

WEBVTT

NOTE duration:"01:03:34"

NOTE recognizability:0.759

NOTE language:en-us

NOTE Confidence: 0.824394778571429

00:00:00.000 --> 00:00:02.936 Today we're going to give an update on

NOTE Confidence: 0.824394778571429

00:00:02.936 --> 00:00:05.347 cellular therapies and stem cell transplant.

NOTE Confidence: 0.815958789166667

00:00:08.180 --> 00:00:11.708 From ash, this session will be

NOTE Confidence: 0.815958789166667

00:00:11.708 --> 00:00:14.937 moderated by myself and Doctor

NOTE Confidence: 0.815958789166667

00:00:14.937 --> 00:00:19.188 Delgado and Doctor Stuart Seropian,

NOTE Confidence: 0.815958789166667

00:00:19.188 --> 00:00:21.540 who's our director of the stem

NOTE Confidence: 0.815958789166667

00:00:21.540 --> 00:00:23.020 Cell Transplant Program and Co.

NOTE Confidence: 0.815958789166667

00:00:23.020 --> 00:00:26.080 Director of the Cellular Therapy program,

NOTE Confidence: 0.815958789166667

00:00:26.080 --> 00:00:29.720 has also joined us and.

NOTE Confidence: 0.815958789166667

00:00:29.720 --> 00:00:31.905 Will help moderate the session

NOTE Confidence: 0.815958789166667

00:00:31.905 --> 00:00:34.700 together with low Heath and myself.

NOTE Confidence: 0.815958789166667

00:00:34.700 --> 00:00:37.470 So we will get started.

NOTE Confidence: 0.815958789166667

00:00:37.470 --> 00:00:41.134 The first, the first half of the talk

NOTE Confidence: 0.815958789166667

00:00:41.134 --> 00:00:45.168 will give some updates on cortisol
NOTE Confidence: 0.815958789166667

00:00:45.168 --> 00:00:48.188 therapy for hematologic malignancies,
NOTE Confidence: 0.815958789166667

00:00:48.190 --> 00:00:50.827 so I'm going to go ahead and get started,
NOTE Confidence: 0.815958789166667

00:00:50.830 --> 00:00:53.980 so thank you again for joining everyone.
NOTE Confidence: 0.815958789166667

00:00:53.980 --> 00:00:55.760 I will probably leave the
NOTE Confidence: 0.815958789166667

00:00:55.760 --> 00:00:57.184 questions for the end.
NOTE Confidence: 0.882645712

00:01:00.760 --> 00:01:03.870 So these are my disclosures.
NOTE Confidence: 0.875363766428572

00:01:05.900 --> 00:01:09.668 And just to to give everyone a little
NOTE Confidence: 0.875363766428572

00:01:09.668 --> 00:01:13.290 bit of a of a background today.
NOTE Confidence: 0.79119031

00:01:15.540 --> 00:01:17.500 I'm just going to show a general
NOTE Confidence: 0.79119031

00:01:17.500 --> 00:01:18.849 schematic for car T cells,
NOTE Confidence: 0.79119031

00:01:18.850 --> 00:01:22.770 so as you know, car T cell therapy.
NOTE Confidence: 0.79119031

00:01:22.770 --> 00:01:25.546 Has been approved in the last in the
NOTE Confidence: 0.79119031

00:01:25.546 --> 00:01:28.162 last five years to treat patients
NOTE Confidence: 0.79119031

00:01:28.162 --> 00:01:30.467 with him to logic malignancies.
NOTE Confidence: 0.79119031

00:01:30.470 --> 00:01:34.642 The the T cells are genetically modified

NOTE Confidence: 0.79119031

00:01:34.642 --> 00:01:38.406 to target tumor cells and this can be

NOTE Confidence: 0.79119031

00:01:38.406 --> 00:01:41.448 done in the absence of MHC one and two.

NOTE Confidence: 0.79119031

00:01:41.450 --> 00:01:44.194 Expression on the surface of the tumor cells.

NOTE Confidence: 0.79119031

00:01:44.200 --> 00:01:46.910 So there's a targeting domain.

NOTE Confidence: 0.79119031

00:01:46.910 --> 00:01:48.520 That binds to the antigen

NOTE Confidence: 0.79119031

00:01:48.520 --> 00:01:49.808 on the cell surface.

NOTE Confidence: 0.79119031

00:01:49.810 --> 00:01:51.046 There's a linker,

NOTE Confidence: 0.79119031

00:01:51.046 --> 00:01:53.106 and then there's a costimulatory

NOTE Confidence: 0.79119031

00:01:53.106 --> 00:01:55.530 domain that gives this car T cells,

NOTE Confidence: 0.79119031

00:01:55.530 --> 00:01:57.410 proliferative capacity,

NOTE Confidence: 0.79119031

00:01:57.410 --> 00:02:02.110 and AT cell activation domain.

NOTE Confidence: 0.79119031

00:02:02.110 --> 00:02:05.086 So we have currently multiple FDA

NOTE Confidence: 0.79119031

00:02:05.086 --> 00:02:08.110 approved car T cell therapies.

NOTE Confidence: 0.79119031

00:02:08.110 --> 00:02:11.463 It's hard to believe the majority of

NOTE Confidence: 0.79119031

00:02:11.463 --> 00:02:14.588 them are approved in the setting of.

NOTE Confidence: 0.79119031

00:02:14.590 --> 00:02:16.366 B cell lymphoma.
NOTE Confidence: 0.79119031

00:02:16.366 --> 00:02:19.918 So we have four products currently
NOTE Confidence: 0.79119031

00:02:19.918 --> 00:02:23.560 axicabtagene sailu so Brexit.
NOTE Confidence: 0.79119031

00:02:23.560 --> 00:02:26.675 Also counted in Merluza Lantis again coucil,
NOTE Confidence: 0.79119031

00:02:26.680 --> 00:02:29.355 and they're currently approved for
NOTE Confidence: 0.79119031

00:02:29.355 --> 00:02:31.495 patients with relapsed refractory
NOTE Confidence: 0.79119031

00:02:31.495 --> 00:02:34.364 B cell lymphoma after at least
NOTE Confidence: 0.79119031

00:02:34.364 --> 00:02:36.619 two lines of systemic therapy.
NOTE Confidence: 0.79119031

00:02:36.620 --> 00:02:38.645 Brecksville Cottage in was recently
NOTE Confidence: 0.79119031

00:02:38.645 --> 00:02:40.670 approved in patients with mantle
NOTE Confidence: 0.79119031

00:02:40.734 --> 00:02:42.840 cell lymphoma as well as in
NOTE Confidence: 0.79119031

00:02:42.840 --> 00:02:44.430 adults with relapsed refractory B.
NOTE Confidence: 0.79119031

00:02:44.430 --> 00:02:47.102 Cell A allows so these are two more
NOTE Confidence: 0.79119031

00:02:47.102 --> 00:02:49.498 recent approvals and then in the
NOTE Confidence: 0.79119031

00:02:49.498 --> 00:02:52.228 multiple myeloma arena the target
NOTE Confidence: 0.79119031

00:02:52.228 --> 00:02:57.010 is bmet and I'm happy to say that

NOTE Confidence: 0.79119031

00:02:57.010 --> 00:03:00.012 we not only have I decapped agenda

NOTE Confidence: 0.79119031

00:03:00.012 --> 00:03:02.010 cluzel approved in patients with

NOTE Confidence: 0.79119031

00:03:02.010 --> 00:03:04.390 with failed at least four lines of

NOTE Confidence: 0.79119031

00:03:04.390 --> 00:03:06.399 prior therapy but very recently.

NOTE Confidence: 0.79119031

00:03:06.400 --> 00:03:08.704 There's a new approval of Celtic

NOTE Confidence: 0.79119031

00:03:08.704 --> 00:03:12.400 captain or the Loosle in the same

NOTE Confidence: 0.79119031

00:03:12.400 --> 00:03:14.560 refractory patient population.

NOTE Confidence: 0.79119031

00:03:14.560 --> 00:03:16.737 So this is the summary of the

NOTE Confidence: 0.79119031

00:03:16.737 --> 00:03:19.030 efficacy after two lines of therapy

NOTE Confidence: 0.79119031

00:03:19.030 --> 00:03:21.180 for the currently approved products.

NOTE Confidence: 0.79119031

00:03:21.180 --> 00:03:22.524 As you can see,

NOTE Confidence: 0.79119031

00:03:22.524 --> 00:03:24.540 there are very high overall response

NOTE Confidence: 0.79119031

00:03:24.610 --> 00:03:26.670 rates from the three randomized

NOTE Confidence: 0.79119031

00:03:26.670 --> 00:03:27.906 phase three trials.

NOTE Confidence: 0.79119031

00:03:27.910 --> 00:03:30.785 Complete response rates vary anywhere

NOTE Confidence: 0.79119031

00:03:30.785 --> 00:03:35.132 between 40 to 58% and you can see that
NOTE Confidence: 0.79119031

00:03:35.132 --> 00:03:38.426 at two years about 40% of patients.
NOTE Confidence: 0.79119031

00:03:38.426 --> 00:03:41.116 There's a 40% progression free survival.
NOTE Confidence: 0.79119031

00:03:41.116 --> 00:03:42.724 Basically at two years,
NOTE Confidence: 0.79119031

00:03:42.730 --> 00:03:46.720 which is definitely not bad for.
NOTE Confidence: 0.79119031

00:03:46.720 --> 00:03:49.126 Refractory patient population
NOTE Confidence: 0.79119031

00:03:49.126 --> 00:03:52.334 that otherwise would have.
NOTE Confidence: 0.79119031

00:03:52.340 --> 00:03:56.020 Expected very poor outcomes.
NOTE Confidence: 0.79119031

00:03:56.020 --> 00:03:58.780 The toxicity is as you are
NOTE Confidence: 0.79119031

00:03:58.780 --> 00:04:01.110 familiar with by now are.
NOTE Confidence: 0.79119031

00:04:01.110 --> 00:04:03.618 Twofold cytokine release syndrome
NOTE Confidence: 0.79119031

00:04:03.618 --> 00:04:07.900 and neurologic toxicity, which.
NOTE Confidence: 0.79119031

00:04:07.900 --> 00:04:09.979 It happens in the majority of patients,
NOTE Confidence: 0.79119031

00:04:09.980 --> 00:04:10.512 however,
NOTE Confidence: 0.79119031

00:04:10.512 --> 00:04:14.236 grade three to four CRS and neurologic
NOTE Confidence: 0.79119031

00:04:14.236 --> 00:04:16.640 toxicity fortunately are less common,

NOTE Confidence: 0.79119031

00:04:16.640 --> 00:04:18.344 and there's some variability

NOTE Confidence: 0.79119031

00:04:18.344 --> 00:04:20.900 between the products in terms of

NOTE Confidence: 0.79119031

00:04:20.973 --> 00:04:23.139 the grades and severity of CRS,

NOTE Confidence: 0.79119031

00:04:23.140 --> 00:04:24.808 and neurologic toxicity.

NOTE Confidence: 0.8164898

00:04:26.850 --> 00:04:31.760 So what was exciting at this year's

NOTE Confidence: 0.8164898

00:04:31.760 --> 00:04:35.114 ASH was that there have been efforts

NOTE Confidence: 0.8164898

00:04:35.114 --> 00:04:38.690 made to move these CAR T cell

NOTE Confidence: 0.8164898

00:04:38.690 --> 00:04:41.825 therapies further up front in the

NOTE Confidence: 0.8164898

00:04:41.825 --> 00:04:44.280 treatment of patients with lymphoma.

NOTE Confidence: 0.8164898

00:04:44.280 --> 00:04:47.199 And you know the question arose well.

NOTE Confidence: 0.8164898

00:04:47.200 --> 00:04:49.108 Given that this type of therapy

NOTE Confidence: 0.8164898

00:04:49.108 --> 00:04:51.818 is doing so well in the relapse

NOTE Confidence: 0.8164898

00:04:51.818 --> 00:04:53.638 refracts that refractory setting,

NOTE Confidence: 0.8164898

00:04:53.640 --> 00:04:55.705 could it potentially replace autologous

NOTE Confidence: 0.8164898

00:04:55.705 --> 00:04:58.623 stem cell transplant so there were three

NOTE Confidence: 0.8164898

00:04:58.623 --> 00:05:00.993 studies that were presented and are
NOTE Confidence: 0.8164898

00:05:00.993 --> 00:05:02.967 currently published and those resume
NOTE Confidence: 0.8164898

00:05:02.967 --> 00:05:04.837 as seven with Axicabtagene sailu.
NOTE Confidence: 0.8164898

00:05:04.840 --> 00:05:07.618 So Belinda with the decision Cluzel
NOTE Confidence: 0.8164898

00:05:07.618 --> 00:05:10.398 and the transform study with Lisa
NOTE Confidence: 0.8164898

00:05:10.398 --> 00:05:12.898 Captain Marlow so and they looked at
NOTE Confidence: 0.8164898

00:05:12.898 --> 00:05:15.285 high risk diffuse large B cell lymphoma
NOTE Confidence: 0.8164898

00:05:15.285 --> 00:05:17.685 patients that were either refractory.
NOTE Confidence: 0.8164898

00:05:17.690 --> 00:05:19.010 First line treatment,
NOTE Confidence: 0.8164898

00:05:19.010 --> 00:05:21.210 which is usually our job.
NOTE Confidence: 0.8164898

00:05:21.210 --> 00:05:23.695 Or that relapse early after
NOTE Confidence: 0.8164898

00:05:23.695 --> 00:05:25.186 first line treatment,
NOTE Confidence: 0.8164898

00:05:25.190 --> 00:05:27.584 and patients were randomized to either
NOTE Confidence: 0.8164898

00:05:27.584 --> 00:05:30.048 cortisol therapy or the standard of
NOTE Confidence: 0.8164898

00:05:30.048 --> 00:05:32.442 care which is salvage therapy with
NOTE Confidence: 0.8164898

00:05:32.442 --> 00:05:34.339 autologous stem cell transplant.

NOTE Confidence: 0.84452435

00:05:37.400 --> 00:05:41.026 So I will start with Zooma 7.

NOTE Confidence: 0.84452435

00:05:41.030 --> 00:05:43.784 Basically, this is again an autologous

NOTE Confidence: 0.84452435

00:05:43.784 --> 00:05:46.483 second generation CD19 directed car T

NOTE Confidence: 0.84452435

00:05:46.483 --> 00:05:48.453 cell therapy that's currently approved

NOTE Confidence: 0.84452435

00:05:48.453 --> 00:05:52.205 after two lines of therapy and in the

NOTE Confidence: 0.84452435

00:05:52.205 --> 00:05:55.895 study design is that patients had

NOTE Confidence: 0.84452435

00:05:55.895 --> 00:05:58.382 relapsed refractory disease within 12

NOTE Confidence: 0.84452435

00:05:58.382 --> 00:06:01.190 months of adequate first line chemo

NOTE Confidence: 0.84452435

00:06:01.268 --> 00:06:03.683 immunotherapy and that were intended

NOTE Confidence: 0.84452435

00:06:03.683 --> 00:06:06.611 to proceed to autologous stem cell

NOTE Confidence: 0.84452435

00:06:06.611 --> 00:06:09.158 transplant so they were stratified

NOTE Confidence: 0.84452435

00:06:09.158 --> 00:06:11.938 by first line treatment response.

NOTE Confidence: 0.84452435

00:06:11.940 --> 00:06:15.559 And second line age adjusted it be

NOTE Confidence: 0.84452435

00:06:15.560 --> 00:06:19.584 they were in demised access L 2 * 10

NOTE Confidence: 0.84452435

00:06:19.584 --> 00:06:22.124 to the 6th chord, T cells per KG.

NOTE Confidence: 0.84452435

00:06:22.124 --> 00:06:23.828 After receiving some Lymphodepletion
NOTE Confidence: 0.84452435

00:06:23.828 --> 00:06:24.680 Kiem Lympho,
NOTE Confidence: 0.84452435

00:06:24.680 --> 00:06:26.604 depleting chemotherapy and cytoxan,
NOTE Confidence: 0.84452435

00:06:26.604 --> 00:06:30.476 or the standard of care which was two
NOTE Confidence: 0.84452435

00:06:30.476 --> 00:06:33.194 to three cycles of investigator selected.
NOTE Confidence: 0.84452435

00:06:33.200 --> 00:06:34.472 Usually platinum based chemotherapy.
NOTE Confidence: 0.84452435

00:06:34.472 --> 00:06:36.880 'cause that's what we use in practice,
NOTE Confidence: 0.84452435

00:06:36.880 --> 00:06:40.160 either rice or our depth.
NOTE Confidence: 0.84452435

00:06:40.160 --> 00:06:43.490 And patients that achieved either complete
NOTE Confidence: 0.84452435

00:06:43.490 --> 00:06:47.125 or partial response went on to achieve
NOTE Confidence: 0.84452435

00:06:47.125 --> 00:06:49.777 to receive a stem cell transplant.
NOTE Confidence: 0.84452435

00:06:49.780 --> 00:06:52.210 Whereas patients that did not achieve
NOTE Confidence: 0.84452435

00:06:52.210 --> 00:06:55.795 a CR or PR were off protocol and
NOTE Confidence: 0.84452435

00:06:55.795 --> 00:06:59.275 this is important as you'll see in a
NOTE Confidence: 0.84452435

00:06:59.275 --> 00:07:01.542 distinction with Belinda trial this
NOTE Confidence: 0.84452435

00:07:01.542 --> 00:07:05.100 the Zuma seven study did not allow for

NOTE Confidence: 0.84452435

00:07:05.100 --> 00:07:08.096 any bridging therapy prior to car T.

NOTE Confidence: 0.84452435

00:07:08.100 --> 00:07:10.400 And there was no crossover,

NOTE Confidence: 0.84452435

00:07:10.400 --> 00:07:12.633 so patients who did not respond and

NOTE Confidence: 0.84452435

00:07:12.633 --> 00:07:15.227 could not go on to transplant or

NOTE Confidence: 0.84452435

00:07:15.227 --> 00:07:18.776 did not crossover to the Axis alarm.

NOTE Confidence: 0.84452435

00:07:18.780 --> 00:07:21.676 Some of them actually 56% did receive

NOTE Confidence: 0.84452435

00:07:21.676 --> 00:07:23.416 subsequent cellular in no therapy.

NOTE Confidence: 0.84452435

00:07:23.420 --> 00:07:26.535 But that was not done on trial.

NOTE Confidence: 0.84452435

00:07:26.540 --> 00:07:29.180 So you know what happened to these patients?

NOTE Confidence: 0.84452435

00:07:29.180 --> 00:07:29.706 Well,

NOTE Confidence: 0.84452435

00:07:29.706 --> 00:07:33.404 you see that they enrolled 359 a

NOTE Confidence: 0.84452435

00:07:33.404 --> 00:07:35.000 180 received access.

