

WEBVTT

NOTE duration:"01:12:11.1040000"

NOTE language:en-us

NOTE Confidence: 0.8132291

00:00:00.000 --> 00:00:00.840 Disclosures.

NOTE Confidence: 0.8046678

00:00:03.080 --> 00:00:05.762 An outline for my talk today would be to

NOTE Confidence: 0.8046678

00:00:05.762 --> 00:00:08.049 briefly talk about 6 important studies.

NOTE Confidence: 0.8046678

00:00:08.050 --> 00:00:10.246 One is a randomized trial comparing

NOTE Confidence: 0.8046678

00:00:10.246 --> 00:00:11.710 best supportive care against

NOTE Confidence: 0.8046678

00:00:11.775 --> 00:00:13.171 allogeneic transplant for patients

NOTE Confidence: 0.8046678

00:00:13.171 --> 00:00:16.305 with MD S between ages of. 50 to 75.

NOTE Confidence: 0.8046678

00:00:16.305 --> 00:00:18.720 Yes second study would be looking into

NOTE Confidence: 0.8046678

00:00:18.798 --> 00:00:21.388 an owl way of mobilizing stem cells.

NOTE Confidence: 0.8046678

00:00:21.390 --> 00:00:23.562 Studies 3, four and five are

NOTE Confidence: 0.8046678

00:00:23.562 --> 00:00:25.010 addressing pharmacologic and cellular

NOTE Confidence: 0.8046678

00:00:25.072 --> 00:00:26.476 manipulations to decrease the

NOTE Confidence: 0.8046678

00:00:26.476 --> 00:00:28.582 risk of graft versus host disease.

NOTE Confidence: 0.8046678

00:00:28.590 --> 00:00:30.030 Post allogeneic stem cell

NOTE Confidence: 0.8046678

00:00:30.030 --> 00:00:31.830 transplant and the final study.

NOTE Confidence: 0.8046678

00:00:31.830 --> 00:00:33.858 We will briefly talk about evolving

NOTE Confidence: 0.8046678

00:00:33.858 --> 00:00:36.419 role of what consolidation is prior to

NOTE Confidence: 0.8046678

00:00:36.419 --> 00:00:37.947 allogeneic stem cell transplantation.

NOTE Confidence: 0.8046678

00:00:37.950 --> 00:00:38.778 In modern era,

NOTE Confidence: 0.8046678

00:00:38.778 --> 00:00:40.710 we will not focus too much about

NOTE Confidence: 0.8046678

00:00:40.774 --> 00:00:42.678 autologous transplantation because my

NOTE Confidence: 0.8046678

00:00:42.678 --> 00:00:45.534 colleagues in lymphoma and myeloma section.

NOTE Confidence: 0.8046678

00:00:45.540 --> 00:00:48.516 I have tested on that concept and once

NOTE Confidence: 0.8046678

00:00:48.516 --> 00:00:51.259 the arrows done I'm going to pass on

NOTE Confidence: 0.8046678

00:00:51.259 --> 00:00:54.517 the talk to Iris for chimeric T cell talk.

NOTE Confidence: 0.8046678

00:00:54.520 --> 00:00:58.012 So the first study was a BMT CTN 1102.

NOTE Confidence: 0.8046678

00:00:58.020 --> 00:00:59.710 This randomized study was a

NOTE Confidence: 0.8046678

00:00:59.710 --> 00:01:01.400 biologic assessment study to be

NOTE Confidence: 0.8046678

00:01:01.457 --> 00:01:03.213 biologically assigned to receive

NOTE Confidence: 0.8046678

00:01:03.213 --> 00:01:05.408 another public stem cell transplant.
NOTE Confidence: 0.8046678

00:01:05.410 --> 00:01:06.970 People should have identified
NOTE Confidence: 0.8046678

00:01:06.970 --> 00:01:09.757 a donor between the 90 days of
NOTE Confidence: 0.8046678

00:01:09.757 --> 00:01:11.637 consenting for this MDS study.
NOTE Confidence: 0.8046678

00:01:11.640 --> 00:01:13.580 Match sibling donors and matched
NOTE Confidence: 0.8046678

00:01:13.580 --> 00:01:15.132 unrelated donors were load.
NOTE Confidence: 0.8046678

00:01:15.140 --> 00:01:18.325 They were all expected to undergo stem
NOTE Confidence: 0.8046678

00:01:18.325 --> 00:01:20.519 cell transplantation within six months.
NOTE Confidence: 0.8046678

00:01:20.520 --> 00:01:23.816 Subjects between ages 50 to 75 were included.
NOTE Confidence: 0.8046678

00:01:23.820 --> 00:01:26.802 Only primary Arduino MD S with the
NOTE Confidence: 0.8046678

00:01:26.802 --> 00:01:29.322 intermediate two or high risk by
NOTE Confidence: 0.8046678

00:01:29.322 --> 00:01:31.638 PSS were included in the study.
NOTE Confidence: 0.8046678

00:01:31.640 --> 00:01:33.330 All these candidates were meant
NOTE Confidence: 0.8046678

00:01:33.330 --> 00:01:36.059 to be in a traditional sense be
NOTE Confidence: 0.8046678

00:01:36.059 --> 00:01:38.007 acceptable to undergo reduced
NOTE Confidence: 0.8046678

00:01:38.007 --> 00:01:39.468 intensity transportation study.

NOTE Confidence: 0.8046678

00:01:39.470 --> 00:01:41.942 Randomized people to either get randomized

NOTE Confidence: 0.8046678

00:01:41.942 --> 00:01:43.590 260 questions to transplantation,

NOTE Confidence: 0.8046678

00:01:43.590 --> 00:01:44.721 or 124 patients.

NOTE Confidence: 0.8046678

00:01:44.721 --> 00:01:46.983 2 best supportive care or whatever

NOTE Confidence: 0.8046678

00:01:46.983 --> 00:01:48.785 other options individual centers

NOTE Confidence: 0.8046678

00:01:48.785 --> 00:01:50.597 would offer to those.

NOTE Confidence: 0.8365025

00:01:55.410 --> 00:01:57.826 So here are the results from that study.

NOTE Confidence: 0.8365025

00:01:57.830 --> 00:01:59.996 The primary endpoint of the trial

NOTE Confidence: 0.8365025

00:01:59.996 --> 00:02:02.130 was a prior overall survival.

NOTE Confidence: 0.8365025

00:02:02.130 --> 00:02:04.050 Looking into the donor and the

NOTE Confidence: 0.8365025

00:02:04.050 --> 00:02:06.516 no donor arms here 3 or estimate

NOTE Confidence: 0.8365025

00:02:06.516 --> 00:02:08.356 overall survival was 47.9% for

NOTE Confidence: 0.8365025

00:02:08.356 --> 00:02:10.778 those who had a donor against at

NOTE Confidence: 0.8365025

00:02:10.778 --> 00:02:13.468 26.6% for people who did not have a

NOTE Confidence: 0.8365025

00:02:13.468 --> 00:02:16.299 donor at the time of randomization.

NOTE Confidence: 0.8365025

00:02:16.300 --> 00:02:18.757 Game when they do the sensitivity analysis,
NOTE Confidence: 0.8365025

00:02:18.760 --> 00:02:19.468 excluding subjects,
NOTE Confidence: 0.8365025

00:02:19.468 --> 00:02:21.946 are assigned to the node on around
NOTE Confidence: 0.8365025

00:02:21.946 --> 00:02:24.067 who either died or withdrew prior
NOTE Confidence: 0.8365025

00:02:24.067 --> 00:02:25.772 to the 90 research window.
NOTE Confidence: 0.8365025

00:02:25.780 --> 00:02:28.125 For the sooner the eventual outcome did
NOTE Confidence: 0.8365025

00:02:28.125 --> 00:02:30.290 not change with the adjusted overall
NOTE Confidence: 0.8365025

00:02:30.290 --> 00:02:32.794 survival of 48% for the donor arm
NOTE Confidence: 0.8365025

00:02:32.794 --> 00:02:35.070 against the 28.1% for the non donor
NOTE Confidence: 0.8365025

00:02:35.070 --> 00:02:36.595 when they specifically looked into
NOTE Confidence: 0.8365025

00:02:36.595 --> 00:02:38.760 the different subgroups for analysis.
NOTE Confidence: 0.8365025

00:02:38.760 --> 00:02:40.520 Use of rat hyperventilation agents.
NOTE Confidence: 0.8365025

00:02:40.520 --> 00:02:42.728 Age groups less than 65 against
NOTE Confidence: 0.8365025

00:02:42.728 --> 00:02:44.730 greater than 65 duration of MBS,
NOTE Confidence: 0.8365025

00:02:44.730 --> 00:02:47.285 less than three months or greater than.
NOTE Confidence: 0.8365025

00:02:47.290 --> 00:02:50.125 Reminds I PS is risk groups that

NOTE Confidence: 0.8365025
00:02:50.125 --> 00:02:53.233 donor arm sent it to do better
NOTE Confidence: 0.8365025
00:02:53.233 --> 00:02:55.037 for the overall survival.
NOTE Confidence: 0.8365025
00:02:55.040 --> 00:02:56.482 One of the secondary endpoints of this
NOTE Confidence: 0.8365025
00:02:56.482 --> 00:02:58.507 video is to look into leukemia free survival.
NOTE Confidence: 0.8365025
00:02:58.510 --> 00:03:00.025 Understanding the risk of my
NOTE Confidence: 0.8365025
00:03:00.025 --> 00:03:00.934 latest plastic syndromes.
NOTE Confidence: 0.8365025
00:03:00.940 --> 00:03:02.170 Clonal evolution here.
NOTE Confidence: 0.8365025
00:03:02.170 --> 00:03:05.040 They don't around again came out superior.
NOTE Confidence: 0.8365025
00:03:05.040 --> 00:03:07.090 Three year leukemia free survival
NOTE Confidence: 0.8365025
00:03:07.090 --> 00:03:09.550 of 35.8% compared to the node
NOTE Confidence: 0.8365025
00:03:09.550 --> 00:03:11.600 on around which was 20.6%.
NOTE Confidence: 0.8365025
00:03:11.600 --> 00:03:13.730 Adjusting with the sensitivity analysis
NOTE Confidence: 0.8365025
00:03:13.730 --> 00:03:16.519 again the leukemia free survival was 35.9%.
NOTE Confidence: 0.8365025
00:03:16.520 --> 00:03:18.980 The donor arm against the 21.8%
NOTE Confidence: 0.8365025
00:03:18.980 --> 00:03:21.241 for the node and are similar to
NOTE Confidence: 0.8365025

00:03:21.241 --> 00:03:23.266 the prior slide within subgroups
NOTE Confidence: 0.8365025

00:03:23.266 --> 00:03:25.711 for all different variables that
NOTE Confidence: 0.8365025

00:03:25.711 --> 00:03:27.178 looked into leukemia.
NOTE Confidence: 0.8365025

00:03:27.180 --> 00:03:29.624 Free survival advantage was
NOTE Confidence: 0.8365025

00:03:29.624 --> 00:03:32.068 seen with the transplantation.
NOTE Confidence: 0.8365025

00:03:32.070 --> 00:03:33.936 This is a slide that is
NOTE Confidence: 0.8365025

00:03:33.936 --> 00:03:35.180 showing as treated analysis.
NOTE Confidence: 0.8365025

00:03:35.180 --> 00:03:35.568 Again,
NOTE Confidence: 0.8365025

00:03:35.568 --> 00:03:37.896 showing the superiority for both overall
NOTE Confidence: 0.8365025

00:03:37.896 --> 00:03:39.910 survival and leukemia free survival.
NOTE Confidence: 0.8365025

00:03:39.910 --> 00:03:41.089 Absolute improvement for
NOTE Confidence: 0.8365025

00:03:41.089 --> 00:03:42.268 overall survival study,
NOTE Confidence: 0.8365025

00:03:42.270 --> 00:03:44.634 one point 4% for the transplantation
NOTE Confidence: 0.8365025

00:03:44.634 --> 00:03:47.392 arm was 28.4% for the leukemia free
NOTE Confidence: 0.8365025

00:03:47.392 --> 00:03:49.357 survival again for the transplantation.
NOTE Confidence: 0.79592305

00:03:52.680 --> 00:03:55.214 So one of the conclusions of this

NOTE Confidence: 0.79592305
00:03:55.214 --> 00:03:57.510 randomized study for a very long time,
NOTE Confidence: 0.79592305
00:03:57.510 --> 00:03:59.240 the field of Miller Park,
NOTE Confidence: 0.79592305
00:03:59.240 --> 00:04:00.272 stem cell transplantation
NOTE Confidence: 0.79592305
00:04:00.272 --> 00:04:01.648 and who to transplant,
NOTE Confidence: 0.79592305
00:04:01.650 --> 00:04:03.720 who not to transplant was based
NOTE Confidence: 0.79592305
00:04:03.720 --> 00:04:05.100 upon Markov decision modeling.
NOTE Confidence: 0.79592305
00:04:05.100 --> 00:04:07.230 This is the first randomized trial
NOTE Confidence: 0.79592305
00:04:07.230 --> 00:04:09.066 comparing best supportive care of
NOTE Confidence: 0.79592305
00:04:09.066 --> 00:04:10.841 best available care against the
NOTE Confidence: 0.79592305
00:04:10.841 --> 00:04:12.723 random against allogeneic stem cell
NOTE Confidence: 0.79592305
00:04:12.723 --> 00:04:14.728 transplantation in a randomized manner.
NOTE Confidence: 0.79592305
00:04:14.730 --> 00:04:16.704 Specifically, in a Common Age group
NOTE Confidence: 0.79592305
00:04:16.704 --> 00:04:18.510 where we encountered this disease,
NOTE Confidence: 0.79592305
00:04:18.510 --> 00:04:19.542 so such patients,
NOTE Confidence: 0.79592305
00:04:19.542 --> 00:04:21.606 if they have a suitable donor,
NOTE Confidence: 0.79592305

00:04:21.610 --> 00:04:23.405 this leads to improved overall
NOTE Confidence: 0.79592305

00:04:23.405 --> 00:04:24.841 survival through leukemia free
NOTE Confidence: 0.79592305

00:04:24.841 --> 00:04:27.193 survival and again after we ask our
NOTE Confidence: 0.79592305

00:04:27.193 --> 00:04:28.485 patients to undergo transplantation,
NOTE Confidence: 0.79592305

00:04:28.490 --> 00:04:31.586 a question that gets asked is can you know,
NOTE Confidence: 0.79592305

00:04:31.590 --> 00:04:33.310 is this covered by Medicare?
NOTE Confidence: 0.79592305

00:04:33.310 --> 00:04:35.025 There's most of these patients
NOTE Confidence: 0.79592305

00:04:35.025 --> 00:04:36.397 are greater than 65.
NOTE Confidence: 0.79592305

00:04:36.400 --> 00:04:36.713 Historically,
NOTE Confidence: 0.79592305

00:04:36.713 --> 00:04:38.591 we had to report those outcomes
NOTE Confidence: 0.79592305

00:04:38.591 --> 00:04:40.529 now within the subgroup analysis,
NOTE Confidence: 0.79592305

00:04:40.530 --> 00:04:43.218 we're clearly able to show that for
NOTE Confidence: 0.79592305

00:04:43.218 --> 00:04:45.768 people greater than 65 in less than 65.
NOTE Confidence: 0.79592305

00:04:45.770 --> 00:04:47.280 Transportation is a good option.
NOTE Confidence: 0.79592305

00:04:47.280 --> 00:04:49.086 I think that goes against transportation.
NOTE Confidence: 0.79592305

00:04:49.090 --> 00:04:50.686 Is there are reports that talk

NOTE Confidence: 0.79592305

00:04:50.686 --> 00:04:51.750 about decreased quality of

NOTE Confidence: 0.79592305

00:04:51.804 --> 00:04:53.019 life post transplantation,

NOTE Confidence: 0.79592305

00:04:53.020 --> 00:04:54.530 so the study had designed.

NOTE Confidence: 0.79592305

00:04:54.530 --> 00:04:56.938 I didn't show you that like the study.

NOTE Confidence: 0.79592305

00:04:56.940 --> 00:04:59.236 I designed a quality of life measurement

NOTE Confidence: 0.79592305

00:04:59.236 --> 00:05:01.321 at different time points for both the

NOTE Confidence: 0.79592305

00:05:01.321 --> 00:05:03.552 arms and it shows that the quality of

NOTE Confidence: 0.79592305

00:05:03.552 --> 00:05:05.382 life was no different or definitely

NOTE Confidence: 0.79592305

00:05:05.382 --> 00:05:08.380 was not included in the transportation.

NOTE Confidence: 0.79592305

00:05:08.380 --> 00:05:08.747 Finally,

NOTE Confidence: 0.79592305

00:05:08.747 --> 00:05:11.316 as I want to emphasize that overall,

NOTE Confidence: 0.79592305

00:05:11.320 --> 00:05:13.150 there's a very strong advantage

NOTE Confidence: 0.79592305

00:05:13.150 --> 00:05:14.614 for stem cell transplantation,

NOTE Confidence: 0.79592305

00:05:14.620 --> 00:05:17.273 particularly to have a match sibling donor

NOTE Confidence: 0.79592305

00:05:17.273 --> 00:05:19.936 or a mass unrelated donor identified

NOTE Confidence: 0.79592305

00:05:19.936 --> 00:05:23.310 early in the course of their treatment.

NOTE Confidence: 0.79592305

00:05:23.310 --> 00:05:25.458 I have next study talks about

NOTE Confidence: 0.79592305

00:05:25.458 --> 00:05:27.609 how to mobilize stem cells at.

NOTE Confidence: 0.79592305

00:05:27.610 --> 00:05:29.400 Traditionally we walked in stem

NOTE Confidence: 0.79592305

00:05:29.400 --> 00:05:31.190 cell sources through several modes,

NOTE Confidence: 0.79592305

00:05:31.190 --> 00:05:32.120 either with G,

NOTE Confidence: 0.79592305

00:05:32.120 --> 00:05:33.670 CSF mobilized the donor bone

NOTE Confidence: 0.79592305

00:05:33.670 --> 00:05:35.600 for bone marrow transplant ago

NOTE Confidence: 0.79592305

00:05:35.600 --> 00:05:37.268 for bone marrow aspiration,

NOTE Confidence: 0.79592305

00:05:37.270 --> 00:05:39.060 or resemble cord blood transplants.

NOTE Confidence: 0.79592305

00:05:39.060 --> 00:05:40.790 There are many different limitations

NOTE Confidence: 0.79592305

00:05:40.790 --> 00:05:43.000 for each one of those things,

NOTE Confidence: 0.79592305

00:05:43.000 --> 00:05:45.148 but the communist platform is G.

NOTE Confidence: 0.79592305

00:05:45.150 --> 00:05:48.380 CSF mobilized peripheral blood graphs.

NOTE Confidence: 0.79592305

00:05:48.380 --> 00:05:49.826 Usually, in order to achieve that,

NOTE Confidence: 0.79592305

00:05:49.830 --> 00:05:51.372 we have to give about four

NOTE Confidence: 0.79592305

00:05:51.372 --> 00:05:53.080 to five days of injection.

NOTE Confidence: 0.79592305

00:05:53.080 --> 00:05:55.180 This is kind of a time sensitive

NOTE Confidence: 0.79592305

00:05:55.180 --> 00:05:57.368 process and with every day we keep

NOTE Confidence: 0.79592305

00:05:57.368 --> 00:05:59.650 giving G CSF phenotype of sounds that

NOTE Confidence: 0.79592305

00:05:59.650 --> 00:06:01.930 we generate along with Democratic stem

NOTE Confidence: 0.79592305

00:06:01.930 --> 00:06:04.254 cells changes with those T cells that

NOTE Confidence: 0.79592305

00:06:04.254 --> 00:06:06.465 are then more likely to induce both

NOTE Confidence: 0.79592305

00:06:06.465 --> 00:06:09.055 acute and chronic graft versus host disease.

NOTE Confidence: 0.79592305

00:06:09.060 --> 00:06:11.209 Currently there is an urgent need rather

NOTE Confidence: 0.79592305

00:06:11.209 --> 00:06:13.728 than unmet need for rapid mobilizing agents.

NOTE Confidence: 0.79592305

00:06:13.730 --> 00:06:16.124 One compound that we tend to use

NOTE Confidence: 0.79592305

00:06:16.124 --> 00:06:17.843 Explorer EXE firing people who

NOTE Confidence: 0.79592305

00:06:17.843 --> 00:06:19.715 do not mobilize with G CSF.

NOTE Confidence: 0.79592305

00:06:19.720 --> 00:06:21.718 It's a CX here for inhibitor.

NOTE Confidence: 0.79592305

00:06:21.720 --> 00:06:24.380 It does generate a lot of cells.

NOTE Confidence: 0.79592305

00:06:24.380 --> 00:06:26.060 But can only mobilize adequate number
NOTE Confidence: 0.79592305

00:06:26.060 --> 00:06:27.949 of cells that we feel are desirable
NOTE Confidence: 0.79592305

00:06:27.949 --> 00:06:29.626 in about 60 to 65% of patients.
NOTE Confidence: 0.79592305

00:06:29.626 --> 00:06:32.070 So in order to come with a rapid solution,
NOTE Confidence: 0.79592305

00:06:32.070 --> 00:06:34.098 people have been looking for alternative
NOTE Confidence: 0.79592305

00:06:34.098 --> 00:06:36.079 options in terms of how to do.
NOTE Confidence: 0.79592305

00:06:36.080 --> 00:06:38.688 CXE R2 seems to be a potential target,
NOTE Confidence: 0.79592305

00:06:38.690 --> 00:06:41.298 so here in this study that we should
NOTE Confidence: 0.79592305

00:06:41.298 --> 00:06:43.342 have presented by the audience they
NOTE Confidence: 0.79592305

00:06:43.342 --> 00:06:45.334 using akcija to organist MDT at
NOTE Confidence: 0.767422140000001

00:06:45.402 --> 00:06:47.544 145 along with product support to try
NOTE Confidence: 0.767422140000001

00:06:47.544 --> 00:06:50.095 and see if a single day mobilization is
NOTE Confidence: 0.767422140000001

00:06:50.095 --> 00:06:52.519 possible to generate * **** wit emitter
NOTE Confidence: 0.767422140000001

00:06:52.519 --> 00:06:55.130 Partick stem cells in addition to Olympus
NOTE Confidence: 0.767422140000001

00:06:55.195 --> 00:06:57.637 suppressive properties of the T cells.
NOTE Confidence: 0.767422140000001

00:06:57.640 --> 00:06:59.761 So here is a condensed version of

NOTE Confidence: 0.767422140000001
00:06:59.761 --> 00:07:01.649 the results that I'm presenting.
NOTE Confidence: 0.767422140000001
00:07:01.650 --> 00:07:03.320 The study included healthy volunteers,
NOTE Confidence: 0.767422140000001
00:07:03.320 --> 00:07:05.993 about 12 of them, of which 92% of
NOTE Confidence: 0.767422140000001
00:07:05.993 --> 00:07:07.658 those volunteers mobilized 20 CD,
NOTE Confidence: 0.767422140000001
00:07:07.660 --> 00:07:09.330 34 cells per microliters combination.
NOTE Confidence: 0.767422140000001
00:07:09.330 --> 00:07:11.689 That is the M GTA145 plus player
NOTE Confidence: 0.767422140000001
00:07:11.689 --> 00:07:14.022 XFR compared to only 57% of the
NOTE Confidence: 0.767422140000001
00:07:14.022 --> 00:07:15.727 patients achieving the same target
NOTE Confidence: 0.767422140000001
00:07:15.727 --> 00:07:17.679 with single agent product so far.
NOTE Confidence: 0.767422140000001
00:07:17.680 --> 00:07:20.152 Just in case you're wondering what is the
NOTE Confidence: 0.767422140000001
00:07:20.152 --> 00:07:22.966 20 CD 34 cells for Michael later before
NOTE Confidence: 0.767422140000001
00:07:22.966 --> 00:07:26.027 the subjects are put on a fresh this machine,
NOTE Confidence: 0.767422140000001
00:07:26.030 --> 00:07:29.158 we do a peripheral blood CD 4 count.
NOTE Confidence: 0.767422140000001
00:07:29.160 --> 00:07:31.239 Most centers would not put people in
NOTE Confidence: 0.767422140000001
00:07:31.239 --> 00:07:33.469 machine if the count is less than 10.
NOTE Confidence: 0.767422140000001

00:07:33.470 --> 00:07:34.870 Here it's showing that they've
NOTE Confidence: 0.767422140000001

00:07:34.870 --> 00:07:36.902 got a decent number of count 2020
NOTE Confidence: 0.767422140000001

00:07:36.902 --> 00:07:38.337 CD 34 cells per microliter,
NOTE Confidence: 0.767422140000001

00:07:38.340 --> 00:07:39.432 suggesting that the eel,
NOTE Confidence: 0.767422140000001

00:07:39.432 --> 00:07:41.500 what we can predict preparing the machine.
NOTE Confidence: 0.767422140000001

00:07:41.500 --> 00:07:42.940 This is a decent deal,
NOTE Confidence: 0.767422140000001

00:07:42.940 --> 00:07:45.412 expecting a good outcome for decent
NOTE Confidence: 0.767422140000001

00:07:45.412 --> 00:07:47.929 collection at the end of the day.
NOTE Confidence: 0.767422140000001

00:07:47.930 --> 00:07:49.595 The Peaks cell concentration that
NOTE Confidence: 0.767422140000001

00:07:49.595 --> 00:07:51.868 we found in the peripheral with the
NOTE Confidence: 0.767422140000001

00:07:51.868 --> 00:07:54.044 combination was 40 CD 34 cells from Mike
NOTE Confidence: 0.767422140000001