NOTE Confidence: 0.84452435

00:07:35.000 --> 00:07:35.560 Actually,

NOTE Confidence: 0.84452435

00:07:35.560 --> 00:07:38.360 we randomized accela 179 the

NOTE Confidence: 0.84452435

00:07:38.360 --> 00:07:40.040 standard of care,

NOTE Confidence: 0.84452435

00:07:40.040 --> 00:07:41.972 and then when you look at what
NOTE Confidence: 0.84452435

00:07:41.972 --> 00:07:46.120 happened to them out of 100 and 8178
NOTE Confidence: 0.84452435

00:07:46.120 --> 00:07:49.312 underwent leukapheresis 172 receiving
NOTE Confidence: 0.84452435

00:07:49.312 --> 00:07:52.104 for depletion chemotherapy and 170
NOTE Confidence: 0.84452435

00:07:52.104 --> 00:07:53.880 received access selling fusion.
NOTE Confidence: 0.84452435

00:07:53.880 --> 00:07:56.526 So 94% of the starting patients.
NOTE Confidence: 0.84452435

00:07:56.530 --> 00:07:59.395 Actually received access out which
NOTE Confidence: 0.84452435

00:07:59.395 --> 00:08:01.687 they were randomized to,
NOTE Confidence: 0.84452435

00:08:01.690 --> 00:08:03.970 whereas in the standard of care
NOTE Confidence: 0.84452435

00:08:03.970 --> 00:08:07.760 arm out of 179 patients.
NOTE Confidence: 0.84452435

00:08:07.760 --> 00:08:12.248 Only about 64 of them received.
NOTE Confidence: 0.84452435

00:08:12.250 --> 00:08:14.090 Stem cell trench transplant,
NOTE Confidence: 0.84452435

00:08:14.090 --> 00:08:16.330 which is 36% of patients,
NOTE Confidence: 0.84452435

00:08:16.330 --> 00:08:18.970 and this actually is not uncommon
NOTE Confidence: 0.84452435

00:08:18.970 --> 00:08:21.977 in clinical practice because many
NOTE Confidence: 0.84452435

00:08:21.977 --> 00:08:24.826 of these patients end up for one

NOTE Confidence: 0.84452435
00:08:24.826 --> 00:08:26.430 reason or another.
NOTE Confidence: 0.84452435
00:08:26.430 --> 00:08:29.028 Not responding to the salvage chemotherapy,
NOTE Confidence: 0.84452435
00:08:29.030 --> 00:08:31.450 or they develop organ toxicity.
NOTE Confidence: 0.84452435
00:08:31.450 --> 00:08:32.978 They may not have.
NOTE Confidence: 0.84452435
00:08:32.978 --> 00:08:35.078 By that point, their lympho depleted,
NOTE Confidence: 0.84452435
00:08:35.078 --> 00:08:37.750 so they may not have fit T cells.
NOTE Confidence: 0.84452435
00:08:37.750 --> 00:08:38.686 They may not.
NOTE Confidence: 0.84452435
00:08:38.686 --> 00:08:40.870 They may not have fit stem cells
NOTE Confidence: 0.84452435
00:08:40.941 --> 00:08:42.908 for us to be able to collect.
NOTE Confidence: 0.84452435
00:08:42.910 --> 00:08:46.870 So a minority actually made it to transplant.
NOTE Confidence: 0.84452435
00:08:46.870 --> 00:08:49.888 So when we look at the
NOTE Confidence: 0.84452435
00:08:49.890 --> 00:08:50.942 baseline characteristics,
NOTE Confidence: 0.84452435
00:08:50.942 --> 00:08:53.572 they were pretty well distributed
NOTE Confidence: 0.84452435
00:08:53.572 --> 00:08:55.150 among the groups.
NOTE Confidence: 0.84452435
00:08:55.150 --> 00:08:56.734 As you can see,
NOTE Confidence: 0.84452435

00:08:56.734 --> 00:08:59.590 74% of patients were primary refractory.
NOTE Confidence: 0.84452435

00:08:59.590 --> 00:09:02.116 And then 26% of patients had
NOTE Confidence: 0.84452435

00:09:02.116 --> 00:09:04.490 relapsed within a 12 months.
NOTE Confidence: 0.84452435

00:09:04.490 --> 00:09:07.210 There were some high grade B cell lymphomas,
NOTE Confidence: 0.84452435

00:09:07.210 --> 00:09:09.350 including double and triple hit,
NOTE Confidence: 0.84452435

00:09:09.350 --> 00:09:11.470 17% dual over X pressers,
NOTE Confidence: 0.84452435

00:09:11.470 --> 00:09:14.530 and Mick rearranged patients.
NOTE Confidence: 0.84452435

00:09:14.530 --> 00:09:17.509 So when we look at the event free survival,
NOTE Confidence: 0.84452435

00:09:17.510 --> 00:09:18.754 which was their primary
NOTE Confidence: 0.84452435

00:09:18.754 --> 00:09:20.309 end point for the study,
NOTE Confidence: 0.84452435

00:09:20.310 --> 00:09:22.818 you can see that the 24
NOTE Confidence: 0.84452435

00:09:22.818 --> 00:09:24.840 month event free survival was
NOTE Confidence: 0.818740913

00:09:24.840 --> 00:09:27.385 40.5% in the access of
NOTE Confidence: 0.818740913

00:09:27.385 --> 00:09:29.930 ARM compared to only 16.
NOTE Confidence: 0.818740913

00:09:29.930 --> 00:09:32.240 .3% in the standard of care arm,
NOTE Confidence: 0.818740913

00:09:32.240 --> 00:09:34.487 and that was actually true when they

NOTE Confidence: 0.818740913

00:09:34.487 --> 00:09:36.650 looked at each of the individual.

NOTE Confidence: 0.818740913

00:09:36.650 --> 00:09:39.812 Subgroups by age response to first

NOTE Confidence: 0.818740913

00:09:39.812 --> 00:09:42.082 line therapy and whether they had

NOTE Confidence: 0.818740913

00:09:42.082 --> 00:09:43.900 high grades at B cell lymphoma,

NOTE Confidence: 0.818740913

00:09:43.900 --> 00:09:44.966 including double,

NOTE Confidence: 0.818740913

00:09:44.966 --> 00:09:48.164 triple hit or double expresser lymphoma.

NOTE Confidence: 0.818740913

00:09:48.170 --> 00:09:51.194 And when you look at the

NOTE Confidence: 0.818740913

00:09:51.194 --> 00:09:52.706 complete response rates,

NOTE Confidence: 0.818740913

00:09:52.710 --> 00:09:55.694 so overall response was 83% in

NOTE Confidence: 0.818740913

00:09:55.694 --> 00:09:58.230 the access alarm and 50% in

NOTE Confidence: 0.818740913

00:09:58.230 --> 00:10:00.430 standard of care and complete

NOTE Confidence: 0.818740913

00:10:00.430 --> 00:10:05.518 remission rates were 65 versus 32%.

NOTE Confidence: 0.818740913

00:10:05.520 --> 00:10:09.384 So there is some confounding in terms of

NOTE Confidence: 0.818740913

00:10:09.384 --> 00:10:13.298 looking at the overall survival benefits,

NOTE Confidence: 0.818740913

00:10:13.300 --> 00:10:15.570 because as I mentioned earlier,

NOTE Confidence: 0.818740913

00:10:15.570 --> 00:10:17.652 56% of patients in the standard
NOTE Confidence: 0.818740913

00:10:17.652 --> 00:10:19.723 of care arm received subsequent
NOTE Confidence: 0.818740913

00:10:19.723 --> 00:10:22.179 cellular immunotherapy of protocol.
NOTE Confidence: 0.818740913

00:10:22.180 --> 00:10:25.300 So this is the event free survival curve,
NOTE Confidence: 0.818740913

00:10:25.300 --> 00:10:29.158 here again showing a dramatic improvement.
NOTE Confidence: 0.818740913

00:10:29.160 --> 00:10:31.830 Median event free survival two months
NOTE Confidence: 0.818740913

00:10:31.830 --> 00:10:34.638 versus 8.3 months in the access arm,
NOTE Confidence: 0.818740913

00:10:34.640 --> 00:10:37.020 the hazard ratio favored accessible
NOTE Confidence: 0.818740913

00:10:37.020 --> 00:10:40.280 for all of the different subgroups,
NOTE Confidence: 0.818740913

00:10:40.280 --> 00:10:45.500 including really high risk disease.
NOTE Confidence: 0.818740913

00:10:45.500 --> 00:10:45.992 Again,
NOTE Confidence: 0.818740913

00:10:45.992 --> 00:10:48.944 this is reflected in the progression
NOTE Confidence: 0.818740913

00:10:48.944 --> 00:10:51.579 free survival curves that separated
NOTE Confidence: 0.818740913

00:10:51.580 --> 00:10:54.124 and then when you look at the median
NOTE Confidence: 0.818740913

00:10:54.124 --> 00:10:56.281 overall survival was 35 months in
NOTE Confidence: 0.818740913

00:10:56.281 --> 00:10:59.809 the standard of care arm and it was

NOTE Confidence: 0.818740913

00:10:59.809 --> 00:11:02.868 not reached in the axle arm and.

NOTE Confidence: 0.818740913

00:11:02.870 --> 00:11:03.986 You know it,

NOTE Confidence: 0.818740913

00:11:03.986 --> 00:11:07.220 it's going again to be difficult to to see.

NOTE Confidence: 0.818740913

00:11:07.220 --> 00:11:10.104 It's curbs here that in terms of

NOTE Confidence: 0.818740913

00:11:10.104 --> 00:11:12.512 overall survival that are dramatically

NOTE Confidence: 0.818740913

00:11:12.512 --> 00:11:14.700 different from each other.

NOTE Confidence: 0.818740913

00:11:14.700 --> 00:11:17.310 So again,

NOTE Confidence: 0.818740913

00:11:17.310 --> 00:11:19.638 nearly three times more patients that

NOTE Confidence: 0.818740913

00:11:19.638 --> 00:11:22.083 were randomized to access L received

NOTE Confidence: 0.818740913

00:11:22.083 --> 00:11:24.573 definitive therapy versus standard of care,

NOTE Confidence: 0.818740913

00:11:24.580 --> 00:11:26.794 and there was a significant improvement

NOTE Confidence: 0.818740913

00:11:26.794 --> 00:11:29.037 in event free survival and response

NOTE Confidence: 0.818740913

00:11:29.037 --> 00:11:31.137 rate compared to standard of care.

NOTE Confidence: 0.818740913

00:11:31.140 --> 00:11:33.876 So this Soma 7 May actually mark a

NOTE Confidence: 0.818740913

00:11:33.876 --> 00:11:36.195 paradigm shift where you access L

NOTE Confidence: 0.818740913

00:11:36.195 --> 00:11:38.855 should be considered the new standard of
NOTE Confidence: 0.818740913

00:11:38.855 --> 00:11:41.980 care for patients with second line relapse.
NOTE Confidence: 0.818740913

00:11:41.980 --> 00:11:45.230 Refractory large B cell lymphoma.
NOTE Confidence: 0.818740913

00:11:45.230 --> 00:11:47.090 This is the transform study,
NOTE Confidence: 0.818740913

00:11:47.090 --> 00:11:49.386 so it looked at Lisa Captain Marlow,
NOTE Confidence: 0.818740913

00:11:49.390 --> 00:11:51.757 so I will not go into a lot of
NOTE Confidence: 0.818740913

00:11:51.757 --> 00:11:53.949 detail because it's very similar,
NOTE Confidence: 0.818740913

00:11:53.950 --> 00:11:56.767 but the I just want to point out that
NOTE Confidence: 0.818740913

00:11:56.767 --> 00:11:59.578 this car T cell therapy is slightly
NOTE Confidence: 0.818740913

00:11:59.578 --> 00:12:01.714 different from access L because
NOTE Confidence: 0.818740913

00:12:01.714 --> 00:12:04.402 there's a defined composition of CD8
NOTE Confidence: 0.818740913

00:12:04.402 --> 00:12:08.210 and CD4T cell components that are.
NOTE Confidence: 0.818740913

00:12:08.210 --> 00:12:09.232 Expanded separately,
NOTE Confidence: 0.818740913

00:12:09.232 --> 00:12:11.787 and then they're administered to
NOTE Confidence: 0.818740913

00:12:11.787 --> 00:12:14.910 the patient in equal target dosing.
NOTE Confidence: 0.818740913

00:12:14.910 --> 00:12:18.534 So when we looked at the study design,

NOTE Confidence: 0.818740913

00:12:18.540 --> 00:12:20.043 it's very similar.

NOTE Confidence: 0.818740913

00:12:20.043 --> 00:12:23.049 This did allow some bridging therapy,

NOTE Confidence: 0.818740913

00:12:23.050 --> 00:12:25.318 but then they.

NOTE Confidence: 0.818740913

00:12:25.320 --> 00:12:29.220 Performed a pet scan prior to

NOTE Confidence: 0.818740913

00:12:29.220 --> 00:12:32.600 LYMPHODEPLETION and Light and Lisle.

NOTE Confidence: 0.818740913

00:12:32.600 --> 00:12:35.296 And if there was no response by 9

NOTE Confidence: 0.818740913

00:12:35.296 --> 00:12:37.898 weeks or progression at anytime,

NOTE Confidence: 0.818740913

00:12:37.900 --> 00:12:43.740 a crossover to the lysis alarm was allowed.

NOTE Confidence: 0.818740913

00:12:43.740 --> 00:12:46.617 So when you look at the event

NOTE Confidence: 0.818740913

00:12:46.617 --> 00:12:49.044 free survival again with a median

NOTE Confidence: 0.818740913

00:12:49.044 --> 00:12:50.636 follow-up of six months,

NOTE Confidence: 0.818740913

00:12:50.640 --> 00:12:53.005 there was a significant improvement

NOTE Confidence: 0.818740913

00:12:53.005 --> 00:12:57.606 in event free survival of 63.3%

NOTE Confidence: 0.818740913

00:12:57.606 --> 00:13:01.428 compared to 33.4% at six months,

NOTE Confidence: 0.818740913

00:13:01.428 --> 00:13:04.519 and that held continue to hold at 12

NOTE Confidence: 0.818740913

00:13:04.519 --> 00:13:07.242 months even though there was some decline.

NOTE Confidence: 0.818740913

00:13:07.250 --> 00:13:11.133 So 44.5% versus 23.7%.

NOTE Confidence: 0.818740913

00:13:11.133 --> 00:13:13.498 Now again very similar results.

NOTE Confidence: 0.818740913

00:13:13.500 --> 00:13:17.329 So what we saw in Zuma 7?

NOTE Confidence: 0.818740913

00:13:17.330 --> 00:13:19.542 The complete response rates

NOTE Confidence: 0.818740913

00:13:19.542 --> 00:13:22.307 in the Lisle arm were

NOTE Confidence: 0.945483056666667

00:13:22.310 --> 00:13:24.710 66% versus only 39% in

NOTE Confidence: 0.945483056666667

00:13:24.710 --> 00:13:27.220 the standard of care arm.

NOTE Confidence: 0.87196846

00:13:29.830 --> 00:13:32.350 This is progression free survival.

NOTE Confidence: 0.87196846

00:13:32.350 --> 00:13:36.316 Again, even looking at 12 month

NOTE Confidence: 0.87196846

00:13:36.316 --> 00:13:40.580 data that is 52% in the Lisle

NOTE Confidence: 0.87196846

00:13:40.580 --> 00:13:44.014 arm compared to 33.9% in the in.

NOTE Confidence: 0.87196846

00:13:44.014 --> 00:13:46.169 The standard of care arm.

NOTE Confidence: 0.87196846

00:13:46.170 --> 00:13:49.224 So significant improvement in PFS median

NOTE Confidence: 0.87196846

00:13:49.224 --> 00:13:53.587 PFS in the light in the Lysol CAP to gene.

NOTE Confidence: 0.87196846

00:13:53.590 --> 00:13:58.790 The lysis alarm was 14.8 months.

NOTE Confidence: 0.87196846

00:13:58.790 --> 00:14:01.050 Versus only 5.7 months in

NOTE Confidence: 0.87196846

00:14:01.050 --> 00:14:03.310 the standard of care arm,

NOTE Confidence: 0.87196846

00:14:03.310 --> 00:14:07.147 which was the transplant arm and

NOTE Confidence: 0.87196846

00:14:07.147 --> 00:14:11.509 you know this is overall survival.

NOTE Confidence: 0.87196846

00:14:11.510 --> 00:14:14.546 Median overall survival was not reached

NOTE Confidence: 0.87196846

00:14:14.546 --> 00:14:17.956 in the Lisle arm and it was 16.4

NOTE Confidence: 0.87196846

00:14:17.956 --> 00:14:20.658 months in the standard of care arm.

NOTE Confidence: 0.778544301428571

00:14:24.480 --> 00:14:29.240 The third phase three study was Belinda,

NOTE Confidence: 0.778544301428571

00:14:29.240 --> 00:14:31.448 which this is kymriah.

NOTE Confidence: 0.778544301428571

00:14:31.448 --> 00:14:35.428 Basically the autologous CD19 CAR T cell

NOTE Confidence: 0.778544301428571

00:14:35.428 --> 00:14:38.838 therapy and this is the study design.

NOTE Confidence: 0.778544301428571

00:14:38.840 --> 00:14:40.046 Patients were looking

NOTE Confidence: 0.778544301428571

00:14:40.046 --> 00:14:41.654 for ease that screening.

NOTE Confidence: 0.778544301428571

00:14:41.660 --> 00:14:44.360 They did receive optional bridging

NOTE Confidence: 0.778544301428571

00:14:44.360 --> 00:14:49.200 with a platinum based chemotherapy and.

NOTE Confidence: 0.778544301428571

00:14:49.200 --> 00:14:52.128 The standard of care arm received
NOTE Confidence: 0.778544301428571

00:14:52.130 --> 00:14:56.250 salvage rice or or depth
NOTE Confidence: 0.778544301428571

00:14:56.250 --> 00:14:58.438 investigators investigators choice.
NOTE Confidence: 0.778544301428571

00:14:58.438 --> 00:15:03.280 They then underwent a week week six pet scan,
NOTE Confidence: 0.778544301428571

00:15:03.280 --> 00:15:06.718 and then they were they received
NOTE Confidence: 0.778544301428571

00:15:06.718 --> 00:15:08.437 either to sigend,
NOTE Confidence: 0.778544301428571

00:15:08.440 --> 00:15:11.710 occlusal or standard of Care now the
NOTE Confidence: 0.778544301428571

00:15:11.710 --> 00:15:13.685 difference here being that patients
NOTE Confidence: 0.778544301428571

00:15:13.685 --> 00:15:16.485 who did not achieve a complete
NOTE Confidence: 0.778544301428571

00:15:16.485 --> 00:15:19.045 remission actually ended up receiving.
NOTE Confidence: 0.778544301428571

00:15:19.050 --> 00:15:22.055 Multiple lines of platinum based
NOTE Confidence: 0.778544301428571

00:15:22.055 --> 00:15:24.340 therapy and including a different
NOTE Confidence: 0.778544301428571

00:15:24.340 --> 00:15:26.440 platinum based therapy altogether so
NOTE Confidence: 0.778544301428571

00:15:26.440 --> 00:15:29.428 they may have had two different two or
NOTE Confidence: 0.778544301428571

00:15:29.428 --> 00:15:31.449 three different salvage regimens here.
NOTE Confidence: 0.778544301428571

00:15:31.450 --> 00:15:33.490 By the time they actually made

NOTE Confidence: 0.778544301428571
00:15:33.490 --> 00:15:37.389 it to stem cell transplant.
NOTE Confidence: 0.778544301428571
00:15:37.390 --> 00:15:37.950 And.
NOTE Confidence: 0.942135833333333
00:15:40.290 --> 00:15:44.454 The fact that. They looked at this.
NOTE Confidence: 0.942135833333333
00:15:44.454 --> 00:15:47.499 They they based a lot of the UM.
NOTE Confidence: 0.942135833333333
00:15:47.500 --> 00:15:52.529 A lot of the criteria for non response
NOTE Confidence: 0.942135833333333
00:15:52.529 --> 00:15:55.490 on the Week 6 assessment actually did
NOTE Confidence: 0.942135833333333
00:15:55.572 --> 00:15:58.628 affect the outcomes as I will show you.
NOTE Confidence: 0.942135833333333
00:15:58.630 --> 00:16:02.406 So the patient characteristics
NOTE Confidence: 0.942135833333333
00:16:02.406 --> 00:16:04.358 were relatively equally
NOTE Confidence: 0.942135833333333
00:16:04.358 --> 00:16:06.878 distributed between the two arms.
NOTE Confidence: 0.942135833333333
00:16:06.880 --> 00:16:09.538 The median time from initial diagnosis.
NOTE Confidence: 0.942135833333333
00:16:09.540 --> 00:16:11.188 The randomization was similar
NOTE Confidence: 0.942135833333333
00:16:11.188 --> 00:16:13.660 about 8 months in both groups
NOTE Confidence: 0.942135833333333
00:16:13.660 --> 00:16:15.844 and the median time from the most
NOTE Confidence: 0.942135833333333
00:16:15.844 --> 00:16:17.781 recent relapse or progression to
NOTE Confidence: 0.942135833333333

00:16:17.781 --> 00:16:19.990 randomization was about 1.4 months.
NOTE Confidence: 0.9421358333333333

00:16:19.990 --> 00:16:22.408 In the decision Lochloosa and 1.1
NOTE Confidence: 0.9421358333333333

00:16:22.408 --> 00:16:25.124 months in the standard of care arm.
NOTE Confidence: 0.9421358333333333

00:16:25.130 --> 00:16:28.196 So if you look now at,
NOTE Confidence: 0.9421358333333333

00:16:28.200 --> 00:16:30.426 you know what patients are received.
NOTE Confidence: 0.9421358333333333

00:16:30.430 --> 00:16:32.854 You can see that in the
NOTE Confidence: 0.9421358333333333

00:16:32.854 --> 00:16:34.470 T sigend occlusal arm,
NOTE Confidence: 0.9421358333333333

00:16:34.470 --> 00:16:36.835 almost 50% of patients received
NOTE Confidence: 0.9421358333333333

00:16:36.835 --> 00:16:40.460 more than one cycle of.
NOTE Confidence: 0.9421358333333333

00:16:40.460 --> 00:16:43.060 Chemotherapy prior to their lymphodepletion
NOTE Confidence: 0.9421358333333333

00:16:43.060 --> 00:16:46.659 and then in the standard of care arm,
NOTE Confidence: 0.9421358333333333

00:16:46.660 --> 00:16:49.295 97% of patients received multiple
NOTE Confidence: 0.9421358333333333

00:16:49.295 --> 00:16:50.876 cycles of chemotherapy,
NOTE Confidence: 0.9421358333333333

00:16:50.880 --> 00:16:51.840 and, importantly,
NOTE Confidence: 0.9421358333333333

00:16:51.840 --> 00:16:55.200 the median time to the actual infusion
NOTE Confidence: 0.9421358333333333

00:16:55.200 --> 00:16:58.842 of the T cells and that isagen occlusal

NOTE Confidence: 0.9421358333333333

00:16:58.842 --> 00:17:02.059 arm was extremely long at 52 days and

NOTE Confidence: 0.9421358333333333

00:17:02.059 --> 00:17:05.520 even in the United States was 41 days.

NOTE Confidence: 0.9421358333333333

00:17:05.520 --> 00:17:07.860 But particularly in Europe,

NOTE Confidence: 0.9421358333333333

00:17:07.860 --> 00:17:10.785 was longer at 57 days.