00:07:54.106 --> 00:07:56.479 later again that suggest that the robust
NOTE Confidence: 0.767422140000001

00:07:56.479 --> 00:07:58.454 aggressive the cells that they were
NOTE Confidence: 0.767422140000001

00:07:58.454 --> 00:08:00.362 able to achieve with this combinations.
NOTE Confidence: 0.767422140000001

00:08:00.370 --> 00:08:02.284 Eight of those donors went voted
NOTE Confidence: 0.767422140000001

00:08:02.284 --> 00:08:03.916 the combination underwent a phrases

NOTE Confidence: 0.767422140000001
00:08:03.916 --> 00:08:06.037 and the median sell those that were
NOTE Confidence: 0.767422140000001
00:08:06.037 --> 00:08:07.993 collected was 4,000,000 cells per cagey
NOTE Confidence: 0.767422140000001
00:08:07.993 --> 00:08:09.937 of their sippy and what's expected.
NOTE Confidence: 0.767422140000001
00:08:09.940 --> 00:08:11.872 So that's a very good number in
NOTE Confidence: 0.767422140000001
00:08:11.872 --> 00:08:13.769 terms of the overall picture.
NOTE Confidence: 0.767422140000001
00:08:13.770 --> 00:08:17.066 How we look at it. Then the design.
NOTE Confidence: 0.767422140000001
00:08:17.066 --> 00:08:17.710 Some industry.
NOTE Confidence: 0.767422140000001
00:08:17.710 --> 00:08:19.756 Most experiment with the primary transparent
NOTE Confidence: 0.767422140000001
00:08:19.756 --> 00:08:21.880 secondary transplant on the left hand side.
NOTE Confidence: 0.767422140000001
00:08:21.880 --> 00:08:24.127 There able to show that using this
NOTE Confidence: 0.767422140000001
00:08:24.127 --> 00:08:26.383 combination they were able to show at
NOTE Confidence: 0.767422140000001
00:08:26.383 --> 00:08:28.237 23 fold higher engraftment compared to
NOTE Confidence: 0.767422140000001
00:08:28.300 --> 00:08:30.226 using donors were mobilized with just
NOTE Confidence: 0.767422140000001
00:08:30.226 --> 00:08:32.698 five days alone or plexi for single agent.
NOTE Confidence: 0.767422140000001
00:08:32.698 --> 00:08:34.889 The graph on the right hand side
NOTE Confidence: 0.767422140000001

00:08:34.889 --> 00:08:37.290 basically show the survival for such mice.
NOTE Confidence: 0.767422140000001

00:08:37.290 --> 00:08:39.275 Post engraftment was pretty good
NOTE Confidence: 0.767422140000001

00:08:39.275 --> 00:08:41.260 compared to the alternative options.
NOTE Confidence: 0.767422140000001

00:08:41.260 --> 00:08:43.980 This study has kind of been an exciting
NOTE Confidence: 0.767422140000001

00:08:43.980 --> 00:08:46.186 development in that now people are
NOTE Confidence: 0.767422140000001

00:08:46.186 --> 00:08:48.006 now exploring alternatives to G,
NOTE Confidence: 0.767422140000001

00:08:48.010 --> 00:08:50.068 CSF and basically trying to mobilize
NOTE Confidence: 0.767422140000001

00:08:50.068 --> 00:08:52.222 a phenotype of cells that are
NOTE Confidence: 0.767422140000001

00:08:52.222 --> 00:08:53.666 immunosuppressive to make sure
NOTE Confidence: 0.767422140000001

00:08:53.666 --> 00:08:55.110 the graph can stain.
NOTE Confidence: 0.767422140000001

00:08:55.110 --> 00:08:57.566 But at the same time they're able to
NOTE Confidence: 0.767422140000001

00:08:57.566 --> 00:09:00.244 generate enough of HSBC's to re populate
NOTE Confidence: 0.767422140000001

00:09:00.244 --> 00:09:01.844 post updated conditioning therapies.
NOTE Confidence: 0.7914078

00:09:04.160 --> 00:09:06.664 For the next three studies were going to
NOTE Confidence: 0.7914078

00:09:06.664 --> 00:09:08.949 talk about graph versus host disease,
NOTE Confidence: 0.7914078

00:09:08.950 --> 00:09:10.660 as many of you know,

NOTE Confidence: 0.7914078

00:09:10.660 --> 00:09:12.028 allogeneic stem cell transplantation

NOTE Confidence: 0.7914078

00:09:12.028 --> 00:09:13.738 is a curative intent treatment,

NOTE Confidence: 0.7914078

00:09:13.740 --> 00:09:15.582 but the graph versus host disease

NOTE Confidence: 0.7914078

00:09:15.582 --> 00:09:17.267 complication that ensures can have

NOTE Confidence: 0.7914078

00:09:17.267 --> 00:09:18.867 significant mortality and morbidity,

NOTE Confidence: 0.7914078

00:09:18.870 --> 00:09:20.916 especially chronic graft versus host disease,

NOTE Confidence: 0.7914078

00:09:20.920 --> 00:09:23.993 can be seen in about 30 to 70% of

NOTE Confidence: 0.7914078

00:09:23.993 --> 00:09:25.708 the patients main frontline therapy.

NOTE Confidence: 0.7914078

00:09:25.710 --> 00:09:26.733 For these patients,

NOTE Confidence: 0.7914078

00:09:26.733 --> 00:09:28.097 we do use corticosteroids.

NOTE Confidence: 0.7914078

00:09:28.100 --> 00:09:29.810 Approximately about 50% of patients,

NOTE Confidence: 0.7914078

00:09:29.810 --> 00:09:32.070 either dependent on it or

NOTE Confidence: 0.7914078

00:09:32.070 --> 00:09:33.426 eventually become refractory.

NOTE Confidence: 0.7914078

00:09:33.430 --> 00:09:35.950 The only FDA approved drugs in their second

NOTE Confidence: 0.7914078

00:09:35.950 --> 00:09:37.989 line setting is the drug in Brittany.

NOTE Confidence: 0.7914078

00:09:37.990 --> 00:09:39.928 People in the CLL vertebrae familiar
NOTE Confidence: 0.7914078

00:09:39.928 --> 00:09:42.195 with this truck and that study was
NOTE Confidence: 0.7914078

00:09:42.195 --> 00:09:44.025 not based on randomized trial is
NOTE Confidence: 0.7914078

00:09:44.025 --> 00:09:46.023 based on a single arm study where
NOTE Confidence: 0.7914078

00:09:46.023 --> 00:09:47.413 they study about 42 patients.
NOTE Confidence: 0.7914078

00:09:47.413 --> 00:09:49.231 The overall response rate was about
NOTE Confidence: 0.7914078

00:09:49.231 --> 00:09:52.865 67% in that in the CRL about 21%.
NOTE Confidence: 0.7914078

00:09:52.870 --> 00:09:54.535 It's interesting to note the
NOTE Confidence: 0.7914078

00:09:54.535 --> 00:09:56.564 median time to response was close
NOTE Confidence: 0.7914078

00:09:56.564 --> 00:09:58.394 to three months on that study.
NOTE Confidence: 0.7914078

00:09:58.400 --> 00:09:58.742 However,
NOTE Confidence: 0.7914078

00:09:58.742 --> 00:10:00.110 there was a D.
NOTE Confidence: 0.7914078

00:10:00.110 --> 00:10:01.980 Saint reduction in Cortico steroid
NOTE Confidence: 0.7914078

00:10:01.980 --> 00:10:04.500 use from .29 two .125 again pretty
NOTE Confidence: 0.7914078

00:10:04.500 --> 00:10:06.796 late in the game by up by both
NOTE Confidence: 0.7914078

00:10:06.872 --> 00:10:08.876 Week 49 after initiating at a

NOTE Confidence: 0.7914078

00:10:08.876 --> 00:10:10.892 median follow up for 14 months.

NOTE Confidence: 0.7914078

00:10:10.892 --> 00:10:14.028 In that study 71% of the patients at

NOTE Confidence: 0.7914078

00:10:14.028 --> 00:10:16.710 discontinue the drug due to toxicities.

NOTE Confidence: 0.7914078

00:10:16.710 --> 00:10:17.023 Again,

NOTE Confidence: 0.7914078

00:10:17.023 --> 00:10:18.901 the other important point to note

NOTE Confidence: 0.7914078

00:10:18.901 --> 00:10:20.927 here is that there are currently

NOTE Confidence: 0.7914078

00:10:20.927 --> 00:10:22.973 no drugs approved in this space.

NOTE Confidence: 0.7914078

00:10:22.980 --> 00:10:24.100 Based on the randomization.

NOTE Confidence: 0.7914078

00:10:24.100 --> 00:10:26.545 This led to the reach three study which

NOTE Confidence: 0.7914078

00:10:26.545 --> 00:10:28.325 was studying ruxolitinib against best

NOTE Confidence: 0.7914078

00:10:28.325 --> 00:10:30.568 available therapy in patients with steroid,

NOTE Confidence: 0.7914078

00:10:30.570 --> 00:10:31.890 refractory or steroid dependent.

NOTE Confidence: 0.7914078

00:10:31.890 --> 00:10:33.540 Chronic graft versus host disease.

NOTE Confidence: 0.7914078

00:10:33.540 --> 00:10:35.200 This was a multinational

NOTE Confidence: 0.7914078

00:10:35.200 --> 00:10:37.275 trial led by Doctor Zaiser.

NOTE Confidence: 0.7914078

00:10:37.280 --> 00:10:38.216 Here's the study.
NOTE Confidence: 0.7914078

00:10:38.216 --> 00:10:39.464 Design included patients greater
NOTE Confidence: 0.7914078

00:10:39.464 --> 00:10:41.733 than 12 years of age who either
NOTE Confidence: 0.7914078

00:10:41.733 --> 00:10:43.017 had steroid refractory independent
NOTE Confidence: 0.7914078

00:10:43.017 --> 00:10:44.690 chronic graft versus host disease.
NOTE Confidence: 0.7914078

00:10:44.690 --> 00:10:46.937 It had to be moderate to severe,
NOTE Confidence: 0.7914078

00:10:46.940 --> 00:10:48.088 as defined here below.
NOTE Confidence: 0.7914078

00:10:48.088 --> 00:10:50.258 That is lack of response or disease
NOTE Confidence: 0.7914078

00:10:50.258 --> 00:10:52.183 progression after Prednisone greater than
NOTE Confidence: 0.7914078

00:10:52.183 --> 00:10:54.988 a MacBook per day for more than a week,
NOTE Confidence: 0.7914078

00:10:54.990 --> 00:10:56.278 or disease progression with
NOTE Confidence: 0.7914078

00:10:56.278 --> 00:10:57.566 Prednisone greater than point,
NOTE Confidence: 0.7914078

00:10:57.570 --> 00:10:59.684 buy mixed bag per day are a
NOTE Confidence: 0.7914078

00:10:59.684 --> 00:11:01.352 milligram per kilogram every other
NOTE Confidence: 0.7914078

00:11:01.352 --> 00:11:03.802 day for greater than four weeks are
NOTE Confidence: 0.7914078

00:11:03.802 --> 00:11:05.665 increasing the dose of Prednisone

NOTE Confidence: 0.7914078

00:11:05.665 --> 00:11:07.475 to greater than .25 milligrams.

NOTE Confidence: 0.7914078

00:11:07.480 --> 00:11:07.832 Today,

NOTE Confidence: 0.7914078

00:11:07.832 --> 00:11:09.240 after two unsuccessful attempts

NOTE Confidence: 0.7914078

00:11:09.240 --> 00:11:10.648 to taper the dose,

NOTE Confidence: 0.7914078

00:11:10.650 --> 00:11:12.054 obviously you're worried about

NOTE Confidence: 0.7914078

00:11:12.054 --> 00:11:13.107 the graft rejection.

NOTE Confidence: 0.7914078

00:11:13.110 --> 00:11:15.216 So prior to the study enrollment,

NOTE Confidence: 0.7914078

00:11:15.220 --> 00:11:16.980 we had to confirm everybody

NOTE Confidence: 0.7914078

00:11:16.980 --> 00:11:18.036 had decent engraftment.

NOTE Confidence: 0.7914078

00:11:18.040 --> 00:11:19.800 The randomization was stratified by

NOTE Confidence: 0.7914078

00:11:19.800 --> 00:11:21.560 chronic graft versus host disease.

NOTE Confidence: 0.7914078

00:11:21.560 --> 00:11:24.045 Great people were allowed to go either

NOTE Confidence: 0.7914078

00:11:24.045 --> 00:11:26.543 on ruxolitinib 10 milligrams to be ID

NOTE Confidence: 0.7914078

00:11:26.543 --> 00:11:28.595 those on the backbone of steroids.

NOTE Confidence: 0.7914078

00:11:28.600 --> 00:11:30.652 Percent minus calcineurin inhibitors

NOTE Confidence: 0.7914078

00:11:30.652 --> 00:11:32.704 or best available therapy.
NOTE Confidence: 0.7914078

00:11:32.710 --> 00:11:33.952 About six cycles.
NOTE Confidence: 0.7914078

00:11:33.952 --> 00:11:36.022 Were given in the intervention
NOTE Confidence: 0.7914078

00:11:36.022 --> 00:11:38.780 alarm and then the analysis was done
NOTE Confidence: 0.7914078

00:11:38.780 --> 00:11:41.639 correctly to the start of summer cycle.
NOTE Confidence: 0.7914078

00:11:41.640 --> 00:11:43.752 At the end of 6 cycle people around
NOTE Confidence: 0.7914078

00:11:43.752 --> 00:11:45.976 the best available therapy are what
NOTE Confidence: 0.7914078

00:11:45.976 --> 00:11:48.670 allowed indeed to crossover the excellent in.
NOTE Confidence: 0.7914078

00:11:48.670 --> 00:11:50.350 If there was a need,
NOTE Confidence: 0.7914078

00:11:50.350 --> 00:11:52.390 the primary endpoint of the study
NOTE Confidence: 0.7914078

00:11:52.390 --> 00:11:54.404 was overall response rate at Week
NOTE Confidence: 0.7914078

00:11:54.404 --> 00:11:56.462 24 as defined by the NIH consensus
NOTE Confidence: 0.7914078

00:11:56.462 --> 00:11:58.251 criteria and the key secondary
NOTE Confidence: 0.7914078

00:11:58.251 --> 00:11:59.683 endpoints were failure free
NOTE Confidence: 0.7914078

00:11:59.683 --> 00:12:00.399 survival and
NOTE Confidence: 0.8022639

00:12:00.400 --> 00:12:02.372 modified lease symptom scale.

NOTE Confidence: 0.8022639

00:12:02.372 --> 00:12:05.330 Assessing the responses at Week 24.

NOTE Confidence: 0.8022639

00:12:05.330 --> 00:12:08.658 This is just a slide to show that

NOTE Confidence: 0.8022639

00:12:08.658 --> 00:12:11.594 across the two arms age, sex, TV,

NOTE Confidence: 0.8022639

00:12:11.594 --> 00:12:13.916 IDF, chronic GV HD the criterias

NOTE Confidence: 0.8022639

00:12:13.916 --> 00:12:16.720 on the score were well matched.

NOTE Confidence: 0.82102114

00:12:18.840 --> 00:12:20.360 The overall response rate,

NOTE Confidence: 0.82102114

00:12:20.360 --> 00:12:23.279 when assessed after six months or weeks 24,

NOTE Confidence: 0.82102114

00:12:23.280 --> 00:12:25.500 was higher in the proximity bomb.

NOTE Confidence: 0.82102114

00:12:25.500 --> 00:12:27.350 It was 49.7% almost doubled

NOTE Confidence: 0.82102114

00:12:27.350 --> 00:12:29.570 compared to the 25.6% seen with

NOTE Confidence: 0.82102114

00:12:29.570 --> 00:12:31.050 the best available therapists.

NOTE Confidence: 0.82102114

00:12:31.050 --> 00:12:33.875 The CRH was about 6.7% or says 3%.

NOTE Confidence: 0.82102114

00:12:33.875 --> 00:12:35.500 Achieving a CR in the

NOTE Confidence: 0.82102114

00:12:35.500 --> 00:12:37.340 setting is extremely hard,

NOTE Confidence: 0.82102114

00:12:37.340 --> 00:12:39.530 although it may look like the

NOTE Confidence: 0.82102114

00:12:39.530 --> 00:12:41.410 sea animals aren't that high.
NOTE Confidence: 0.82102114

00:12:41.410 --> 00:12:44.298 What we really need to take into account
NOTE Confidence: 0.82102114

00:12:44.298 --> 00:12:47.354 is the OR or are you know when you
NOTE Confidence: 0.82102114

00:12:47.354 --> 00:12:50.250 talk to people who take transportation.
NOTE Confidence: 0.82102114

00:12:50.250 --> 00:12:51.612 It will be agrees that this
NOTE Confidence: 0.82102114

00:12:51.612 --> 00:12:52.520 is a good endpoint.
NOTE Confidence: 0.82102114

00:12:52.520 --> 00:12:55.850 Rather than focusing on CR alone.
NOTE Confidence: 0.82102114

00:12:55.850 --> 00:12:57.285 When they looked into failure
NOTE Confidence: 0.82102114

00:12:57.285 --> 00:12:58.720 free survival at week 24,
NOTE Confidence: 0.82102114

00:12:58.720 --> 00:13:00.456 failure fix around being defined as a
NOTE Confidence: 0.82102114

00:13:00.456 --> 00:13:02.540 time to the earliest of recurrence of
NOTE Confidence: 0.82102114

00:13:02.540 --> 00:13:04.460 underlying disease or the start menu.
NOTE Confidence: 0.82102114

00:13:04.460 --> 00:13:06.028 Systemic treatment for chronic
NOTE Confidence: 0.82102114

00:13:06.028 --> 00:13:07.596 GV HD or death.
NOTE Confidence: 0.82102114

00:13:07.600 --> 00:13:09.325 But the rock selection of
NOTE Confidence: 0.82102114

00:13:09.325 --> 00:13:11.050 arm it was not raised,

NOTE Confidence: 0.82102114

00:13:11.050 --> 00:13:13.120 but as it was 5.7 months

NOTE Confidence: 0.82102114

00:13:13.120 --> 00:13:14.500 with the observation log.

NOTE Confidence: 0.8165663

00:13:16.950 --> 00:13:18.720 One thing that is often

NOTE Confidence: 0.8165663

00:13:18.720 --> 00:13:19.428 understood understood,

NOTE Confidence: 0.8165663

00:13:19.430 --> 00:13:21.195 he did incorporate that is

NOTE Confidence: 0.8165663

00:13:21.195 --> 00:13:22.607 the symptom scale modified.

NOTE Confidence: 0.8165663

00:13:22.610 --> 00:13:24.602 Lee Symptom Scale is well validated

NOTE Confidence: 0.8165663

00:13:24.602 --> 00:13:26.510 in chronic GV HD setting,

NOTE Confidence: 0.8165663

00:13:26.510 --> 00:13:28.634 investigators were able to show that

NOTE Confidence: 0.8165663

00:13:28.634 --> 00:13:30.452 for patients who are investigational

NOTE Confidence: 0.8165663

00:13:30.452 --> 00:13:33.132 arm had a better quality of life as

NOTE Confidence: 0.8165663

00:13:33.132 --> 00:13:35.332 is being measured by the symptomatic

NOTE Confidence: 0.8165663

00:13:35.332 --> 00:13:37.478 score with a 24.2% here compared

NOTE Confidence: 0.8165663

00:13:37.478 --> 00:13:40.640 to the 11% the controller.

NOTE Confidence: 0.8165663

00:13:40.640 --> 00:13:42.842 Which is the best overall response

NOTE Confidence: 0.8165663

00:13:42.842 --> 00:13:44.360 rate right? But again,
NOTE Confidence: 0.8165663

00:13:44.360 --> 00:13:46.700 with the intervention arm with excellent
NOTE Confidence: 0.8165663

00:13:46.700 --> 00:13:49.486 and M it was 76.4% compared to 60.4%.
NOTE Confidence: 0.8165663

00:13:49.486 --> 00:13:51.718 But the best available therapy are
NOTE Confidence: 0.8165663

00:13:51.718 --> 00:13:54.114 the median duration or best overall
NOTE Confidence: 0.8165663

00:13:54.114 --> 00:13:56.796 response was 6.2 four months unpaid but
NOTE Confidence: 0.8165663

00:13:56.796 --> 00:14:01.000 was not reached in their excellent in a bar.
NOTE Confidence: 0.8165663

00:14:01.000 --> 00:14:03.994 In conclusion this is the first
NOTE Confidence: 0.8165663

00:14:03.994 --> 00:14:05.990 successful randomized phase three
NOTE Confidence: 0.8165663

00:14:06.069 --> 00:14:08.680 trial for the chronic GV HD space,
NOTE Confidence: 0.8165663

00:14:08.680 --> 00:14:11.428 or excellent in a demonstrated significantly
NOTE Confidence: 0.8165663

00:14:11.428 --> 00:14:14.019 higher overall response rate at Week 24.
NOTE Confidence: 0.8165663

00:14:14.020 --> 00:14:16.310 There was improvement in failure
NOTE Confidence: 0.8165663

00:14:16.310 --> 00:14:17.684 free survival significantly
NOTE Confidence: 0.8165663

00:14:17.684 --> 00:14:19.380 improved symptom improvement.
NOTE Confidence: 0.8165663

00:14:19.380 --> 00:14:20.454 There was hype.

NOTE Confidence: 0.8165663

00:14:20.454 --> 00:14:22.602 It was the highest best overall

NOTE Confidence: 0.8165663

00:14:22.602 --> 00:14:25.019 response rate at Week 24 with excellent.

NOTE Confidence: 0.8165663

00:14:25.020 --> 00:14:26.800 The most frequent adverse event

NOTE Confidence: 0.8165663

00:14:26.800 --> 00:14:29.205 seemed the setting was similar to what

NOTE Confidence: 0.8165663

00:14:29.205 --> 00:14:30.891 we've seen in acute GBS resetting

NOTE Confidence: 0.8165663

00:14:30.891 --> 00:14:32.838 when we use our excellent name,

NOTE Confidence: 0.8165663

00:14:32.840 --> 00:14:34.384 namely anemia and thrombocytopenia.

NOTE Confidence: 0.8165663

00:14:34.384 --> 00:14:35.928 Based on this finding,

NOTE Confidence: 0.8165663

00:14:35.930 --> 00:14:37.664 there is increasing enthusiasm to start

NOTE Confidence: 0.8165663

00:14:37.664 --> 00:14:39.969 using this drug as a second line setting.

NOTE Confidence: 0.7725647

00:14:42.080 --> 00:14:44.414 The other important progress in the

NOTE Confidence: 0.7725647

00:14:44.414 --> 00:14:47.519 chronic GV HD space is in studying this

NOTE Confidence: 0.7725647

00:14:47.519 --> 00:14:50.283 pathway called the rock Pot Rock here

NOTE Confidence: 0.7725647

00:14:50.283 --> 00:14:52.688 stands for through associated coiled

NOTE Confidence: 0.7725647

00:14:52.688 --> 00:14:55.038 coiled coil protein kinase pathway.

NOTE Confidence: 0.7725647

00:14:55.038 --> 00:14:57.546 Rock essentially comes in two isoforms,
NOTE Confidence: 0.7725647

00:14:57.550 --> 00:14:59.850 rock one and Rock 2.
NOTE Confidence: 0.7725647

00:14:59.850 --> 00:15:02.734 These are sitting three on TuneIn kinases.
NOTE Confidence: 0.7725647

00:15:02.740 --> 00:15:05.729 Most of this study is coming systemic
NOTE Confidence: 0.7725647

00:15:05.729 --> 00:15:07.026 sclerosis, another autoimmune
NOTE Confidence: 0.7725647

00:15:07.026 --> 00:15:09.191 disease models where altering rock
NOTE Confidence: 0.7725647

00:15:09.191 --> 00:15:11.728 to re balance the immune system,
NOTE Confidence: 0.7725647

00:15:11.730 --> 00:15:13.438 which down regulates drugs
NOTE Confidence: 0.7725647

00:15:13.438 --> 00:15:15.146 that's blocking the rock.
NOTE Confidence: 0.7725647

00:15:15.150 --> 00:15:16.040 Two parter.
NOTE Confidence: 0.7725647

00:15:16.040 --> 00:15:17.375 Basically, downregulate proinflammatory
NOTE Confidence: 0.7725647

00:15:17.375 --> 00:15:20.438 side intensity at 17 and it also
NOTE Confidence: 0.7725647

00:15:20.438 --> 00:15:21.998 increases your Excel production.
NOTE Confidence: 0.7725647

00:15:22.000 --> 00:15:22.788 In addition,
NOTE Confidence: 0.7725647

00:15:22.788 --> 00:15:24.758 what is interesting about this
NOTE Confidence: 0.7725647

00:15:24.758 --> 00:15:27.408 pathway is that it also controls

NOTE Confidence: 0.7725647

00:15:27.408 --> 00:15:29.276 multiple pro fibrotic processes,

NOTE Confidence: 0.7725647

00:15:29.280 --> 00:15:30.678 including myofibroblast activation.

NOTE Confidence: 0.7725647

00:15:30.678 --> 00:15:33.940 Rock is a downstream of major Pro.

NOTE Confidence: 0.7725647

00:15:33.940 --> 00:15:35.128 Fibrotic mediators mediate

NOTE Confidence: 0.7725647

00:15:35.128 --> 00:15:36.316 stress fiber formation.

NOTE Confidence: 0.7725647

00:15:36.320 --> 00:15:37.900 It also regulates transcription

NOTE Confidence: 0.7725647

00:15:37.900 --> 00:15:39.875 of several pro fibrotic genes.