NOTE Confidence: 0.9421358333333333

00:17:10.790 --> 00:17:12.950 So when they looked,

NOTE Confidence: 0.9421358333333333

00:17:12.950 --> 00:17:13.490 surprisingly,

NOTE Confidence: 0.9421358333333333

00:17:13.490 --> 00:17:15.834 when they looked at the event free survival,

NOTE Confidence: 0.9421358333333333

00:17:15.840 --> 00:17:17.830 which was their primary endpoint,

NOTE Confidence: 0.9421358333333333

00:17:17.830 --> 00:17:19.794 that was actually disappointingly

NOTE Confidence: 0.9421358333333333

00:17:19.794 --> 00:17:22.740 the same in both the tisagenlecleucel

NOTE Confidence: 0.9421358333333333

00:17:22.818 --> 00:17:27.070 and standard of care arm, so.

NOTE Confidence: 0.9421358333333333

00:17:27.070 --> 00:17:29.268 You know why? Why did this happen?

NOTE Confidence: 0.9421358333333333

00:17:29.270 --> 00:17:30.034 I mean,

NOTE Confidence: 0.9421358333333333

00:17:30.034 --> 00:17:32.326 why was this study different from

NOTE Confidence: 0.9421358333333333

00:17:32.326 --> 00:17:35.219 the prior to when you look at the

NOTE Confidence: 0.9421358333333333

00:17:35.219 --> 00:17:38.094 Week 6 assessment that they did after
NOTE Confidence: 0.9421358333333333

00:17:38.094 --> 00:17:39.938 these patients received bridging
NOTE Confidence: 0.9421358333333333

00:17:39.938 --> 00:17:42.469 therapy or salvage chemotherapy,
NOTE Confidence: 0.9421358333333333

00:17:42.470 --> 00:17:44.654 you can see that in that isagen
NOTE Confidence: 0.9421358333333333

00:17:44.654 --> 00:17:45.278 lochloosa ORM.
NOTE Confidence: 0.9071260133333333

00:17:48.290 --> 00:17:50.990 26% of patients actually had
NOTE Confidence: 0.9071260133333333

00:17:50.990 --> 00:17:53.150 progressive disease compared to
NOTE Confidence: 0.9071260133333333

00:17:53.150 --> 00:17:55.124 14% in the standard of care arm,
NOTE Confidence: 0.9071260133333333

00:17:55.130 --> 00:17:57.445 so they progressed before they
NOTE Confidence: 0.9071260133333333

00:17:57.445 --> 00:18:00.433 were able to receive the lympho
NOTE Confidence: 0.9071260133333333

00:18:00.433 --> 00:18:02.789 depleting regimen and Corti.
NOTE Confidence: 0.9071260133333333

00:18:02.790 --> 00:18:07.295 So they they investigators for
NOTE Confidence: 0.9071260133333333

00:18:07.295 --> 00:18:10.640 the study did point that out,
NOTE Confidence: 0.9071260133333333

00:18:10.640 --> 00:18:12.565 that the progressive disease at
NOTE Confidence: 0.9071260133333333

00:18:12.565 --> 00:18:15.019 week six was more frequent in
NOTE Confidence: 0.9071260133333333

00:18:15.019 --> 00:18:17.014 patients in that isagen lochloosa

NOTE Confidence: 0.907126013333333

00:18:17.086 --> 00:18:21.510 arm versus the standard of care and.

NOTE Confidence: 0.907126013333333

00:18:21.510 --> 00:18:24.186 There were multiple meetings and and

NOTE Confidence: 0.907126013333333

00:18:24.186 --> 00:18:27.369 experts in the field were asked about

NOTE Confidence: 0.907126013333333

00:18:27.369 --> 00:18:30.435 why they thought that Belinda failed to

NOTE Confidence: 0.907126013333333

00:18:30.521 --> 00:18:33.888 show an improvement in event free survival.

NOTE Confidence: 0.907126013333333

00:18:33.890 --> 00:18:36.270 And there are several factors for this

NOTE Confidence: 0.907126013333333

00:18:36.270 --> 00:18:38.907 that I'm sure will guide their the

NOTE Confidence: 0.907126013333333

00:18:38.907 --> 00:18:41.223 development of future trials for them.

NOTE Confidence: 0.907126013333333

00:18:41.230 --> 00:18:43.300 So the first was the longtime

NOTE Confidence: 0.907126013333333

00:18:43.300 --> 00:18:45.563 to infusion with that Kymriah in

NOTE Confidence: 0.907126013333333

00:18:45.563 --> 00:18:49.740 Belinda 52 days compared to 29 days

NOTE Confidence: 0.907126013333333

00:18:49.740 --> 00:18:51.930 with this card and Zuma 7.

NOTE Confidence: 0.907126013333333

00:18:51.930 --> 00:18:53.448 Abelinda allowed multiple

NOTE Confidence: 0.907126013333333

00:18:53.448 --> 00:18:54.966 lines of chemotherapy,

NOTE Confidence: 0.907126013333333

00:18:54.970 --> 00:18:56.371 as bridging therapy,

NOTE Confidence: 0.907126013333333

00:18:56.371 --> 00:18:58.239 which was different from
NOTE Confidence: 0.9071260133333333

00:18:58.239 --> 00:19:00.560 Zuma 7 and transform.
NOTE Confidence: 0.9071260133333333

00:19:00.560 --> 00:19:03.335 And Belinda also used lower
NOTE Confidence: 0.9071260133333333

00:19:03.335 --> 00:19:06.110 dosing of lympho depleting agents,
NOTE Confidence: 0.9071260133333333

00:19:06.110 --> 00:19:08.426 which are important for to obtain
NOTE Confidence: 0.9071260133333333

00:19:08.426 --> 00:19:10.458 Disease Control in these patients
NOTE Confidence: 0.9071260133333333

00:19:10.458 --> 00:19:12.972 that are not as heavily pretreated
NOTE Confidence: 0.9071260133333333

00:19:12.972 --> 00:19:15.477 right because these patients had only
NOTE Confidence: 0.9071260133333333

00:19:15.477 --> 00:19:17.829 received one prior line of therapy.
NOTE Confidence: 0.9071260133333333

00:19:17.830 --> 00:19:18.970 So in Belinda,
NOTE Confidence: 0.9071260133333333

00:19:18.970 --> 00:19:21.250 Cytosan was only 900 milligram per
NOTE Confidence: 0.9071260133333333

00:19:21.250 --> 00:19:23.368 meter squared over three days,
NOTE Confidence: 0.9071260133333333

00:19:23.370 --> 00:19:26.387 and fludarabine was 75 per meter squared,
NOTE Confidence: 0.9071260133333333

00:19:26.390 --> 00:19:28.832 whereas the other two trials had
NOTE Confidence: 0.9071260133333333

00:19:28.832 --> 00:19:31.198 a higher cytoxin dose of 1500
NOTE Confidence: 0.9071260133333333

00:19:31.198 --> 00:19:33.230 milligrams and 90 milligrams.

NOTE Confidence: 0.907126013333333

00:19:33.230 --> 00:19:35.780 Perimeter squared off loader being

NOTE Confidence: 0.907126013333333

00:19:35.780 --> 00:19:38.420 over three days. There were some.

NOTE Confidence: 0.907126013333333

00:19:38.420 --> 00:19:39.900 There were some differences

NOTE Confidence: 0.907126013333333

00:19:39.900 --> 00:19:41.010 in disease criteria.

NOTE Confidence: 0.907126013333333

00:19:41.010 --> 00:19:42.830 So Zuma 7 for example,

NOTE Confidence: 0.907126013333333

00:19:42.830 --> 00:19:45.866 enrolled only diffuse large B cell

NOTE Confidence: 0.907126013333333

00:19:45.866 --> 00:19:48.032 lymphoma patients whereas transform

NOTE Confidence: 0.907126013333333

00:19:48.032 --> 00:19:50.600 and Belinda allowed patients

NOTE Confidence: 0.907126013333333

00:19:50.600 --> 00:19:53.168 with 3B follicular lymphoma,

NOTE Confidence: 0.907126013333333

00:19:53.170 --> 00:19:56.290 which one could argue may be less aggressive.

NOTE Confidence: 0.907126013333333

00:19:56.290 --> 00:19:59.428 And the Belinda Trials definition of

NOTE Confidence: 0.907126013333333

00:19:59.428 --> 00:20:02.092 event free survival actually counts

NOTE Confidence: 0.907126013333333

00:20:02.092 --> 00:20:05.322 failure to achieve a response at the

NOTE Confidence: 0.907126013333333

00:20:05.322 --> 00:20:08.164 week 12 assessment as a negative incident.

NOTE Confidence: 0.907126013333333

00:20:08.170 --> 00:20:10.706 But due to the long gap to treatment,

NOTE Confidence: 0.907126013333333

00:20:10.710 --> 00:20:13.248 some patients may did not adequately
NOTE Confidence: 0.9071260133333333

00:20:13.248 --> 00:20:15.819 respond to kymriah at that point,
NOTE Confidence: 0.9071260133333333

00:20:15.820 --> 00:20:19.388 and they responded to kymriah after the 12
NOTE Confidence: 0.9071260133333333

00:20:19.388 --> 00:20:23.029 week mark without any additional therapy.
NOTE Confidence: 0.9071260133333333

00:20:23.030 --> 00:20:25.400 So several factors for White failed.
NOTE Confidence: 0.9071260133333333

00:20:25.400 --> 00:20:27.374 So what is Novartis going to do?
NOTE Confidence: 0.9071260133333333

00:20:27.380 --> 00:20:29.575 Are they gonna pursue another
NOTE Confidence: 0.9071260133333333

00:20:29.575 --> 00:20:31.770 trial using the same product?
NOTE Confidence: 0.9071260133333333

00:20:31.770 --> 00:20:32.656 You know,
NOTE Confidence: 0.9071260133333333

00:20:32.656 --> 00:20:35.757 trying to mimic the other two studies?
NOTE Confidence: 0.9071260133333333

00:20:35.760 --> 00:20:37.380 They have moved away from that.
NOTE Confidence: 0.9071260133333333

00:20:37.380 --> 00:20:40.383 They have moved on and what they
NOTE Confidence: 0.9071260133333333

00:20:40.383 --> 00:20:42.870 actually announced was this a next
NOTE Confidence: 0.9071260133333333

00:20:42.870 --> 00:20:44.490 generation platform that's called
NOTE Confidence: 0.9071260133333333

00:20:44.490 --> 00:20:46.894 T Charge that aims to revolutionize
NOTE Confidence: 0.9071260133333333

00:20:46.894 --> 00:20:49.750 car T cell therapy and what it does

NOTE Confidence: 0.907126013333333

00:20:49.818 --> 00:20:52.268 is that it preserves T cell stemness

NOTE Confidence: 0.907126013333333

00:20:52.268 --> 00:20:54.824 the ability to self renew and mature

NOTE Confidence: 0.907126013333333

00:20:54.824 --> 00:20:57.659 that results in a product that has

NOTE Confidence: 0.907126013333333

00:20:57.659 --> 00:20:59.177 greater proliferative potential

NOTE Confidence: 0.907126013333333

00:20:59.177 --> 00:21:02.330 and fewer exhausted T cells and.

NOTE Confidence: 0.907126013333333

00:21:02.330 --> 00:21:05.430 They already presented at Ash.

NOTE Confidence: 0.907126013333333

00:21:05.430 --> 00:21:08.986 Now data from two first in human

NOTE Confidence: 0.907126013333333

00:21:08.986 --> 00:21:10.510 dose escalation trials.

NOTE Confidence: 0.907126013333333

00:21:10.510 --> 00:21:14.745 So Y TB323IN lymphoma and PHE

NOTE Confidence: 0.907126013333333

00:21:14.745 --> 00:21:17.093 885 in multiple myeloma.

NOTE Confidence: 0.907126013333333

00:21:17.100 --> 00:21:19.812 So there were two scientific posters

NOTE Confidence: 0.907126013333333

00:21:19.812 --> 00:21:23.038 that went along with the 1st in

NOTE Confidence: 0.907126013333333

00:21:23.038 --> 00:21:25.702 human clinical trials and what they

NOTE Confidence: 0.907126013333333

00:21:25.702 --> 00:21:29.397 basically showed is that this T cell T

NOTE Confidence: 0.907126013333333

00:21:29.397 --> 00:21:33.370 charge manufacturing process actually.

NOTE Confidence: 0.907126013333333

00:21:33.370 --> 00:21:34.130 Uhm?

NOTE Confidence: 0.8136206225

00:21:36.730 --> 00:21:39.215 Give us a product that

NOTE Confidence: 0.8136206225

00:21:39.215 --> 00:21:40.706 retains the immunophenotype,

NOTE Confidence: 0.8136206225

00:21:40.710 --> 00:21:43.218 the of the input leukapheresis material,

NOTE Confidence: 0.8136206225

00:21:43.220 --> 00:21:47.606 where naive and T central memory

NOTE Confidence: 0.8136206225

00:21:47.606 --> 00:21:51.190 cells that are city 45 RO negative

NOTE Confidence: 0.8136206225

00:21:51.190 --> 00:21:54.152 and CCR 7 positive are actually

NOTE Confidence: 0.8136206225

00:21:54.152 --> 00:21:56.807 preserved as you see here.

NOTE Confidence: 0.8136206225

00:21:56.810 --> 00:21:58.556 I don't know if you can

NOTE Confidence: 0.8136206225

00:21:58.556 --> 00:22:00.529 see this here on the right.

NOTE Confidence: 0.8136206225

00:22:00.530 --> 00:22:04.694 As opposed to the traditional manufacturing

NOTE Confidence: 0.8136206225

00:22:04.694 --> 00:22:08.298 approaches where the cells are.

NOTE Confidence: 0.514413965

00:22:11.350 --> 00:22:16.620 City 45 Arrow positive CCR, seven negative.

NOTE Confidence: 0.514413965

00:22:16.620 --> 00:22:21.266 So the the thought is that these cells

NOTE Confidence: 0.514413965

00:22:21.266 --> 00:22:24.645 this is the time will reduce the

NOTE Confidence: 0.514413965

00:22:24.645 --> 00:22:27.795 manufacturing time basically to less than

NOTE Confidence: 0.514413965

00:22:27.881 --> 00:22:30.878 than two days because these cells are

NOTE Confidence: 0.514413965

00:22:30.878 --> 00:22:34.860 going to be able to go into the patient

NOTE Confidence: 0.514413965

00:22:34.860 --> 00:22:38.220 and expand and proliferate in vivo.

NOTE Confidence: 0.8323023

00:22:40.570 --> 00:22:43.894 So when you look again,

NOTE Confidence: 0.8323023

00:22:43.894 --> 00:22:48.520 these are called violent plots, there is.

NOTE Confidence: 0.8323023

00:22:48.520 --> 00:22:53.835 The. Y TB323 core T cells here actually

NOTE Confidence: 0.8323023

00:22:53.835 --> 00:22:55.900 showed very similar central memory.

NOTE Confidence: 0.8323023

00:22:55.900 --> 00:22:58.540 T cell phenotype and stemness gene

NOTE Confidence: 0.8323023

00:22:58.540 --> 00:23:00.760 signatures as the input material

NOTE Confidence: 0.8323023

00:23:00.760 --> 00:23:05.430 here in red compared to to the

NOTE Confidence: 0.8323023

00:23:05.430 --> 00:23:07.680 standard autologous city 19 product

NOTE Confidence: 0.8323023

00:23:07.680 --> 00:23:10.139 where there's more of a T factor,

NOTE Confidence: 0.8323023

00:23:10.140 --> 00:23:14.310 memory phenotype and.

NOTE Confidence: 0.8323023

00:23:14.310 --> 00:23:18.360 The Stemness high signature is retained

NOTE Confidence: 0.8323023

00:23:18.360 --> 00:23:21.374 in the the new product where TP323

NOTE Confidence: 0.8323023

00:23:21.374 --> 00:23:24.698 versus low stamina signature in the
NOTE Confidence: 0.8323023

00:23:24.698 --> 00:23:26.360 conventional autologous product,
NOTE Confidence: 0.8323023

00:23:26.360 --> 00:23:29.690 and this what this did is that it actually
NOTE Confidence: 0.8323023

00:23:29.690 --> 00:23:31.610 when you they looked at a tumor model,
NOTE Confidence: 0.8323023

00:23:31.610 --> 00:23:33.895 it showed better in vivo
NOTE Confidence: 0.8323023

00:23:33.895 --> 00:23:35.723 and to tumor efficacy.
NOTE Confidence: 0.8323023

00:23:35.730 --> 00:23:37.475 This is a traditional manufacturing
NOTE Confidence: 0.8323023

00:23:37.475 --> 00:23:39.945 and this is the T charge platform
NOTE Confidence: 0.8323023

00:23:39.945 --> 00:23:41.919 where you can see that even
NOTE Confidence: 0.8323023

00:23:41.919 --> 00:23:44.027 as low overdose as .1 times.
NOTE Confidence: 0.8323023

00:23:44.030 --> 00:23:47.446 Went to the six here shown in blue.
NOTE Confidence: 0.8323023

00:23:47.450 --> 00:23:50.396 Gives a response compared to .5.
NOTE Confidence: 0.8323023

00:23:50.396 --> 00:23:53.168 Times tends to the six in the
NOTE Confidence: 0.8323023

00:23:53.168 --> 00:23:54.360 traditional manufacturing so
NOTE Confidence: 0.8323023

00:23:54.360 --> 00:23:56.316 fewer cells are actually a car.
NOTE Confidence: 0.8323023

00:23:56.320 --> 00:24:00.114 T cells are required for tumor suppression

NOTE Confidence: 0.8323023

00:24:00.114 --> 00:24:04.646 and even when they looked at the expansion.

NOTE Confidence: 0.8323023

00:24:04.650 --> 00:24:07.177 The that they looked at in the

NOTE Confidence: 0.8323023

00:24:07.177 --> 00:24:09.170 blood by flow cytometry.

NOTE Confidence: 0.8323023

00:24:09.170 --> 00:24:11.879 These cells were were very potent and

NOTE Confidence: 0.8323023

00:24:11.879 --> 00:24:14.670 they actually had much better expansion.

NOTE Confidence: 0.8323023

00:24:14.670 --> 00:24:17.958 So there C Max was 40 times higher

NOTE Confidence: 0.8323023

00:24:17.958 --> 00:24:21.756 and AUC in the 1st 21 days was 33

NOTE Confidence: 0.8323023

00:24:21.756 --> 00:24:24.830 times higher for Y TB323 as compared

NOTE Confidence: 0.8323023

00:24:24.830 --> 00:24:26.670 to their traditional manufacturing.

NOTE Confidence: 0.8323023

00:24:26.670 --> 00:24:29.630 So this is what they used in the

NOTE Confidence: 0.8323023

00:24:29.630 --> 00:24:32.858 first in human study in patients with

NOTE Confidence: 0.8323023

00:24:32.858 --> 00:24:35.198 relapsed diffuse, large B cell lymphoma.

NOTE Confidence: 0.8323023

00:24:35.198 --> 00:24:37.690 And they saw some very encouraging data.

NOTE Confidence: 0.8323023

00:24:37.690 --> 00:24:40.336 They had two dose levels and

NOTE Confidence: 0.8323023

00:24:40.336 --> 00:24:43.166 they treated about 20 patients.

NOTE Confidence: 0.8323023

00:24:43.170 --> 00:24:45.930 15 patients who received this
NOTE Confidence: 0.8323023

00:24:45.930 --> 00:24:48.490 product at those level 2.
NOTE Confidence: 0.8323023

00:24:48.490 --> 00:24:50.650 They had a very high complete
NOTE Confidence: 0.8323023

00:24:50.650 --> 00:24:54.594 response rate of 73%. And they didn't.
NOTE Confidence: 0.8323023

00:24:54.594 --> 00:24:55.310 Importantly.
NOTE Confidence: 0.8323023

00:24:55.310 --> 00:24:58.402 Also they didn't see any safety
NOTE Confidence: 0.8323023

00:24:58.402 --> 00:25:01.474 signals beyond what was known and
NOTE Confidence: 0.8323023

00:25:01.474 --> 00:25:05.794 expected with the with the kymriah.
NOTE Confidence: 0.8323023

00:25:05.794 --> 00:25:07.650 So so.
NOTE Confidence: 0.8323023

00:25:07.650 --> 00:25:10.364 I think that all of the future studies
NOTE Confidence: 0.8323023

00:25:10.364 --> 00:25:12.513 that we're going to see coming out
NOTE Confidence: 0.8323023

00:25:12.513 --> 00:25:14.601 of Novartis will be utilizing this
NOTE Confidence: 0.8323023

00:25:14.601 --> 00:25:17.026 platform and at some point they will
NOTE Confidence: 0.8323023

00:25:17.026 --> 00:25:18.976 probably compare this to the standard
NOTE Confidence: 0.8323023

00:25:18.976 --> 00:25:21.595 of care which is autologous stem cell
NOTE Confidence: 0.8323023

00:25:21.595 --> 00:25:24.010 transplant and this eventually I think,

NOTE Confidence: 0.8323023

00:25:24.010 --> 00:25:25.615 will replace kymriah.