NOTE Confidence: 0.7725647

00:15:39.880 --> 00:15:41.860 It is important because when

NOTE Confidence: 0.7725647

00:15:41.860 --> 00:15:43.840 you study chronic GV HD,

NOTE Confidence: 0.7725647

00:15:43.840 --> 00:15:47.024 there are milder versions of GV HD where

NOTE Confidence: 0.7725647

00:15:47.024 --> 00:15:49.779 people are just ocular or oral GST,

NOTE Confidence: 0.7725647

00:15:49.780 --> 00:15:53.344 which is not really that much of morbid GST.

NOTE Confidence: 0.7725647

00:15:53.350 --> 00:15:54.930 In contrast, that sclerotic,

NOTE Confidence: 0.7725647

00:15:54.930 --> 00:15:56.115 longer sclerotic pericardium,

NOTE Confidence: 0.7725647

00:15:56.120 --> 00:15:58.544 those are the most serious one

NOTE Confidence: 0.7725647

00:15:58.544 --> 00:16:00.160 where inflammation with fibrosis
NOTE Confidence: 0.7725647

00:16:00.227 --> 00:16:02.277 eventually lead to bad outcomes.
NOTE Confidence: 0.7725647

00:16:02.280 --> 00:16:04.518 So a drug which controls inflammation
NOTE Confidence: 0.7725647

00:16:04.518 --> 00:16:06.010 alters the fibrotic trajectory
NOTE Confidence: 0.7725647

00:16:06.065 --> 00:16:07.815 is a big welcome into the field.
NOTE Confidence: 0.84766275

00:16:10.100 --> 00:16:12.074 Study results are being eagerly awaited
NOTE Confidence: 0.84766275

00:16:12.074 --> 00:16:14.410 in the field for the last couple
NOTE Confidence: 0.84766275

00:16:14.410 --> 00:16:16.330 of years based on its mechanisms.
NOTE Confidence: 0.84766275

00:16:16.330 --> 00:16:18.437 And here's a slide on the right
NOTE Confidence: 0.84766275

00:16:18.437 --> 00:16:20.110 hand side that was presented
NOTE Confidence: 0.84766275

00:16:20.110 --> 00:16:22.553 initially in as 2018 and that ECT.
NOTE Confidence: 0.84766275

00:16:22.560 --> 00:16:25.437 And they're trying to find the dose.
NOTE Confidence: 0.84766275

00:16:25.440 --> 00:16:27.115 That intention to treat analysis
NOTE Confidence: 0.84766275

00:16:27.115 --> 00:16:29.130 about 59% of the patients showed
NOTE Confidence: 0.84766275

00:16:29.130 --> 00:16:31.140 overall response rate in that state.
NOTE Confidence: 0.84766275

00:16:31.140 --> 00:16:32.910 The inclusion criteria included people

NOTE Confidence: 0.84766275

00:16:32.910 --> 00:16:35.351 or greater than two prior lines of

NOTE Confidence: 0.84766275

00:16:35.351 --> 00:16:37.479 therapy and a significant number of those

NOTE Confidence: 0.84766275

00:16:37.479 --> 00:16:39.507 have more than four organ involved,

NOTE Confidence: 0.84766275

00:16:39.510 --> 00:16:42.180 and many of those are traditionally

NOTE Confidence: 0.84766275

00:16:42.180 --> 00:16:44.729 classified as what we call as

NOTE Confidence: 0.84766275

00:16:44.729 --> 00:16:46.454 a severe chronic GV HD.

NOTE Confidence: 0.84766275

00:16:46.460 --> 00:16:48.015 This lady is recapitulating what

NOTE Confidence: 0.84766275

00:16:48.015 --> 00:16:50.309 the study design was on the left

NOTE Confidence: 0.84766275

00:16:50.309 --> 00:16:51.677 of the eligibility criteria,

NOTE Confidence: 0.84766275

00:16:51.680 --> 00:16:53.702 which is basically age greater than

NOTE Confidence: 0.84766275

00:16:53.702 --> 00:16:55.719 to all active chronic Jamie ST2

NOTE Confidence: 0.84766275

00:16:55.719 --> 00:16:57.537 to five prior lines of therapy.

NOTE Confidence: 0.84766275

00:16:57.540 --> 00:17:00.004 They were allowed to go on the one

NOTE Confidence: 0.84766275

00:17:00.004 --> 00:17:02.430 of two arms either once a day.

NOTE Confidence: 0.84766275

00:17:02.430 --> 00:17:04.060 Those are twice a day.

NOTE Confidence: 0.84766275

00:17:04.060 --> 00:17:06.130 Those you would continue to tell
NOTE Confidence: 0.84766275

00:17:06.130 --> 00:17:07.165 clinically significant progression
NOTE Confidence: 0.84766275

00:17:07.165 --> 00:17:08.871 or unacceptable toxicity with the
NOTE Confidence: 0.84766275

00:17:08.871 --> 00:17:10.501 primary endpoint looking in four
NOTE Confidence: 0.84766275

00:17:10.501 --> 00:17:12.652 or R as per the consensus criteria
NOTE Confidence: 0.84766275

00:17:12.652 --> 00:17:14.206 and secondary endpoints with safety
NOTE Confidence: 0.84766275

00:17:14.206 --> 00:17:16.768 duration of response, at least symptoms care.
NOTE Confidence: 0.84766275

00:17:16.770 --> 00:17:19.570 Can you free survival and overall survival?
NOTE Confidence: 0.84766275

00:17:19.570 --> 00:17:21.000 The study population was well
NOTE Confidence: 0.84766275

00:17:21.000 --> 00:17:23.064 balanced for both the once a day dose
NOTE Confidence: 0.84766275

00:17:23.064 --> 00:17:24.739 and twice a day dose on the right
NOTE Confidence: 0.84766275

00:17:24.739 --> 00:17:26.594 hand side is giving you the overall
NOTE Confidence: 0.84766275

00:17:26.594 --> 00:17:28.650 output for all of those things.
NOTE Confidence: 0.84766275

00:17:28.650 --> 00:17:30.170 There was nothing significantly
NOTE Confidence: 0.84766275

00:17:30.170 --> 00:17:31.908 different between these two groups,
NOTE Confidence: 0.84766275

00:17:31.910 --> 00:17:33.938 but what is of interest here?

NOTE Confidence: 0.84766275

00:17:33.940 --> 00:17:35.630 Ways there were several people.

NOTE Confidence: 0.84766275

00:17:35.630 --> 00:17:37.315 Approximately 30% of the patients

NOTE Confidence: 0.84766275

00:17:37.315 --> 00:17:38.663 had used up ibrutinib.

NOTE Confidence: 0.84766275

00:17:38.670 --> 00:17:40.698 Other option ruxolitinib bugs are option,

NOTE Confidence: 0.84766275

00:17:40.700 --> 00:17:42.695 suggesting that the drug the the design

NOTE Confidence: 0.84766275

00:17:42.695 --> 00:17:45.149 of the study should be interpreted taking

NOTE Confidence: 0.84766275

00:17:45.149 --> 00:17:47.453 into account what are currently approved,

NOTE Confidence: 0.84766275

00:17:47.460 --> 00:17:49.865 or at least what's commonly

NOTE Confidence: 0.84766275

00:17:49.865 --> 00:17:51.789 used in the field.

NOTE Confidence: 0.84766275

00:17:51.790 --> 00:17:53.776 Here is the safety and tolerability

NOTE Confidence: 0.84766275

00:17:53.776 --> 00:17:56.049 of the of the study design.

NOTE Confidence: 0.84766275

00:17:56.050 --> 00:17:57.825 It has issues with gastrointestinal

NOTE Confidence: 0.84766275

00:17:57.825 --> 00:17:59.972 stuff in terms of diarrhea, nausea,

NOTE Confidence: 0.84766275

00:17:59.972 --> 00:18:02.576 which is a common thing that we

NOTE Confidence: 0.84766275

00:18:02.576 --> 00:18:05.048 encounter in our patient population.

NOTE Confidence: 0.84766275

00:18:05.050 --> 00:18:07.060 When we looked at specifically the
NOTE Confidence: 0.84766275

00:18:07.060 --> 00:18:08.746 great prior higher events, pneumonia,
NOTE Confidence: 0.84766275

00:18:08.746 --> 00:18:09.438 hypertension, hyperglycemia,
NOTE Confidence: 0.84766275

00:18:09.438 --> 00:18:11.514 or some of the common events
NOTE Confidence: 0.84766275

00:18:11.514 --> 00:18:12.759 that might come across.
NOTE Confidence: 0.84766275

00:18:12.760 --> 00:18:13.111 Again,
NOTE Confidence: 0.84766275

00:18:13.111 --> 00:18:15.568 keep in mind chronic GV HD patients
NOTE Confidence: 0.84766275

00:18:15.568 --> 00:18:17.447 are highly immunocompromised and
NOTE Confidence: 0.84766275

00:18:17.447 --> 00:18:19.655 infections are not uncommon.
NOTE Confidence: 0.84766275

00:18:19.660 --> 00:18:21.610 The primary endpoint was easily
NOTE Confidence: 0.84766275

00:18:21.610 --> 00:18:23.560 met for both the arms.
NOTE Confidence: 0.84766275

00:18:23.560 --> 00:18:26.290 It was 73% with once a day,
NOTE Confidence: 0.84766275

00:18:26.290 --> 00:18:29.410 those 77% with the twice a day dose.
NOTE Confidence: 0.84766275

00:18:29.410 --> 00:18:31.588 What was presented in this Patch
NOTE Confidence: 0.84766275

00:18:31.588 --> 00:18:34.152 was basically the 12 months follow
NOTE Confidence: 0.84766275

00:18:34.152 --> 00:18:36.747 compared to the previous presentations.

NOTE Confidence: 0.84766275

00:18:36.750 --> 00:18:38.304 Offered to show that seven patients

NOTE Confidence: 0.84766275

00:18:38.304 --> 00:18:40.162 were able to reach a CR Interestingly

NOTE Confidence: 0.84766275

00:18:40.162 --> 00:18:41.692 median time to the response in

NOTE Confidence: 0.84766275

00:18:41.692 --> 00:18:42.908 the studies four weeks,

NOTE Confidence: 0.84766275

00:18:42.910 --> 00:18:45.800 which is a welcome change.

NOTE Confidence: 0.84766275

00:18:45.800 --> 00:18:47.612 Here's the responses across the different

NOTE Confidence: 0.84766275

00:18:47.612 --> 00:18:48.990 subgroups they were interested in,

NOTE Confidence: 0.84766275

00:18:48.990 --> 00:18:51.174 no matter whether using it once

NOTE Confidence: 0.84766275

00:18:51.174 --> 00:18:53.189 a day or twice a day.

NOTE Confidence: 0.84766275

00:18:53.190 --> 00:18:55.030 Whether they had severe chronic

NOTE Confidence: 0.84766275

00:18:55.030 --> 00:18:56.870 GV HD screening or not,

NOTE Confidence: 0.84766275

00:18:56.870 --> 00:18:59.078 but it was refractory and refractory

NOTE Confidence: 0.84766275

00:18:59.078 --> 00:19:00.550 number of organs involved.

NOTE Confidence: 0.84766275

00:19:00.550 --> 00:19:02.932 Number of prior lines of therapy

NOTE Confidence: 0.84766275

00:19:02.932 --> 00:19:04.970 prior originate are excellent in it,

NOTE Confidence: 0.7602978

00:19:04.970 --> 00:19:08.144 this drug was able to show
NOTE Confidence: 0.7602978

00:19:08.144 --> 00:19:10.260 good overall response rate.
NOTE Confidence: 0.7602978

00:19:10.260 --> 00:19:12.540 The duration of Response rather than
NOTE Confidence: 0.7602978

00:19:12.540 --> 00:19:14.895 median duration of response was 50 weeks
NOTE Confidence: 0.7602978

00:19:14.895 --> 00:19:17.566 and about 60% of the patients maintain
NOTE Confidence: 0.7602978

00:19:17.566 --> 00:19:20.410 responses for greater than five months.
NOTE Confidence: 0.7602978

00:19:20.410 --> 00:19:21.774 Can you see survival
NOTE Confidence: 0.7602978

00:19:21.774 --> 00:19:23.138 Rasterizer reported six months?
NOTE Confidence: 0.7602978

00:19:23.140 --> 00:19:25.688 This ones reporting at 12 months of
NOTE Confidence: 0.7602978

00:19:25.688 --> 00:19:28.172 failure free survival at 58% is an
NOTE Confidence: 0.7602978

00:19:28.172 --> 00:19:30.998 extremely encouraging data for this field.
NOTE Confidence: 0.7602978

00:19:31.000 --> 00:19:32.770 Overall survival again is impressive,
NOTE Confidence: 0.7602978

00:19:32.770 --> 00:19:35.428 but 89% understanding the mortality that
NOTE Confidence: 0.7602978

00:19:35.428 --> 00:19:38.640 comes with chronic graft versus host disease.
NOTE Confidence: 0.7602978

00:19:38.640 --> 00:19:40.315 Additional endpoints that they talk
NOTE Confidence: 0.7602978

00:19:40.315 --> 00:19:42.380 about is reduction in the doors.

NOTE Confidence: 0.7602978

00:19:42.380 --> 00:19:44.964 They were able to show that the main

NOTE Confidence: 0.7602978

00:19:44.964 --> 00:19:46.739 cortico steroid dose reduction was

NOTE Confidence: 0.7602978

00:19:46.739 --> 00:19:49.180 possible in about 44% of the people.

NOTE Confidence: 0.7602978

00:19:49.180 --> 00:19:51.560 It was higher in those who responded.

NOTE Confidence: 0.7602978

00:19:51.560 --> 00:19:54.320 Obviously 52% and lower in those who are

NOTE Confidence: 0.7602978

00:19:54.320 --> 00:19:56.340 not responding about 17% in addition

NOTE Confidence: 0.7602978

00:19:56.340 --> 00:19:58.090 to the steroids calcineurin inhibitor

NOTE Confidence: 0.7602978

00:19:58.090 --> 00:20:00.178 dose reduction was also possible with.

NOTE Confidence: 0.7602978

00:20:00.180 --> 00:20:02.378 More patients in the treatment arm able

NOTE Confidence: 0.7602978

00:20:02.378 --> 00:20:05.329 to do that with compared to what we've

NOTE Confidence: 0.7602978

00:20:05.329 --> 00:20:07.274 seen historically in other trials.

NOTE Confidence: 0.7602978

00:20:07.280 --> 00:20:09.170 Symptoms scale The least scale

NOTE Confidence: 0.7602978

00:20:09.170 --> 00:20:11.330 as I presented you earlier on.

NOTE Confidence: 0.7602978

00:20:11.330 --> 00:20:11.678 Again,

NOTE Confidence: 0.7602978

00:20:11.678 --> 00:20:14.114 it was a meaningful difference with both

NOTE Confidence: 0.7602978

00:20:14.114 --> 00:20:15.870 responders or nonresponders achieving
NOTE Confidence: 0.7602978

00:20:15.870 --> 00:20:18.360 improvement in their symptoms scores.
NOTE Confidence: 0.7602978

00:20:18.360 --> 00:20:20.820 In conclusion this drug element Bell
NOTE Confidence: 0.7602978

00:20:20.820 --> 00:20:23.566 incident is well tolerated and has
NOTE Confidence: 0.7602978

00:20:23.566 --> 00:20:25.646 achieved clinically meaningful outcomes.
NOTE Confidence: 0.7602978

00:20:25.650 --> 00:20:27.705 Response rates are greater than
NOTE Confidence: 0.7602978

00:20:27.705 --> 00:20:29.756 70% with both treatment arms,
NOTE Confidence: 0.7602978

00:20:29.756 --> 00:20:31.801 including in patients who failed
NOTE Confidence: 0.7602978

00:20:31.801 --> 00:20:33.479 ibrutinib and Jack inhibitors.
NOTE Confidence: 0.78034705

00:20:36.110 --> 00:20:37.727 Switching gears will talk about the cells.
NOTE Confidence: 0.78034705

00:20:37.730 --> 00:20:39.550 The reason for graft versus host disease
NOTE Confidence: 0.78034705

00:20:39.550 --> 00:20:41.827 or the T cells that are coming here.
NOTE Confidence: 0.78034705

00:20:41.830 --> 00:20:43.774 The trial initially done at Stanford
NOTE Confidence: 0.78034705

00:20:43.774 --> 00:20:46.519 is explored to see if we can isolate
NOTE Confidence: 0.78034705

00:20:46.519 --> 00:20:48.254 self populations to decrease after
NOTE Confidence: 0.78034705

00:20:48.254 --> 00:20:49.989 sostis is historically the way

NOTE Confidence: 0.78034705

00:20:49.989 --> 00:20:51.969 we've tried to diploid cells are

NOTE Confidence: 0.78034705

00:20:51.970 --> 00:20:54.336 XY or we try to extract pantycelyn,

NOTE Confidence: 0.78034705

00:20:54.340 --> 00:20:57.036 plead or use drugs like ATG Witcher invite.

NOTE Confidence: 0.78034705

00:20:57.040 --> 00:20:59.168 We're depleting agents toxin is more recent

NOTE Confidence: 0.78034705

00:20:59.168 --> 00:21:01.429 addition to the field of transplantation,

NOTE Confidence: 0.78034705

00:21:01.430 --> 00:21:03.718 which kinds of depletes the cell in the

NOTE Confidence: 0.78034705

00:21:03.718 --> 00:21:06.129 setting of haploidentical transplantation?

NOTE Confidence: 0.78034705

00:21:06.130 --> 00:21:08.010 What investigators at Stanford Ed.

NOTE Confidence: 0.78034705

00:21:08.010 --> 00:21:09.880 Was in the preclinical models.

NOTE Confidence: 0.78034705

00:21:09.880 --> 00:21:11.820 Initially, they showed that regulatory

NOTE Confidence: 0.78034705

00:21:11.820 --> 00:21:14.890 cells which in the PD 1 field with

NOTE Confidence: 0.78034705

00:21:14.890 --> 00:21:17.002 solid tumors as a different meaning,

NOTE Confidence: 0.78034705

00:21:17.010 --> 00:21:19.761 is a welcome change in the post

NOTE Confidence: 0.78034705

00:21:19.761 --> 00:21:21.346 transplantation setting because it

NOTE Confidence: 0.78034705

00:21:21.346 --> 00:21:23.380 in users tolerance decreases GV HD.

NOTE Confidence: 0.78034705

00:21:23.380 --> 00:21:25.652 So the design the study with the my
NOTE Confidence: 0.78034705

00:21:25.652 --> 00:21:27.588 love letter transplant setting wherein
NOTE Confidence: 0.78034705

00:21:27.588 --> 00:21:29.763 you would give your chemotherapy
NOTE Confidence: 0.78034705

00:21:29.763 --> 00:21:31.878 or radiation and then subsequently
NOTE Confidence: 0.78034705

00:21:31.878 --> 00:21:33.843 confuse equal volumes of regulatory
NOTE Confidence: 0.78034705

00:21:33.843 --> 00:21:35.812 T cells and conventional cells.
NOTE Confidence: 0.78034705

00:21:35.812 --> 00:21:36.600 So basically.
NOTE Confidence: 0.78034705

00:21:36.600 --> 00:21:39.015 And a -- 2 prior to transplantation.
NOTE Confidence: 0.78034705

00:21:39.020 --> 00:21:41.090 Amateur quite stem cells and T.
NOTE Confidence: 0.78034705

00:21:41.090 --> 00:21:42.810 Rex cells were extracted out,
NOTE Confidence: 0.78034705

00:21:42.810 --> 00:21:43.922 kept and then infused,
NOTE Confidence: 0.78034705

00:21:43.922 --> 00:21:46.481 and a 0 two days later the conventional
NOTE Confidence: 0.78034705

00:21:46.481 --> 00:21:49.365 cells were then infused into the recipient.
NOTE Confidence: 0.78034705

00:21:49.370 --> 00:21:51.690 Here instead of a conventional two or a
NOTE Confidence: 0.78034705

00:21:51.690 --> 00:21:53.509 combination of suppression regiments,
NOTE Confidence: 0.78034705

00:21:53.510 --> 00:21:56.270 they were able to show that single agent,

NOTE Confidence: 0.78034705

00:21:56.270 --> 00:21:57.305 even a suppressive.

NOTE Confidence: 0.78034705

00:21:57.305 --> 00:21:59.030 Agents like tacrolimus was adequate.

NOTE Confidence: 0.8181829

00:22:01.340 --> 00:22:02.948 The amount of total cells that

NOTE Confidence: 0.8181829

00:22:02.948 --> 00:22:04.579 they chose would 3,000,000 T cells

NOTE Confidence: 0.8181829

00:22:04.579 --> 00:22:06.103 and almost everybody got more than

NOTE Confidence: 0.8181829

00:22:06.103 --> 00:22:07.649 two million CD 34 positive cells,

NOTE Confidence: 0.8181829

00:22:07.650 --> 00:22:10.362 which is what we normally like

NOTE Confidence: 0.8181829

00:22:10.362 --> 00:22:12.170 in the transportation context.

NOTE Confidence: 0.8181829

00:22:12.170 --> 00:22:13.304 Extrapolating the data,

NOTE Confidence: 0.8181829

00:22:13.304 --> 00:22:16.761 they now went at a multi site level and

NOTE Confidence: 0.8181829

00:22:16.761 --> 00:22:19.721 showed that when you try to go commercial,

NOTE Confidence: 0.8181829

00:22:19.730 --> 00:22:21.580 it's feasible showed on the

NOTE Confidence: 0.8181829

00:22:21.580 --> 00:22:24.269 left hand side the CD 34 purity.

NOTE Confidence: 0.8181829

00:22:24.270 --> 00:22:26.846 Here XL doses anti Rexel purity when

NOTE Confidence: 0.8181829

00:22:26.846 --> 00:22:29.160 taking into account the logistics that

NOTE Confidence: 0.8181829

00:22:29.160 --> 00:22:31.827 comes with it for mobilizing the donor.

NOTE Confidence: 0.8181829

00:22:31.830 --> 00:22:34.511 Collecting at a site shipping it to

NOTE Confidence: 0.8181829

00:22:34.511 --> 00:22:36.762 this company would then analyze extract

NOTE Confidence: 0.8181829

00:22:36.762 --> 00:22:40.037 HSP season T Rex to one bag and then

NOTE Confidence: 0.8181829

00:22:40.037 --> 00:22:42.485 conventional T cells to another back.

NOTE Confidence: 0.8181829

00:22:42.490 --> 00:22:45.514 They were able to show that that process

NOTE Confidence: 0.8181829

00:22:45.514 --> 00:22:47.739 work efficiently and the rest of this,

NOTE Confidence: 0.8181829

00:22:47.740 --> 00:22:49.840 like basically show the clinical data,

NOTE Confidence: 0.8181829

00:22:49.840 --> 00:22:51.868 were able to show this interphil

NOTE Confidence: 0.8181829

00:22:51.868 --> 00:22:53.220 engraftment later engagement and

NOTE Confidence: 0.8181829

00:22:53.280 --> 00:22:54.740 time of hospital discharges,

NOTE Confidence: 0.8181829

00:22:54.740 --> 00:22:56.840 or all favoring this novel approach.

NOTE Confidence: 0.8181829

00:22:56.840 --> 00:22:58.164 What is more important,

NOTE Confidence: 0.8181829

00:22:58.164 --> 00:23:00.690 or patients is graft versus host disease,

NOTE Confidence: 0.8181829

00:23:00.690 --> 00:23:03.259 both grades two or higher acute graft

NOTE Confidence: 0.8181829

00:23:03.259 --> 00:23:05.534 versus host disease and chronic GBS T

NOTE Confidence: 0.8181829

00:23:05.534 --> 00:23:08.437 as shown on the left hand side here was

NOTE Confidence: 0.8181829

00:23:08.437 --> 00:23:10.397 significantly lowered when they use

NOTE Confidence: 0.8181829

00:23:10.397 --> 00:23:13.080 this design of infusing regulatory T cells.

NOTE Confidence: 0.8181829

00:23:13.080 --> 00:23:14.744 Along with the conventional

NOTE Confidence: 0.8181829

00:23:14.744 --> 00:23:16.824 cells at different time points.

NOTE Confidence: 0.8181829

00:23:16.830 --> 00:23:18.150 GPS direction is important,

NOTE Confidence: 0.8181829

00:23:18.150 --> 00:23:20.130 So what happens to the relapse?

NOTE Confidence: 0.8181829

00:23:20.130 --> 00:23:22.338 A good out point for that is what

NOTE Confidence: 0.8181829

00:23:22.338 --> 00:23:24.735 we call the GFS on the right hand

NOTE Confidence: 0.8181829

00:23:24.735 --> 00:23:27.605 side there able to show that GFS was

NOTE Confidence: 0.8181829

00:23:27.605 --> 00:23:29.625 significantly better with using this

NOTE Confidence: 0.8181829

00:23:29.625 --> 00:23:31.680 novel approach and TRM was almost

NOTE Confidence: 0.8181829

00:23:31.680 --> 00:23:33.000 nonexistent with this approach,

NOTE Confidence: 0.8181829

00:23:33.000 --> 00:23:34.788 suggesting and paving way for future

NOTE Confidence: 0.8181829

00:23:34.788 --> 00:23:36.768 study designs for cell manipulation to

NOTE Confidence: 0.8181829

00:23:36.768 --> 00:23:38.608 decrease graph versus host disease,
NOTE Confidence: 0.8181829

00:23:38.610 --> 00:23:41.658 with a special emphasis on regulatory
NOTE Confidence: 0.8181829

00:23:41.658 --> 00:23:42.674 T cells.
NOTE Confidence: 0.8181829

00:23:42.680 --> 00:23:43.816 In this last light,
NOTE Confidence: 0.8181829

00:23:43.816 --> 00:23:45.961 we're going to talk about how they
NOTE Confidence: 0.8181829

00:23:45.961 --> 00:23:47.846 feel if consolidation is evolving.
NOTE Confidence: 0.8181829

00:23:47.850 --> 00:23:49.944 Loading my colleague presented a couple
NOTE Confidence: 0.8181829

00:23:49.944 --> 00:23:52.064 of weeks ago and this interesting
NOTE Confidence: 0.8181829

00:23:52.064 --> 00:23:54.374 trial from oral is cited in in
NOTE Confidence: 0.8181829

00:23:54.374 --> 00:23:56.598 terms of how this is a game changer
NOTE Confidence: 0.8181829

00:23:56.598 --> 00:23:58.210 to the field of transplantation,
NOTE Confidence: 0.8181829

00:23:58.210 --> 00:24:00.670 the drug has now been approved.
NOTE Confidence: 0.8181829

00:24:00.670 --> 00:24:01.420 To recap,
NOTE Confidence: 0.8181829

00:24:01.420 --> 00:24:02.920 essentially patients get intensive
NOTE Confidence: 0.8181829

00:24:02.920 --> 00:24:05.299 chemotherapy at the time of recruitment.
NOTE Confidence: 0.8181829

00:24:05.300 --> 00:24:07.435 These people are all in the older

NOTE Confidence: 0.8181829

00:24:07.435 --> 00:24:09.891 age group and were thought not

NOTE Confidence: 0.8181829

00:24:09.891 --> 00:24:11.855 eligible to receive transplantation,

NOTE Confidence: 0.8181829

00:24:11.860 --> 00:24:14.612 but 44% of the patient get one cycle

NOTE Confidence: 0.8181829

00:24:14.612 --> 00:24:16.321 of intensive chemo consolidation

NOTE Confidence: 0.8181829

00:24:16.321 --> 00:24:19.435 and 38% get second layer of chemo

NOTE Confidence: 0.8181829

00:24:19.435 --> 00:24:21.600 consolidation and then their random

NOTE Confidence: 0.8181829

00:24:21.675 --> 00:24:24.015 honest to get either placebo osrs

NOTE Confidence: 0.8181829

00:24:24.015 --> 00:24:26.291 study agent which was CC-486 which

NOTE Confidence: 0.8181829

00:24:26.291 --> 00:24:28.843 is or a laser sighted in in that

NOTE Confidence: 0.8181829

00:24:28.850 --> 00:24:30.960 there was overall survival advantage

NOTE Confidence: 0.8181829

00:24:30.960 --> 00:24:33.949 as shown in the right top corner.

NOTE Confidence: 0.8181829

00:24:33.950 --> 00:24:36.218 I adore you present it as an extension of

NOTE Confidence: 0.8181829

00:24:36.218 --> 00:24:38.666 that people have now done subgroup analysis,

NOTE Confidence: 0.8181829

00:24:38.670 --> 00:24:40.764 coming back to the left hand

NOTE Confidence: 0.8181829

00:24:40.764 --> 00:24:43.153 side here Doctor Way and up to

NOTE Confidence: 0.8181829

00:24:43.153 --> 00:24:45.295 remind you are able to show that.

NOTE Confidence: 0.8181829

00:24:45.300 --> 00:24:46.998 Irrespective of consolidation,

NOTE Confidence: 0.8181829

00:24:46.998 --> 00:24:50.394 whether they got consolidation or not.

NOTE Confidence: 0.8181829

00:24:50.400 --> 00:24:52.040 Are they got one consolidation

NOTE Confidence: 0.8181829

00:24:52.040 --> 00:24:54.399 or greater than or equal to two

NOTE Confidence: 0.8181829

00:24:54.399 --> 00:24:55.711 consolidation there showing that

NOTE Confidence: 0.8181829

00:24:55.711 --> 00:24:58.295 CC 4X6 was able to improve overall

NOTE Confidence: 0.8181829

00:24:58.295 --> 00:25:00.310 survival and relapse free survival?

NOTE Confidence: 0.8181829

00:25:00.310 --> 00:25:02.446 I'm not showing the slide but

NOTE Confidence: 0.8181829

00:25:02.446 --> 00:25:03.870 in the more recent

NOTE Confidence: 0.82386875

00:25:03.945 --> 00:25:06.227 ECD a couple of weeks ago as

NOTE Confidence: 0.82386875

00:25:06.227 --> 00:25:08.100 an extension of this study,

NOTE Confidence: 0.82386875

00:25:08.100 --> 00:25:09.796 investigators showed that many

NOTE Confidence: 0.82386875

00:25:09.796 --> 00:25:11.916 people in the placebo arm.

NOTE Confidence: 0.82386875

00:25:11.920 --> 00:25:14.074 Went on to get eventual allogeneic

NOTE Confidence: 0.82386875

00:25:14.074 --> 00:25:15.861 stem cell transplantation and they

NOTE Confidence: 0.82386875

00:25:15.861 --> 00:25:17.613 make a case suggesting that we

NOTE Confidence: 0.82386875

00:25:17.613 --> 00:25:18.930 are getting more transplantation

NOTE Confidence: 0.82386875

00:25:18.930 --> 00:25:21.240 at higher frequency in that arm.

NOTE Confidence: 0.82386875

00:25:21.240 --> 00:25:22.965 Basically did not alter the

NOTE Confidence: 0.82386875

00:25:22.965 --> 00:25:24.305 eventual overall survival, however,

NOTE Confidence: 0.82386875

00:25:24.305 --> 00:25:26.745 we should keep in mind the study was

NOTE Confidence: 0.82386875

00:25:26.745 --> 00:25:29.169 not designed to answer that question,

NOTE Confidence: 0.82386875

00:25:29.170 --> 00:25:31.340 so that leads us to the next

NOTE Confidence: 0.82386875

00:25:31.340 --> 00:25:34.224 segment of this as to how we can

NOTE Confidence: 0.82386875

00:25:34.224 --> 00:25:35.728 address limitations and propel.

NOTE Confidence: 0.82386875

00:25:35.730 --> 00:25:36.765 Understands of allogeneic

NOTE Confidence: 0.82386875

00:25:36.765 --> 00:25:37.800 stem cell transplant,

NOTE Confidence: 0.82386875

00:25:37.800 --> 00:25:40.760 so in this coming year ALR several study

NOTE Confidence: 0.82386875

00:25:40.760 --> 00:25:43.540 designs to do this in the backdrop of.

NOTE Confidence: 0.82386875

00:25:43.540 --> 00:25:45.350 Was that animal study design

NOTE Confidence: 0.82386875

00:25:45.350 --> 00:25:46.798 working with Doctor Probie?
NOTE Confidence: 0.82386875

00:25:46.800 --> 00:25:48.610 We have a multicenter study
NOTE Confidence: 0.82386875

00:25:48.610 --> 00:25:50.058 that we we initiating's,
NOTE Confidence: 0.82386875

00:25:50.060 --> 00:25:51.344 been supported by Celgene.
NOTE Confidence: 0.82386875

00:25:51.344 --> 00:25:52.628 That is basically looking
NOTE Confidence: 0.82386875

00:25:52.628 --> 00:25:54.586 into the potential role of
NOTE Confidence: 0.82386875

00:25:54.586 --> 00:25:55.849 novel consolidation regiments.
NOTE Confidence: 0.82386875

00:25:55.850 --> 00:25:58.088 We all know that reaching CR
NOTE Confidence: 0.82386875

00:25:58.088 --> 00:26:00.189 is a major milestone in AML.
NOTE Confidence: 0.82386875

00:26:00.190 --> 00:26:01.189 The question is,
NOTE Confidence: 0.82386875

00:26:01.189 --> 00:26:03.520 how long do you need to consolidate
NOTE Confidence: 0.82386875

00:26:03.586 --> 00:26:06.658 them prior to you get them to the
NOTE Confidence: 0.82386875

00:26:06.658 --> 00:26:08.518 allogeneic transplantation in that premise,
NOTE Confidence: 0.82386875

00:26:08.520 --> 00:26:09.848 using some immunological correlates
NOTE Confidence: 0.82386875

00:26:09.848 --> 00:26:11.840 will be studying the role of
NOTE Confidence: 0.82386875

00:26:11.896 --> 00:26:13.868 epigenetic priming post consolidation.

NOTE Confidence: 0.82386875

00:26:13.870 --> 00:26:15.893 And also using the concept of Fortaleza

NOTE Confidence: 0.82386875

00:26:15.893 --> 00:26:17.298 cited in increasing regulatory T

NOTE Confidence: 0.82386875

00:26:17.298 --> 00:26:18.978 cell output to decrease GV HD in

NOTE Confidence: 0.82386875

00:26:18.978 --> 00:26:20.700 the post transplantation setting,

NOTE Confidence: 0.82386875

00:26:20.700 --> 00:26:22.122 we have designed a study that

NOTE Confidence: 0.82386875

00:26:22.122 --> 00:26:23.798 will look into an extended period

NOTE Confidence: 0.82386875

00:26:23.798 --> 00:26:25.802 use of over laser setting prior

NOTE Confidence: 0.82386875

00:26:25.802 --> 00:26:27.138 to transplantation and post

NOTE Confidence: 0.82386875

00:26:27.138 --> 00:26:28.678 transplantation with the hope of

NOTE Confidence: 0.82386875

00:26:28.678 --> 00:26:30.204 decreasing both GST and relaxed

NOTE Confidence: 0.82386875

00:26:30.204 --> 00:26:31.986 survival and that would start recording.

NOTE Confidence: 0.82386875

00:26:31.990 --> 00:26:33.910 So this study has implications to

NOTE Confidence: 0.82386875

00:26:33.910 --> 00:26:35.539 the satellite centers because many

NOTE Confidence: 0.82386875

00:26:35.539 --> 00:26:36.989 of these patients after transferring

NOTE Confidence: 0.82386875

00:26:36.989 --> 00:26:39.278 will go back to you as primary and

NOTE Confidence: 0.82386875

00:26:39.278 --> 00:26:40.892 that's something you guys would be
NOTE Confidence: 0.82386875

00:26:40.900 --> 00:26:43.000 able to get access to the drugs
NOTE Confidence: 0.82386875

00:26:43.000 --> 00:26:45.018 and treat them in the practice.
NOTE Confidence: 0.82386875

00:26:45.020 --> 00:26:46.754 The other two studies of interest
NOTE Confidence: 0.82386875

00:26:46.754 --> 00:26:49.178 is led by my boss that are open.
NOTE Confidence: 0.82386875

00:26:49.180 --> 00:26:51.161 We looking into the role of allogeneic
NOTE Confidence: 0.82386875

00:26:51.161 --> 00:26:52.679 stem cell transplantation for patients
NOTE Confidence: 0.82386875

00:26:52.679 --> 00:26:54.229 who are relapsed refractory setting.
NOTE Confidence: 0.82386875

00:26:54.230 --> 00:26:56.598 There are many new drugs that are coming.
NOTE Confidence: 0.82386875

00:26:56.600 --> 00:26:59.064 I didn't have a chance to talk all
NOTE Confidence: 0.82386875

00:26:59.064 --> 00:27:01.056 about them up for all of them,
NOTE Confidence: 0.82386875

00:27:01.060 --> 00:27:03.004 but I have is 1 set strike which is
NOTE Confidence: 0.82386875

00:27:03.004 --> 00:27:04.121 using Radionucleotide radionucleotide
NOTE Confidence: 0.82386875

00:27:04.121 --> 00:27:05.809 to target CD 45.
NOTE Confidence: 0.82386875

00:27:05.810 --> 00:27:07.010 Comparing against the conventional
NOTE Confidence: 0.82386875

00:27:07.010 --> 00:27:08.810 care which is currently ongoing and

NOTE Confidence: 0.82386875

00:27:08.855 --> 00:27:10.270 there's also a multicenter trial.

NOTE Confidence: 0.82386875

00:27:10.270 --> 00:27:11.155 As you know,

NOTE Confidence: 0.82386875

00:27:11.155 --> 00:27:12.925 afflict Rena bitter guilty name is

NOTE Confidence: 0.82386875

00:27:12.925 --> 00:27:15.018 approved to treat relapsed refractory AML.

NOTE Confidence: 0.82386875

00:27:15.020 --> 00:27:16.882 But now we're studying that in a

NOTE Confidence: 0.82386875

00:27:16.882 --> 00:27:18.707 randomized fashion to see if preventing

NOTE Confidence: 0.82386875

00:27:18.707 --> 00:27:20.657 relapse is better rather than treating

NOTE Confidence: 0.82386875

00:27:20.657 --> 00:27:22.170 relapsing relapse refractory AML.

NOTE Confidence: 0.82386875

00:27:22.170 --> 00:27:23.725 And that's a study that's

NOTE Confidence: 0.82386875

00:27:23.725 --> 00:27:24.969 currently ongoing with that.

NOTE Confidence: 0.82386875

00:27:24.970 --> 00:27:27.910 I'd like to thank you all and.

NOTE Confidence: 0.82386875

00:27:27.910 --> 00:27:30.412 I would ask you all to hold your questions

NOTE Confidence: 0.82386875

00:27:30.412 --> 00:27:32.617 at the end of it while I pass on.

NOTE Confidence: 0.82386875

00:27:32.620 --> 00:27:34.860 So the more interesting phase of T cell

NOTE Confidence: 0.82386875

00:27:34.860 --> 00:27:36.259 engineering talks by my colleague,

NOTE Confidence: 0.82386875

00:27:36.260 --> 00:27:36.820 Doctor Sophie,
NOTE Confidence: 0.82386875

00:27:36.820 --> 00:27:37.940 thank you very much.
NOTE Confidence: 0.5139432

00:27:45.490 --> 00:27:46.618 Thank you, Louise.
NOTE Confidence: 0.84160817

00:28:03.250 --> 00:28:06.850 So I'll focus my talk today on cellular
NOTE Confidence: 0.84160817

00:28:06.850 --> 00:28:09.538 therapies for B cell malignancy's.
NOTE Confidence: 0.84160817

00:28:09.540 --> 00:28:11.272 These are my disclosures.
NOTE Confidence: 0.84160817

00:28:11.272 --> 00:28:14.523 And I'd like to start by reminding
NOTE Confidence: 0.84160817

00:28:14.523 --> 00:28:17.338 everyone of the approved city
NOTE Confidence: 0.84160817

00:28:17.338 --> 00:28:20.102 19 cortisol products that are
NOTE Confidence: 0.84160817

00:28:20.102 --> 00:28:23.056 currently on the market for B cell.
NOTE Confidence: 0.84160817

00:28:23.060 --> 00:28:25.616 Non Hodgkin lymphoma is we have
NOTE Confidence: 0.84160817

00:28:25.616 --> 00:28:27.881 exit Captain James I'll alusil
NOTE Confidence: 0.84160817

00:28:27.881 --> 00:28:31.241 targeting City 19 with the city 28
NOTE Confidence: 0.84160817

00:28:31.241 --> 00:28:33.120 costimulatory domain tyssa gentle
NOTE Confidence: 0.84160817

00:28:33.120 --> 00:28:36.046 occlusal also targeting CD 19 with a
NOTE Confidence: 0.84160817

00:28:36.046 --> 00:28:38.254 four one baby costimulatory domain.

NOTE Confidence: 0.84160817

00:28:38.254 --> 00:28:40.038 The newly approved lie.

NOTE Confidence: 0.84160817

00:28:40.040 --> 00:28:42.124 So Captain Jean meluso.

NOTE Confidence: 0.84160817

00:28:42.124 --> 00:28:45.970 With a four one baby costimulatory domain,

NOTE Confidence: 0.84160817

00:28:45.970 --> 00:28:49.092 these are all approved for large cell

NOTE Confidence: 0.84160817

00:28:49.092 --> 00:28:51.939 lymphoma and transformed follicular lymphoma,

NOTE Confidence: 0.84160817

00:28:51.940 --> 00:28:54.430 whereas T Sergeant occlusal is

NOTE Confidence: 0.84160817

00:28:54.430 --> 00:28:56.920 currently the only approved product.

NOTE Confidence: 0.84160817

00:28:56.920 --> 00:28:59.950 Also for the treatment of relapsed

NOTE Confidence: 0.84160817

00:28:59.950 --> 00:29:02.532 refractory pediatric LL and then

NOTE Confidence: 0.84160817

00:29:02.532 --> 00:29:04.897 finally a recent another recent

NOTE Confidence: 0.84160817

00:29:04.897 --> 00:29:07.871 approval last year of Brexit captain

NOTE Confidence: 0.84160817

00:29:07.871 --> 00:29:10.865 Jean Autolux so in mental relapse,

NOTE Confidence: 0.84160817

00:29:10.870 --> 00:29:12.782 refractory mantle cell lymphoma.

NOTE Confidence: 0.84160817

00:29:12.782 --> 00:29:15.650 Targeting CD19 with the CD 28

NOTE Confidence: 0.84160817

00:29:15.728 --> 00:29:18.232 costimulatory domain for relapsed

NOTE Confidence: 0.84160817

00:29:18.232 --> 00:29:20.736 refractory large cell lymphoma,
NOTE Confidence: 0.84160817

00:29:20.740 --> 00:29:22.627 transformed follicular lymphoma.
NOTE Confidence: 0.84160817

00:29:22.627 --> 00:29:25.772 The overall response rates seen
NOTE Confidence: 0.84160817

00:29:25.772 --> 00:29:28.464 in clinical trials have varied
NOTE Confidence: 0.84160817

00:29:28.464 --> 00:29:31.164 between 50 and upwards of 80%.
NOTE Confidence: 0.84160817

00:29:31.170 --> 00:29:33.574 Complete remission rates, however,
NOTE Confidence: 0.84160817

00:29:33.574 --> 00:29:38.298 are only in the order of 40 to 50%.
NOTE Confidence: 0.84160817

00:29:38.300 --> 00:29:40.808 This is significantly improved
NOTE Confidence: 0.84160817

00:29:40.808 --> 00:29:43.316 compared to the previously
NOTE Confidence: 0.84160817

00:29:43.316 --> 00:29:45.289 established standards of care.
NOTE Confidence: 0.84160817

00:29:45.290 --> 00:29:47.900 But still leaves some room for
NOTE Confidence: 0.84160817

00:29:47.900 --> 00:29:50.245 improvement and then with Brexit
NOTE Confidence: 0.84160817

00:29:50.245 --> 00:29:52.835 catagen and mantle cell lymphoma.
NOTE Confidence: 0.84160817

00:29:52.840 --> 00:29:55.200 Also very remarkable results with
NOTE Confidence: 0.84160817

00:29:55.200 --> 00:29:58.031 overall response rates of 93% and
NOTE Confidence: 0.84160817

00:29:58.031 --> 00:30:00.386 complete response rates of 67%.

NOTE Confidence: 0.8383559

00:30:02.440 --> 00:30:05.140 Looking at studies of these cellular

NOTE Confidence: 0.8383559

00:30:05.140 --> 00:30:08.724 therapies and some of the risk factors

NOTE Confidence: 0.8383559

00:30:08.724 --> 00:30:10.988 associated with worse progression,

NOTE Confidence: 0.8383559

00:30:10.990 --> 00:30:13.510 free survival and overall survival,

NOTE Confidence: 0.8383559

00:30:13.510 --> 00:30:16.695 it has become clear that there are

NOTE Confidence: 0.8383559

00:30:16.695 --> 00:30:19.789 some factors that are patient related

NOTE Confidence: 0.8383559

00:30:19.789 --> 00:30:23.059 and some that are treatment related.

NOTE Confidence: 0.8383559

00:30:23.060 --> 00:30:26.574 For example, having a very poor performance,

NOTE Confidence: 0.8383559

00:30:26.580 --> 00:30:29.225 equal performance status prior to

NOTE Confidence: 0.8383559

00:30:29.225 --> 00:30:32.729 receiving car T cell therapy and also.

NOTE Confidence: 0.8383559

00:30:32.730 --> 00:30:35.222 Very elevated LDH have actually been shown

NOTE Confidence: 0.8383559

00:30:35.222 --> 00:30:38.338 to be very poor prognostic markers for

NOTE Confidence: 0.8383559

00:30:38.338 --> 00:30:40.803 progression free and overall survival.

NOTE Confidence: 0.8383559

00:30:40.810 --> 00:30:44.350 Post car T cell therapy.

NOTE Confidence: 0.8383559

00:30:44.350 --> 00:30:47.126 And and this is a study just published

NOTE Confidence: 0.8383559

00:30:47.126 --> 00:30:50.403 in JCO this year where they did
NOTE Confidence: 0.8383559

00:30:50.403 --> 00:30:52.407 multivariable models in patients
NOTE Confidence: 0.8383559

00:30:52.407 --> 00:30:55.379 treated with AXI cottage inside alusil.
NOTE Confidence: 0.8383559

00:30:55.380 --> 00:30:58.170 And again they really showed clear
NOTE Confidence: 0.8383559

00:30:58.170 --> 00:31:00.512 distinction between the progression free
NOTE Confidence: 0.8383559

00:31:00.512 --> 00:31:02.572 survival and overall survival curves
NOTE Confidence: 0.8383559

00:31:02.572 --> 00:31:05.153 in patients that had poor performance
NOTE Confidence: 0.8383559

00:31:05.153 --> 00:31:07.745 status and high disease burden as
NOTE Confidence: 0.8383559

00:31:07.745 --> 00:31:09.930 represented by elevated LDH levels.
NOTE Confidence: 0.8386046

00:31:11.970 --> 00:31:14.676 You know what about what about
NOTE Confidence: 0.8386046

00:31:14.676 --> 00:31:17.769 the biology of the tumor itself?
NOTE Confidence: 0.8386046

00:31:17.770 --> 00:31:22.153 What we know now is that anywhere from 1/4
NOTE Confidence: 0.8386046

00:31:22.153 --> 00:31:25.490 to 30% of patients with relapsed refractory,
NOTE Confidence: 0.8386046

00:31:25.490 --> 00:31:27.488 large cell lymphoma,
NOTE Confidence: 0.8386046

00:31:27.488 --> 00:31:30.818 who progress after cortisol therapy.
NOTE Confidence: 0.8386046

00:31:30.820 --> 00:31:32.969 1/4 of them will have loss of

NOTE Confidence: 0.8386046

00:31:32.969 --> 00:31:35.668 CD 19 in their tumor biopsies.

NOTE Confidence: 0.8386046

00:31:35.670 --> 00:31:37.126 So not all patients,

NOTE Confidence: 0.8386046

00:31:37.126 --> 00:31:39.879 but at least in some this is

NOTE Confidence: 0.8386046

00:31:39.879 --> 00:31:42.795 responsible for their for their relapse.

NOTE Confidence: 0.8386046

00:31:42.800 --> 00:31:45.938 So how can we circumvent that?

NOTE Confidence: 0.8386046

00:31:45.940 --> 00:31:49.138 A very important study published in

NOTE Confidence: 0.8386046

00:31:49.138 --> 00:31:52.868 Nature of Medicine also this year by

NOTE Confidence: 0.8386046

00:31:52.868 --> 00:31:55.880 Nirav Shah at University of Medicine,

NOTE Confidence: 0.8386046

00:31:55.880 --> 00:31:59.012 Wisconsin, looked at by specific anti

NOTE Confidence: 0.8386046

00:31:59.012 --> 00:32:03.461 CD 20 and CD19 car sales for relapsed

NOTE Confidence: 0.8386046

00:32:03.461 --> 00:32:06.839 diffuse large B cell lymphoma and

NOTE Confidence: 0.8386046

00:32:06.939 --> 00:32:09.996 they have seen a 40% of patients

NOTE Confidence: 0.8386046

00:32:09.996 --> 00:32:12.088 having ongoing response rates.

NOTE Confidence: 0.8386046

00:32:12.090 --> 00:32:12.924 There's the.

NOTE Confidence: 0.8386046

00:32:12.924 --> 00:32:16.260 The follow-up is still short on this study,

NOTE Confidence: 0.8386046

00:32:16.260 --> 00:32:17.704 but there were definitely
NOTE Confidence: 0.8386046

00:32:17.704 --> 00:32:18.787 complete remission rates,
NOTE Confidence: 0.8386046

00:32:18.790 --> 00:32:20.230 including in patients with
NOTE Confidence: 0.8386046

00:32:20.230 --> 00:32:21.670 previously received CD 19,
NOTE Confidence: 0.8386046

00:32:21.670 --> 00:32:23.022 car T cell therapy,
NOTE Confidence: 0.8386046

00:32:23.022 --> 00:32:26.634 and they did not see loss of CD 19 in
NOTE Confidence: 0.8386046

00:32:26.634 --> 00:32:28.890 any of the progressing patient tumors.
NOTE Confidence: 0.84797

00:32:31.100 --> 00:32:34.684 In addition to antigen CD 19 antigen Escape,
NOTE Confidence: 0.84797

00:32:34.690 --> 00:32:36.482 the tumor micro environment
NOTE Confidence: 0.84797

00:32:36.482 --> 00:32:38.722 is very important as well,
NOTE Confidence: 0.84797

00:32:38.730 --> 00:32:41.196 with PDL one upregulation which can
NOTE Confidence: 0.84797

00:32:41.196 --> 00:32:44.120 contribute to car T cell exhaustion,
NOTE Confidence: 0.84797

00:32:44.120 --> 00:32:47.136 and so this brings me to a very
NOTE Confidence: 0.84797

00:32:47.136 --> 00:32:49.053 important study called Alexander
NOTE Confidence: 0.84797

00:32:49.053 --> 00:32:51.748 Auto Three that was presented.
NOTE Confidence: 0.8052864

00:32:54.010 --> 00:32:56.360 Initially at ASCO where they

NOTE Confidence: 0.8052864

00:32:56.360 --> 00:32:58.240 looked at targeting Bicistronic,

NOTE Confidence: 0.8052864

00:32:58.240 --> 00:33:00.885 assisting with a bicistronic vector

NOTE Confidence: 0.8052864

00:33:00.885 --> 00:33:04.803 target targeting CD 19 and CD 22 and

NOTE Confidence: 0.8052864

00:33:04.803 --> 00:33:07.554 the importance of this is that there

NOTE Confidence: 0.8052864

00:33:07.640 --> 00:33:10.460 are two independent cars that are

NOTE Confidence: 0.8052864

00:33:10.460 --> 00:33:13.262 delivered in a single retroviral vector.