NOTE Confidence: 0.8323023

00:25:25.615 --> 00:25:28.825 So just to shift gears quickly

NOTE Confidence: 0.8323023

00:25:28.825 --> 00:25:30.969 towards multiple myeloma,

NOTE Confidence: 0.8323023

00:25:30.970 --> 00:25:32.152 as you know,

NOTE Confidence: 0.8323023

00:25:32.152 --> 00:25:34.516 bmet is highly expressed and malignant.

NOTE Confidence: 0.8323023

00:25:34.520 --> 00:25:37.030 Plasma cells and multiple myeloma,

NOTE Confidence: 0.8323023

00:25:37.030 --> 00:25:40.066 and then higher concentrations of soluble

NOTE Confidence: 0.8323023

00:25:40.066 --> 00:25:43.239 BCMA are associated with poor outcomes,

NOTE Confidence: 0.8323023

00:25:43.240 --> 00:25:46.126 and that's why this presented a

NOTE Confidence: 0.8323023

00:25:46.126 --> 00:25:48.830 very rational target for therapy.

NOTE Confidence: 0.8323023

00:25:48.830 --> 00:25:51.146 There's a lot of competition in

NOTE Confidence: 0.8323023

00:25:51.146 --> 00:25:53.425 terms of antibody drug conjugates

NOTE Confidence: 0.8323023

00:25:53.425 --> 00:25:55.408 and bispecific antibodies,

NOTE Confidence: 0.8323023

00:25:55.410 --> 00:25:58.090 but in terms of car T cell therapies.

NOTE Confidence: 0.8323023

00:25:58.090 --> 00:25:59.410 The advantages that hopefully

NOTE Confidence: 0.8323023

00:25:59.410 --> 00:26:01.390 it's a one and done deal.
NOTE Confidence: 0.8323023

00:26:01.390 --> 00:26:03.703 If you have a good product and you don't
NOTE Confidence: 0.8323023

00:26:03.703 --> 00:26:05.968 have to continuously infuse antibodies.
NOTE Confidence: 0.8323023

00:26:05.970 --> 00:26:08.556 So currently either captured in blue
NOTE Confidence: 0.8323023

00:26:08.556 --> 00:26:11.689 so and Celtic after Geno Deluso are
NOTE Confidence: 0.8323023

00:26:11.689 --> 00:26:14.353 both approved in patients who've had
NOTE Confidence: 0.8323023

00:26:14.360 --> 00:26:18.434 four lines of therapy exposures to
NOTE Confidence: 0.8323023

00:26:18.434 --> 00:26:20.471 immunomodulatory agent proteasome
NOTE Confidence: 0.8323023

00:26:20.471 --> 00:26:23.970 inhibitors and also anti CD 38
NOTE Confidence: 0.8323023

00:26:23.970 --> 00:26:26.150 monoclonal antibody like daratumumab.
NOTE Confidence: 0.8323023

00:26:26.150 --> 00:26:28.150 So.
NOTE Confidence: 0.8323023

00:26:28.150 --> 00:26:30.950 This is the phase one two data
NOTE Confidence: 0.8323023

00:26:30.950 --> 00:26:32.150 with BCM a
NOTE Confidence: 0.784530236470588

00:26:32.249 --> 00:26:36.246 directed CAR T cells in multiple myeloma.
NOTE Confidence: 0.784530236470588

00:26:36.250 --> 00:26:39.426 So BB 2121 was the first product approved.
NOTE Confidence: 0.784530236470588

00:26:39.430 --> 00:26:44.270 You see it has a 73% overall response rate,

NOTE Confidence: 0.784530236470588

00:26:44.270 --> 00:26:47.510 31% complete response rate in a

NOTE Confidence: 0.784530236470588

00:26:47.510 --> 00:26:49.670 heavily pretreated patient population.

NOTE Confidence: 0.784530236470588

00:26:49.670 --> 00:26:50.650 However, disappointingly,

NOTE Confidence: 0.784530236470588

00:26:50.650 --> 00:26:52.610 the median progression free

NOTE Confidence: 0.784530236470588

00:26:52.610 --> 00:26:55.470 survival was only about a year,

NOTE Confidence: 0.784530236470588

00:26:55.470 --> 00:26:58.620 and so people realize very early that.

NOTE Confidence: 0.784530236470588

00:26:58.620 --> 00:27:01.190 Uhm? Something else that needed

NOTE Confidence: 0.784530236470588

00:27:01.190 --> 00:27:03.497 to be done and that we need to

NOTE Confidence: 0.784530236470588

00:27:03.497 --> 00:27:05.534 improve upon upon this product.

NOTE Confidence: 0.784530236470588

00:27:05.534 --> 00:27:09.667 So Elk, RB 38 M is a car construct

NOTE Confidence: 0.784530236470588

00:27:09.667 --> 00:27:12.205 that actually has CV targeting

NOTE Confidence: 0.784530236470588

00:27:12.205 --> 00:27:15.433 2 bfme epitopes instead of 1.

NOTE Confidence: 0.784530236470588

00:27:15.440 --> 00:27:19.184 So it targets both VH1 and VH two,

NOTE Confidence: 0.784530236470588

00:27:19.190 --> 00:27:21.710 and when they looked at the data,

NOTE Confidence: 0.784530236470588

00:27:21.710 --> 00:27:24.413 the overall response rate was 100%

NOTE Confidence: 0.784530236470588

00:27:24.413 --> 00:27:27.262 with complete response rate of 76%.
NOTE Confidence: 0.784530236470588

00:27:27.262 --> 00:27:30.454 And there's also another product where.
NOTE Confidence: 0.784530236470588

00:27:30.460 --> 00:27:32.624 Which is fully humanized,
NOTE Confidence: 0.784530236470588

00:27:32.624 --> 00:27:35.329 and that's enriched for early
NOTE Confidence: 0.784530236470588

00:27:35.329 --> 00:27:36.840 memory phenotype,
NOTE Confidence: 0.784530236470588

00:27:36.840 --> 00:27:38.772 so this kind of kills two
NOTE Confidence: 0.784530236470588

00:27:38.772 --> 00:27:40.060 birds with one stone.
NOTE Confidence: 0.784530236470588

00:27:40.060 --> 00:27:42.660 The cells hopefully persist longer,
NOTE Confidence: 0.784530236470588

00:27:42.660 --> 00:27:45.820 but because of their memory,
NOTE Confidence: 0.784530236470588

00:27:45.820 --> 00:27:49.200 early memory phenotype, but.
NOTE Confidence: 0.784530236470588

00:27:49.200 --> 00:27:49.964 Also,
NOTE Confidence: 0.784530236470588

00:27:49.964 --> 00:27:53.020 and being fully humanized,
NOTE Confidence: 0.784530236470588

00:27:53.020 --> 00:27:56.562 there is less development of of antibodies
NOTE Confidence: 0.784530236470588

00:27:56.562 --> 00:27:59.574 that result in destruction of these.
NOTE Confidence: 0.784530236470588

00:27:59.580 --> 00:28:03.171 Court T cells soak attitude one was
NOTE Confidence: 0.784530236470588

00:28:03.171 --> 00:28:06.370 a phase 1B2 study of Celtic catagen

NOTE Confidence: 0.784530236470588
00:28:06.370 --> 00:28:09.260 all deluso and they presented at ash
NOTE Confidence: 0.784530236470588
00:28:09.260 --> 00:28:12.568 their two year update and this is
NOTE Confidence: 0.784530236470588
00:28:12.568 --> 00:28:15.940 very similar in terms of leukapheresis
NOTE Confidence: 0.784530236470588
00:28:15.940 --> 00:28:17.230 lymphodepletion with fludarabine
NOTE Confidence: 0.784530236470588
00:28:17.230 --> 00:28:20.608 cytoxan and then they had the soul to sell.
NOTE Confidence: 0.784530236470588
00:28:20.610 --> 00:28:24.143 Infusion the baseline characteristics.
NOTE Confidence: 0.784530236470588
00:28:24.143 --> 00:28:27.674 Just important to note that 87% of
NOTE Confidence: 0.784530236470588
00:28:27.674 --> 00:28:30.234 patients were triple class refractory
NOTE Confidence: 0.784530236470588
00:28:30.234 --> 00:28:33.132 and 42% were pentad drug refractory so
NOTE Confidence: 0.784530236470588
00:28:33.132 --> 00:28:35.430 very heavily pretreated and resistant.
NOTE Confidence: 0.784530236470588
00:28:35.430 --> 00:28:36.598 Patient population.
NOTE Confidence: 0.784530236470588
00:28:36.598 --> 00:28:40.102 When you look at their overall
NOTE Confidence: 0.784530236470588
00:28:40.102 --> 00:28:41.270 response rates.
NOTE Confidence: 0.784530236470588
00:28:41.270 --> 00:28:45.846 I mean dramatic 97.9% and when you
NOTE Confidence: 0.784530236470588
00:28:45.846 --> 00:28:48.766 look at stringent complete response
NOTE Confidence: 0.784530236470588

00:28:48.766 --> 00:28:51.262 extremely high 82.5% the median
NOTE Confidence: 0.784530236470588

00:28:51.262 --> 00:28:54.166 time to first response was quick
NOTE Confidence: 0.784530236470588

00:28:54.166 --> 00:28:57.546 a month and median time to CR or
NOTE Confidence: 0.784530236470588

00:28:57.546 --> 00:28:59.929 better with two point 9 months.
NOTE Confidence: 0.784530236470588

00:28:59.930 --> 00:29:02.355 The percentage of patients that
NOTE Confidence: 0.784530236470588

00:29:02.355 --> 00:29:04.295 are remaining progression free
NOTE Confidence: 0.784530236470588

00:29:04.295 --> 00:29:06.272 at two years with 60.5%.
NOTE Confidence: 0.784530236470588

00:29:06.272 --> 00:29:08.806 So that was better than what we
NOTE Confidence: 0.784530236470588

00:29:08.806 --> 00:29:11.192 saw with the with Ida Captain Jean.
NOTE Confidence: 0.784530236470588

00:29:11.192 --> 00:29:14.164 Then you can see that this is important
NOTE Confidence: 0.784530236470588

00:29:14.164 --> 00:29:16.774 because basically for two years these
NOTE Confidence: 0.784530236470588

00:29:16.774 --> 00:29:19.646 patients did not get any other therapies.
NOTE Confidence: 0.784530236470588

00:29:19.650 --> 00:29:21.845 Which is you know important
NOTE Confidence: 0.784530236470588

00:29:21.845 --> 00:29:24.570 in terms of quality of life?
NOTE Confidence: 0.784530236470588

00:29:24.570 --> 00:29:27.080 And preservation of organ function.
NOTE Confidence: 0.784530236470588

00:29:27.080 --> 00:29:30.203 So when we look at PFS and overall survival,

NOTE Confidence: 0.784530236470588

00:29:30.210 --> 00:29:36.580 the two year PFS was a 71% median PFS

NOTE Confidence: 0.784530236470588

00:29:36.580 --> 00:29:40.680 and not reached compared to 60.5%.

NOTE Confidence: 0.17822057

00:29:42.890 --> 00:29:43.540 Uhm?

NOTE Confidence: 0.89654931

00:29:46.420 --> 00:29:51.968 Here in blue for patients who the all

NOTE Confidence: 0.89654931

00:29:51.968 --> 00:29:54.542 comers compared to patients who achieve

NOTE Confidence: 0.89654931

00:29:54.542 --> 00:29:56.924 stringent CR that did significantly

NOTE Confidence: 0.89654931

00:29:56.924 --> 00:29:59.339 better in terms of progression.

NOTE Confidence: 0.89654931

00:29:59.340 --> 00:30:02.000 Free survival at two years.

NOTE Confidence: 0.89654931

00:30:02.000 --> 00:30:05.213 So, so that's what denoted here in blue and.

NOTE Confidence: 0.89654931

00:30:05.220 --> 00:30:07.386 And as expected, the stringent CR

NOTE Confidence: 0.89654931

00:30:07.386 --> 00:30:09.440 patients would have better outcomes.

NOTE Confidence: 0.89654931

00:30:09.440 --> 00:30:12.128 And if you look at progression free and

NOTE Confidence: 0.89654931

00:30:12.128 --> 00:30:14.060 overall survival by MRD status again,

NOTE Confidence: 0.89654931

00:30:14.060 --> 00:30:15.522 significantly better.

NOTE Confidence: 0.89654931

00:30:15.522 --> 00:30:21.460 In patients who were MRD negative.

NOTE Confidence: 0.89654931

00:30:21.460 --> 00:30:24.925 And MRD negativity negative patients

NOTE Confidence: 0.89654931

00:30:24.925 --> 00:30:27.697 actually maintain their progression

NOTE Confidence: 0.89654931

00:30:27.697 --> 00:30:30.740 free survival beyond the year.

NOTE Confidence: 0.89654931

00:30:30.740 --> 00:30:35.225 So I'm going to switch gears

NOTE Confidence: 0.89654931

00:30:35.225 --> 00:30:38.200 now finally to a LL briefly.

NOTE Confidence: 0.89654931

00:30:38.200 --> 00:30:39.246 But importantly,

NOTE Confidence: 0.89654931

00:30:39.246 --> 00:30:42.907 we now do not have just the

NOTE Confidence: 0.89654931

00:30:42.907 --> 00:30:43.876 tisagenlecleucel approval

NOTE Confidence: 0.89654931

00:30:43.876 --> 00:30:46.700 for a LL up to 25 years old.

NOTE Confidence: 0.89654931

00:30:46.700 --> 00:30:49.156 We also have Rex Cottage in Auto Lusso,

NOTE Confidence: 0.89654931

00:30:49.160 --> 00:30:50.772 recently approved in adults

NOTE Confidence: 0.89654931

00:30:50.772 --> 00:30:52.787 with relapsed refractory B cell

NOTE Confidence: 0.71652823375

00:30:54.820 --> 00:30:57.704 LALLLA much anticipated approval.

NOTE Confidence: 0.71652823375

00:30:57.704 --> 00:31:00.588 So Ileana was in.

NOTE Confidence: 0.71652823375

00:31:00.590 --> 00:31:03.025 Children and young adults are

NOTE Confidence: 0.71652823375

00:31:03.025 --> 00:31:04.973 showing a significant improvement

NOTE Confidence: 0.71652823375
00:31:04.973 --> 00:31:07.912 in event free and overall survival
NOTE Confidence: 0.71652823375
00:31:07.912 --> 00:31:09.812 with this agenda Clouseau.
NOTE Confidence: 0.71652823375
00:31:09.820 --> 00:31:11.708 In this patient population,
NOTE Confidence: 0.71652823375
00:31:11.708 --> 00:31:14.068 including patients who did not
NOTE Confidence: 0.71652823375
00:31:14.068 --> 00:31:16.908 go onto to receive an allogeneic
NOTE Confidence: 0.71652823375
00:31:16.908 --> 00:31:19.193 stem cell transplant and this
NOTE Confidence: 0.71652823375
00:31:19.271 --> 00:31:21.683 is zooma 3 with Brexit captain
NOTE Confidence: 0.71652823375
00:31:21.683 --> 00:31:24.700 Jean with that showed 70.9% CR.
NOTE Confidence: 0.71652823375
00:31:24.700 --> 00:31:28.900 Or CR with incomplete hematologic response.
NOTE Confidence: 0.71652823375
00:31:28.900 --> 00:31:31.475 Pretty high in adults with
NOTE Confidence: 0.71652823375
00:31:31.475 --> 00:31:33.020 relapsed refractory LL,
NOTE Confidence: 0.71652823375
00:31:33.020 --> 00:31:34.975 so this has already previously
NOTE Confidence: 0.71652823375
00:31:34.975 --> 00:31:35.757 been published.
NOTE Confidence: 0.71652823375
00:31:35.760 --> 00:31:38.868 But to point out what was interesting
NOTE Confidence: 0.71652823375
00:31:38.868 --> 00:31:42.648 at ASH is that patients are relapsing
NOTE Confidence: 0.71652823375

00:31:42.648 --> 00:31:46.584 mainly because they're losing CD 19
NOTE Confidence: 0.71652823375

00:31:46.584 --> 00:31:49.954 and so a lot of effort has gone into
NOTE Confidence: 0.71652823375

00:31:49.954 --> 00:31:52.120 finding ways to mitigate that risk.
NOTE Confidence: 0.71652823375

00:31:52.120 --> 00:31:55.602 So either by giving dual cars like City 1920.
NOTE Confidence: 0.71652823375

00:31:55.602 --> 00:31:58.498 Two giving off the shelf CAR products or
NOTE Confidence: 0.71652823375

00:31:58.498 --> 00:32:01.323 by re infusing CAR T cells in patients
NOTE Confidence: 0.71652823375

00:32:01.323 --> 00:32:04.350 who may be at high risk of free labs.
NOTE Confidence: 0.71652823375

00:32:04.350 --> 00:32:08.688 And so this was a study from CHOP at
NOTE Confidence: 0.71652823375

00:32:08.688 --> 00:32:11.420 Upenn in children and young adults
NOTE Confidence: 0.71652823375

00:32:11.420 --> 00:32:14.318 with relapsed refractory LL and they
NOTE Confidence: 0.71652823375

00:32:14.318 --> 00:32:16.598 basically followed patients from.
NOTE Confidence: 0.71652823375

00:32:16.600 --> 00:32:18.136 The time of their first scene,
NOTE Confidence: 0.71652823375

00:32:18.140 --> 00:32:21.290 19 Carty and if they had,
NOTE Confidence: 0.71652823375

00:32:21.290 --> 00:32:23.060 if they were minimal residual disease,
NOTE Confidence: 0.71652823375

00:32:23.060 --> 00:32:24.612 positive if they relapsed,
NOTE Confidence: 0.71652823375

00:32:24.612 --> 00:32:28.157 or if they saw that they had early B

NOTE Confidence: 0.71652823375

00:32:28.157 --> 00:32:30.955 cell recovery and or city 19 hematogen's

NOTE Confidence: 0.71652823375

00:32:30.955 --> 00:32:34.021 in the bone marrow they basically re

NOTE Confidence: 0.71652823375

00:32:34.021 --> 00:32:36.493 infuse them with the autologous CAR.

NOTE Confidence: 0.71652823375

00:32:36.493 --> 00:32:38.599 T cell products within six months

NOTE Confidence: 0.71652823375

00:32:38.599 --> 00:32:41.035 of their initial treatment and

NOTE Confidence: 0.71652823375

00:32:41.035 --> 00:32:45.060 you can see that in patients who.

NOTE Confidence: 0.71652823375

00:32:45.060 --> 00:32:49.239 Were reinfused because of him at Agones.

NOTE Confidence: 0.71652823375

00:32:49.240 --> 00:32:52.152 Actually the majority of them 76%

NOTE Confidence: 0.71652823375

00:32:52.152 --> 00:32:56.180 achieved a complete remission and also

NOTE Confidence: 0.71652823375

00:32:56.180 --> 00:32:59.974 patients who had early B cell recovery

NOTE Confidence: 0.71652823375

00:32:59.974 --> 00:33:02.470 but did not have measurable disease.

NOTE Confidence: 0.71652823375

00:33:02.470 --> 00:33:06.262 A good proportion of them achieved CR without

NOTE Confidence: 0.71652823375

00:33:06.262 --> 00:33:08.560 needing consolidation with a transplant.

NOTE Confidence: 0.71652823375

00:33:08.560 --> 00:33:09.049 However,

NOTE Confidence: 0.71652823375

00:33:09.049 --> 00:33:11.983 patients who were reinfused for non

NOTE Confidence: 0.71652823375

00:33:11.983 --> 00:33:15.007 response actually all of them pretty much.

NOTE Confidence: 0.71652823375

00:33:15.010 --> 00:33:18.466 Did not respond to the car T product,

NOTE Confidence: 0.71652823375

00:33:18.470 --> 00:33:21.595 so the clinical implications

NOTE Confidence: 0.71652823375

00:33:21.595 --> 00:33:24.085 for this are that cortisol re

NOTE Confidence: 0.71652823375

00:33:24.085 --> 00:33:25.847 infusions can prolong be sold.

NOTE Confidence: 0.71652823375

00:33:25.850 --> 00:33:28.664 A plasias in a subset of patients

NOTE Confidence: 0.71652823375

00:33:28.664 --> 00:33:30.986 with short car persistence and

NOTE Confidence: 0.71652823375

00:33:30.986 --> 00:33:34.064 this can reduce risk of relapse.

NOTE Confidence: 0.71652823375

00:33:34.070 --> 00:33:35.780 Rain fusions can induce remission

NOTE Confidence: 0.71652823375

00:33:35.780 --> 00:33:37.490 in patients with prior relapse,

NOTE Confidence: 0.71652823375

00:33:37.490 --> 00:33:40.286 but the remissions have limited durability,

NOTE Confidence: 0.71652823375

00:33:40.290 --> 00:33:42.922 and really it does not make sense to

NOTE Confidence: 0.71652823375

00:33:42.922 --> 00:33:44.687 reinfuse patients who were refractory

NOTE Confidence: 0.71652823375

00:33:44.687 --> 00:33:46.422 the first time around because

NOTE Confidence: 0.71652823375

00:33:46.422 --> 00:33:48.649 none of them actually responded.