NOTE Confidence: 0.8052864

00:33:13.262 --> 00:33:16.489 They have humanized binders and in addition

NOTE Confidence: 0.8052864

00:33:16.489 --> 00:33:19.860 to the four one baby costimulatory domains,

NOTE Confidence: 0.8052864

00:33:19.860 --> 00:33:21.740 there's also an OX40

NOTE Confidence: 0.8052864

00:33:21.740 --> 00:33:23.245 costimulatory domain, which.

NOTE Confidence: 0.8052864

00:33:23.245 --> 00:33:26.070 Would lead to improved persistence,

NOTE Confidence: 0.8052864

00:33:26.070 --> 00:33:28.611 and so from this study presented at

NOTE Confidence: 0.8052864

00:33:28.611 --> 00:33:31.824 ASCO now we have the Auto 3 Alexander

NOTE Confidence: 0.8052864

00:33:31.824 --> 00:33:34.384 study that was presented at this

NOTE Confidence: 0.8052864

00:33:34.384 --> 00:33:37.408 year's ASH where in addition to dewali

NOTE Confidence: 0.8052864

00:33:37.408 --> 00:33:40.500 targeting CD 19 and CD 22 they also
NOTE Confidence: 0.8052864

00:33:40.500 --> 00:33:43.178 edit Pember Lizum app in relapsed
NOTE Confidence: 0.8052864

00:33:43.178 --> 00:33:46.520 refractory diffuse large B cell lymphoma.
NOTE Confidence: 0.8052864

00:33:46.520 --> 00:33:49.327 They had a cohort of patients that
NOTE Confidence: 0.8052864

00:33:49.327 --> 00:33:51.038 received the cortisol therapy
NOTE Confidence: 0.8052864

00:33:51.038 --> 00:33:53.618 alone and then they had another
NOTE Confidence: 0.8052864

00:33:53.618 --> 00:33:55.905 cohort that received three doses
NOTE Confidence: 0.8052864

00:33:55.905 --> 00:33:58.210 of pembrolizumab every two weeks,
NOTE Confidence: 0.8052864

00:33:58.210 --> 00:34:01.754 as well as a third cord that received
NOTE Confidence: 0.8052864

00:34:01.754 --> 00:34:05.680 just one dose of Pembroke on day
NOTE Confidence: 0.8052864

00:34:05.680 --> 00:34:08.032 one following conditioning and.
NOTE Confidence: 0.8052864

00:34:08.040 --> 00:34:10.488 Based on the.
NOTE Confidence: 0.8052864

00:34:10.490 --> 00:34:13.666 MTD that was established from the phase one.
NOTE Confidence: 0.8052864

00:34:13.670 --> 00:34:15.896 There is currently an ongoing phase
NOTE Confidence: 0.8052864

00:34:15.896 --> 00:34:18.292 two looking at efficacy for relapsed
NOTE Confidence: 0.8052864

00:34:18.292 --> 00:34:20.836 refractory diffuse large B cell lymphoma.

NOTE Confidence: 0.8052864

00:34:20.840 --> 00:34:23.619 So these are some of the characteristics.

NOTE Confidence: 0.8052864

00:34:23.620 --> 00:34:25.212 As you can see,

NOTE Confidence: 0.8052864

00:34:25.212 --> 00:34:27.600 the median age was 59 years,

NOTE Confidence: 0.8052864

00:34:27.600 --> 00:34:30.729 but they did give this cortisol therapy

NOTE Confidence: 0.8052864

00:34:30.729 --> 00:34:33.570 to patients up to the age of 83.

NOTE Confidence: 0.8052864

00:34:33.570 --> 00:34:36.754 The majority of them had high risk features,

NOTE Confidence: 0.8052864

00:34:36.760 --> 00:34:38.488 55% were double hit,

NOTE Confidence: 0.8052864

00:34:38.488 --> 00:34:41.080 dual overexpresses or even triple hits.

NOTE Confidence: 0.8052864

00:34:41.080 --> 00:34:44.314 At the majority, 71% had stage four

NOTE Confidence: 0.8052864

00:34:44.314 --> 00:34:47.880 disease and the majority were relapsed.

NOTE Confidence: 0.8052864

00:34:47.880 --> 00:34:48.403 Actually,

NOTE Confidence: 0.8052864

00:34:48.403 --> 00:34:51.541 about 50% were both relapsed and

NOTE Confidence: 0.8052864

00:34:51.541 --> 00:34:53.734 refractory and interesting, Lee.

NOTE Confidence: 0.8052864

00:34:53.734 --> 00:34:56.230 With this novel technology,

NOTE Confidence: 0.8052864

00:34:56.230 --> 00:34:59.086 they saw that great three of

NOTE Confidence: 0.8052864

00:34:59.086 --> 00:35:00.514 cytokine release syndrome,
NOTE Confidence: 0.8052864

00:35:00.520 --> 00:35:03.382 or grades three and above of
NOTE Confidence: 0.8052864

00:35:03.382 --> 00:35:05.290 neurotoxicity were quite low.
NOTE Confidence: 0.8052864

00:35:05.290 --> 00:35:08.629 So CRS over grades three and above.
NOTE Confidence: 0.8052864

00:35:08.630 --> 00:35:11.015 Only 2% and neurotoxicity City
NOTE Confidence: 0.8052864

00:35:11.015 --> 00:35:13.400 green above only four percent.
NOTE Confidence: 0.8052864

00:35:13.400 --> 00:35:13.885 Importantly,
NOTE Confidence: 0.8052864

00:35:13.885 --> 00:35:16.795 none of these patients received any
NOTE Confidence: 0.8052864

00:35:16.795 --> 00:35:19.229 prophylactic measures to prevent the
NOTE Confidence: 0.8052864

00:35:19.229 --> 00:35:21.504 development of CRS or neurotoxicity.
NOTE Confidence: 0.8052864

00:35:21.510 --> 00:35:22.630 An overall,
NOTE Confidence: 0.8052864

00:35:22.630 --> 00:35:25.990 the number of patients that received
NOTE Confidence: 0.8052864

00:35:25.990 --> 00:35:28.169 tocilizumab was low at 16%.
NOTE Confidence: 0.8052864

00:35:28.170 --> 00:35:30.837 And an patients did not receive steroids.
NOTE Confidence: 0.89521617

00:35:33.350 --> 00:35:35.280 So what are the results?
NOTE Confidence: 0.89521617

00:35:35.280 --> 00:35:37.266 As you can see, particularly if

NOTE Confidence: 0.89521617

00:35:37.266 --> 00:35:39.996 we go to the higher dose levels

NOTE Confidence: 0.89521617

00:35:39.996 --> 00:35:42.206 of the cell therapy product,

NOTE Confidence: 0.89521617

00:35:42.210 --> 00:35:43.833 the overall response.

NOTE Confidence: 0.89521617

00:35:43.833 --> 00:35:50.260 Rate is 87% with 73% complete response rates.

NOTE Confidence: 0.89521617

00:35:50.260 --> 00:35:51.811 It's still early,

NOTE Confidence: 0.89521617

00:35:51.811 --> 00:35:53.879 so durability remains unclear,

NOTE Confidence: 0.89521617

00:35:53.880 --> 00:35:56.976 but the patients, particularly the patients,

NOTE Confidence: 0.89521617

00:35:56.980 --> 00:35:58.038 were achieved.

NOTE Confidence: 0.89521617

00:35:58.038 --> 00:35:59.625 Complete remission actually

NOTE Confidence: 0.89521617

00:35:59.625 --> 00:36:01.741 have had ongoing complete

NOTE Confidence: 0.89521617

00:36:01.741 --> 00:36:03.698 remission beyond three months.

NOTE Confidence: 0.8766074

00:36:06.140 --> 00:36:08.620 And also when we look at the cellular

NOTE Confidence: 0.8766074

00:36:08.620 --> 00:36:10.699 kinetics by best overall response,

NOTE Confidence: 0.8766074

00:36:10.700 --> 00:36:13.380 you can see that.

NOTE Confidence: 0.8766074

00:36:13.380 --> 00:36:16.145 Particularly in patients who achieved

NOTE Confidence: 0.8766074

00:36:16.145 --> 00:36:19.810 CR PR as designated here in green,
NOTE Confidence: 0.8766074

00:36:19.810 --> 00:36:22.802 they have ongoing persistency
NOTE Confidence: 0.8766074

00:36:22.802 --> 00:36:25.046 beyond 18 months.
NOTE Confidence: 0.8766074

00:36:25.050 --> 00:36:27.684 So CRP are associated with higher
NOTE Confidence: 0.8766074

00:36:27.684 --> 00:36:29.440 expansion and longer persistence.
NOTE Confidence: 0.8766074

00:36:29.440 --> 00:36:32.248 So in conclusion, auto three is
NOTE Confidence: 0.8766074

00:36:32.248 --> 00:36:35.149 well tolerated with low rates of C,
NOTE Confidence: 0.8766074

00:36:35.150 --> 00:36:36.464 Rs and neurotoxicity.
NOTE Confidence: 0.8766074

00:36:36.464 --> 00:36:37.778 Particularly higher grades.
NOTE Confidence: 0.8766074

00:36:37.780 --> 00:36:40.180 They did also include an outpatient
NOTE Confidence: 0.8766074

00:36:40.180 --> 00:36:43.122 cohort and more than half of the
NOTE Confidence: 0.8766074

00:36:43.122 --> 00:36:45.654 patients were managed in the outpatient
NOTE Confidence: 0.8766074

00:36:45.654 --> 00:36:47.599 setting without requiring admission
NOTE Confidence: 0.8766074

00:36:47.599 --> 00:36:50.503 of the patients who got admitted.
NOTE Confidence: 0.8766074

00:36:50.510 --> 00:36:53.150 None of them were into baited,
NOTE Confidence: 0.8766074

00:36:53.150 --> 00:36:54.930 and the complete response

NOTE Confidence: 0.8766074

00:36:54.930 --> 00:36:56.710 rates were particularly high.

NOTE Confidence: 0.8766074

00:36:56.710 --> 00:37:00.064 Especially if we look at the

NOTE Confidence: 0.8766074

00:37:00.064 --> 00:37:02.300 higher cortisol dose levels.

NOTE Confidence: 0.8766074

00:37:02.300 --> 00:37:06.800 With a CR rate of 73%.

NOTE Confidence: 0.8766074

00:37:06.800 --> 00:37:09.140 Um?

NOTE Confidence: 0.8766074

00:37:09.140 --> 00:37:12.129 So the next study that I will

NOTE Confidence: 0.8766074

00:37:12.129 --> 00:37:14.896 talk about that I found very

NOTE Confidence: 0.8766074

00:37:14.896 --> 00:37:17.680 interesting and I will just give

NOTE Confidence: 0.8766074

00:37:17.680 --> 00:37:20.810 you a bit of a background here,

NOTE Confidence: 0.8766074

00:37:20.810 --> 00:37:24.482 is that about 20 to 30% of these

NOTE Confidence: 0.8766074

00:37:24.482 --> 00:37:26.426 relapsed refractory diffuse large

NOTE Confidence: 0.8766074

00:37:26.426 --> 00:37:28.895 B cell informers were actually

NOTE Confidence: 0.8766074

00:37:28.895 --> 00:37:31.135 found to have either mutations

NOTE Confidence: 0.8766074

00:37:31.135 --> 00:37:33.838 or copy number loss in City 58.

NOTE Confidence: 0.8766074

00:37:33.840 --> 00:37:36.450 And there was this study that

NOTE Confidence: 0.8766074

00:37:36.450 --> 00:37:38.860 was published in Uncle Target.
NOTE Confidence: 0.8766074

00:37:38.860 --> 00:37:42.199 That has looked at TP 53 and 358 and
NOTE Confidence: 0.8766074

00:37:42.199 --> 00:37:45.640 here just to focus on wild type CD
NOTE Confidence: 0.8766074

00:37:45.640 --> 00:37:49.186 58 versus mutated both in terms of
NOTE Confidence: 0.8766074

00:37:49.186 --> 00:37:52.444 progression free but also overall survival.
NOTE Confidence: 0.8766074

00:37:52.450 --> 00:37:55.324 Both patients who had mutations in
NOTE Confidence: 0.8766074

00:37:55.324 --> 00:37:58.665 city 58 and patients who had copy
NOTE Confidence: 0.8766074

00:37:58.665 --> 00:38:01.329 number loss actually had a much
NOTE Confidence: 0.8766074

00:38:01.329 --> 00:38:05.177 poorer progression free and overall survival.
NOTE Confidence: 0.8766074

00:38:05.180 --> 00:38:06.740 And why is that important?
NOTE Confidence: 0.8766074

00:38:06.740 --> 00:38:07.117 Well,
NOTE Confidence: 0.8766074

00:38:07.117 --> 00:38:10.133 it turns out to be 58 is actually
NOTE Confidence: 0.8766074

00:38:10.133 --> 00:38:12.799 the receptor of for the city.
NOTE Confidence: 0.8766074

00:38:12.800 --> 00:38:15.278 Of the city to molecule that's
NOTE Confidence: 0.8766074

00:38:15.278 --> 00:38:17.894 expressed by T cells and also
NOTE Confidence: 0.8766074

00:38:17.894 --> 00:38:20.522 by natural killer cells and its

NOTE Confidence: 0.8766074

00:38:20.522 --> 00:38:23.459 expression is necessary for T cell

NOTE Confidence: 0.8766074

00:38:23.459 --> 00:38:25.934 and NK cell mediated cytotoxicity.

NOTE Confidence: 0.8766074

00:38:25.940 --> 00:38:28.200 So in this study published,

NOTE Confidence: 0.8766074

00:38:28.200 --> 00:38:30.616 it actually presented as

NOTE Confidence: 0.8766074

00:38:30.616 --> 00:38:33.636 an oral abstract by Misner.

NOTE Confidence: 0.8766074

00:38:33.640 --> 00:38:34.596 Stanford group.

NOTE Confidence: 0.8766074

00:38:34.596 --> 00:38:37.942 They looked at city 58 mutations in

NOTE Confidence: 0.8766074

00:38:37.942 --> 00:38:40.725 circulating tumor DNA by cap seek and also

NOTE Confidence: 0.8766074

00:38:40.725 --> 00:38:43.889 looked at a city 58 expression by email,

NOTE Confidence: 0.8766074

00:38:43.890 --> 00:38:44.300 history,

NOTE Confidence: 0.8766074

00:38:44.300 --> 00:38:46.760 chemistry and as you can see,

NOTE Confidence: 0.8766074

00:38:46.760 --> 00:38:49.256 patients who carried these city 58

NOTE Confidence: 0.8766074

00:38:49.256 --> 00:38:51.915 mutations in their tumors actually had

NOTE Confidence: 0.8766074

00:38:51.915 --> 00:38:54.205 much worse progression free survival

NOTE Confidence: 0.8766074

00:38:54.205 --> 00:38:56.675 compared to wild type patients and

NOTE Confidence: 0.8766074

00:38:56.675 --> 00:38:59.055 also when it looked at city 58,
NOTE Confidence: 0.8766074

00:38:59.060 --> 00:39:00.515 expression by IHC.
NOTE Confidence: 0.8766074

00:39:00.515 --> 00:39:03.910 And again this is a pre treatment.
NOTE Confidence: 0.8766074

00:39:03.910 --> 00:39:07.278 Precarity and this is.
NOTE Confidence: 0.8766074

00:39:07.280 --> 00:39:09.716 Post treatment with Corti
NOTE Confidence: 0.8766074

00:39:09.716 --> 00:39:13.370 in the study that looked at.
NOTE Confidence: 0.8766074

00:39:13.370 --> 00:39:16.914 They had used exit captain Jean style Alusil.
NOTE Confidence: 0.8766074

00:39:16.920 --> 00:39:20.574 What they saw is that the complete
NOTE Confidence: 0.8766074

00:39:20.574 --> 00:39:23.271 remission rates were actually much
NOTE Confidence: 0.8766074

00:39:23.271 --> 00:39:26.890 lower in the patient group who had.
NOTE Confidence: 0.8766074

00:39:26.890 --> 00:39:32.330 Low levels of CD 58. Expression and.
NOTE Confidence: 0.8766074

00:39:32.330 --> 00:39:35.210 Even though even in the patients with a
NOTE Confidence: 0.8766074

00:39:35.210 --> 00:39:38.627 C 58 loss who responded to treatment,
NOTE Confidence: 0.8766074

00:39:38.630 --> 00:39:42.270 at best they had a short PR and
NOTE Confidence: 0.8766074

00:39:42.270 --> 00:39:47.340 then they progressed. And so, um.
NOTE Confidence: 0.8766074

00:39:47.340 --> 00:39:49.370 So this was very interesting.

NOTE Confidence: 0.8766074

00:39:49.370 --> 00:39:51.806 So how can we circumvent that and

NOTE Confidence: 0.8766074

00:39:51.806 --> 00:39:54.609 how can we probe the biology of

NOTE Confidence: 0.8766074

00:39:54.609 --> 00:39:57.123 the car T cell responses towards

NOTE Confidence: 0.8766074

00:39:57.210 --> 00:39:59.110 tumors that are lacking?

NOTE Confidence: 0.8766074

00:39:59.110 --> 00:40:02.274 This functional city 58 So what the

NOTE Confidence: 0.8766074

00:40:02.274 --> 00:40:05.242 authors did is they generated the

NOTE Confidence: 0.8766074

00:40:05.242 --> 00:40:08.784 city 58 knockout via CRISPR and they.

NOTE Confidence: 0.8078168

00:40:08.790 --> 00:40:11.260 Integrated a city to Costimulation

NOTE Confidence: 0.8078168

00:40:11.260 --> 00:40:15.289 within cars so when you look here on

NOTE Confidence: 0.8078168

00:40:15.289 --> 00:40:17.739 the left they actually generated.

NOTE Confidence: 0.8078168

00:40:17.740 --> 00:40:20.694 They looked as a control it either

NOTE Confidence: 0.8078168

00:40:20.694 --> 00:40:24.275 CD19 or CD22 targeting cars that were

NOTE Confidence: 0.8078168

00:40:24.275 --> 00:40:28.204 similar to exit cottage inside Alusil or

NOTE Confidence: 0.8078168

00:40:28.204 --> 00:40:31.662 Tisagenlecleucel that are on the market and

NOTE Confidence: 0.8078168

00:40:31.662 --> 00:40:35.626 and they actually did not see any response.

NOTE Confidence: 0.8078168

00:40:35.630 --> 00:40:39.186 However, when they integrated a city too.
NOTE Confidence: 0.8078168

00:40:39.190 --> 00:40:41.545 Costimulation here represented in red
NOTE Confidence: 0.8078168

00:40:41.545 --> 00:40:44.762 what they saw is that that actually
NOTE Confidence: 0.8078168

00:40:44.762 --> 00:40:48.450 overcame the loss of CD 58 in tumor cells.
NOTE Confidence: 0.8078168

00:40:48.450 --> 00:40:51.677 And when you look at the percent
NOTE Confidence: 0.8078168

00:40:51.677 --> 00:40:53.720 survival that was significantly
NOTE Confidence: 0.8078168

00:40:53.720 --> 00:40:57.116 higher in the cells that had.
NOTE Confidence: 0.8078168

00:40:57.120 --> 00:41:01.384 That contained CV 2 and you know initially
NOTE Confidence: 0.8078168

00:41:01.384 --> 00:41:04.412 they incorporated city two in SIS and
NOTE Confidence: 0.8078168

00:41:04.412 --> 00:41:08.329 that did not result in any responses in vivo.
NOTE Confidence: 0.8078168

00:41:08.330 --> 00:41:11.744 However, when they introduced it in
NOTE Confidence: 0.8078168

00:41:11.744 --> 00:41:15.069 trends that actually did the trick.
NOTE Confidence: 0.8078168

00:41:15.070 --> 00:41:17.608 So they put in an additional,
NOTE Confidence: 0.8078168

00:41:17.610 --> 00:41:18.882 so to speak.
NOTE Confidence: 0.8078168

00:41:18.882 --> 00:41:20.578 City two receptor entrance,
NOTE Confidence: 0.8078168

00:41:20.580 --> 00:41:22.775 and that's what mediated significant

NOTE Confidence: 0.8078168

00:41:22.775 --> 00:41:25.428 antitumor activity in in Vivo Anet

NOTE Confidence: 0.8078168

00:41:25.428 --> 00:41:27.368 overcame the city 58 knockout.

NOTE Confidence: 0.8078168

00:41:27.370 --> 00:41:29.902 So this data was actually extremely

NOTE Confidence: 0.8078168

00:41:29.902 --> 00:41:31.620 important, in my view,

NOTE Confidence: 0.8078168

00:41:31.620 --> 00:41:35.419 because it it shows us that City two Co.

NOTE Confidence: 0.8078168

00:41:35.420 --> 00:41:37.116 Stimulation is very important.

NOTE Confidence: 0.8078168

00:41:37.116 --> 00:41:39.236 This wasn't known before we,

NOTE Confidence: 0.8078168

00:41:39.240 --> 00:41:42.552 we thought that these car T cells were

NOTE Confidence: 0.8078168

00:41:42.552 --> 00:41:45.526 already endowed with all the necessary

NOTE Confidence: 0.8078168

00:41:45.526 --> 00:41:47.594 costimulation that they needed.

NOTE Confidence: 0.8078168

00:41:47.600 --> 00:41:50.896 However, we now know based on this study,

NOTE Confidence: 0.8078168

00:41:50.900 --> 00:41:53.336 that there are other Co stimulators

NOTE Confidence: 0.8078168

00:41:53.336 --> 00:41:56.270 on the surface of the tumor cells,

NOTE Confidence: 0.8078168

00:41:56.270 --> 00:41:59.807 such as CD 58 that also really matter and

NOTE Confidence: 0.8078168

00:41:59.807 --> 00:42:03.290 that they can drive car T cell efficacy.

NOTE Confidence: 0.82577026

00:42:05.440 --> 00:42:08.457 So this CD 5832 is a novel
NOTE Confidence: 0.82577026

00:42:08.457 --> 00:42:11.080 axis for car resistance.
NOTE Confidence: 0.82577026

00:42:11.080 --> 00:42:13.128 It's important in large
NOTE Confidence: 0.82577026

00:42:13.128 --> 00:42:14.664 cell lymphoma because,
NOTE Confidence: 0.82577026

00:42:14.670 --> 00:42:19.806 as I said to you 25 to 30% of patients
NOTE Confidence: 0.82577026

00:42:19.806 --> 00:42:23.910 will have either city 58 loss or mutations.
NOTE Confidence: 0.82577026

00:42:23.910 --> 00:42:26.470 And if we engineer cars,
NOTE Confidence: 0.82577026

00:42:26.470 --> 00:42:28.598 integrating City two signaling
NOTE Confidence: 0.82577026

00:42:28.598 --> 00:42:32.120 entrance we can overcome this city 58.
NOTE Confidence: 0.82577026

00:42:32.120 --> 00:42:33.840 Lawson reestablished car efficacy.
NOTE Confidence: 0.82577026

00:42:33.840 --> 00:42:36.904 And and this is important because there
NOTE Confidence: 0.82577026

00:42:36.904 --> 00:42:39.400 are other cancers like multiple myeloma,
NOTE Confidence: 0.82577026

00:42:39.400 --> 00:42:42.172 Hodgkin lymphoma as well as solid tumors
NOTE Confidence: 0.82577026

00:42:42.172 --> 00:42:44.521 like colon cancer for example that
NOTE Confidence: 0.82577026

00:42:44.521 --> 00:42:47.055 do carry city 58 loss and mutations,
NOTE Confidence: 0.82577026

00:42:47.060 --> 00:42:49.685 and we expect that in the next

NOTE Confidence: 0.82577026

00:42:49.685 --> 00:42:52.040 couple of years there will be.

NOTE Confidence: 0.71786034

00:42:54.070 --> 00:43:00.580 Cortisol studies looking at this.

NOTE Confidence: 0.71786034

00:43:00.580 --> 00:43:05.915 In humans. Another study that I found

NOTE Confidence: 0.71786034

00:43:05.915 --> 00:43:10.020 of interest was also this abstract.

NOTE Confidence: 0.71786034

00:43:10.020 --> 00:43:12.978 1194, where they looked at Amick,

NOTE Confidence: 0.71786034

00:43:12.980 --> 00:43:15.935 expression and tumor infiltrated the

NOTE Confidence: 0.71786034

00:43:15.935 --> 00:43:19.455 cells in patients who received his

NOTE Confidence: 0.71786034

00:43:19.455 --> 00:43:22.787 agenda cluzel in the Juliet study for

NOTE Confidence: 0.71786034

00:43:22.787 --> 00:43:25.815 lymphoma and what they were able to

NOTE Confidence: 0.71786034

00:43:25.815 --> 00:43:28.830 show was that having a baseline Nick

NOTE Confidence: 0.71786034

00:43:28.830 --> 00:43:31.405 negative Myc positive studies make

NOTE Confidence: 0.71786034

00:43:31.405 --> 00:43:34.720 positive study was actually here in blue.

NOTE Confidence: 0.71786034

00:43:34.720 --> 00:43:38.818 Associated with a worse probability of.

NOTE Confidence: 0.71786034

00:43:38.820 --> 00:43:42.761 Survival and then also having fewer tumor

NOTE Confidence: 0.71786034

00:43:42.761 --> 00:43:46.488 infiltrating CD 3 positive cells were

NOTE Confidence: 0.71786034

00:43:46.488 --> 00:43:50.370 was also associated with poorer outcomes.

NOTE Confidence: 0.71786034

00:43:50.370 --> 00:43:51.864 And particularly,

NOTE Confidence: 0.71786034

00:43:51.864 --> 00:43:55.599 if those infiltrating cells had.

NOTE Confidence: 0.71786034

00:43:55.600 --> 00:43:57.420 Exhausted immunophenotype

NOTE Confidence: 0.83085793

00:43:59.750 --> 00:44:03.040 so I I talked to you about you know how

NOTE Confidence: 0.83085793

00:44:03.134 --> 00:44:05.972 this works in the relapse refractory

NOTE Confidence: 0.83085793

00:44:05.972 --> 00:44:09.795 setting and what we can do in that

NOTE Confidence: 0.83085793

00:44:09.795 --> 00:44:12.095 setting to to overcome resistance.

NOTE Confidence: 0.83085793

00:44:12.100 --> 00:44:15.164 But what about patients who never go into

NOTE Confidence: 0.83085793

00:44:15.164 --> 00:44:17.640 remission with their frontline therapy?

NOTE Confidence: 0.83085793

00:44:17.640 --> 00:44:19.770 So this study Zooma, 12,

NOTE Confidence: 0.83085793

00:44:19.770 --> 00:44:22.326 looked at exit cottage inside Alusil,

NOTE Confidence: 0.83085793

00:44:22.330 --> 00:44:24.880 in patients with very high risk,

NOTE Confidence: 0.83085793

00:44:24.880 --> 00:44:27.320 large diffuse large B cell

NOTE Confidence: 0.83085793

00:44:27.320 --> 00:44:29.760 lymphoma in the first line.

NOTE Confidence: 0.83085793

00:44:29.760 --> 00:44:32.298 Um and and at ash they

NOTE Confidence: 0.83085793

00:44:32.298 --> 00:44:33.990 presented the interim efficacy,

NOTE Confidence: 0.83085793

00:44:33.990 --> 00:44:35.818 safety and PK data,

NOTE Confidence: 0.83085793

00:44:35.818 --> 00:44:38.103 so patients qualified for this

NOTE Confidence: 0.83085793

00:44:38.103 --> 00:44:40.997 study if they had high grade B

NOTE Confidence: 0.83085793

00:44:40.997 --> 00:44:43.299 cell lymphoma with Mick and BCL,

NOTE Confidence: 0.83085793

00:44:43.300 --> 00:44:45.410 two or BCL six translocations,

NOTE Confidence: 0.83085793

00:44:45.410 --> 00:44:49.026 so double hit or triple hit large cell

NOTE Confidence: 0.83085793

00:44:49.026 --> 00:44:52.362 lymphoma with an epic score of three

NOTE Confidence: 0.83085793

00:44:52.362 --> 00:44:55.457 or above before enrollment they had to

NOTE Confidence: 0.83085793

00:44:55.457 --> 00:44:59.160 have had at least 2 lines of an anti CD.

NOTE Confidence: 0.83085793

00:44:59.160 --> 00:45:00.750 20 monoclonal antibody.

NOTE Confidence: 0.83085793

00:45:00.750 --> 00:45:03.630 Sorry not 2 lines but two cycles and

NOTE Confidence: 0.83085793

00:45:03.630 --> 00:45:06.015 enter second containing regimen and they

NOTE Confidence: 0.83085793

00:45:06.015 --> 00:45:09.207 had to have had a positive PET scan

NOTE Confidence: 0.83085793

00:45:09.207 --> 00:45:11.776 after two Step 2 cycles of treatment

NOTE Confidence: 0.83085793

00:45:11.776 --> 00:45:14.430 they enrolled them look at free stem.
NOTE Confidence: 0.83085793

00:45:14.430 --> 00:45:17.076 They had the option of getting some
NOTE Confidence: 0.83085793

00:45:17.076 --> 00:45:18.649 non chemotherapy bridging such
NOTE Confidence: 0.83085793

00:45:18.649 --> 00:45:20.509 as radiation or maybe REVLIMID.
NOTE Confidence: 0.83085793

00:45:20.510 --> 00:45:23.126 And then they give them flu
NOTE Confidence: 0.83085793

00:45:23.126 --> 00:45:25.488 side conditioning and a single
NOTE Confidence: 0.83085793

00:45:25.488 --> 00:45:27.608 infusion of access cell.
NOTE Confidence: 0.83085793

00:45:27.610 --> 00:45:30.238 Again, median was 61 years old,
NOTE Confidence: 0.83085793

00:45:30.240 --> 00:45:31.996 but they treated patients
NOTE Confidence: 0.83085793

00:45:31.996 --> 00:45:34.630 up to the age of 86.
NOTE Confidence: 0.83085793

00:45:34.630 --> 00:45:37.270 They all had advanced stage disease,
NOTE Confidence: 0.83085793

00:45:37.270 --> 00:45:39.856 53% were double hit or triple
NOTE Confidence: 0.83085793

00:45:39.856 --> 00:45:42.100 hit as determined by fish.
NOTE Confidence: 0.83085793

00:45:42.100 --> 00:45:43.426 A 72% had.
NOTE Confidence: 0.83085793

00:45:43.426 --> 00:45:47.070 Keeping score of greater than or equal to 3.
NOTE Confidence: 0.84949166

00:45:49.290 --> 00:45:51.882 And when they looked at overall

NOTE Confidence: 0.84949166

00:45:51.882 --> 00:45:54.494 response rates, remarkably high 85% and

NOTE Confidence: 0.84949166

00:45:54.494 --> 00:45:57.520 CR rate for these patients was 74%,

NOTE Confidence: 0.84949166

00:45:57.520 --> 00:45:59.680 and they have followed them.

NOTE Confidence: 0.84949166

00:45:59.680 --> 00:46:02.704 The median follow-up was a 9.5 months,

NOTE Confidence: 0.84949166

00:46:02.710 --> 00:46:05.734 so not very long follow up yet,

NOTE Confidence: 0.84949166

00:46:05.740 --> 00:46:08.164 but it's important to realize that

NOTE Confidence: 0.84949166

00:46:08.164 --> 00:46:10.806 the majority of these patients with

NOTE Confidence: 0.84949166

00:46:10.806 --> 00:46:13.662 double or triple hit INFORMALS will

NOTE Confidence: 0.84949166

00:46:13.662 --> 00:46:15.698 actually relapse within a year.

NOTE Confidence: 0.84949166

00:46:15.700 --> 00:46:16.996 Post initial therapy.

NOTE Confidence: 0.84949166

00:46:16.996 --> 00:46:19.153 So so you know, really.

NOTE Confidence: 0.84949166

00:46:19.153 --> 00:46:21.268 Really great outcomes and the

NOTE Confidence: 0.84949166

00:46:21.268 --> 00:46:24.069 most common grade three and above

NOTE Confidence: 0.84949166

00:46:24.069 --> 00:46:26.149 adverse events were encephalopathy.

NOTE Confidence: 0.84949166

00:46:26.150 --> 00:46:29.643 In 16% of the patients and cytopenias

NOTE Confidence: 0.84949166

00:46:29.643 --> 00:46:33.779 there was one grade 5 adverse event that
NOTE Confidence: 0.84949166

00:46:33.779 --> 00:46:37.600 occurred on the study due to COVID-19.
NOTE Confidence: 0.84949166

00:46:37.600 --> 00:46:39.730 When they looked at cortisol
NOTE Confidence: 0.84949166

00:46:39.730 --> 00:46:42.374 expansion and compared that to their
NOTE Confidence: 0.84949166

00:46:42.374 --> 00:46:45.014 Zuma one study where people had
NOTE Confidence: 0.84949166

00:46:45.014 --> 00:46:46.990 had relapsed refractory disease,
NOTE Confidence: 0.84949166

00:46:46.990 --> 00:46:51.031 what they saw is that the car T cell
NOTE Confidence: 0.84949166

00:46:51.031 --> 00:46:53.961 expansion was significantly greater in
NOTE Confidence: 0.84949166

00:46:53.961 --> 00:46:58.808 this study in summer 12 compared to Zuma one.
NOTE Confidence: 0.84949166

00:46:58.810 --> 00:47:00.289 And that perhaps,
NOTE Confidence: 0.84949166

00:47:00.289 --> 00:47:03.740 maybe because these patients had very little
NOTE Confidence: 0.84949166

00:47:03.819 --> 00:47:06.920 treatment before they went on to party.
NOTE Confidence: 0.84949166

00:47:06.920 --> 00:47:07.958 Um?
NOTE Confidence: 0.84949166

00:47:07.958 --> 00:47:12.110 And in Zuma 12.
NOTE Confidence: 0.84949166

00:47:12.110 --> 00:47:15.166 There was higher frequency of CCR seven 3045
NOTE Confidence: 0.84949166

00:47:15.166 --> 00:47:18.337 RAT cells in the pre infusion product which

NOTE Confidence: 0.84949166

00:47:18.337 --> 00:47:21.240 was associated with a greater expansion.

NOTE Confidence: 0.84949166

00:47:21.240 --> 00:47:24.586 Again, this is suggestive of improved T

NOTE Confidence: 0.84949166

00:47:24.586 --> 00:47:28.290 cell fitness in the first line treatment.

NOTE Confidence: 0.84949166

00:47:28.290 --> 00:47:31.195 So it's this study you know well

NOTE Confidence: 0.84949166

00:47:31.195 --> 00:47:33.780 doesn't have very long follow up.

NOTE Confidence: 0.84949166

00:47:33.780 --> 00:47:36.384 It does provide us with some

NOTE Confidence: 0.84949166

00:47:36.384 --> 00:47:38.120 insights into the pharmacology

NOTE Confidence: 0.84949166

00:47:38.199 --> 00:47:40.719 of access L for patients who are

NOTE Confidence: 0.84949166

00:47:40.719 --> 00:47:43.060 exposed to fewer prior therapies.

NOTE Confidence: 0.84949166

00:47:43.060 --> 00:47:46.252 Now I'm going to shift gears to relapse

NOTE Confidence: 0.84949166

00:47:46.252 --> 00:47:48.549 refractory indolent non Hodgkin lymphoma.

NOTE Confidence: 0.84949166

00:47:48.550 --> 00:47:51.469 I'll present you the data from Zuma

NOTE Confidence: 0.84949166

00:47:51.469 --> 00:47:55.866 five with AXI Cap to Gene and then from

NOTE Confidence: 0.84949166

00:47:55.866 --> 00:47:58.679 ilaris study with tisagenlecleucel cell so.

NOTE Confidence: 0.84949166

00:47:58.680 --> 00:48:00.312 In this study zoomify,

NOTE Confidence: 0.84949166

00:48:00.312 --> 00:48:02.760 they looked at follicular and marginal
NOTE Confidence: 0.84949166

00:48:02.834 --> 00:48:05.126 zone lymphoma patients who had relapsed
NOTE Confidence: 0.84949166

00:48:05.126 --> 00:48:07.858 after two or more lines of therapy.
NOTE Confidence: 0.84949166

00:48:07.860 --> 00:48:09.850 This was the study design.
NOTE Confidence: 0.84949166

00:48:09.850 --> 00:48:10.249 Again,
NOTE Confidence: 0.84949166

00:48:10.249 --> 00:48:13.840 very standard flu Cy followed by by Access L.
NOTE Confidence: 0.84949166

00:48:13.840 --> 00:48:17.305 They all had to have had anti CD 20
NOTE Confidence: 0.84949166

00:48:17.305 --> 00:48:20.055 monoclonal antibody plus an alkylating
NOTE Confidence: 0.84949166

00:48:20.055 --> 00:48:22.895 agent with their prior therapies.
NOTE Confidence: 0.84949166

00:48:22.900 --> 00:48:25.684 68% of the patients had refractory
NOTE Confidence: 0.84949166

00:48:25.684 --> 00:48:27.076 disease and importantly,
NOTE Confidence: 0.84949166

00:48:27.080 --> 00:48:29.744 over half of the patients had
NOTE Confidence: 0.84949166

00:48:29.744 --> 00:48:31.520 actually progressed within two
NOTE Confidence: 0.84949166

00:48:31.597 --> 00:48:34.037 years from their initial therapy,
NOTE Confidence: 0.84949166

00:48:34.040 --> 00:48:36.360 which is this P OH,
NOTE Confidence: 0.84949166

00:48:36.360 --> 00:48:39.111 D20 four group that we now know

NOTE Confidence: 0.84949166

00:48:39.111 --> 00:48:41.455 is associated with worse survival

NOTE Confidence: 0.84949166

00:48:41.455 --> 00:48:44.165 in both follicular lymphoma and

NOTE Confidence: 0.84949166

00:48:44.165 --> 00:48:46.756 marginal zone lymphoma when they

NOTE Confidence: 0.84949166

00:48:46.756 --> 00:48:49.396 looked at the overall response rates

NOTE Confidence: 0.84949166

00:48:49.396 --> 00:48:52.890 very high again in the above 90%.

NOTE Confidence: 0.84949166

00:48:52.890 --> 00:48:53.878 And CRA,

NOTE Confidence: 0.84949166

00:48:53.878 --> 00:48:56.348 it's also very high anywhere

NOTE Confidence: 0.84949166

00:48:56.348 --> 00:48:59.190 from 70 to 80% progression free.

NOTE Confidence: 0.84949166

00:48:59.190 --> 00:49:02.010 Survival was actually noted to be

NOTE Confidence: 0.84949166

00:49:02.010 --> 00:49:05.040 longer in the follicular lymphoma group

NOTE Confidence: 0.84949166

00:49:05.040 --> 00:49:08.046 compared to the marginal as opposed

NOTE Confidence: 0.84949166

00:49:08.131 --> 00:49:10.909 to the marginal Zone lymphoma group.

NOTE Confidence: 0.84949166

00:49:10.910 --> 00:49:13.748 But the response rates importantly were

NOTE Confidence: 0.84949166

00:49:13.748 --> 00:49:16.749 consistent across all of the subgroups,

NOTE Confidence: 0.84949166

00:49:16.750 --> 00:49:18.616 including Flapi score,

NOTE Confidence: 0.84949166

00:49:18.616 --> 00:49:22.348 high tumor burden or prior therapies.

NOTE Confidence: 0.84949166

00:49:22.350 --> 00:49:25.608 And the median duration of response,

NOTE Confidence: 0.84949166

00:49:25.610 --> 00:49:28.335 particularly in the follicular lymphoma

NOTE Confidence: 0.84949166

00:49:28.335 --> 00:49:33.110 Group, has not been reached and.

NOTE Confidence: 0.84949166

00:49:33.110 --> 00:49:38.241 Is a 78% duration of response in

NOTE Confidence: 0.84949166

00:49:38.241 --> 00:49:41.906 patients who, with follicular lymphoma,

NOTE Confidence: 0.84949166

00:49:41.906 --> 00:49:44.834 who achieved a CR.

NOTE Confidence: 0.84090036

00:49:46.960 --> 00:49:49.744 There were important to note a

NOTE Confidence: 0.84090036

00:49:49.744 --> 00:49:52.163 grade three and above adverse

NOTE Confidence: 0.84090036

00:49:52.163 --> 00:49:55.010 events in 86% of the patients.

NOTE Confidence: 0.84090036

00:49:55.010 --> 00:49:57.410 Most of them were cytopenias

NOTE Confidence: 0.84090036

00:49:57.410 --> 00:49:59.806 and infections and their worst

NOTE Confidence: 0.84090036

00:49:59.806 --> 00:50:02.056 three Grade 5 adverse events,

NOTE Confidence: 0.84090036

00:50:02.060 --> 00:50:05.140 one of which was related to multisystem

NOTE Confidence: 0.84090036

00:50:05.140 --> 00:50:07.727 organ failure with cytokine release

NOTE Confidence: 0.84090036

00:50:07.727 --> 00:50:11.279 syndrome and another one due to

NOTE Confidence: 0.84090036

00:50:11.279 --> 00:50:12.463 coccidioidomycosis infection.

NOTE Confidence: 0.84090036

00:50:12.470 --> 00:50:16.306 So the the other important thing to

NOTE Confidence: 0.84090036

00:50:16.306 --> 00:50:20.030 note is that 82% of patients experienced

NOTE Confidence: 0.84090036

00:50:20.030 --> 00:50:23.270 some grade of cytokine release syndrome.

NOTE Confidence: 0.84090036

00:50:23.270 --> 00:50:25.430 The only 7% experienced

NOTE Confidence: 0.84090036

00:50:25.430 --> 00:50:27.590 grade three and above.

NOTE Confidence: 0.84090036

00:50:27.590 --> 00:50:30.830 Almost half the patients received socialism

NOTE Confidence: 0.84090036

00:50:30.830 --> 00:50:35.510 AB and 17% received corticosteroids.

NOTE Confidence: 0.84090036

00:50:35.510 --> 00:50:37.840 As far as neurologic events,

NOTE Confidence: 0.84090036

00:50:37.840 --> 00:50:39.700 60% at any grade,

NOTE Confidence: 0.84090036

00:50:39.700 --> 00:50:42.497 neurologic events an almost 20% had

NOTE Confidence: 0.84090036

00:50:42.497 --> 00:50:45.299 grade three and above neurologic events.

NOTE Confidence: 0.84090036

00:50:45.300 --> 00:50:47.625 36% of patients received steroids

NOTE Confidence: 0.84090036

00:50:47.625 --> 00:50:49.020 for neurologic toxicity,

NOTE Confidence: 0.84090036

00:50:49.020 --> 00:50:52.748 so when they looked at serum cytokine levels,

NOTE Confidence: 0.84090036

00:50:52.750 --> 00:50:56.551 they saw that cortisol peak levels were
NOTE Confidence: 0.84090036

00:50:56.551 --> 00:50:59.371 associated with grade three and above
NOTE Confidence: 0.84090036

00:50:59.371 --> 00:51:03.000 CR S and then some of the other side.
NOTE Confidence: 0.84090036

00:51:03.000 --> 00:51:06.800 It kinds like interferon gamma L6 TNF Alpha.
NOTE Confidence: 0.84090036

00:51:06.800 --> 00:51:09.460 Were also associated with grade
NOTE Confidence: 0.84090036

00:51:09.460 --> 00:51:12.120 three and above neurologic events.
NOTE Confidence: 0.84090036

00:51:12.120 --> 00:51:15.627 So the response rates were very high,
NOTE Confidence: 0.84090036

00:51:15.630 --> 00:51:19.653 but as I've just shown you there is still
NOTE Confidence: 0.84090036

00:51:19.653 --> 00:51:22.639 significant toxicity with this treatment,
NOTE Confidence: 0.84090036

00:51:22.640 --> 00:51:24.143 particularly for follicular
NOTE Confidence: 0.84090036

00:51:24.143 --> 00:51:25.646 and marginal zone.
NOTE Confidence: 0.84090036

00:51:25.650 --> 00:51:29.178 Lymphoma is where we now do have available
NOTE Confidence: 0.84090036

00:51:29.178 --> 00:51:31.660 other available therapeutic options.
NOTE Confidence: 0.84090036

00:51:31.660 --> 00:51:36.169 This is a sort of a similar design study.
NOTE Confidence: 0.84090036

00:51:36.170 --> 00:51:39.642 The Ilara which looked at this urgent
NOTE Confidence: 0.84090036

00:51:39.642 --> 00:51:42.269 occlusal for follicular lymphoma and.

NOTE Confidence: 0.84090036

00:51:42.270 --> 00:51:45.007 And I will not spend much time.

NOTE Confidence: 0.84090036

00:51:45.010 --> 00:51:47.866 Suffice it to say that the complete response

NOTE Confidence: 0.84090036

00:51:47.866 --> 00:51:50.320 rates and overall response rates were

NOTE Confidence: 0.84090036

00:51:50.320 --> 00:51:53.220 extremely high with this therapy as well,

NOTE Confidence: 0.84090036

00:51:53.220 --> 00:51:55.170 but it was better tolerated,

NOTE Confidence: 0.84090036

00:51:55.170 --> 00:51:58.284 and indeed they did not have any cases of

NOTE Confidence: 0.84090036

00:51:58.284 --> 00:52:01.429 Grade 3 or above cytokine release syndrome.

NOTE Confidence: 0.84090036

00:52:01.430 --> 00:52:04.188 There was very little use of anti

NOTE Confidence: 0.84090036

00:52:04.188 --> 00:52:06.970 cytokine therapy and very low rate of

NOTE Confidence: 0.84090036

00:52:06.970 --> 00:52:11.440 severe neurologic events of only 1% so.

NOTE Confidence: 0.84090036

00:52:11.440 --> 00:52:12.076 You know,

NOTE Confidence: 0.84090036

00:52:12.076 --> 00:52:13.984 it's important to again keep in

NOTE Confidence: 0.84090036

00:52:13.984 --> 00:52:15.748 mind that these treatments are

NOTE Confidence: 0.84090036

00:52:15.748 --> 00:52:17.878 not created equal and that there

NOTE Confidence: 0.84090036

00:52:17.878 --> 00:52:19.858 are differences between them,

NOTE Confidence: 0.84090036

00:52:19.860 --> 00:52:22.422 some of which have to do with
NOTE Confidence: 0.84090036

00:52:22.422 --> 00:52:23.520 the costimulatory domain,
NOTE Confidence: 0.84090036

00:52:23.520 --> 00:52:26.019 but many of which have to do
NOTE Confidence: 0.84090036

00:52:26.019 --> 00:52:28.279 with other parts of the design.
NOTE Confidence: 0.84090036

00:52:28.280 --> 00:52:30.260 So toxicities are very different
NOTE Confidence: 0.84090036

00:52:30.260 --> 00:52:32.855 and and there's much work to be
NOTE Confidence: 0.84090036

00:52:32.855 --> 00:52:35.039 done to see how they will stack up
NOTE Confidence: 0.84090036

00:52:35.108 --> 00:52:37.428 against other types of treatments,
NOTE Confidence: 0.84090036

00:52:37.430 --> 00:52:40.130 particularly these novel.
NOTE Confidence: 0.84090036

00:52:40.130 --> 00:52:45.362 Body drug conjugates or or CD20
NOTE Confidence: 0.84090036

00:52:45.362 --> 00:52:48.850 CD 1963 by specifics.
NOTE Confidence: 0.84090036

00:52:48.850 --> 00:52:51.724 I will now briefly shift gears
NOTE Confidence: 0.84090036

00:52:51.724 --> 00:52:53.640 to mantle cell lymphoma,
NOTE Confidence: 0.84090036

00:52:53.640 --> 00:52:56.508 which also remains an unmet need.
NOTE Confidence: 0.84090036

00:52:56.510 --> 00:52:59.238 As you can see with one year and
NOTE Confidence: 0.84090036

00:52:59.238 --> 00:53:02.013 five year outcomes relative in terms

NOTE Confidence: 0.84090036

00:53:02.013 --> 00:53:05.031 of relative survival that are worse

NOTE Confidence: 0.84090036

00:53:05.116 --> 00:53:07.420 compared to follicular lymphoma

NOTE Confidence: 0.84090036

00:53:07.420 --> 00:53:10.300 in marginal zone lymphoma and

NOTE Confidence: 0.84090036

00:53:10.300 --> 00:53:12.796 certainly lower cure rates compared

NOTE Confidence: 0.84090036

00:53:12.796 --> 00:53:15.670 to diffuse large B cell lymphoma.

NOTE Confidence: 0.84090036

00:53:15.670 --> 00:53:19.590 So this is the study that got.

NOTE Confidence: 0.84090036

00:53:19.590 --> 00:53:21.690 Actually, that got Brexit.

NOTE Confidence: 0.84090036

00:53:21.690 --> 00:53:23.265 Captain Jean approved,

NOTE Confidence: 0.84090036

00:53:23.270 --> 00:53:25.900 published in New England Journal

NOTE Confidence: 0.84090036

00:53:25.900 --> 00:53:28.530 in 2020 targeting CD 19,

NOTE Confidence: 0.84090036

00:53:28.530 --> 00:53:31.650 where you see that the overall

NOTE Confidence: 0.84090036

00:53:31.650 --> 00:53:34.320 response rate was very high,

NOTE Confidence: 0.84090036

00:53:34.320 --> 00:53:37.470 93% and 67% of patients actually

NOTE Confidence: 0.84090036

00:53:37.470 --> 00:53:39.045 achieved complete remission.