NOTE Confidence: 0.71652823375

00:33:48.650 --> 00:33:51.135 So this is just the class effects

NOTE Confidence: 0.71652823375
00:33:51.135 --> 00:33:53.040 of the immune responses,
NOTE Confidence: 0.71652823375
00:33:53.040 --> 00:33:54.736 CRS, and neurologic toxicity.
NOTE Confidence: 0.71652823375
00:33:54.736 --> 00:33:57.870 You see that they're very very variable
NOTE Confidence: 0.71652823375
00:33:57.870 --> 00:34:00.730 amongst the products in terms of
NOTE Confidence: 0.71652823375
00:34:00.730 --> 00:34:02.930 both CRS and neurologic toxicity,
NOTE Confidence: 0.71652823375
00:34:02.930 --> 00:34:04.565 and so then.
NOTE Confidence: 0.71652823375
00:34:04.565 --> 00:34:08.124 The the less disease burden patients have.
NOTE Confidence: 0.71652823375
00:34:08.124 --> 00:34:12.029 At the time of treatment at the better,
NOTE Confidence: 0.71652823375
00:34:12.030 --> 00:34:15.117 the outcomes and and the less toxicity.
NOTE Confidence: 0.71652823375
00:34:15.120 --> 00:34:16.765 And this is this is a lesson
NOTE Confidence: 0.71652823375
00:34:16.765 --> 00:34:17.470 that we've learned.
NOTE Confidence: 0.71652823375
00:34:17.470 --> 00:34:20.557 So the studies now are moving to
NOTE Confidence: 0.71652823375
00:34:20.560 --> 00:34:22.140 incorporate these therapies earlier
NOTE Confidence: 0.71652823375
00:34:22.140 --> 00:34:24.967 in the disease course or to debulk
NOTE Confidence: 0.71652823375
00:34:24.967 --> 00:34:26.912 the patients before we actually
NOTE Confidence: 0.71652823375

00:34:26.912 --> 00:34:28.468 give them the products.
NOTE Confidence: 0.71652823375

00:34:28.470 --> 00:34:31.406 And and I think that's all I have.
NOTE Confidence: 0.71652823375

00:34:31.410 --> 00:34:33.831 So what I'm going to do is I'm going
NOTE Confidence: 0.71652823375

00:34:33.831 --> 00:34:36.177 to pass it over to to low heath.
NOTE Confidence: 0.96360756625

00:34:36.180 --> 00:34:38.084 And then we'll do questions at the end.
NOTE Confidence: 0.742589505625

00:34:57.610 --> 00:34:58.801 Good afternoon everyone.
NOTE Confidence: 0.742589505625

00:34:58.801 --> 00:35:01.183 Anika I thank you for that
NOTE Confidence: 0.742589505625

00:35:01.183 --> 00:35:02.737 beautiful presentation that
NOTE Confidence: 0.742589505625

00:35:02.737 --> 00:35:04.909 really indeed is transformative.
NOTE Confidence: 0.742589505625

00:35:04.910 --> 00:35:07.046 Yeah, these are the people who led the
NOTE Confidence: 0.742589505625

00:35:07.046 --> 00:35:09.050 studies that I'm going to be presenting.
NOTE Confidence: 0.742589505625

00:35:09.050 --> 00:35:10.527 Most of them have said this slides.
NOTE Confidence: 0.742589505625

00:35:10.530 --> 00:35:13.038 I'm grateful for that.
NOTE Confidence: 0.742589505625

00:35:13.040 --> 00:35:15.422 Objectives are DOC today would be
NOTE Confidence: 0.742589505625

00:35:15.422 --> 00:35:17.325 to mainly look into the therapeutic
NOTE Confidence: 0.742589505625

00:35:17.325 --> 00:35:18.830 avenues in which allogeneic stem

NOTE Confidence: 0.742589505625

00:35:18.877 --> 00:35:20.242 cell transplant has been making

NOTE Confidence: 0.742589505625

00:35:20.242 --> 00:35:22.250 progress in order to reduce some of

NOTE Confidence: 0.742589505625

00:35:22.250 --> 00:35:23.735 the complications associated with it,

NOTE Confidence: 0.742589505625

00:35:23.740 --> 00:35:25.963 which ultimately results in a better

NOTE Confidence: 0.742589505625

00:35:25.963 --> 00:35:28.364 curative promise on the quality of life.

NOTE Confidence: 0.742589505625

00:35:28.370 --> 00:35:30.714 I'm going to present a trial wherein we're

NOTE Confidence: 0.742589505625

00:35:30.714 --> 00:35:33.818 going to use pre and post transplant.

NOTE Confidence: 0.742589505625

00:35:33.818 --> 00:35:36.826 Uh, and I'll present some data from

NOTE Confidence: 0.742589505625

00:35:36.826 --> 00:35:39.340 University of Minnesota that looked into.

NOTE Confidence: 0.742589505625

00:35:39.340 --> 00:35:40.848 One Cody Anaconda troping.

NOTE Confidence: 0.742589505625

00:35:40.848 --> 00:35:42.733 In addition to standard immunosuppression,

NOTE Confidence: 0.742589505625

00:35:42.740 --> 00:35:44.950 for patients with acute GVHD,

NOTE Confidence: 0.742589505625

00:35:44.950 --> 00:35:48.806 also present 2 two phase two trials looking

NOTE Confidence: 0.742589505625

00:35:48.806 --> 00:35:52.870 a chronic DVT targeting different pathways.

NOTE Confidence: 0.742589505625

00:35:52.870 --> 00:35:55.190 This this was a trial that was like that MGS.

NOTE Confidence: 0.742589505625

00:35:55.190 --> 00:35:56.834 There was a multi site study
NOTE Confidence: 0.742589505625

00:35:56.834 --> 00:35:58.270 led by Doctor Hobson team.
NOTE Confidence: 0.742589505625

00:35:58.270 --> 00:36:00.272 Basically the study is looking to use
NOTE Confidence: 0.742589505625

00:36:00.272 --> 00:36:02.029 of ruxolitinib which is a Jack anybody
NOTE Confidence: 0.742589505625

00:36:02.030 --> 00:36:04.319 prior to during and after stem cell
NOTE Confidence: 0.742589505625

00:36:04.319 --> 00:36:05.718 transplantation for patients with
NOTE Confidence: 0.742589505625

00:36:05.718 --> 00:36:07.548 primary or secondary modified process.
NOTE Confidence: 0.742589505625

00:36:07.550 --> 00:36:09.062 So for those of you who manage my life,
NOTE Confidence: 0.742589505625

00:36:09.070 --> 00:36:09.594 I process.
NOTE Confidence: 0.742589505625

00:36:09.594 --> 00:36:11.166 This is a very common slide.
NOTE Confidence: 0.742589505625

00:36:11.170 --> 00:36:13.010 The disease can be classified
NOTE Confidence: 0.742589505625

00:36:13.010 --> 00:36:14.482 into five different categories.
NOTE Confidence: 0.742589505625

00:36:14.490 --> 00:36:16.596 Things on the left here usually
NOTE Confidence: 0.742589505625

00:36:16.596 --> 00:36:17.649 get managed conservatively,
NOTE Confidence: 0.742589505625

00:36:17.650 --> 00:36:19.775 or using cytokines and things
NOTE Confidence: 0.742589505625

00:36:19.775 --> 00:36:21.050 symptomatic splenomegaly patients.

NOTE Confidence: 0.742589505625
00:36:21.050 --> 00:36:21.875 We use ruxolitinib,
NOTE Confidence: 0.742589505625
00:36:21.875 --> 00:36:23.250 and more recently the strike
NOTE Confidence: 0.742589505625
00:36:23.250 --> 00:36:24.290 has been approved.
NOTE Confidence: 0.742589505625
00:36:24.290 --> 00:36:26.610 Once they start coming intermediate
NOTE Confidence: 0.742589505625
00:36:26.610 --> 00:36:29.104 risk or have bad gene signatures
NOTE Confidence: 0.742589505625
00:36:29.104 --> 00:36:30.689 or higher very high risk.
NOTE Confidence: 0.742589505625
00:36:30.690 --> 00:36:30.954 OK,
NOTE Confidence: 0.742589505625
00:36:30.954 --> 00:36:32.538 those are the people if they're
NOTE Confidence: 0.742589505625
00:36:32.538 --> 00:36:33.330 eligible for transplant,
NOTE Confidence: 0.742589505625
00:36:33.330 --> 00:36:35.646 they'll be considered for stem cell
NOTE Confidence: 0.742589505625
00:36:35.646 --> 00:36:37.190 transplantation of clinical trials.
NOTE Confidence: 0.742589505625
00:36:37.190 --> 00:36:38.606 This is just a slide that
NOTE Confidence: 0.742589505625
00:36:38.606 --> 00:36:40.250 shows that for the groups here,
NOTE Confidence: 0.742589505625
00:36:40.250 --> 00:36:41.630 starting from grey, yellow,
NOTE Confidence: 0.742589505625
00:36:41.630 --> 00:36:43.630 and blue median, overall survival is less.
NOTE Confidence: 0.742589505625

00:36:43.630 --> 00:36:45.070 Those are the people that are
NOTE Confidence: 0.742589505625

00:36:45.123 --> 00:36:46.695 normally considered for a stem cell.
NOTE Confidence: 0.742589505625

00:36:46.700 --> 00:36:49.380 Transplantation based on clinical scenarios.
NOTE Confidence: 0.742589505625

00:36:49.380 --> 00:36:52.133 So why is it that stem cell transplantation,
NOTE Confidence: 0.742589505625

00:36:52.133 --> 00:36:53.246 although being curative,
NOTE Confidence: 0.742589505625

00:36:53.250 --> 00:36:55.700 has been a little bit of a problem for us?
NOTE Confidence: 0.742589505625

00:36:55.700 --> 00:36:55.936 Well,
NOTE Confidence: 0.742589505625

00:36:55.936 --> 00:36:57.116 most of these patients have
NOTE Confidence: 0.742589505625

00:36:57.116 --> 00:36:58.128 a ***** fibrotic condition.
NOTE Confidence: 0.742589505625

00:36:58.128 --> 00:37:00.011 Have you know Mega League and patients
NOTE Confidence: 0.742589505625

00:37:00.011 --> 00:37:02.053 who come in with splenomegaly at the
NOTE Confidence: 0.742589505625

00:37:02.053 --> 00:37:03.201 time of transplantation generally
NOTE Confidence: 0.742589505625

00:37:03.245 --> 00:37:05.040 tend to do poorly compared to others.
NOTE Confidence: 0.742589505625

00:37:05.040 --> 00:37:07.080 You can consider options to take
NOTE Confidence: 0.742589505625

00:37:07.139 --> 00:37:08.579 over spleen do variation,
NOTE Confidence: 0.742589505625

00:37:08.580 --> 00:37:09.820 surgery and things like that,

NOTE Confidence: 0.742589505625
00:37:09.820 --> 00:37:12.095 but it has its own infectious risk,
NOTE Confidence: 0.742589505625
00:37:12.100 --> 00:37:13.836 robotic risk which ultimately
NOTE Confidence: 0.742589505625
00:37:13.836 --> 00:37:16.006 decreases the promise of transplant.
NOTE Confidence: 0.742589505625
00:37:16.010 --> 00:37:16.700 In addition,
NOTE Confidence: 0.742589505625
00:37:16.700 --> 00:37:18.770 we've seen people have poor graft
NOTE Confidence: 0.742589505625
00:37:18.770 --> 00:37:20.017 function graph failure rates
NOTE Confidence: 0.742589505625
00:37:20.017 --> 00:37:21.267 can be up to 15%.
NOTE Confidence: 0.742589505625
00:37:21.270 --> 00:37:23.370 That all adds up to the non
NOTE Confidence: 0.742589505625
00:37:23.370 --> 00:37:24.462 relapse mortality and there
NOTE Confidence: 0.742589505625
00:37:24.462 --> 00:37:25.446 are some transwitch reports.
NOTE Confidence: 0.742589505625
00:37:25.450 --> 00:37:27.165 Pretty high rates of GVHD and on
NOTE Confidence: 0.742589505625
00:37:27.165 --> 00:37:28.954 the left mortality for my life I
NOTE Confidence: 0.742589505625
00:37:28.954 --> 00:37:30.209 process compared to other people.
NOTE Confidence: 0.742589505625
00:37:30.210 --> 00:37:31.704 The real question is if regulating
NOTE Confidence: 0.742589505625
00:37:31.704 --> 00:37:33.503 even the rest of the drugs which
NOTE Confidence: 0.742589505625

00:37:33.503 --> 00:37:34.997 are now making foray into the
NOTE Confidence: 0.742589505625

00:37:34.997 --> 00:37:36.327 field of my life I process,
NOTE Confidence: 0.742589505625

00:37:36.330 --> 00:37:37.530 is it possible to continue
NOTE Confidence: 0.742589505625

00:37:37.530 --> 00:37:39.020 this trucks in a longer term?
NOTE Confidence: 0.732006483363637

00:37:41.080 --> 00:37:42.652 Because, as I said,
NOTE Confidence: 0.732006483363637

00:37:42.652 --> 00:37:44.617 Jackie Ken has implications on
NOTE Confidence: 0.732006483363637

00:37:44.617 --> 00:37:46.626 symptomatic control for people who
NOTE Confidence: 0.732006483363637

00:37:46.626 --> 00:37:48.948 have multiple process can decrease the
NOTE Confidence: 0.732006483363637

00:37:49.012 --> 00:37:50.856 screen size or the last couple of years.
NOTE Confidence: 0.732006483363637

00:37:50.860 --> 00:37:52.897 We've learned that this drug is pretty
NOTE Confidence: 0.732006483363637

00:37:52.897 --> 00:37:55.098 active in both acute and chronic GVHD.
NOTE Confidence: 0.732006483363637

00:37:55.100 --> 00:37:57.326 Now we have a label for it.
NOTE Confidence: 0.732006483363637

00:37:57.330 --> 00:37:59.184 If people are being a Jack iffy and you
NOTE Confidence: 0.732006483363637

00:37:59.184 --> 00:38:00.808 start with prior to transplantation,
NOTE Confidence: 0.732006483363637

00:38:00.810 --> 00:38:02.610 there are some reports which suggest that it
NOTE Confidence: 0.732006483363637

00:38:02.610 --> 00:38:04.247 can manifest in cytokine release syndrome.

NOTE Confidence: 0.732006483363637
00:38:04.250 --> 00:38:06.506 Kind of clinical spectrum and there have been
NOTE Confidence: 0.732006483363637
00:38:06.506 --> 00:38:08.784 efforts to see if this drug can continue on.
NOTE Confidence: 0.732006483363637
00:38:08.790 --> 00:38:10.428 And there are also people who think
NOTE Confidence: 0.732006483363637
00:38:10.428 --> 00:38:12.002 if you suddenly stop it will rebound
NOTE Confidence: 0.732006483363637
00:38:12.002 --> 00:38:13.906 or bounce back and things like that
NOTE Confidence: 0.732006483363637
00:38:13.906 --> 00:38:15.410 which ultimately has negative impact.
NOTE Confidence: 0.732006483363637
00:38:15.410 --> 00:38:17.188 So the real question this study is
NOTE Confidence: 0.732006483363637
00:38:17.188 --> 00:38:18.999 trying to answer is, is it safe,
NOTE Confidence: 0.732006483363637
00:38:18.999 --> 00:38:21.747 effective to use a drug pre and post
NOTE Confidence: 0.732006483363637
00:38:21.747 --> 00:38:24.060 transplantation? This is a study schema.
NOTE Confidence: 0.732006483363637
00:38:24.060 --> 00:38:25.698 It included patients with mild fibrosis,
NOTE Confidence: 0.732006483363637
00:38:25.700 --> 00:38:27.415 both primary and secondary pre
NOTE Confidence: 0.732006483363637
00:38:27.415 --> 00:38:29.130 transplantation they would start a
NOTE Confidence: 0.732006483363637
00:38:29.188 --> 00:38:31.260 drug at 5 milligrams which is a lower
NOTE Confidence: 0.732006483363637
00:38:31.260 --> 00:38:33.310 dose around day minus 14 continued
NOTE Confidence: 0.732006483363637

00:38:33.310 --> 00:38:34.420 with conditioning regimen.
NOTE Confidence: 0.732006483363637

00:38:34.420 --> 00:38:36.114 Use it in the post transplant period.
NOTE Confidence: 0.732006483363637

00:38:36.120 --> 00:38:38.045 Reevaluate the patients at day
NOTE Confidence: 0.732006483363637

00:38:38.045 --> 00:38:39.200 30 post transplantation,
NOTE Confidence: 0.732006483363637

00:38:39.200 --> 00:38:40.999 at which time if the Council recovered,
NOTE Confidence: 0.732006483363637

00:38:41.000 --> 00:38:42.624 you bump them up to the 10
NOTE Confidence: 0.732006483363637

00:38:42.624 --> 00:38:43.320 milligrams vid dose,
NOTE Confidence: 0.732006483363637

00:38:43.320 --> 00:38:47.380 which is what we kind of use it in our set.
NOTE Confidence: 0.732006483363637

00:38:47.380 --> 00:38:49.102 The key inclusion for mainly adult
NOTE Confidence: 0.732006483363637

00:38:49.102 --> 00:38:50.571 patient population, as I said,
NOTE Confidence: 0.732006483363637

00:38:50.571 --> 00:38:51.759 both primary and secondary.
NOTE Confidence: 0.732006483363637

00:38:51.760 --> 00:38:53.180 This is a classification system.
NOTE Confidence: 0.732006483363637

00:38:53.180 --> 00:38:55.035 This is a dip system that intermediate
NOTE Confidence: 0.732006483363637

00:38:55.035 --> 00:38:57.144 one risk group in addition to adverse
NOTE Confidence: 0.732006483363637

00:38:57.144 --> 00:38:59.034 molecular markers or people greater than
NOTE Confidence: 0.732006483363637

00:38:59.088 --> 00:39:00.888 intermediate 2 running through that,

NOTE Confidence: 0.732006483363637
00:39:00.890 --> 00:39:03.134 they went with the Disney intensity
NOTE Confidence: 0.732006483363637
00:39:03.134 --> 00:39:06.004 regimen as receipts was 140 or lesser
NOTE Confidence: 0.732006483363637
00:39:06.004 --> 00:39:08.392 dose commonly used regimen prophylaxis.
NOTE Confidence: 0.732006483363637
00:39:08.392 --> 00:39:10.344 Methotrexate and climbers was
NOTE Confidence: 0.732006483363637
00:39:10.350 --> 00:39:12.530 applied in the set.
NOTE Confidence: 0.732006483363637
00:39:12.530 --> 00:39:13.738 Here is some characteristics.
NOTE Confidence: 0.732006483363637
00:39:13.738 --> 00:39:15.550 I know it's a busy slide,
NOTE Confidence: 0.732006483363637
00:39:15.550 --> 00:39:17.166 but all that I want you to focus
NOTE Confidence: 0.732006483363637
00:39:17.166 --> 00:39:19.006 on is that most of these people,
NOTE Confidence: 0.732006483363637
00:39:19.010 --> 00:39:20.543 about 85% of the people in this
NOTE Confidence: 0.732006483363637
00:39:20.543 --> 00:39:22.428 trial had a split omegle coming in.
NOTE Confidence: 0.732006483363637
00:39:22.430 --> 00:39:23.990 The study largely consisted of
NOTE Confidence: 0.732006483363637
00:39:23.990 --> 00:39:25.550 match related and unrelated donors,
NOTE Confidence: 0.732006483363637
00:39:25.550 --> 00:39:27.806 number of mismatched donors was less.
NOTE Confidence: 0.732006483363637
00:39:27.810 --> 00:39:29.959 The first thing that you think about
NOTE Confidence: 0.732006483363637

00:39:29.959 --> 00:39:31.868 when putting in a post transplant
NOTE Confidence: 0.732006483363637

00:39:31.868 --> 00:39:33.270 period is housing grafman.
NOTE Confidence: 0.732006483363637

00:39:33.270 --> 00:39:35.790 This is a pretty mild toxic drug.
NOTE Confidence: 0.732006483363637

00:39:35.790 --> 00:39:37.800 People can have deep cytopenias
NOTE Confidence: 0.732006483363637

00:39:37.800 --> 00:39:40.690 and here's a report and they thirty
NOTE Confidence: 0.732006483363637

00:39:40.690 --> 00:39:43.690 23124 patients had engrafted.
NOTE Confidence: 0.732006483363637

00:39:43.690 --> 00:39:45.898 On the platelet count tend to lag behind
NOTE Confidence: 0.732006483363637

00:39:45.898 --> 00:39:47.712 a little bit, whether it's the drug,
NOTE Confidence: 0.732006483363637

00:39:47.712 --> 00:39:48.684 whether it's the spleen.
NOTE Confidence: 0.732006483363637

00:39:48.690 --> 00:39:49.260 It's debatable,
NOTE Confidence: 0.732006483363637

00:39:49.260 --> 00:39:50.685 you follow them up today,
NOTE Confidence: 0.732006483363637

00:39:50.690 --> 00:39:52.262 60 neutrophils have recovered,
NOTE Confidence: 0.732006483363637

00:39:52.262 --> 00:39:54.975 or the platelets still lags behind by
NOTE Confidence: 0.732006483363637

00:39:54.975 --> 00:39:56.984 around a little more than 100 days,
NOTE Confidence: 0.732006483363637

00:39:56.990 --> 00:39:58.354 almost everybody recovers their
NOTE Confidence: 0.732006483363637

00:39:58.354 --> 00:39:59.036 platelet count.

NOTE Confidence: 0.797700432222222

00:40:01.280 --> 00:40:02.760 I'm here with the clinical

NOTE Confidence: 0.797700432222222

00:40:02.760 --> 00:40:03.944 outcomes that are reported.

NOTE Confidence: 0.797700432222222

00:40:03.950 --> 00:40:06.924 The one year OS is about 77% the

NOTE Confidence: 0.797700432222222

00:40:06.924 --> 00:40:08.734 one year cumulative incidence of

NOTE Confidence: 0.797700432222222

00:40:08.734 --> 00:40:11.131 relapse is about 17%. One year.

NOTE Confidence: 0.797700432222222

00:40:11.131 --> 00:40:13.611 Incidence of chronic GVHD is 14%.

NOTE Confidence: 0.797700432222222

00:40:13.611 --> 00:40:15.939 I think it's also important in the six

NOTE Confidence: 0.797700432222222

00:40:15.939 --> 00:40:18.386 months incidence of great leader for acute,

NOTE Confidence: 0.797700432222222

00:40:18.390 --> 00:40:20.166 which can be lethal. It's about

NOTE Confidence: 0.797700432222222

00:40:20.166 --> 00:40:21.976 four percent is kind of impressive.

NOTE Confidence: 0.797700432222222

00:40:21.976 --> 00:40:24.234 So based on this trial now people

NOTE Confidence: 0.797700432222222

00:40:24.234 --> 00:40:26.418 are starting to contemplate the C.

NOTE Confidence: 0.797700432222222

00:40:26.420 --> 00:40:28.328 Yes, this drug has benefits in

NOTE Confidence: 0.797700432222222

00:40:28.328 --> 00:40:29.600 pre and post transplantation

NOTE Confidence: 0.797700432222222

00:40:29.663 --> 00:40:31.497 setting in terms of the high risk.

NOTE Confidence: 0.797700432222222

00:40:31.500 --> 00:40:31.988 In population,
NOTE Confidence: 0.797700432222222

00:40:31.988 --> 00:40:33.696 maybe this can be translated into clinically.
NOTE Confidence: 0.633647803583333

00:40:35.850 --> 00:40:38.328 We will now just switch gears and
NOTE Confidence: 0.633647803583333

00:40:38.328 --> 00:40:41.214 go to an acute graft history that
NOTE Confidence: 0.633647803583333

00:40:41.214 --> 00:40:43.224 is presented by Minnesota Group.
NOTE Confidence: 0.633647803583333

00:40:43.230 --> 00:40:45.288 This was a phase two study
NOTE Confidence: 0.633647803583333

00:40:45.290 --> 00:40:46.130 a couple of years ago.
NOTE Confidence: 0.633647803583333

00:40:46.130 --> 00:40:47.831 They presented their phase one data that
NOTE Confidence: 0.633647803583333

00:40:47.831 --> 00:40:49.598 was published in Blood Advances, Dr.
NOTE Confidence: 0.633647803583333

00:40:49.598 --> 00:40:52.718 Holton and ET al had led this study.
NOTE Confidence: 0.633647803583333

00:40:52.718 --> 00:40:54.602 Basically, the rationale behind
NOTE Confidence: 0.633647803583333

00:40:54.602 --> 00:40:57.022 using human chorionic troepen and
NOTE Confidence: 0.633647803583333

00:40:57.022 --> 00:40:59.089 epidermal growth factor is that.
NOTE Confidence: 0.633647803583333

00:40:59.090 --> 00:41:00.017 Acute GVHD happens.
NOTE Confidence: 0.633647803583333

00:41:00.017 --> 00:41:02.180 It's usually in the setting of an
NOTE Confidence: 0.633647803583333

00:41:02.244 --> 00:41:04.416 immune attack due to the discordance

NOTE Confidence: 0.633647803583333

00:41:04.416 --> 00:41:06.450 between the recipient and the host.

NOTE Confidence: 0.633647803583333

00:41:06.450 --> 00:41:07.890 Communist therapeutic interventions that

NOTE Confidence: 0.633647803583333

00:41:07.890 --> 00:41:10.050 we apply are all deeply immunosuppressive.

NOTE Confidence: 0.633647803583333

00:41:10.050 --> 00:41:12.732 But by the time the immune cells have caused

NOTE Confidence: 0.633647803583333

00:41:12.732 --> 00:41:15.449 an destruction to the epithelial lining.

NOTE Confidence: 0.633647803583333

00:41:15.450 --> 00:41:16.728 In the absence of anything else,

NOTE Confidence: 0.633647803583333

00:41:16.730 --> 00:41:18.826 we continue to escalate him in a suppression,

NOTE Confidence: 0.633647803583333

00:41:18.830 --> 00:41:20.830 but here they're trying to come up with

NOTE Confidence: 0.633647803583333

00:41:20.830 --> 00:41:22.640 the concept of using tissue repair

NOTE Confidence: 0.633647803583333

00:41:22.640 --> 00:41:24.524 mechanisms by using growth factor support

NOTE Confidence: 0.633647803583333

00:41:24.576 --> 00:41:26.586 mechanisms like epidermal growth factors.

NOTE Confidence: 0.633647803583333

00:41:26.590 --> 00:41:29.306 We also know the concept of pregnancy.

NOTE Confidence: 0.633647803583333

00:41:29.310 --> 00:41:31.590 We've all known that HCG is

NOTE Confidence: 0.633647803583333

00:41:31.590 --> 00:41:33.528 kind of taller rising rising,

NOTE Confidence: 0.633647803583333

00:41:33.528 --> 00:41:35.618 it increases the regular population

NOTE Confidence: 0.633647803583333

00:41:35.618 --> 00:41:37.290 compared to conventional subpopulation.

NOTE Confidence: 0.633647803583333

00:41:37.290 --> 00:41:39.414 It also has impact on anabolic

NOTE Confidence: 0.633647803583333

00:41:39.414 --> 00:41:40.830 sides of metabol ISM,

NOTE Confidence: 0.633647803583333

00:41:40.830 --> 00:41:43.018 and as I said.

NOTE Confidence: 0.633647803583333

00:41:43.020 --> 00:41:46.920 GF also decreases and regulation,

NOTE Confidence: 0.633647803583333

00:41:46.920 --> 00:41:48.708 which is kind of being thought

NOTE Confidence: 0.633647803583333

00:41:48.708 --> 00:41:50.935 as a marker of inflammation in

NOTE Confidence: 0.633647803583333

00:41:50.935 --> 00:41:53.350 addition to promoting promoting it.

NOTE Confidence: 0.633647803583333

00:41:53.350 --> 00:41:55.708 More and more T cell metabolic

NOTE Confidence: 0.633647803583333

00:41:55.708 --> 00:41:57.723 studies suggests that bit rate

NOTE Confidence: 0.633647803583333

00:41:57.723 --> 00:41:59.049 seems to promote expansion,

NOTE Confidence: 0.633647803583333

00:41:59.049 --> 00:42:00.801 which is kind of a thing we like

NOTE Confidence: 0.633647803583333

00:42:00.801 --> 00:42:02.449 in the field of transplantation.

NOTE Confidence: 0.633647803583333

00:42:02.450 --> 00:42:05.072 Unlike neoplasms where T Rex are not

NOTE Confidence: 0.633647803583333

00:42:05.072 --> 00:42:07.389 well liked upon but to develop tolerance,

NOTE Confidence: 0.633647803583333

00:42:07.390 --> 00:42:09.832 we, like any agents that increases

NOTE Confidence: 0.633647803583333
00:42:09.832 --> 00:42:10.646 direct population.
NOTE Confidence: 0.633647803583333
00:42:10.650 --> 00:42:13.517 So based on their phase one design they
NOTE Confidence: 0.633647803583333
00:42:13.517 --> 00:42:16.799 now where they identified 2000 units.
NOTE Confidence: 0.633647803583333
00:42:16.800 --> 00:42:19.686 Sorry, 2000 units as appropriate dose,
NOTE Confidence: 0.633647803583333
00:42:19.690 --> 00:42:20.986 and they included two risk groups.
NOTE Confidence: 0.633647803583333
00:42:20.990 --> 00:42:21.734 In Minnesota,
NOTE Confidence: 0.633647803583333
00:42:21.734 --> 00:42:23.594 High Risk Group and the.
NOTE Confidence: 0.633647803583333
00:42:23.600 --> 00:42:24.868 Second line therapeutic group.
NOTE Confidence: 0.633647803583333
00:42:24.868 --> 00:42:26.770 I can give references for this
NOTE Confidence: 0.633647803583333
00:42:26.826 --> 00:42:27.710 at a later stage.
NOTE Confidence: 0.633647803583333
00:42:27.710 --> 00:42:29.691 They were used to drug subq every
NOTE Confidence: 0.633647803583333
00:42:29.691 --> 00:42:31.581 other day for seven days in
NOTE Confidence: 0.633647803583333
00:42:31.581 --> 00:42:33.543 addition to the high dose steroids,
NOTE Confidence: 0.633647803583333
00:42:33.550 --> 00:42:35.320 which is the commonest Firstline agent
NOTE Confidence: 0.633647803583333
00:42:35.320 --> 00:42:37.710 we use for the second line cohort,
NOTE Confidence: 0.633647803583333

00:42:37.710 --> 00:42:39.210 they would use this combination

NOTE Confidence: 0.633647803583333

00:42:39.210 --> 00:42:40.337 the same dose subq.

NOTE Confidence: 0.633647803583333

00:42:40.337 --> 00:42:42.380 Or if you're going to use it at 5000

NOTE Confidence: 0.633647803583333

00:42:42.443 --> 00:42:44.564 units for those who are refractory was

NOTE Confidence: 0.633647803583333

00:42:44.564 --> 00:42:46.780 given every other day for 14 days in

NOTE Confidence: 0.633647803583333

00:42:46.780 --> 00:42:48.706 addition to the standard of care and

NOTE Confidence: 0.633647803583333

00:42:48.706 --> 00:42:51.072 that standard of care was left with

NOTE Confidence: 0.633647803583333

00:42:51.072 --> 00:42:53.809 the physicians based on their choice.

NOTE Confidence: 0.633647803583333

00:42:53.810 --> 00:42:55.376 This is just a brief synopsis

NOTE Confidence: 0.633647803583333

00:42:55.376 --> 00:42:57.219 of what were the cohorts like.

NOTE Confidence: 0.633647803583333

00:42:57.220 --> 00:42:57.438 Largely,

NOTE Confidence: 0.633647803583333

00:42:57.438 --> 00:42:58.964 I wanted to focus on the fact

NOTE Confidence: 0.633647803583333

00:42:58.964 --> 00:43:00.487 that in the first line cohort,

NOTE Confidence: 0.633647803583333

00:43:00.490 --> 00:43:02.260 most of those people were stage

NOTE Confidence: 0.633647803583333

00:43:02.260 --> 00:43:03.970 three to four lower GI GVHD,

NOTE Confidence: 0.633647803583333

00:43:03.970 --> 00:43:05.446 which is what is more challenging

NOTE Confidence: 0.633647803583333
00:43:05.446 --> 00:43:07.223 to manage in the second line cohort
NOTE Confidence: 0.633647803583333
00:43:07.223 --> 00:43:08.945 that did have a few skin cases,
NOTE Confidence: 0.633647803583333
00:43:08.950 --> 00:43:10.666 that was stage three or four,
NOTE Confidence: 0.633647803583333
00:43:10.670 --> 00:43:11.880 they have some pictures in
NOTE Confidence: 0.633647803583333
00:43:11.880 --> 00:43:12.364 their presentation.
NOTE Confidence: 0.633647803583333
00:43:12.370 --> 00:43:13.566 I'm not showing that,
NOTE Confidence: 0.633647803583333
00:43:13.566 --> 00:43:15.770 but they were pretty bad skin stays,
NOTE Confidence: 0.633647803583333
00:43:15.770 --> 00:43:16.402 but regardless,
NOTE Confidence: 0.633647803583333
00:43:16.402 --> 00:43:18.298 most of them are a grade
NOTE Confidence: 0.633647803583333
00:43:18.298 --> 00:43:20.029 three to four acute GVHD,
NOTE Confidence: 0.633647803583333
00:43:20.030 --> 00:43:22.606 which is kind of challenging to manage.
NOTE Confidence: 0.633647803583333
00:43:22.610 --> 00:43:24.490 Here are the response rates
NOTE Confidence: 0.573978271428571
00:43:24.490 --> 00:43:27.528 in the acute GVHD clinical drug development.
NOTE Confidence: 0.573978271428571
00:43:27.530 --> 00:43:29.462 28 year responses being kind of validated
NOTE Confidence: 0.573978271428571
00:43:29.462 --> 00:43:31.867 as a nice marker to predict responses,
NOTE Confidence: 0.573978271428571

00:43:31.870 --> 00:43:35.048 so date 28 for all patient cohorts.
NOTE Confidence: 0.573978271428571

00:43:35.050 --> 00:43:37.819 There was a 57% CR and 11% had
NOTE Confidence: 0.573978271428571

00:43:37.819 --> 00:43:39.564 partial responses for the high
NOTE Confidence: 0.573978271428571

00:43:39.564 --> 00:43:41.430 risk Minnesota Risk Group to see.
NOTE Confidence: 0.573978271428571

00:43:41.430 --> 00:43:43.686 Our rate was 64% in the second line,
NOTE Confidence: 0.573978271428571

00:43:43.690 --> 00:43:46.060 it was 50% CR rates.
NOTE Confidence: 0.573978271428571

00:43:46.060 --> 00:43:47.890 And here's a non elapsed
NOTE Confidence: 0.573978271428571

00:43:47.890 --> 00:43:50.380 mortality can easily lead to that.
NOTE Confidence: 0.573978271428571

00:43:50.380 --> 00:43:52.068 This is for the entire cohort in the
NOTE Confidence: 0.573978271428571

00:43:52.068 --> 00:43:53.577 dark clients for the high risk group.
NOTE Confidence: 0.573978271428571

00:43:53.580 --> 00:43:55.268 And this is for the second line group.
NOTE Confidence: 0.573978271428571

00:43:55.270 --> 00:43:57.118 The P value was not significant,
NOTE Confidence: 0.573978271428571

00:43:57.120 --> 00:43:58.737 but based on those who are responding,
NOTE Confidence: 0.573978271428571

00:43:58.740 --> 00:44:00.978 CR or PR is not responding.
NOTE Confidence: 0.573978271428571

00:44:00.980 --> 00:44:03.220 There seems to be a train that the
NOTE Confidence: 0.573978271428571

00:44:03.220 --> 00:44:05.413 non relapse mortality at two years

NOTE Confidence: 0.573978271428571

00:44:05.413 --> 00:44:07.373 is declining with this information.

NOTE Confidence: 0.573978271428571

00:44:07.380 --> 00:44:10.004 And here is the same analysis for overall

NOTE Confidence: 0.573978271428571

00:44:10.004 --> 00:44:11.898 survival based on the whole cohort.

NOTE Confidence: 0.573978271428571

00:44:11.900 --> 00:44:13.996 And this is for those who are responding

NOTE Confidence: 0.573978271428571

00:44:14.000 --> 00:44:15.710 based on this kind of response

NOTE Confidence: 0.573978271428571

00:44:15.710 --> 00:44:17.650 we elicit with this intervention.

NOTE Confidence: 0.573978271428571

00:44:17.650 --> 00:44:19.904 When they presented the causes of that,

NOTE Confidence: 0.573978271428571

00:44:19.910 --> 00:44:22.304 it's really interesting that happens to be

NOTE Confidence: 0.573978271428571

00:44:22.304 --> 00:44:24.467 still a communist cause of death, right?

NOTE Confidence: 0.573978271428571

00:44:24.467 --> 00:44:25.986 About half of the patients had died,

NOTE Confidence: 0.573978271428571

00:44:25.990 --> 00:44:28.027 with a median follow-up of 17 months.

NOTE Confidence: 0.573978271428571

00:44:28.030 --> 00:44:30.228 Relapse is the second most common stuff,

NOTE Confidence: 0.573978271428571

00:44:30.230 --> 00:44:31.680 and infections and organ damage

NOTE Confidence: 0.573978271428571

00:44:31.680 --> 00:44:32.550 with common livery,

NOTE Confidence: 0.573978271428571

00:44:32.550 --> 00:44:34.310 and that didn't seem to be that much.

NOTE Confidence: 0.573978271428571

00:44:34.310 --> 00:44:37.348 But again, it's a small patient population.
NOTE Confidence: 0.573978271428571

00:44:37.350 --> 00:44:37.920 In summary,
NOTE Confidence: 0.573978271428571

00:44:37.920 --> 00:44:40.601 I think they show that the response rate of
NOTE Confidence: 0.573978271428571

00:44:40.601 --> 00:44:42.665 68 percent is pretty reasonably accepted,
NOTE Confidence: 0.573978271428571

00:44:42.670 --> 00:44:43.636 and day 28,
NOTE Confidence: 0.573978271428571

00:44:43.636 --> 00:44:45.568 and doesn't significantly impact on relapse.
NOTE Confidence: 0.573978271428571

00:44:45.570 --> 00:44:47.593 Mortality based on the fact that people
NOTE Confidence: 0.573978271428571

00:44:47.593 --> 00:44:49.670 are still dying with GST and relapses,
NOTE Confidence: 0.573978271428571

00:44:49.670 --> 00:44:53.390 they're recommending either using biomarkers,
NOTE Confidence: 0.573978271428571

00:44:53.390 --> 00:44:55.448 and they have some nice profile of
NOTE Confidence: 0.573978271428571

00:44:55.448 --> 00:44:56.888 metabolic stuff that they reported
NOTE Confidence: 0.573978271428571

00:44:56.888 --> 00:44:58.896 which I can talk to you later on,
NOTE Confidence: 0.573978271428571

00:44:58.900 --> 00:45:00.573 but it's kind of now in development
NOTE Confidence: 0.573978271428571

00:45:00.573 --> 00:45:02.622 in the field that we don't necessarily
NOTE Confidence: 0.573978271428571

00:45:02.622 --> 00:45:04.536 have to keep thinking about escalating
NOTE Confidence: 0.573978271428571

00:45:04.591 --> 00:45:05.490 immunosuppression,

NOTE Confidence: 0.573978271428571

00:45:05.490 --> 00:45:07.135 but now we need to start focusing.

NOTE Confidence: 0.573978271428571

00:45:07.140 --> 00:45:11.610 On getting the right immunomodulation in

NOTE Confidence: 0.573978271428571

00:45:11.610 --> 00:45:15.080 addition to tissue repair pathway drugs.

NOTE Confidence: 0.573978271428571

00:45:15.080 --> 00:45:17.600 In the other half of the talk,

NOTE Confidence: 0.573978271428571

00:45:17.600 --> 00:45:20.687 I'm going to talk about chronic GVHD.

NOTE Confidence: 0.573978271428571

00:45:20.690 --> 00:45:23.320 For some of us who do this on a daily basis,

NOTE Confidence: 0.573978271428571

00:45:23.320 --> 00:45:24.904 we see this in up to about 50%

NOTE Confidence: 0.573978271428571

00:45:24.910 --> 00:45:27.046 of patient population use of post

NOTE Confidence: 0.573978271428571

00:45:27.046 --> 00:45:28.114 transplant cyclophosphamide has

NOTE Confidence: 0.573978271428571

00:45:28.114 --> 00:45:29.349 brought that number down,

NOTE Confidence: 0.573978271428571

00:45:29.350 --> 00:45:31.132 but most people don't get it

NOTE Confidence: 0.573978271428571

00:45:31.132 --> 00:45:32.320 because cyclophosphamide does have

NOTE Confidence: 0.573978271428571

00:45:32.374 --> 00:45:33.976 some issues in terms of infection,

NOTE Confidence: 0.573978271428571

00:45:33.980 --> 00:45:36.040 cardiac toxicity and other things,

NOTE Confidence: 0.573978271428571

00:45:36.040 --> 00:45:37.570 and again it's largely applied in

NOTE Confidence: 0.573978271428571

00:45:37.570 --> 00:45:38.900 the setting of unrelated donors
NOTE Confidence: 0.573978271428571

00:45:38.900 --> 00:45:40.832 and not commonly used in massively
NOTE Confidence: 0.573978271428571

00:45:40.832 --> 00:45:41.476 donor transplantation.
NOTE Confidence: 0.573978271428571

00:45:41.480 --> 00:45:43.000 For those who develop,
NOTE Confidence: 0.573978271428571

00:45:43.000 --> 00:45:45.410 chronic steroids has been the workhorse
NOTE Confidence: 0.573978271428571

00:45:45.410 --> 00:45:47.034 for multiple multiple decades.
NOTE Confidence: 0.573978271428571

00:45:47.040 --> 00:45:48.520 About half of those patients
NOTE Confidence: 0.573978271428571

00:45:48.520 --> 00:45:50.000 eventually need second line treatment
NOTE Confidence: 0.573978271428571

00:45:50.051 --> 00:45:51.128 for disease progression.
NOTE Confidence: 0.573978271428571

00:45:51.130 --> 00:45:53.710 And they don't tend to do well at that stage.
NOTE Confidence: 0.573978271428571

00:45:53.710 --> 00:45:54.886 Up until a year,
NOTE Confidence: 0.573978271428571

00:45:54.886 --> 00:45:56.650 year and half ago really didn't
NOTE Confidence: 0.573978271428571

00:45:56.714 --> 00:45:58.570 have that many drugs in Brittany
NOTE Confidence: 0.573978271428571

00:45:58.570 --> 00:46:00.460 was approved a few years ago.
NOTE Confidence: 0.573978271428571

00:46:00.460 --> 00:46:01.552 Based on this trial,
NOTE Confidence: 0.573978271428571

00:46:01.552 --> 00:46:02.644 it's a boutique inhibitor.