NOTE Confidence: 0.84090036

00:53:39.050 --> 00:53:42.188 These were patients that had relapsed

NOTE Confidence: 0.84090036

00:53:42.188 --> 00:53:44.881 refractory disease and the duration
NOTE Confidence: 0.84090036

00:53:44.881 --> 00:53:47.466 of response is quite durable,
NOTE Confidence: 0.84090036

00:53:47.470 --> 00:53:51.320 with with a plateau in this curve.
NOTE Confidence: 0.9070388

00:53:51.320 --> 00:53:54.140 I'm reaching three years now.
NOTE Confidence: 0.9070388

00:53:54.140 --> 00:53:57.756 As so, um, this is the transcendent study.
NOTE Confidence: 0.9070388

00:53:57.760 --> 00:53:59.540 The mantle cell cohort.
NOTE Confidence: 0.9070388

00:53:59.540 --> 00:54:02.210 This was just presented at ASH
NOTE Confidence: 0.9070388

00:54:02.299 --> 00:54:04.771 and this is looking at lysosome
NOTE Confidence: 0.9070388

00:54:04.771 --> 00:54:07.250 now in mantle cell lymphoma.
NOTE Confidence: 0.9070388

00:54:07.250 --> 00:54:09.914 This product is different from AXA
NOTE Confidence: 0.9070388

00:54:09.914 --> 00:54:12.826 capture Gene because it has a defined
NOTE Confidence: 0.9070388

00:54:12.826 --> 00:54:15.290 composition of T of CD8 and CD4T
NOTE Confidence: 0.9070388

00:54:15.371 --> 00:54:18.086 cell components that are administered
NOTE Confidence: 0.9070388

00:54:18.086 --> 00:54:20.801 separately at equal target doses.
NOTE Confidence: 0.9070388

00:54:20.810 --> 00:54:23.408 So flu Cy conditioning lies to
NOTE Confidence: 0.9070388

00:54:23.408 --> 00:54:26.678 sell and they had two dose levels.

NOTE Confidence: 0.820293
00:54:28.770 --> 00:54:31.843 70% of patients had more than or
NOTE Confidence: 0.820293
00:54:31.843 --> 00:54:34.760 equal to three prior therapies.
NOTE Confidence: 0.820293
00:54:34.760 --> 00:54:37.748 A 75% had received prior ibrutinib,
NOTE Confidence: 0.820293
00:54:37.750 --> 00:54:39.750 including 31% that were
NOTE Confidence: 0.820293
00:54:39.750 --> 00:54:41.250 refractory to ibrutinib,
NOTE Confidence: 0.820293
00:54:41.250 --> 00:54:44.834 25% a quarter had received prior Boneta
NOTE Confidence: 0.820293
00:54:44.834 --> 00:54:48.227 klaxon there were 16% of patients that
NOTE Confidence: 0.820293
00:54:48.227 --> 00:54:51.720 were also refractory to prior Boneta clocks.
NOTE Confidence: 0.820293
00:54:51.720 --> 00:54:55.220 There was a significant number of patients,
NOTE Confidence: 0.820293
00:54:55.220 --> 00:54:57.710 41% that had blastoid morphology,
NOTE Confidence: 0.820293
00:54:57.710 --> 00:54:59.069 22% with P50.
NOTE Confidence: 0.820293
00:54:59.069 --> 00:55:02.240 Three mutations and the majority of patients.
NOTE Confidence: 0.820293
00:55:02.240 --> 00:55:05.640 2/3 of patients actually had an elevated key.
NOTE Confidence: 0.820293
00:55:05.640 --> 00:55:06.873 67 proliferation index,
NOTE Confidence: 0.820293
00:55:06.873 --> 00:55:09.750 which we know is associated with worse
NOTE Confidence: 0.820293

00:55:09.820 --> 00:55:12.010 outcomes in mantle cell lymphoma.
NOTE Confidence: 0.820293

00:55:12.010 --> 00:55:15.490 When we look at the toxicity.
NOTE Confidence: 0.820293

00:55:15.490 --> 00:55:19.928 I'm with Lisa cell CRS grade three
NOTE Confidence: 0.820293

00:55:19.928 --> 00:55:24.422 and above very low 3% and Grade
NOTE Confidence: 0.820293

00:55:24.422 --> 00:55:28.627 3 or above neurotoxicity 12.5%.
NOTE Confidence: 0.820293

00:55:28.630 --> 00:55:31.780 When they looked at response by subgroup,
NOTE Confidence: 0.820293

00:55:31.780 --> 00:55:34.300 again remarkable that the overall
NOTE Confidence: 0.820293

00:55:34.300 --> 00:55:36.820 response rates and complete response
NOTE Confidence: 0.820293

00:55:36.893 --> 00:55:39.311 rates in patients with High Ki
NOTE Confidence: 0.820293

00:55:39.311 --> 00:55:41.430 67 blastoid morphology or P53
NOTE Confidence: 0.820293

00:55:41.430 --> 00:55:43.590 mutations are actually quite so.
NOTE Confidence: 0.820293

00:55:43.590 --> 00:55:46.453 Miller to the group that does not
NOTE Confidence: 0.820293

00:55:46.453 --> 00:55:49.600 have any of these poor features.
NOTE Confidence: 0.820293

00:55:49.600 --> 00:55:51.905 The median follow-up is still
NOTE Confidence: 0.820293

00:55:51.905 --> 00:55:53.749 relatively short 5.9 months.
NOTE Confidence: 0.820293

00:55:53.750 --> 00:55:56.522 This type of therapy works fast

NOTE Confidence: 0.820293

00:55:56.522 --> 00:56:00.990 within a month. You see the responses.

NOTE Confidence: 0.820293

00:56:00.990 --> 00:56:03.738 And when they looked at the

NOTE Confidence: 0.820293

00:56:03.738 --> 00:56:04.654 cellular kinetics,

NOTE Confidence: 0.820293

00:56:04.660 --> 00:56:08.020 what they saw is that at one year

NOTE Confidence: 0.820293

00:56:08.020 --> 00:56:10.991 sick there was life cell persistence

NOTE Confidence: 0.820293

00:56:10.991 --> 00:56:16.000 in 67% and 33% even out to two years.

NOTE Confidence: 0.820293

00:56:16.000 --> 00:56:19.010 Am so now they are ongoing with

NOTE Confidence: 0.820293

00:56:19.010 --> 00:56:21.978 enrollment at the higher dose level.

NOTE Confidence: 0.820293

00:56:21.980 --> 00:56:24.848 Dose level 2.

NOTE Confidence: 0.820293

00:56:24.850 --> 00:56:26.533 And and again,

NOTE Confidence: 0.820293

00:56:26.533 --> 00:56:29.899 this is remarkable for mantle cell

NOTE Confidence: 0.820293

00:56:29.899 --> 00:56:33.850 lymphoma with with no significant toxicity,

NOTE Confidence: 0.820293

00:56:33.850 --> 00:56:37.618 grade three toxicity.

NOTE Confidence: 0.820293

00:56:37.620 --> 00:56:41.298 What about CLL?

NOTE Confidence: 0.820293

00:56:41.300 --> 00:56:44.090 This study transcend CLL 004,

NOTE Confidence: 0.820293

00:56:44.090 --> 00:56:46.958 looked at lice or sell in
NOTE Confidence: 0.820293

00:56:46.958 --> 00:56:50.230 relapse CLL and very interesting.
NOTE Confidence: 0.820293

00:56:50.230 --> 00:56:53.572 Lee had very high complete response
NOTE Confidence: 0.820293

00:56:53.572 --> 00:56:56.921 rates of 45% and and really
NOTE Confidence: 0.820293

00:56:56.921 --> 00:56:59.706 high rates of undetectable MRD,
NOTE Confidence: 0.820293

00:56:59.710 --> 00:57:03.483 both in the blood flow and in
NOTE Confidence: 0.820293

00:57:03.483 --> 00:57:07.571 the bone marrow by NGS and even
NOTE Confidence: 0.820293

00:57:07.571 --> 00:57:11.093 when they looked at patients with
NOTE Confidence: 0.820293

00:57:11.215 --> 00:57:14.809 failed BTK here in the second.
NOTE Confidence: 0.820293

00:57:14.810 --> 00:57:18.210 Bar what failed BTK or or phonetic lacks.
NOTE Confidence: 0.820293

00:57:18.210 --> 00:57:20.335 They had a very impressive
NOTE Confidence: 0.820293

00:57:20.335 --> 00:57:22.035 rates of complete response,
NOTE Confidence: 0.820293

00:57:22.040 --> 00:57:25.148 so so this was already presented at
NOTE Confidence: 0.820293

00:57:25.148 --> 00:57:28.587 Ash of 2019 and what was actually
NOTE Confidence: 0.820293

00:57:28.587 --> 00:57:31.593 presented this year at Ash was.
NOTE Confidence: 0.820293

00:57:31.600 --> 00:57:33.164 A combination of lice,

NOTE Confidence: 0.820293

00:57:33.164 --> 00:57:36.573 a cell with a brute nip based on

NOTE Confidence: 0.820293

00:57:36.573 --> 00:57:38.998 preclinical data that shows that

NOTE Confidence: 0.820293

00:57:38.998 --> 00:57:42.158 imbrued nip can improve car T cell,

NOTE Confidence: 0.820293

00:57:42.160 --> 00:57:44.644 anti tumor efficacy and reduce the

NOTE Confidence: 0.820293

00:57:44.644 --> 00:57:47.000 rates of cytokine release syndrome.

NOTE Confidence: 0.820293

00:57:47.000 --> 00:57:49.863 So so this was the study patients

NOTE Confidence: 0.820293

00:57:49.863 --> 00:57:52.401 had progressed on ibrutinib or they

NOTE Confidence: 0.820293

00:57:52.401 --> 00:57:56.054 had mutations of BTK and they had no

NOTE Confidence: 0.820293

00:57:56.054 --> 00:57:58.878 contraindication to restarting ibrutinib.

NOTE Confidence: 0.820293

00:57:58.880 --> 00:58:01.586 And they were again very high

NOTE Confidence: 0.820293

00:58:01.586 --> 00:58:04.120 risk patients in all groups.

NOTE Confidence: 0.820293

00:58:04.120 --> 00:58:06.970 100% had some high risk features

NOTE Confidence: 0.820293

00:58:06.970 --> 00:58:09.352 like deletion 17, P 53,

NOTE Confidence: 0.820293

00:58:09.352 --> 00:58:10.780 mutation complex karyotype,

NOTE Confidence: 0.820293

00:58:10.780 --> 00:58:13.636 100% had had priori brute Nip,

NOTE Confidence: 0.820293

00:58:13.640 --> 00:58:16.444 100% were relapsed refractory
NOTE Confidence: 0.820293

00:58:16.444 --> 00:58:18.547 to ibrutinib and.
NOTE Confidence: 0.820293

00:58:18.550 --> 00:58:20.570 Half of the patients had
NOTE Confidence: 0.820293

00:58:20.570 --> 00:58:22.186 actually seen vanetta clocks,
NOTE Confidence: 0.820293

00:58:22.190 --> 00:58:25.568 in addition to two BTK inhibitors.
NOTE Confidence: 0.820293

00:58:25.570 --> 00:58:28.048 When we looked at grade three
NOTE Confidence: 0.820293

00:58:28.048 --> 00:58:29.287 cytokine release syndrome,
NOTE Confidence: 0.820293

00:58:29.290 --> 00:58:31.534 only 5% again and or logic
NOTE Confidence: 0.820293

00:58:31.534 --> 00:58:33.574 toxicity grade three and above
NOTE Confidence: 0.820293

00:58:33.574 --> 00:58:35.899 similar to mantle cell lymphoma.
NOTE Confidence: 0.820293

00:58:35.900 --> 00:58:37.216 Only 16%.
NOTE Confidence: 0.820293

00:58:37.216 --> 00:58:37.874 Um,
NOTE Confidence: 0.820293

00:58:37.874 --> 00:58:39.848 complete response rates,
NOTE Confidence: 0.820293

00:58:39.850 --> 00:58:42.154 particularly when you look
NOTE Confidence: 0.820293

00:58:42.154 --> 00:58:44.458 at dose level 200%
NOTE Confidence: 0.8644943

00:58:44.460 --> 00:58:47.565 overall response rate 67% complete

NOTE Confidence: 0.8644943

00:58:47.565 --> 00:58:51.397 response rate and the majority of

NOTE Confidence: 0.8644943

00:58:51.397 --> 00:58:53.917 patients had undetectable MRD.

NOTE Confidence: 0.8644943

00:58:53.920 --> 00:58:56.960 In their in their blood.

NOTE Confidence: 0.8644943

00:58:56.960 --> 00:59:00.456 So in summary, you have very rapid responses,

NOTE Confidence: 0.8644943

00:59:00.460 --> 00:59:02.956 high overall response rate, high rates

NOTE Confidence: 0.8644943

00:59:02.956 --> 00:59:06.138 of CR with lysis cell and ibrutinib.

NOTE Confidence: 0.8644943

00:59:06.140 --> 00:59:09.628 And even though this is no direct comparison,

NOTE Confidence: 0.8644943

00:59:09.630 --> 00:59:11.630 it certainly looks better than

NOTE Confidence: 0.8644943

00:59:11.630 --> 00:59:14.207 the data with lysis cell alone

NOTE Confidence: 0.8644943

00:59:14.207 --> 00:59:16.187 for relapsed refractory CLL.

NOTE Confidence: 0.8644943

00:59:16.190 --> 00:59:19.235 So I just wanted to I know

NOTE Confidence: 0.8644943

00:59:19.235 --> 00:59:21.429 we're running out of time,

NOTE Confidence: 0.8644943

00:59:21.430 --> 00:59:24.046 but for people who treat leukemia,

NOTE Confidence: 0.8644943

00:59:24.050 --> 00:59:28.082 I did want to mention some of the upcoming.

NOTE Confidence: 0.8644943

00:59:28.090 --> 00:59:31.247 Studies in a allow that are important,

NOTE Confidence: 0.8644943

00:59:31.250 --> 00:59:33.805 including the comparison of tisagenlecleucel

NOTE Confidence: 0.8644943

00:59:33.805 --> 00:59:37.129 cell versus plain attuma Bob or I know,

NOTE Confidence: 0.8644943

00:59:37.130 --> 00:59:40.056 choose a map, Osaka mice and this

NOTE Confidence: 0.8644943

00:59:40.056 --> 00:59:43.008 is the Auburn phase three study,

NOTE Confidence: 0.8644943

00:59:43.010 --> 00:59:43.510 Cassiopeia,

NOTE Confidence: 0.8644943

00:59:43.510 --> 00:59:47.010 which looks at his agenda occlusal in

NOTE Confidence: 0.8644943

00:59:47.010 --> 00:59:49.867 patients who are MRD positive after

NOTE Confidence: 0.8644943

00:59:49.867 --> 00:59:53.010 first line therapy and then also summa

NOTE Confidence: 0.8644943

00:59:53.010 --> 00:59:56.170 for looking at exit cap to gene in

NOTE Confidence: 0.8644943

00:59:56.170 --> 00:59:58.370 patients with relapsed refractory LL.

NOTE Confidence: 0.8644943

00:59:58.370 --> 01:00:00.170 So so with that,

NOTE Confidence: 0.8644943

01:00:00.170 --> 01:00:02.634 you know I'd like to end and and

NOTE Confidence: 0.8644943

01:00:02.634 --> 01:00:04.948 I'm happy to take any questions.

NOTE Confidence: 0.9340173

01:00:16.570 --> 01:00:20.450 OK. So, Doctor Gordon Dr Sophie.

NOTE Confidence: 0.8303818

01:00:20.450 --> 01:00:22.520 Thanks for those great reviews.

NOTE Confidence: 0.8303818

01:00:22.520 --> 01:00:25.425 We do have a number of questions.

NOTE Confidence: 0.8303818

01:00:25.430 --> 01:00:27.920 All remind people who are listening.

NOTE Confidence: 0.8303818

01:00:27.920 --> 01:00:29.688 If you have questions,

NOTE Confidence: 0.8303818

01:00:29.688 --> 01:00:33.090 submit them in the Chatter Q&A section.

NOTE Confidence: 0.8303818

01:00:33.090 --> 01:00:37.318 I and. I'll start with some

NOTE Confidence: 0.8303818

01:00:37.318 --> 01:00:38.806 questions about Milo dysplasia,

NOTE Confidence: 0.8303818

01:00:38.810 --> 01:00:41.098 starting from the top.

NOTE Confidence: 0.8303818

01:00:41.098 --> 01:00:43.958 This is for Doctor Gowda.

NOTE Confidence: 0.8303818

01:00:43.960 --> 01:00:46.660 And I'll just, I'll paraphrase this,

NOTE Confidence: 0.8303818

01:00:46.660 --> 01:00:49.252 given the results of the randomized

NOTE Confidence: 0.8303818

01:00:49.252 --> 01:00:51.610 trial led by Doctor Cutler.

NOTE Confidence: 0.8303818

01:00:51.610 --> 01:00:54.050 Mild displeasure.

NOTE Confidence: 0.8303818

01:00:54.050 --> 01:00:55.106 Should we in?

NOTE Confidence: 0.8303818

01:00:55.106 --> 01:00:56.866 This isn't naturally to donor.

NOTE Confidence: 0.8303818

01:00:56.870 --> 01:00:58.306 Should we be considering

NOTE Confidence: 0.8303818

01:00:58.306 --> 01:00:59.742 haploidentical transplant in older

NOTE Confidence: 0.8303818

01:00:59.742 --> 01:01:01.460 high risk MD's patients low?
NOTE Confidence: 0.8303818

01:01:01.460 --> 01:01:04.120 What do you think?
NOTE Confidence: 0.8303818

01:01:04.120 --> 01:01:04.370 It's
NOTE Confidence: 0.9250498

01:01:04.370 --> 01:01:06.340 a great question, I think.
NOTE Confidence: 0.9250498

01:01:06.340 --> 01:01:08.340 It was an exclusion criteria in this trial,
NOTE Confidence: 0.9250498

01:01:08.340 --> 01:01:10.746 so that's the number one point.
NOTE Confidence: 0.9250498

01:01:10.750 --> 01:01:12.222 Essentially, this pistol betas
NOTE Confidence: 0.9250498

01:01:12.222 --> 01:01:14.430 lingered on for as many years
NOTE Confidence: 0.9250498

01:01:14.491 --> 01:01:16.267 as we've all been doing this.
NOTE Confidence: 0.9250498

01:01:16.270 --> 01:01:19.396 That haploidentical outcomes similar to
NOTE Confidence: 0.9250498

01:01:19.396 --> 01:01:21.580 match siblings and matched unrelated donors.
NOTE Confidence: 0.9250498

01:01:21.580 --> 01:01:23.764 There has never been a randomized
NOTE Confidence: 0.9250498

01:01:23.764 --> 01:01:25.220 study in this population.
NOTE Confidence: 0.9250498

01:01:25.220 --> 01:01:27.355 There are multiple registry studies
NOTE Confidence: 0.9250498

01:01:27.355 --> 01:01:29.063 that have shown feasibility's.
NOTE Confidence: 0.9250498

01:01:29.070 --> 01:01:31.310 And then also just studies that shows

NOTE Confidence: 0.9250498

01:01:31.310 --> 01:01:34.181 you kind of laid these people so you have

NOTE Confidence: 0.9250498

01:01:34.181 --> 01:01:36.847 to take all those with a pinch of salt.

NOTE Confidence: 0.9250498

01:01:36.850 --> 01:01:39.020 I would say enter specific protocol based.

NOTE Confidence: 0.9250498

01:01:39.020 --> 01:01:40.845 Certainly worth considering that the

NOTE Confidence: 0.9250498

01:01:40.845 --> 01:01:42.987 reason that prospective study that says

NOTE Confidence: 0.9250498

01:01:42.987 --> 01:01:45.043 in elderly people Apple may not be that

NOTE Confidence: 0.9250498

01:01:45.043 --> 01:01:47.110 great for email from the registry again,

NOTE Confidence: 0.9250498

01:01:47.110 --> 01:01:49.460 but there are at the same time you do the

NOTE Confidence: 0.9250498

01:01:49.526 --> 01:01:51.766 mismatches in the registry limitations.

NOTE Confidence: 0.9250498

01:01:51.770 --> 01:01:53.325 There are equal numbers that

NOTE Confidence: 0.9250498

01:01:53.325 --> 01:01:54.258 suggest it's efficacious.

NOTE Confidence: 0.9250498

01:01:54.260 --> 01:01:56.684 So if you think there's a high risk

NOTE Confidence: 0.9250498

01:01:56.684 --> 01:01:59.297 disease and there's no really good option.

NOTE Confidence: 0.9250498

01:01:59.300 --> 01:02:00.395 I would certainly get an

NOTE Confidence: 0.9250498

01:02:00.395 --> 01:02:01.490 Apple down and go forward.

NOTE Confidence: 0.7872994

01:02:02.870 --> 01:02:05.505 OK alright thanks Doctor Assoufia
NOTE Confidence: 0.7872994

01:02:05.505 --> 01:02:08.140 question about car T cells.
NOTE Confidence: 0.7872994

01:02:08.140 --> 01:02:10.825 Given the encouraging Zuma 12
NOTE Confidence: 0.7872994

01:02:10.825 --> 01:02:14.760 results or were car T cells child
NOTE Confidence: 0.7872994

01:02:14.760 --> 01:02:17.605 at all and frontline setting
NOTE Confidence: 0.7872994

01:02:17.605 --> 01:02:20.740 for high risk lymphoma. So
NOTE Confidence: 0.8666774

01:02:20.740 --> 01:02:23.225 this is this is the first study
NOTE Confidence: 0.8666774

01:02:23.225 --> 01:02:25.918 that I know of where this is
NOTE Confidence: 0.8666774

01:02:25.918 --> 01:02:27.843 being tested in up front,
NOTE Confidence: 0.8666774

01:02:27.850 --> 01:02:29.980 in upfront lymphoma and that's why
NOTE Confidence: 0.8666774

01:02:29.980 --> 01:02:32.708 they chose such a high disease risk.
NOTE Confidence: 0.8666774

01:02:32.710 --> 01:02:34.918 Group of patients that had double
NOTE Confidence: 0.8666774

01:02:34.918 --> 01:02:37.205 or triple hit disease or were
NOTE Confidence: 0.8666774

01:02:37.205 --> 01:02:39.070 primary refractory on PET scan.
NOTE Confidence: 0.8725645

01:02:40.830 --> 01:02:43.357 I'll follow up with my own question.
NOTE Confidence: 0.8725645

01:02:43.360 --> 01:02:45.880 Do you think this data is sufficient?

NOTE Confidence: 0.8725645

01:02:45.880 --> 01:02:48.540 We should consider this.

NOTE Confidence: 0.8725645

01:02:48.540 --> 01:02:50.958 Or this requires further study and

NOTE Confidence: 0.8725645

01:02:50.958 --> 01:02:52.970 end insurance approval, of course.

NOTE Confidence: 0.86581653

01:02:53.630 --> 01:02:56.006 Yeah, I mean, I think that

NOTE Confidence: 0.86581653

01:02:56.006 --> 01:02:58.200 the the duration is short,

NOTE Confidence: 0.86581653

01:02:58.200 --> 01:02:59.856 we need longer duration,

NOTE Confidence: 0.86581653

01:02:59.856 --> 01:03:01.926 at least beyond the year.

NOTE Confidence: 0.86581653

01:03:01.930 --> 01:03:04.010 For these patients, you know.

NOTE Confidence: 0.86581653

01:03:04.010 --> 01:03:05.060 That being said,

NOTE Confidence: 0.86581653

01:03:05.060 --> 01:03:07.510 we we have treated here and also

NOTE Confidence: 0.86581653

01:03:07.588 --> 01:03:09.838 other institutions have reported that

NOTE Confidence: 0.86581653

01:03:09.838 --> 01:03:13.025 PET scan after two cycles of therapy

NOTE Confidence: 0.86581653

01:03:13.025 --> 01:03:15.599 does not have the same prognostic

NOTE Confidence: 0.86581653

01:03:15.599 --> 01:03:17.702 significance in large cell lymphoma

NOTE Confidence: 0.86581653

01:03:17.702 --> 01:03:20.186 that it has in Hodgkin lymphoma,

NOTE Confidence: 0.86581653

01:03:20.190 --> 01:03:23.638 and that indeed we are able to cure.
NOTE Confidence: 0.86581653

01:03:23.640 --> 01:03:27.217 Um, many of those patients when we
NOTE Confidence: 0.86581653

01:03:27.217 --> 01:03:30.168 complete six cycles of therapy so.
NOTE Confidence: 0.86581653

01:03:30.170 --> 01:03:31.802 I certainly don't think
NOTE Confidence: 0.86581653

01:03:31.802 --> 01:03:33.842 that based on these data,
NOTE Confidence: 0.86581653

01:03:33.850 --> 01:03:37.114 you know we would change standard of care.
NOTE Confidence: 0.86581653

01:03:37.120 --> 01:03:39.574 I think that this requires you
NOTE Confidence: 0.86581653

01:03:39.574 --> 01:03:42.790 know further further follow up.
NOTE Confidence: 0.86581653

01:03:42.790 --> 01:03:45.340 Right, and I think that most importantly,
NOTE Confidence: 0.86581653

01:03:45.340 --> 01:03:47.727 we really need to see the data
NOTE Confidence: 0.86581653

01:03:47.727 --> 01:03:49.340 in relapsed refractory disease.
NOTE Confidence: 0.86581653

01:03:49.340 --> 01:03:52.250 As to how this stacks up to too high dose
NOTE Confidence: 0.86581653

01:03:52.326 --> 01:03:55.170 therapy and autologous stem cell rescue,
NOTE Confidence: 0.86581653

01:03:55.170 --> 01:03:57.826 I think if indeed there is an improvement
NOTE Confidence: 0.86581653

01:03:57.826 --> 01:04:00.259 in cure rates with that approach.
NOTE Confidence: 0.86581653

01:04:00.260 --> 01:04:01.352 For these patients,

NOTE Confidence: 0.86581653

01:04:01.352 --> 01:04:04.683 I think that will be a stronger push to

NOTE Confidence: 0.86581653

01:04:04.683 --> 01:04:07.531 move it to frontline for high risk groups.

NOTE Confidence: 0.826792846153846

01:04:09.140 --> 01:04:10.396 Right, right?