NOTE Confidence: 0.573978271428571

00:46:02.650 --> 00:46:03.814 As you all know,

NOTE Confidence: 0.573978271428571

00:46:03.814 --> 00:46:05.713 the overall response rate was 67%,

NOTE Confidence: 0.573978271428571

00:46:05.713 --> 00:46:07.928 CR was 21% in that

NOTE Confidence: 0.794081502857143

00:46:07.930 --> 00:46:09.498 in the last 12 to 24 months.

NOTE Confidence: 0.794081502857143

00:46:09.500 --> 00:46:11.656 Now we have two drugs belimo saddle

NOTE Confidence: 0.794081502857143

00:46:11.656 --> 00:46:13.930 which is a rock to inhibition.

NOTE Confidence: 0.794081502857143

00:46:13.930 --> 00:46:15.680 That's not only has anti-inflammatory

NOTE Confidence: 0.794081502857143

00:46:15.680 --> 00:46:17.590 properties, but it also kind of

NOTE Confidence: 0.794081502857143

00:46:17.590 --> 00:46:19.630 targets the scarring part of it,

NOTE Confidence: 0.794081502857143

00:46:19.630 --> 00:46:21.366 which is kind of a novel mechanisms.

NOTE Confidence: 0.794081502857143

00:46:21.370 --> 00:46:24.430 Here the overall rate was 73% in the CR.

NOTE Confidence: 0.794081502857143

00:46:24.430 --> 00:46:26.743 CRA despite being low the PR was

NOTE Confidence: 0.794081502857143

00:46:26.743 --> 00:46:28.941 high but based on the fact that

NOTE Confidence: 0.794081502857143

00:46:28.941 --> 00:46:30.672 it targets the scarring pathway,

NOTE Confidence: 0.794081502857143

00:46:30.672 --> 00:46:32.084 it's been approved recently.

NOTE Confidence: 0.794081502857143

00:46:32.090 --> 00:46:34.600 In addition to controlling gived.
NOTE Confidence: 0.794081502857143

00:46:34.600 --> 00:46:37.897 Uh, I spoke to you earlier on.
NOTE Confidence: 0.794081502857143

00:46:37.900 --> 00:46:40.210 Fracture GBST in the last six months.
NOTE Confidence: 0.794081502857143

00:46:40.210 --> 00:46:42.919 It's also been approved for chronic GVHD.
NOTE Confidence: 0.794081502857143

00:46:42.920 --> 00:46:46.016 Again, the rates of CR is close to about 50%.
NOTE Confidence: 0.794081502857143

00:46:46.016 --> 00:46:47.552 Most of these drugs are approved
NOTE Confidence: 0.794081502857143

00:46:47.552 --> 00:46:49.076 for people who fail at least
NOTE Confidence: 0.794081502857143

00:46:49.076 --> 00:46:50.486 two or more lines of therapy,
NOTE Confidence: 0.794081502857143

00:46:50.490 --> 00:46:52.638 but these lines of response rate
NOTE Confidence: 0.794081502857143

00:46:52.638 --> 00:46:54.885 suggests there is still more that's
NOTE Confidence: 0.794081502857143

00:46:54.885 --> 00:46:56.755 needed to optimize the speed.
NOTE Confidence: 0.794081502857143

00:46:56.760 --> 00:46:58.620 One of the yes,
NOTE Confidence: 0.794081502857143

00:46:58.620 --> 00:47:01.620 which is kind of not that commonly explored,
NOTE Confidence: 0.794081502857143

00:47:01.620 --> 00:47:02.760 but it's kind of.
NOTE Confidence: 0.794081502857143

00:47:02.760 --> 00:47:04.060 It's a welcome change.
NOTE Confidence: 0.794081502857143

00:47:04.060 --> 00:47:04.710 It's commonly,

NOTE Confidence: 0.794081502857143
00:47:04.710 --> 00:47:07.097 we think about jobs as a T
NOTE Confidence: 0.794081502857143
00:47:07.097 --> 00:47:08.120 cell mediated pathway.
NOTE Confidence: 0.794081502857143
00:47:08.120 --> 00:47:10.316 This work that was presented by
NOTE Confidence: 0.794081502857143
00:47:10.316 --> 00:47:12.260 Stephanie Lee's group from Fred
NOTE Confidence: 0.794081502857143
00:47:12.260 --> 00:47:14.756 Hutch is now looking into targeting
NOTE Confidence: 0.794081502857143
00:47:14.756 --> 00:47:16.546 macrophage driven chronic drug
NOTE Confidence: 0.794081502857143
00:47:16.546 --> 00:47:19.171 Physiology colony stimulating factor
NOTE Confidence: 0.794081502857143
00:47:19.171 --> 00:47:22.039 1 receptor mediated pathways.
NOTE Confidence: 0.794081502857143
00:47:22.040 --> 00:47:23.312 Once someone is circulating,
NOTE Confidence: 0.794081502857143
00:47:23.312 --> 00:47:25.611 they can get into the tissues and
NOTE Confidence: 0.794081502857143
00:47:25.611 --> 00:47:27.585 then they can differentiate in either.
NOTE Confidence: 0.794081502857143
00:47:27.590 --> 00:47:30.290 I'm wondering 2 phenotypes of macrophages,
NOTE Confidence: 0.794081502857143
00:47:30.290 --> 00:47:32.606 which them one being pro inflammatory,
NOTE Confidence: 0.794081502857143
00:47:32.610 --> 00:47:33.798 this being anti inflammatory.
NOTE Confidence: 0.794081502857143
00:47:33.798 --> 00:47:35.580 But now people are looking into
NOTE Confidence: 0.794081502857143

00:47:35.630 --> 00:47:37.146 developing drugs against tests
NOTE Confidence: 0.794081502857143

00:47:37.146 --> 00:47:38.662 which promotes this differentiation
NOTE Confidence: 0.794081502857143

00:47:38.662 --> 00:47:40.236 to decrease the inflammation and
NOTE Confidence: 0.794081502857143

00:47:40.236 --> 00:47:42.007 the drug that I'm going to talk
NOTE Confidence: 0.794081502857143

00:47:42.010 --> 00:47:44.712 to you is a CC colony stimulating
NOTE Confidence: 0.794081502857143

00:47:44.712 --> 00:47:46.630 factor 1 receptor antibody.
NOTE Confidence: 0.794081502857143

00:47:46.630 --> 00:47:48.496 Inhibition of that is start to
NOTE Confidence: 0.794081502857143

00:47:48.496 --> 00:47:50.857 decrease 5 process and make bring about
NOTE Confidence: 0.794081502857143

00:47:50.857 --> 00:47:52.617 changes in collagen structure which
NOTE Confidence: 0.794081502857143

00:47:52.617 --> 00:47:55.084 kind of then has impact and tissue
NOTE Confidence: 0.794081502857143

00:47:55.084 --> 00:47:58.830 healing for people with chronic dry.
NOTE Confidence: 0.794081502857143

00:47:58.830 --> 00:48:02.370 The drug is exactly exactly map.
NOTE Confidence: 0.794081502857143

00:48:02.370 --> 00:48:03.966 As I said, it's a humanized IgG.
NOTE Confidence: 0.794081502857143

00:48:03.970 --> 00:48:06.595 4 monoclonal antibody binds to
NOTE Confidence: 0.794081502857143

00:48:06.595 --> 00:48:08.170 CSF 1 receptor.
NOTE Confidence: 0.794081502857143

00:48:08.170 --> 00:48:10.346 In addition, it also binds to oil 34,

NOTE Confidence: 0.794081502857143
00:48:10.350 --> 00:48:13.409 which has informative properties in the skin.
NOTE Confidence: 0.794081502857143
00:48:13.410 --> 00:48:14.695 It's administered over 30 minutes
NOTE Confidence: 0.794081502857143
00:48:14.695 --> 00:48:16.310 for every two to four weeks.
NOTE Confidence: 0.794081502857143
00:48:16.310 --> 00:48:17.790 It's highly effective in decreasing
NOTE Confidence: 0.794081502857143
00:48:17.790 --> 00:48:19.270 the fiber optic signals on
NOTE Confidence: 0.794081502857143
00:48:19.320 --> 00:48:20.610 the nonclassical monocytes.
NOTE Confidence: 0.794081502857143
00:48:20.610 --> 00:48:21.352 In addition,
NOTE Confidence: 0.794081502857143
00:48:21.352 --> 00:48:23.207 using this intermittent dosing pathway,
NOTE Confidence: 0.794081502857143
00:48:23.210 --> 00:48:25.310 they found that you know gives
NOTE Confidence: 0.794081502857143
00:48:25.310 --> 00:48:27.372 opportunities to keep the drugs going
NOTE Confidence: 0.794081502857143
00:48:27.372 --> 00:48:29.027 frequently because the cells do.
NOTE Confidence: 0.794081502857143
00:48:29.030 --> 00:48:30.810 So in the mean time this was
NOTE Confidence: 0.794081502857143
00:48:30.810 --> 00:48:32.550 a phase one two study design.
NOTE Confidence: 0.794081502857143
00:48:32.550 --> 00:48:34.446 They wanted to test the phase
NOTE Confidence: 0.794081502857143
00:48:34.446 --> 00:48:35.710 one about 17 patients,
NOTE Confidence: 0.794081502857143

00:48:35.710 --> 00:48:36.120 a point
NOTE Confidence: 0.649108285555556

00:48:39.150 --> 00:48:41.886 15.5133 given over Q4 weeks at Q 2 weeks,
NOTE Confidence: 0.649108285555556

00:48:41.890 --> 00:48:43.591 and then they went to the phase
NOTE Confidence: 0.649108285555556

00:48:43.591 --> 00:48:45.589 expansion at 1 milligram per kilogram.
NOTE Confidence: 0.649108285555556

00:48:45.590 --> 00:48:47.630 That included a larger number
NOTE Confidence: 0.649108285555556

00:48:47.630 --> 00:48:48.854 of patient population.
NOTE Confidence: 0.649108285555556

00:48:48.860 --> 00:48:50.845 Presented here is a baseline
NOTE Confidence: 0.649108285555556

00:48:50.845 --> 00:48:52.036 characteristics for patients.
NOTE Confidence: 0.649108285555556

00:48:52.040 --> 00:48:54.035 A quick summary of this is that
NOTE Confidence: 0.649108285555556

00:48:54.035 --> 00:48:56.168 most of these people were heavily
NOTE Confidence: 0.649108285555556

00:48:56.168 --> 00:48:58.625 treated that more than half of the
NOTE Confidence: 0.649108285555556

00:48:58.625 --> 00:49:00.919 people in both phase one and two.
NOTE Confidence: 0.649108285555556

00:49:00.920 --> 00:49:03.636 I had four or more organs involved
NOTE Confidence: 0.649108285555556

00:49:03.640 --> 00:49:05.360 consistent with modern tactics.
NOTE Confidence: 0.649108285555556

00:49:05.360 --> 00:49:08.272 People have been exposed to Brittany and
NOTE Confidence: 0.649108285555556

00:49:08.272 --> 00:49:10.928 which is the rock number that I showed.

NOTE Confidence: 0.649108285555556
00:49:10.930 --> 00:49:12.058 I'm I'm there,
NOTE Confidence: 0.649108285555556
00:49:12.058 --> 00:49:14.314 basically show that there's no differences
NOTE Confidence: 0.649108285555556
00:49:14.314 --> 00:49:16.380 between Android patient populations.
NOTE Confidence: 0.649108285555556
00:49:16.380 --> 00:49:19.020 Uh, and the drug seems to be pretty
NOTE Confidence: 0.649108285555556
00:49:19.020 --> 00:49:21.279 well tolerated across both groups.
NOTE Confidence: 0.649108285555556
00:49:21.279 --> 00:49:22.878 The discontinuation rate,
NOTE Confidence: 0.649108285555556
00:49:22.880 --> 00:49:23.960 although seems to be high,
NOTE Confidence: 0.649108285555556
00:49:23.960 --> 00:49:26.298 but in this context it's pretty challenging,
NOTE Confidence: 0.649108285555556
00:49:26.300 --> 00:49:28.295 and about 30% in the phase one,
NOTE Confidence: 0.649108285555556
00:49:28.300 --> 00:49:30.196 and about 58% are still continuing.
NOTE Confidence: 0.649108285555556
00:49:30.200 --> 00:49:33.398 This drug in the phase two.
NOTE Confidence: 0.649108285555556
00:49:33.400 --> 00:49:34.650 More interestingly,
NOTE Confidence: 0.649108285555556
00:49:34.650 --> 00:49:37.150 is the response rate.
NOTE Confidence: 0.649108285555556
00:49:37.150 --> 00:49:38.425 Most of the responses we
NOTE Confidence: 0.649108285555556
00:49:38.425 --> 00:49:39.445 do show that responsive,
NOTE Confidence: 0.649108285555556

00:49:39.450 --> 00:49:41.305 especially with this one milligram per KQ,
NOTE Confidence: 0.649108285555556

00:49:41.310 --> 00:49:43.790 2 weeks our sponsor seems to be pretty
NOTE Confidence: 0.649108285555556

00:49:43.790 --> 00:49:46.094 durable and same is the case with
NOTE Confidence: 0.649108285555556

00:49:46.094 --> 00:49:47.956 three milligrams per kick and when
NOTE Confidence: 0.649108285555556

00:49:47.956 --> 00:49:49.654 you look around their best overall
NOTE Confidence: 0.649108285555556

00:49:49.654 --> 00:49:51.448 response rates and time from responses,
NOTE Confidence: 0.649108285555556

00:49:51.450 --> 00:49:53.091 that's reasonably impressive,
NOTE Confidence: 0.649108285555556

00:49:53.091 --> 00:49:55.279 but time to responsive.
NOTE Confidence: 0.649108285555556

00:49:55.280 --> 00:49:56.784 One month it's something
NOTE Confidence: 0.649108285555556

00:49:56.784 --> 00:49:58.664 that you don't often see,
NOTE Confidence: 0.649108285555556

00:49:58.670 --> 00:50:01.190 and that's a welcome change.
NOTE Confidence: 0.649108285555556

00:50:01.190 --> 00:50:03.381 The next question people come commonly ask
NOTE Confidence: 0.649108285555556

00:50:03.381 --> 00:50:05.809 is how about organ specific responses?
NOTE Confidence: 0.649108285555556

00:50:05.810 --> 00:50:07.735 Well, light light Gray or blue ish
NOTE Confidence: 0.649108285555556

00:50:07.735 --> 00:50:10.069 is the CR rates in the dark ones.
NOTE Confidence: 0.649108285555556

00:50:10.070 --> 00:50:11.646 The PR lower GI?

NOTE Confidence: 0.649108285555556

00:50:11.646 --> 00:50:14.010 Everybody seems to have good responses.

NOTE Confidence: 0.649108285555556

00:50:14.010 --> 00:50:15.648 What what's of interest to us

NOTE Confidence: 0.649108285555556

00:50:15.648 --> 00:50:17.330 is the Giants and the skin,

NOTE Confidence: 0.649108285555556

00:50:17.330 --> 00:50:20.025 which seems to be PR based on

NOTE Confidence: 0.649108285555556

00:50:20.025 --> 00:50:21.180 its antifibrotic mechanisms.

NOTE Confidence: 0.649108285555556

00:50:21.180 --> 00:50:22.684 People ask me what happens to the lung,

NOTE Confidence: 0.649108285555556

00:50:22.690 --> 00:50:24.952 which is more common and challenging

NOTE Confidence: 0.649108285555556

00:50:24.952 --> 00:50:25.706 to handle?

NOTE Confidence: 0.649108285555556

00:50:25.710 --> 00:50:27.897 Seems like you know at least five out of

NOTE Confidence: 0.649108285555556

00:50:27.897 --> 00:50:30.226 15 patients is a reasonable one for CR.

NOTE Confidence: 0.649108285555556

00:50:30.230 --> 00:50:31.660 When it types the lung.

NOTE Confidence: 0.649108285555556

00:50:31.660 --> 00:50:34.482 And and and about 88% at serious

NOTE Confidence: 0.649108285555556

00:50:34.482 --> 00:50:36.512 skin sclerosis are baseline close

NOTE Confidence: 0.649108285555556

00:50:36.512 --> 00:50:40.000 to 16% on improvement in sclerosis.

NOTE Confidence: 0.649108285555556

00:50:40.000 --> 00:50:41.645 Another aspect that we tend to ignore

NOTE Confidence: 0.649108285555556

00:50:41.645 --> 00:50:43.719 is you might have clinical manifestation,
NOTE Confidence: 0.649108285555556

00:50:43.720 --> 00:50:45.520 but what about the quality of
NOTE Confidence: 0.649108285555556

00:50:45.520 --> 00:50:46.720 lives and symptom burden?
NOTE Confidence: 0.649108285555556

00:50:46.720 --> 00:50:48.939 And here's just a graph in somebody
NOTE Confidence: 0.649108285555556

00:50:48.939 --> 00:50:50.502 that's depicting that across the
NOTE Confidence: 0.649108285555556

00:50:50.502 --> 00:50:52.820 dose people had good responses
NOTE Confidence: 0.649108285555556

00:50:52.820 --> 00:50:54.860 in the symptom scale.
NOTE Confidence: 0.649108285555556

00:50:54.860 --> 00:50:55.500 In conclusion,
NOTE Confidence: 0.649108285555556

00:50:55.500 --> 00:50:57.100 I think the investigators were
NOTE Confidence: 0.649108285555556

00:50:57.100 --> 00:50:59.065 able to show that targeting
NOTE Confidence: 0.649108285555556

00:50:59.065 --> 00:51:00.487 monocyte macrophage pathway,
NOTE Confidence: 0.649108285555556

00:51:00.490 --> 00:51:04.434 the CSF one receptor ligand seems to be
NOTE Confidence: 0.649108285555556

00:51:04.434 --> 00:51:07.422 meaningful leads to decent response rates.
NOTE Confidence: 0.649108285555556

00:51:07.430 --> 00:51:10.190 Sclerosis seems to go down on it now.
NOTE Confidence: 0.649108285555556

00:51:10.190 --> 00:51:12.206 There's a trial that they're going
NOTE Confidence: 0.649108285555556

00:51:12.206 --> 00:51:13.550 to randomize different doses,

NOTE Confidence: 0.649108285555556

00:51:13.550 --> 00:51:15.896 potentially as a group with contemplating

NOTE Confidence: 0.649108285555556

00:51:15.900 --> 00:51:17.168 participating in this thing,

NOTE Confidence: 0.649108285555556

00:51:17.168 --> 00:51:19.873 but it's kind of opened up the concept

NOTE Confidence: 0.649108285555556

00:51:19.873 --> 00:51:21.718 of targeting monocyte macrophages in

NOTE Confidence: 0.649108285555556

00:51:21.718 --> 00:51:24.138 addition to the T cell thing that

NOTE Confidence: 0.649108285555556

00:51:24.138 --> 00:51:26.010 we commonly pursued in chronic GVHD.

NOTE Confidence: 0.649108285555556

00:51:26.010 --> 00:51:27.340 On the last day that I'm going

NOTE Confidence: 0.649108285555556

00:51:27.340 --> 00:51:28.650 to talk about is a better set,

NOTE Confidence: 0.649108285555556

00:51:28.650 --> 00:51:31.495 this was a study that was done at Boston.

NOTE Confidence: 0.649108285555556

00:51:31.495 --> 00:51:34.165 Abbott stepped as you all know,

NOTE Confidence: 0.649108285555556

00:51:34.170 --> 00:51:37.668 is a T cell costimulation modulator,

NOTE Confidence: 0.616817497777778

00:51:37.670 --> 00:51:39.650 the T cell receptors.

NOTE Confidence: 0.616817497777778

00:51:39.650 --> 00:51:42.125 After recognizing the APKS would

NOTE Confidence: 0.616817497777778

00:51:42.130 --> 00:51:44.754 interact with them and the CD 20 would

NOTE Confidence: 0.616817497777778

00:51:44.754 --> 00:51:47.640 normally interact with the CD 86.