NOTE Confidence: 0.826792846153846

01:04:10.396 --> 01:04:14.164 OK couple of questions on the

NOTE Confidence: 0.826792846153846

01:04:14.164 --> 01:04:17.889 graft versus host disease studies.

NOTE Confidence: 0.826792846153846

01:04:17.890 --> 01:04:19.570 I from Doctor Challace,

NOTE Confidence: 0.826792846153846

01:04:19.570 --> 01:04:22.650 do we have a sense of what?

NOTE Confidence: 0.826792846153846

01:04:22.650 --> 01:04:25.740 Best alternative therapies patients received.

NOTE Confidence: 0.826792846153846

01:04:25.740 --> 01:04:27.380 Monoclonal antibodies.

NOTE Confidence: 0.826792846153846

01:04:27.380 --> 01:04:32.300 Did any receive a brute nib?

NOTE Confidence: 0.826792846153846

01:04:32.300 --> 01:04:33.620 And now it's just.

NOTE Confidence: 0.826792846153846

01:04:33.620 --> 01:04:34.940 Did anyone receive rocks?

NOTE Confidence: 0.826792846153846

01:04:34.940 --> 01:04:39.007 Although that may refer to the crossover.

NOTE Confidence: 0.826792846153846

01:04:39.010 --> 01:04:39.412 Hello diary,

NOTE Confidence: 0.826792846153846

01:04:39.412 --> 01:04:41.020 I probably also know the answer to this.

NOTE Confidence: 0.826792846153846

01:04:41.020 --> 01:04:43.068 I don't know if you want me to

NOTE Confidence: 0.826792846153846

01:04:43.068 --> 01:04:44.099 feel this one or.

NOTE Confidence: 0.826792846153846

01:04:44.100 --> 01:04:45.400 Yeah, sure yeah.

NOTE Confidence: 0.826792846153846

01:04:45.400 --> 01:04:46.262 So yes.

NOTE Confidence: 0.826792846153846

01:04:46.262 --> 01:04:47.986 It says it says.

NOTE Confidence: 0.826792846153846

01:04:47.990 --> 01:04:50.270 Why was the local investigator on

NOTE Confidence: 0.826792846153846

01:04:50.270 --> 01:04:52.740 this study so best alternative?

NOTE Confidence: 0.826792846153846

01:04:52.740 --> 01:04:55.435 Therapy was a long list of standard

NOTE Confidence: 0.826792846153846

01:04:55.435 --> 01:04:57.649 non FDA approved treatments 'cause

NOTE Confidence: 0.826792846153846

01:04:57.649 --> 01:05:00.094 there aren't any FDA approved

NOTE Confidence: 0.826792846153846

01:05:00.094 --> 01:05:02.679 treatments for for chronic GV HD,

NOTE Confidence: 0.826792846153846

01:05:02.680 --> 01:05:04.840 but they did include ibrutinib.

NOTE Confidence: 0.826792846153846

01:05:04.840 --> 01:05:06.564 They included photo pheresis.

NOTE Confidence: 0.826792846153846

01:05:06.564 --> 01:05:08.288 Those were common ones.

NOTE Confidence: 0.826792846153846

01:05:08.290 --> 01:05:10.278 Other agents for Mycophenolate

NOTE Confidence: 0.826792846153846

01:05:10.278 --> 01:05:12.266 sirolimus occasionally and the

NOTE Confidence: 0.826792846153846
01:05:12.266 --> 01:05:14.987 brute name was added to this trial.
NOTE Confidence: 0.826792846153846
01:05:14.990 --> 01:05:15.851 Pretty early on,
NOTE Confidence: 0.826792846153846
01:05:15.851 --> 01:05:17.860 and so patients did receive many of
NOTE Confidence: 0.826792846153846
01:05:17.917 --> 01:05:19.737 those best alternative therapies.
NOTE Confidence: 0.7581872
01:05:21.860 --> 01:05:24.380 In comparison, and that was up to
NOTE Confidence: 0.7581872
01:05:24.380 --> 01:05:25.521 investigators choice, corollary,
NOTE Confidence: 0.7581872
01:05:25.521 --> 01:05:28.047 question, how do you recite decide
NOTE Confidence: 0.7581872
01:05:28.047 --> 01:05:29.945 between ruxolitinib and a brute
NOTE Confidence: 0.7581872
01:05:29.945 --> 01:05:31.940 knipfer GV HD based on this phase,
NOTE Confidence: 0.7581872
01:05:31.940 --> 01:05:33.380 three data looks like.
NOTE Confidence: 0.7581872
01:05:33.380 --> 01:05:36.260 Take a stab at that. Yeah, I think
NOTE Confidence: 0.7581872
01:05:36.260 --> 01:05:38.964 we should understand that I put in the
NOTE Confidence: 0.7581872
01:05:38.964 --> 01:05:41.656 beta was approved based on Phase 1B.
NOTE Confidence: 0.7581872
01:05:41.660 --> 01:05:43.300 Phase two study design.
NOTE Confidence: 0.7581872
01:05:43.300 --> 01:05:46.100 In another, we really didn't have many drugs.
NOTE Confidence: 0.7581872

01:05:46.100 --> 01:05:47.424 Well, certainly it's challenging.
NOTE Confidence: 0.7581872

01:05:47.424 --> 01:05:48.443 You know, practice.
NOTE Confidence: 0.7581872

01:05:48.443 --> 01:05:51.267 We see a lot of cases with Orange
NOTE Confidence: 0.7581872

01:05:51.267 --> 01:05:53.707 ebstein a little bit of Raskin GV HD.
NOTE Confidence: 0.7581872

01:05:53.710 --> 01:05:55.370 Those stones care of us.
NOTE Confidence: 0.7581872

01:05:55.370 --> 01:05:57.025 I'm really excited about this
NOTE Confidence: 0.7581872

01:05:57.025 --> 01:05:58.707 new drug that Katie, 025,
NOTE Confidence: 0.7581872

01:05:58.707 --> 01:06:00.492 especially for what we traditionally
NOTE Confidence: 0.7581872

01:06:00.492 --> 01:06:02.319 called the marleybone versions of GST,
NOTE Confidence: 0.7581872

01:06:02.320 --> 01:06:04.020 including highly fibrotic questions of
NOTE Confidence: 0.7581872

01:06:04.020 --> 01:06:06.619 that and those are the ones that kill.
NOTE Confidence: 0.7581872

01:06:06.620 --> 01:06:08.275 Your patience is defining it
NOTE Confidence: 0.7581872

01:06:08.275 --> 01:06:09.271 highly immunosuppressive, right?
NOTE Confidence: 0.7581872

01:06:09.271 --> 01:06:11.257 So, coming back to her then,
NOTE Confidence: 0.7581872

01:06:11.260 --> 01:06:14.005 I think I might be tempted to use it
NOTE Confidence: 0.7581872

01:06:14.005 --> 01:06:16.874 earlier on again in a clinical trial design,

NOTE Confidence: 0.7581872

01:06:16.880 --> 01:06:17.228 because.

NOTE Confidence: 0.7581872

01:06:17.228 --> 01:06:18.620 It's not a prude,

NOTE Confidence: 0.7581872

01:06:18.620 --> 01:06:20.608 although we are waiting for the approval

NOTE Confidence: 0.7581872

01:06:20.608 --> 01:06:22.449 to come through anytime I might be

NOTE Confidence: 0.7581872

01:06:22.449 --> 01:06:24.515 tempted to try that if it's a highly

NOTE Confidence: 0.7581872

01:06:24.515 --> 01:06:26.040 fibrotic question earlier on but.

NOTE Confidence: 0.7581872

01:06:26.040 --> 01:06:27.452 Side effects of reboot.

NOTE Confidence: 0.7581872

01:06:27.452 --> 01:06:29.217 Your name can be significant

NOTE Confidence: 0.7581872

01:06:29.217 --> 01:06:31.379 in my personal biased opinion.

NOTE Confidence: 0.7581872

01:06:31.380 --> 01:06:33.207 Set opinions with Rocks is an issue,

NOTE Confidence: 0.7581872

01:06:33.210 --> 01:06:33.672 but again,

NOTE Confidence: 0.7581872

01:06:33.672 --> 01:06:35.058 in this trial the show that

NOTE Confidence: 0.7581872

01:06:35.058 --> 01:06:36.394 quality of life cytopenias taking

NOTE Confidence: 0.7581872

01:06:36.394 --> 01:06:38.038 all that into account rocks was

NOTE Confidence: 0.7581872

01:06:38.038 --> 01:06:39.730 way better compared to the other,

NOTE Confidence: 0.7581872

01:06:39.730 --> 01:06:41.610 so I may be tempted to use that
NOTE Confidence: 0.7581872

01:06:41.610 --> 01:06:43.230 up front and we're already doing
NOTE Confidence: 0.7581872

01:06:43.230 --> 01:06:45.210 it in some of our case this,
NOTE Confidence: 0.7581872

01:06:45.210 --> 01:06:47.298 but it's not studied in a randomized fashion.
NOTE Confidence: 0.7581872

01:06:47.300 --> 01:06:48.380 It's worth studying it.
NOTE Confidence: 0.7581872

01:06:48.380 --> 01:06:50.429 If somebody sponsors that kind of a study.
NOTE Confidence: 0.7981567

01:06:52.990 --> 01:06:56.329 So when you short answer the data support for
NOTE Confidence: 0.7981567

01:06:56.329 --> 01:06:58.855 ruxolitinib is probably a more active agent.
NOTE Confidence: 0.7981567

01:06:58.860 --> 01:07:01.842 The I'll add the ibrutinib study required
NOTE Confidence: 0.7981567

01:07:01.842 --> 01:07:04.366 inflammatory erythema in the skin or oral
NOTE Confidence: 0.7981567

01:07:04.366 --> 01:07:07.140 GV HD is entry criteria. So as you said,
NOTE Confidence: 0.7981567

01:07:07.140 --> 01:07:09.870 it was probably a group of patients.
NOTE Confidence: 0.7981567

01:07:09.870 --> 01:07:12.438 Might be a little bit easier to treat
NOTE Confidence: 0.7981567

01:07:12.438 --> 01:07:14.280 those particular clinical scenarios,
NOTE Confidence: 0.7981567

01:07:14.280 --> 01:07:16.332 whereas ruxolitinib seems to be a
NOTE Confidence: 0.7981567

01:07:16.332 --> 01:07:18.561 more broadly active agent and it

NOTE Confidence: 0.7981567
01:07:18.561 --> 01:07:20.149 doesn't cause atrial fibrillation,
NOTE Confidence: 0.7981567
01:07:20.150 --> 01:07:23.426 which is an issue with the brunette.
NOTE Confidence: 0.7981567
01:07:23.430 --> 01:07:29.250 Um? OK, another Milo dysplasia question.
NOTE Confidence: 0.7981567
01:07:29.250 --> 01:07:31.338 Given the recent randomized study from
NOTE Confidence: 0.7981567
01:07:31.338 --> 01:07:33.244 MD Anderson showing no improvement
NOTE Confidence: 0.7981567
01:07:33.244 --> 01:07:35.068 in outcome with maintenance,
NOTE Confidence: 0.7981567
01:07:35.070 --> 01:07:37.786 Ivy is a sighted in versus placebo.
NOTE Confidence: 0.7981567
01:07:37.790 --> 01:07:42.515 This is post transplant in AML and MD S.
NOTE Confidence: 0.7981567
01:07:42.520 --> 01:07:45.256 Do we think or Eliza would be different?
NOTE Confidence: 0.8174205
01:07:48.000 --> 01:07:49.869 So I'm glad I'm with paying attention
NOTE Confidence: 0.8174205
01:07:49.869 --> 01:07:51.799 to MD Anderson clinical trial output
NOTE Confidence: 0.8174205
01:07:51.799 --> 01:07:54.585 very closely, and I guess he likes
NOTE Confidence: 0.8174205
01:07:54.585 --> 01:07:56.650 those results with that background.
NOTE Confidence: 0.8174205
01:07:56.650 --> 01:07:58.810 I think we should first
NOTE Confidence: 0.8174205
01:07:58.810 --> 01:08:00.538 dichotomize those two things,
NOTE Confidence: 0.8174205

01:08:00.540 --> 01:08:03.390 So what battle showed was.

NOTE Confidence: 0.8174205

01:08:03.390 --> 01:08:05.070 Every every come are getting

NOTE Confidence: 0.8174205

01:08:05.070 --> 01:08:06.750 randomized and they've only median

NOTE Confidence: 0.8174205

01:08:06.810 --> 01:08:08.674 of 4 four cycles of that was given.

NOTE Confidence: 0.8174205

01:08:08.680 --> 01:08:10.150 As for the trial right?

NOTE Confidence: 0.8174205

01:08:10.150 --> 01:08:13.435 And it was it was tested in a randomized

NOTE Confidence: 0.8174205

01:08:13.435 --> 01:08:16.238 fashion that turned out to be negative.

NOTE Confidence: 0.8174205

01:08:16.240 --> 01:08:18.725 We can argue that Ivy and oral,

NOTE Confidence: 0.8174205

01:08:18.730 --> 01:08:19.798 despite mechanistic things,

NOTE Confidence: 0.8174205

01:08:19.798 --> 01:08:21.578 are not the same drug.

NOTE Confidence: 0.8174205

01:08:21.580 --> 01:08:24.010 What we're trying to achieve is

NOTE Confidence: 0.8174205

01:08:24.010 --> 01:08:26.220 couple of two different things.

NOTE Confidence: 0.8174205

01:08:26.220 --> 01:08:28.068 There's some confusion now with the

NOTE Confidence: 0.8174205

01:08:28.068 --> 01:08:30.097 CC-486 clinical trial data as to what

NOTE Confidence: 0.8174205

01:08:30.097 --> 01:08:31.833 is the right timing for the transplant,

NOTE Confidence: 0.8174205

01:08:31.840 --> 01:08:33.344 because it's very cleverly

NOTE Confidence: 0.8174205

01:08:33.344 --> 01:08:35.600 articulated by the company in terms

NOTE Confidence: 0.8174205

01:08:35.661 --> 01:08:37.418 of how this needs to be done.

NOTE Confidence: 0.8174205

01:08:37.420 --> 01:08:39.415 So we all agree CR one is

NOTE Confidence: 0.8174205

01:08:39.415 --> 01:08:40.790 a major entry point,

NOTE Confidence: 0.8174205

01:08:40.790 --> 01:08:41.705 especially for intermediate

NOTE Confidence: 0.8174205

01:08:41.705 --> 01:08:42.620 and advanced rest.

NOTE Confidence: 0.8174205

01:08:42.620 --> 01:08:44.755 How many cycles of consolidations are needed?

NOTE Confidence: 0.8174205

01:08:44.760 --> 01:08:46.108 It's an open field,

NOTE Confidence: 0.8174205

01:08:46.108 --> 01:08:49.030 unlike the hydac for the good risk groups.

NOTE Confidence: 0.8174205

01:08:49.030 --> 01:08:51.232 So if we can create outpatient

NOTE Confidence: 0.8174205

01:08:51.232 --> 01:08:52.700 based regiments with oral

NOTE Confidence: 0.8174205

01:08:52.772 --> 01:08:54.608 set aside in equal and drug.

NOTE Confidence: 0.8174205

01:08:54.610 --> 01:08:56.356 And the rationale that we build

NOTE Confidence: 0.8174205

01:08:56.356 --> 01:08:58.399 for the trial is the initial

NOTE Confidence: 0.8174205

01:08:58.399 --> 01:09:00.019 scandura trial from Cornell,

NOTE Confidence: 0.8174205

01:09:00.020 --> 01:09:02.090 where they show that epigenetic priming
NOTE Confidence: 0.8174205

01:09:02.090 --> 01:09:04.205 enhances cancer test is an antigen
NOTE Confidence: 0.8174205

01:09:04.205 --> 01:09:05.900 exposure now antigen expression that
NOTE Confidence: 0.8174205

01:09:05.900 --> 01:09:08.127 then makes the T cell attack better.
NOTE Confidence: 0.8174205

01:09:08.130 --> 01:09:10.426 You generate a lot of tumor infiltrating
NOTE Confidence: 0.8174205

01:09:10.426 --> 01:09:11.850 lymphocytes with epigenetic priming,
NOTE Confidence: 0.8174205

01:09:11.850 --> 01:09:13.740 so you kind of also make the
NOTE Confidence: 0.8174205

01:09:13.740 --> 01:09:15.353 people less fragile coming into
NOTE Confidence: 0.8174205

01:09:15.353 --> 01:09:17.208 the transparent by rather than
NOTE Confidence: 0.8174205

01:09:17.208 --> 01:09:18.950 giving hydac equivalent intensity,
NOTE Confidence: 0.8174205

01:09:18.950 --> 01:09:20.302 you make it better.
NOTE Confidence: 0.8174205

01:09:20.302 --> 01:09:20.640 Third,
NOTE Confidence: 0.8174205

01:09:20.640 --> 01:09:21.920 in the pre transplantation
NOTE Confidence: 0.8174205

01:09:21.920 --> 01:09:23.520 setting this synergy when you
NOTE Confidence: 0.8174205

01:09:23.520 --> 01:09:25.088 prime with epigenetic agents.
NOTE Confidence: 0.8174205

01:09:25.090 --> 01:09:26.450 Bracton Alcalay to yourself

NOTE Confidence: 0.8174205

01:09:26.450 --> 01:09:27.130 and cyclophosphamide.

NOTE Confidence: 0.8174205

01:09:27.130 --> 01:09:28.950 So those are the 3 three concepts

NOTE Confidence: 0.8174205

01:09:28.950 --> 01:09:31.209 in the pre transplantation setting.

NOTE Confidence: 0.8174205

01:09:31.210 --> 01:09:32.454 The post transplantation setting.

NOTE Confidence: 0.8174205

01:09:32.454 --> 01:09:33.698 When you continue that

NOTE Confidence: 0.8174205

01:09:33.698 --> 01:09:35.290 as a maintenance again,

NOTE Confidence: 0.8174205

01:09:35.290 --> 01:09:36.650 that's the dichotomy between

NOTE Confidence: 0.8174205

01:09:36.650 --> 01:09:38.350 BI tools file and mine.

NOTE Confidence: 0.8174205

01:09:38.350 --> 01:09:40.050 Is that increase the regulatory

NOTE Confidence: 0.8174205

01:09:40.050 --> 01:09:41.070 T cell expressions,

NOTE Confidence: 0.8174205

01:09:41.070 --> 01:09:42.770 which is beneficial for GST.

NOTE Confidence: 0.8174205

01:09:42.770 --> 01:09:45.474 But there's also a lot of data that

NOTE Confidence: 0.8174205

01:09:45.474 --> 01:09:47.224 epigenetics increases hedging idea or

NOTE Confidence: 0.8174205

01:09:47.224 --> 01:09:49.252 expression which then makes it easier

NOTE Confidence: 0.8174205

01:09:49.252 --> 01:09:51.641 for the T cell attack that makes

NOTE Confidence: 0.8174205

01:09:51.641 --> 01:09:53.340 relapse less likely because there's
NOTE Confidence: 0.8174205

01:09:53.340 --> 01:09:55.560 an ongoing TNR GVL surveillance so.
NOTE Confidence: 0.8174205

01:09:55.560 --> 01:09:57.476 We're redefining consolidation differently.
NOTE Confidence: 0.8174205

01:09:57.476 --> 01:10:01.156 Trying to get into the space of a
NOTE Confidence: 0.8174205

01:10:01.156 --> 01:10:03.021 traditional hydac plus hydac against
NOTE Confidence: 0.8174205

01:10:03.021 --> 01:10:04.529 probably lower intensity therapy,
NOTE Confidence: 0.8174205

01:10:04.530 --> 01:10:06.414 which can be given an extended
NOTE Confidence: 0.8174205

01:10:06.414 --> 01:10:09.149 period of time at the target on
NOTE Confidence: 0.8174205

01:10:09.149 --> 01:10:10.556 decreasing events downstream,
NOTE Confidence: 0.8174205

01:10:10.560 --> 01:10:13.288 either due to relapse GST so that those
NOTE Confidence: 0.8174205

01:10:13.288 --> 01:10:15.665 are some of the subtle differences
NOTE Confidence: 0.8174205

01:10:15.665 --> 01:10:18.095 in how this can be interpreted.
NOTE Confidence: 0.7608803

01:10:20.090 --> 01:10:22.278 OK, one last question.
NOTE Confidence: 0.7608803

01:10:22.278 --> 01:10:25.013 I were there patients with
NOTE Confidence: 0.7608803

01:10:25.013 --> 01:10:27.215 bronchiolitis obliterans and the
NOTE Confidence: 0.7608803

01:10:27.215 --> 01:10:30.372 Rockstar study an important question.

NOTE Confidence: 0.7608803
01:10:30.372 --> 01:10:32.196 Alright, do you recall?
NOTE Confidence: 0.7608803
01:10:32.196 --> 01:10:34.930 It's not clear to me. I mean, I
NOTE Confidence: 0.81454706
01:10:34.930 --> 01:10:36.290 think this is abstract.
NOTE Confidence: 0.81454706
01:10:36.290 --> 01:10:38.741 I want to look at the paper
NOTE Confidence: 0.81454706
01:10:38.741 --> 01:10:40.745 myself to see what it is,
NOTE Confidence: 0.81454706
01:10:40.750 --> 01:10:42.310 but the initial dose finding
NOTE Confidence: 0.81454706
01:10:42.310 --> 01:10:43.558 study they said greater
NOTE Confidence: 0.81454706
01:10:43.558 --> 01:10:45.189 than four organ involvement.
NOTE Confidence: 0.81454706
01:10:45.190 --> 01:10:47.871 And there was a lot of multiple
NOTE Confidence: 0.81454706
01:10:47.871 --> 01:10:50.218 people at severe chronic GV HD.
NOTE Confidence: 0.81454706
01:10:50.220 --> 01:10:51.755 I'm assuming there was some
NOTE Confidence: 0.81454706
01:10:51.755 --> 01:10:52.676 representation of Bill,
NOTE Confidence: 0.81454706
01:10:52.680 --> 01:10:55.088 but I want to look at the fine
NOTE Confidence: 0.81454706
01:10:55.088 --> 01:10:56.669 print before it comes out,
NOTE Confidence: 0.81454706
01:10:56.670 --> 01:10:58.296 especially for all the noise it's
NOTE Confidence: 0.81454706

01:10:58.296 --> 01:10:59.380 making saying it's antifibrotic
NOTE Confidence: 0.81454706

01:10:59.430 --> 01:11:00.350 and anti-inflammatory.
NOTE Confidence: 0.81454706

01:11:00.350 --> 01:11:01.890 That would be a breakthrough.
NOTE Confidence: 0.7963529

01:11:04.350 --> 01:11:06.612 Right, so I think we we
NOTE Confidence: 0.7963529

01:11:06.612 --> 01:11:08.460 probably need to wrap up.
NOTE Confidence: 0.7963529

01:11:08.460 --> 01:11:11.490 There's a kudos to Doctor Trophy
NOTE Confidence: 0.7963529

01:11:11.490 --> 01:11:14.120 for pronouncing the Carty names.
NOTE Confidence: 0.7963529

01:11:14.120 --> 01:11:15.444 I'm sure I was.
NOTE Confidence: 0.7963529

01:11:15.444 --> 01:11:17.672 I was very impressed actually and
NOTE Confidence: 0.7963529

01:11:17.672 --> 01:11:21.104 thank you so much buddy else.
NOTE Confidence: 0.7963529

01:11:21.110 --> 01:11:23.742 Can do that? Yeah yeah thank you so
NOTE Confidence: 0.7963529

01:11:23.742 --> 01:11:25.979 much Stewart for moderating such a,
NOTE Confidence: 0.7963529

01:11:25.980 --> 01:11:28.068 you know, a very lively Q&A.
NOTE Confidence: 0.7963529

01:11:28.070 --> 01:11:30.116 And thank you Doctor Sufyan doctor
NOTE Confidence: 0.7963529

01:11:30.116 --> 01:11:31.900 Gowda for such amazing talks.
NOTE Confidence: 0.7963529

01:11:31.900 --> 01:11:33.982 I would also like to thank

NOTE Confidence: 0.7963529

01:11:33.982 --> 01:11:36.070 me go day to work very

NOTE Confidence: 0.8184527

01:11:36.070 --> 01:11:38.507 hard behind the scenes to get this

NOTE Confidence: 0.8184527

01:11:38.507 --> 01:11:40.950 series going and this is recorded as

NOTE Confidence: 0.8184527

01:11:40.950 --> 01:11:42.685 we discussed all of the

NOTE Confidence: 0.8184527

01:11:42.685 --> 01:11:44.073 recordings will be available.

NOTE Confidence: 0.8184527

01:11:44.080 --> 01:11:46.376 You can claim CME credit if you

NOTE Confidence: 0.8184527

01:11:46.376 --> 01:11:49.027 provide us some feedback about how we

NOTE Confidence: 0.8184527

01:11:49.027 --> 01:11:51.415 can improve this going forward and.

NOTE Confidence: 0.8184527

01:11:51.420 --> 01:11:53.959 Hopefully next year we will have

NOTE Confidence: 0.8184527

01:11:53.960 --> 01:11:56.795 a hybrid model of in person and

NOTE Confidence: 0.8184527

01:11:56.795 --> 01:11:59.055 virtual component and looking forward

NOTE Confidence: 0.8184527

01:11:59.055 --> 01:12:01.600 for a great 2021 for everybody.

NOTE Confidence: 0.8184527

01:12:01.600 --> 01:12:04.138 Thank you so much and looking

NOTE Confidence: 0.8184527

01:12:04.138 --> 01:12:06.680 forward to next year post Ash.

NOTE Confidence: 0.8184527

01:12:06.680 --> 01:12:11.104 Thank you. Excellent, thank you.