NOTE Confidence: 0.616817497777778

00:51:47.640 --> 00:51:49.840 For this is necessary for T cell activation,
NOTE Confidence: 0.616817497777778

00:51:49.840 --> 00:51:51.370 proliferation and production
NOTE Confidence: 0.616817497777778

00:51:51.370 --> 00:51:52.900 of inflammatory mediators,
NOTE Confidence: 0.616817497777778

00:51:52.900 --> 00:51:55.260 whereas inhibits this pathway
NOTE Confidence: 0.616817497777778

00:51:55.260 --> 00:51:57.234 by targeting CD 1886,
NOTE Confidence: 0.616817497777778

00:51:57.234 --> 00:51:58.822 and this costimulation doesn't
NOTE Confidence: 0.616817497777778

00:51:58.822 --> 00:52:00.455 happen and the hypothesis here is
NOTE Confidence: 0.616817497777778

00:52:00.455 --> 00:52:02.076 that if you somehow can prevent
NOTE Confidence: 0.616817497777778

00:52:02.076 --> 00:52:03.420 this T cell costimulation,
NOTE Confidence: 0.616817497777778

00:52:03.420 --> 00:52:04.359 maybe the proliferation
NOTE Confidence: 0.616817497777778

00:52:04.359 --> 00:52:05.298 activation doesn't happen.
NOTE Confidence: 0.616817497777778

00:52:05.300 --> 00:52:08.408 That leads to decrease chronic dry.
NOTE Confidence: 0.616817497777778

00:52:08.410 --> 00:52:10.670 About six months ago I.
NOTE Confidence: 0.616817497777778

00:52:10.670 --> 00:52:12.329 I know I'm using the six months
NOTE Confidence: 0.616817497777778

00:52:12.329 --> 00:52:13.678 one year commonly because that's
NOTE Confidence: 0.616817497777778

00:52:13.678 --> 00:52:14.850 how frequently the drugs are

NOTE Confidence: 0.616817497777778
00:52:14.850 --> 00:52:15.950 getting approved in this space.
NOTE Confidence: 0.616817497777778
00:52:15.950 --> 00:52:16.416 Recently,
NOTE Confidence: 0.616817497777778
00:52:16.416 --> 00:52:18.746 the drug was actually approved
NOTE Confidence: 0.616817497777778
00:52:18.746 --> 00:52:21.050 for prevention of acute GVHD.
NOTE Confidence: 0.616817497777778
00:52:21.050 --> 00:52:23.230 Yeah, mainly for unrelated donors,
NOTE Confidence: 0.616817497777778
00:52:23.230 --> 00:52:25.170 so this is a study in the backdrop of that,
NOTE Confidence: 0.616817497777778
00:52:25.170 --> 00:52:26.822 but obviously the context
NOTE Confidence: 0.616817497777778
00:52:26.822 --> 00:52:28.887 is in a chronic dbcontext,
NOTE Confidence: 0.616817497777778
00:52:28.890 --> 00:52:30.444 so people are wanting to say yes.
NOTE Confidence: 0.616817497777778
00:52:30.450 --> 00:52:31.692 This is a drug that's not
NOTE Confidence: 0.616817497777778
00:52:31.692 --> 00:52:32.790 going to be commonly used.
NOTE Confidence: 0.616817497777778
00:52:32.790 --> 00:52:35.184 What happens in the chronic dry setting?
NOTE Confidence: 0.616817497777778
00:52:35.190 --> 00:52:37.142 So the design was this close to 40
NOTE Confidence: 0.616817497777778
00:52:37.142 --> 00:52:39.060 patients who had both are bleeding
NOTE Confidence: 0.616817497777778
00:52:39.060 --> 00:52:40.432 and reduced density transplants
NOTE Confidence: 0.616817497777778

00:52:40.432 --> 00:52:41.913 and declared themselves steroid
NOTE Confidence: 0.616817497777778

00:52:41.913 --> 00:52:43.389 refractory and the definition
NOTE Confidence: 0.616817497777778

00:52:43.389 --> 00:52:45.156 of that was persistent science
NOTE Confidence: 0.616817497777778

00:52:45.156 --> 00:52:46.586 and symptoms of chronic GVHD.
NOTE Confidence: 0.616817497777778

00:52:46.590 --> 00:52:47.842 Despite use of steroids,
NOTE Confidence: 0.616817497777778

00:52:47.842 --> 00:52:49.720 .5 mix perchik per day for
NOTE Confidence: 0.616817497777778

00:52:49.789 --> 00:52:51.017 at least four weeks.
NOTE Confidence: 0.616817497777778

00:52:51.020 --> 00:52:51.955 They were to be getting
NOTE Confidence: 0.616817497777778

00:52:51.955 --> 00:52:53.140 this to stand mix for cake,
NOTE Confidence: 0.616817497777778

00:52:53.140 --> 00:52:54.598 which is what was acute GVHD.
NOTE Confidence: 0.616817497777778

00:52:54.600 --> 00:52:56.434 Dose was every two weeks for three
NOTE Confidence: 0.616817497777778

00:52:56.434 --> 00:52:58.383 doses and then they would go on to
NOTE Confidence: 0.616817497777778

00:52:58.383 --> 00:53:00.484 get it for every four weeks for three
NOTE Confidence: 0.616817497777778

00:53:00.484 --> 00:53:02.380 doses based on the clinical response,
NOTE Confidence: 0.616817497777778

00:53:02.380 --> 00:53:03.814 there was no response will come
NOTE Confidence: 0.616817497777778

00:53:03.814 --> 00:53:05.503 off that a clinical response for

NOTE Confidence: 0.616817497777778
00:53:05.503 --> 00:53:06.875 their continuation was allowed.
NOTE Confidence: 0.616817497777778
00:53:06.880 --> 00:53:09.504 The aim was to look into the rates
NOTE Confidence: 0.616817497777778
00:53:09.504 --> 00:53:11.260 of overall response rates and
NOTE Confidence: 0.616817497777778
00:53:11.260 --> 00:53:13.390 see how things were playing out.
NOTE Confidence: 0.616817497777778
00:53:13.390 --> 00:53:15.030 And this is just a description of things.
NOTE Confidence: 0.616817497777778
00:53:15.030 --> 00:53:18.003 Go on the oral response rate was 49%.
NOTE Confidence: 0.616817497777778
00:53:18.003 --> 00:53:18.356 Unfortunately,
NOTE Confidence: 0.616817497777778
00:53:18.356 --> 00:53:20.827 CR was zero and most of them
NOTE Confidence: 0.616817497777778
00:53:20.827 --> 00:53:22.119 were PR responses.
NOTE Confidence: 0.616817497777778
00:53:22.120 --> 00:53:23.710 This is just a spread
NOTE Confidence: 0.616817497777778
00:53:23.710 --> 00:53:24.664 across different organs.
NOTE Confidence: 0.616817497777778
00:53:24.670 --> 00:53:25.480 In the interest of time,
NOTE Confidence: 0.616817497777778
00:53:25.480 --> 00:53:27.230 I'm going to quit that and this
NOTE Confidence: 0.616817497777778
00:53:27.230 --> 00:53:29.228 is the slide that basically shows.
NOTE Confidence: 0.616817497777778
00:53:29.230 --> 00:53:30.650 While look at response rates,
NOTE Confidence: 0.616817497777778

00:53:30.650 --> 00:53:32.939 its importance to Ryan has been the
NOTE Confidence: 0.616817497777778

00:53:32.939 --> 00:53:34.873 main drug that we've used quite
NOTE Confidence: 0.616817497777778

00:53:34.873 --> 00:53:36.434 a few other people were able to
NOTE Confidence: 0.616817497777778

00:53:36.434 --> 00:53:37.928 decrease down their dose of steroids,
NOTE Confidence: 0.616817497777778

00:53:37.930 --> 00:53:39.560 which has long term implications
NOTE Confidence: 0.616817497777778

00:53:39.560 --> 00:53:40.864 on their metabolic health,
NOTE Confidence: 0.616817497777778

00:53:40.870 --> 00:53:41.566 mental health,
NOTE Confidence: 0.616817497777778

00:53:41.566 --> 00:53:43.654 cardiovascular risk and things like that.
NOTE Confidence: 0.616817497777778

00:53:43.660 --> 00:53:46.848 So with that the.
NOTE Confidence: 0.616817497777778

00:53:46.848 --> 00:53:49.288 Investigators conclude now a 50%
NOTE Confidence: 0.616817497777778

00:53:49.290 --> 00:53:51.582 objective response rate or are in
NOTE Confidence: 0.616817497777778

00:53:51.582 --> 00:53:54.298 the cirrhotic factory is a welcome change.
NOTE Confidence: 0.616817497777778

00:53:54.300 --> 00:53:54.704 Importantly,
NOTE Confidence: 0.616817497777778

00:53:54.704 --> 00:53:57.128 there was a durable reduction in
NOTE Confidence: 0.616817497777778

00:53:57.128 --> 00:53:58.789 Prednisone dosing overtime infections
NOTE Confidence: 0.616817497777778

00:53:58.789 --> 00:54:00.709 were uncommon in this context,

NOTE Confidence: 0.616817497777778
00:54:00.710 --> 00:54:02.546 and infusions were pretty well tolerated.
NOTE Confidence: 0.616817497777778
00:54:02.550 --> 00:54:04.128 Their ongoing studies,
NOTE Confidence: 0.616817497777778
00:54:04.128 --> 00:54:05.706 correlate's and biomarkers,
NOTE Confidence: 0.616817497777778
00:54:05.710 --> 00:54:06.654 and things like that.
NOTE Confidence: 0.616817497777778
00:54:06.654 --> 00:54:07.126 With that,
NOTE Confidence: 0.616817497777778
00:54:07.130 --> 00:54:08.775 I'll end the top and thank everybody
NOTE Confidence: 0.616817497777778
00:54:08.775 --> 00:54:10.406 for coming and I'll open it up
NOTE Confidence: 0.616817497777778
00:54:10.406 --> 00:54:11.060 for the audience.
NOTE Confidence: 0.9663661
00:54:15.530 --> 00:54:17.690 So we're going to open this up to questions.
NOTE Confidence: 0.946120445
00:54:17.690 --> 00:54:21.050 Now you can feel free to ask them
NOTE Confidence: 0.946120445
00:54:21.050 --> 00:54:24.794 or or write them down in the chat.
NOTE Confidence: 0.946120445
00:54:24.800 --> 00:54:26.190 For each of the talks.
NOTE Confidence: 0.822578278571429
00:54:29.780 --> 00:54:31.796 And maybe in the. In the meantime,
NOTE Confidence: 0.822578278571429
00:54:31.800 --> 00:54:35.220 I'll just ask Lohith lohith.
NOTE Confidence: 0.822578278571429
00:54:35.220 --> 00:54:38.752 Do you think that given the good
NOTE Confidence: 0.822578278571429

00:54:38.752 --> 00:54:41.407 efficacy we've seen with ruxolitinib
NOTE Confidence: 0.822578278571429

00:54:41.410 --> 00:54:43.910 in patients with steroid refractory?
NOTE Confidence: 0.82662060625

00:54:46.010 --> 00:54:48.314 Jigged, do you think that there's
NOTE Confidence: 0.82662060625

00:54:48.314 --> 00:54:51.036 and given the safe the what seems
NOTE Confidence: 0.82662060625

00:54:51.036 --> 00:54:53.619 to be fairly good safety profile of
NOTE Confidence: 0.82662060625

00:54:53.700 --> 00:54:56.140 the human chorionic gonadotropin?
NOTE Confidence: 0.82662060625

00:54:56.140 --> 00:54:58.748 Do you see a role for the combination
NOTE Confidence: 0.82662060625

00:54:58.748 --> 00:55:03.196 of that with ruxolitinib and in
NOTE Confidence: 0.82662060625

00:55:03.196 --> 00:55:06.088 terms of steroid sparing effects
NOTE Confidence: 0.82662060625

00:55:06.088 --> 00:55:07.800 in this patient population?
NOTE Confidence: 0.82662060625

00:55:07.800 --> 00:55:09.627 I don't know if there is such
NOTE Confidence: 0.82662060625

00:55:09.627 --> 00:55:11.239 a trial that's already been.
NOTE Confidence: 0.82662060625

00:55:11.240 --> 00:55:13.496 That University of Minnesota is doing or not,
NOTE Confidence: 0.82662060625

00:55:13.500 --> 00:55:15.474 but that would seem like a
NOTE Confidence: 0.82662060625

00:55:15.474 --> 00:55:16.790 reasonable trial to conduct.
NOTE Confidence: 0.7046359992

00:55:17.560 --> 00:55:19.108 Yeah, I think I think that's

NOTE Confidence: 0.7046359992

00:55:19.108 --> 00:55:21.530 that's a great question, Alice.

NOTE Confidence: 0.7046359992

00:55:21.530 --> 00:55:23.945 Obviously, the CR rates around 60 to

NOTE Confidence: 0.7046359992

00:55:23.945 --> 00:55:25.808 70% based on which trial you look

NOTE Confidence: 0.7046359992

00:55:25.808 --> 00:55:28.300 around it or our response rate.

NOTE Confidence: 0.7046359992

00:55:28.300 --> 00:55:31.740 Real question is the day 28 is the

NOTE Confidence: 0.7046359992

00:55:31.740 --> 00:55:34.270 magic bullet, at least in most trials.

NOTE Confidence: 0.7046359992

00:55:34.270 --> 00:55:37.528 How much are we going to?

NOTE Confidence: 0.7046359992

00:55:37.530 --> 00:55:38.122 Miles suppressed?

NOTE Confidence: 0.7046359992

00:55:38.122 --> 00:55:40.490 The good thing about this drug is it's

NOTE Confidence: 0.7046359992

00:55:40.543 --> 00:55:42.238 not deeply Mila suppressive right?

NOTE Confidence: 0.7046359992

00:55:42.238 --> 00:55:44.650 I think that's that's a great part of this.

NOTE Confidence: 0.7046359992

00:55:44.650 --> 00:55:46.528 There's always been this concern in

NOTE Confidence: 0.7046359992

00:55:46.528 --> 00:55:48.478 the field that if the inflammation

NOTE Confidence: 0.7046359992

00:55:48.478 --> 00:55:51.030 kicks in and the tissue is wiped out.

NOTE Confidence: 0.7046359992

00:55:51.030 --> 00:55:54.016 You're in a losing cause that that

NOTE Confidence: 0.7046359992

00:55:54.016 --> 00:55:56.388 combination makes rational sense,
NOTE Confidence: 0.7046359992

00:55:56.390 --> 00:55:58.280 but I'm not certain the group
NOTE Confidence: 0.7046359992

00:55:58.280 --> 00:55:59.225 is pursuing this.
NOTE Confidence: 0.7046359992

00:55:59.230 --> 00:55:59.502 Clearly,
NOTE Confidence: 0.7046359992

00:55:59.502 --> 00:56:01.678 I think what it's showing is we just
NOTE Confidence: 0.7046359992

00:56:01.678 --> 00:56:04.064 probably need to start thinking and
NOTE Confidence: 0.7046359992

00:56:04.064 --> 00:56:05.228 deescalating immunosuppression sooner
NOTE Confidence: 0.7046359992

00:56:05.228 --> 00:56:07.256 rather than keep harping on it,
NOTE Confidence: 0.7046359992

00:56:07.260 --> 00:56:09.508 which is what we've done for many decades.
NOTE Confidence: 0.7046359992

00:56:09.510 --> 00:56:11.980 Hopefully we'll get a good
NOTE Confidence: 0.7046359992

00:56:11.980 --> 00:56:13.796 antimotility drugs, good tissue,
NOTE Confidence: 0.7046359992

00:56:13.796 --> 00:56:15.448 healing, drugs going forwards,
NOTE Confidence: 0.7046359992

00:56:15.450 --> 00:56:18.170 and this seems to be the right start.
NOTE Confidence: 0.7046359992

00:56:18.170 --> 00:56:18.800 But there's
NOTE Confidence: 0.857819911428572

00:56:18.810 --> 00:56:21.358 a question in the chat about the
NOTE Confidence: 0.837721745

00:56:22.230 --> 00:56:25.618 the mechanism of rock

NOTE Confidence: 0.730805488

00:56:23.830 --> 00:56:25.610 two and Rock 2 inhibition. Can you

NOTE Confidence: 0.928397435714286

00:56:25.620 --> 00:56:28.770 tell us a little more about that? So.

NOTE Confidence: 0.527086646666667

00:56:31.510 --> 00:56:33.285 I think it's mass general

NOTE Confidence: 0.527086646666667

00:56:33.285 --> 00:56:35.476 identified a few years ago.

NOTE Confidence: 0.527086646666667

00:56:35.476 --> 00:56:38.860 They came up with this idea that.

NOTE Confidence: 0.527086646666667

00:56:38.860 --> 00:56:41.508 You know, just like most things you know,

NOTE Confidence: 0.527086646666667

00:56:41.510 --> 00:56:43.338 we have anti-inflammatory drugs.

NOTE Confidence: 0.527086646666667

00:56:43.338 --> 00:56:45.623 But we don't really have

NOTE Confidence: 0.527086646666667

00:56:45.623 --> 00:56:47.629 good antifibrotic trucks.

NOTE Confidence: 0.527086646666667

00:56:47.630 --> 00:56:49.835 I think this rock pathway has been

NOTE Confidence: 0.527086646666667

00:56:49.835 --> 00:56:51.700 shown in systemic sclerosis and,

NOTE Confidence: 0.527086646666667

00:56:51.700 --> 00:56:53.758 at least in this clematis GBST,

NOTE Confidence: 0.527086646666667

00:56:53.760 --> 00:56:57.004 most models targeting rock

NOTE Confidence: 0.527086646666667

00:56:57.004 --> 00:57:01.059 Pathway Rock 2 results in.

NOTE Confidence: 0.527086646666667

00:57:01.060 --> 00:57:03.236 Grease scarring, decreased fibrosis,

NOTE Confidence: 0.527086646666667

00:57:03.236 --> 00:57:06.990 and that was the rationale for that.
NOTE Confidence: 0.527086646666667

00:57:06.990 --> 00:57:08.550 Considering most of chronic GVHD,
NOTE Confidence: 0.527086646666667

00:57:08.550 --> 00:57:10.914 people have facial involvement,
NOTE Confidence: 0.527086646666667

00:57:10.914 --> 00:57:13.278 synovitis myositis and things.
NOTE Confidence: 0.527086646666667

00:57:13.280 --> 00:57:14.942 There's a lot of interest that's
NOTE Confidence: 0.527086646666667

00:57:14.942 --> 00:57:16.765 going on a couple of our dermatology
NOTE Confidence: 0.527086646666667

00:57:16.765 --> 00:57:17.777 colleagues and our banking.
NOTE Confidence: 0.527086646666667

00:57:17.780 --> 00:57:19.970 These samples at least my patients.
NOTE Confidence: 0.527086646666667

00:57:19.970 --> 00:57:22.959 Uh, trying to address what are the
NOTE Confidence: 0.527086646666667

00:57:22.959 --> 00:57:25.278 synergistic things that we could use?
NOTE Confidence: 0.527086646666667

00:57:25.280 --> 00:57:27.947 In addition to the rock pathway that
NOTE Confidence: 0.527086646666667

00:57:27.950 --> 00:57:30.942 further subprocess fibrotic mechanisms,
NOTE Confidence: 0.527086646666667

00:57:30.942 --> 00:57:31.908 because really,
NOTE Confidence: 0.527086646666667

00:57:31.908 --> 00:57:34.196 we do see that some of them come up with
NOTE Confidence: 0.527086646666667

00:57:34.196 --> 00:57:35.840 contracted arms and things like that
NOTE Confidence: 0.527086646666667

00:57:35.840 --> 00:57:37.930 and that has functional implications.

NOTE Confidence: 0.527086646666667
00:57:37.930 --> 00:57:38.782 More importantly,
NOTE Confidence: 0.527086646666667
00:57:38.782 --> 00:57:40.486 it's not deeply immunosuppressive,
NOTE Confidence: 0.527086646666667
00:57:40.490 --> 00:57:42.090 and that's a welcome change.
NOTE Confidence: 0.527086646666667
00:57:42.090 --> 00:57:44.682 Rates of infections are low and and.
NOTE Confidence: 0.527086646666667
00:57:44.682 --> 00:57:46.062 Stating that this is something
NOTE Confidence: 0.527086646666667
00:57:46.062 --> 00:57:47.528 that you had in the car,
NOTE Confidence: 0.527086646666667
00:57:47.530 --> 00:57:49.462 I say I've seen good responses
NOTE Confidence: 0.527086646666667
00:57:49.462 --> 00:57:50.750 even in lung GVHD,
NOTE Confidence: 0.527086646666667
00:57:50.750 --> 00:57:53.000 but I think as a special code I would
NOTE Confidence: 0.527086646666667
00:57:53.000 --> 00:57:55.311 like to see a little more to see if
NOTE Confidence: 0.527086646666667
00:57:55.311 --> 00:57:57.043 that brings up on field changing shift,
NOTE Confidence: 0.527086646666667
00:57:57.043 --> 00:57:59.080 but that's still a work in progress.
NOTE Confidence: 0.7297306075
00:58:01.090 --> 00:58:02.398 There's also a question
NOTE Confidence: 0.457523812
00:58:02.410 --> 00:58:05.170 for Aris about immune approaches.
NOTE Confidence: 0.457523812
00:58:05.170 --> 00:58:07.920 Postcard T to enhance attention
NOTE Confidence: 0.457523812

00:58:07.920 --> 00:58:10.670 of cells for continued response.
NOTE Confidence: 0.457523812

00:58:10.670 --> 00:58:12.018 Thank you. Touched on that a little
NOTE Confidence: 0.457523812

00:58:12.018 --> 00:58:14.510 bit with that new Novartis platform.
NOTE Confidence: 0.457523812

00:58:14.510 --> 00:58:16.494 But people doing other things try and
NOTE Confidence: 0.457523812

00:58:16.494 --> 00:58:18.286 get car T cells to persist to work
NOTE Confidence: 0.457523812

00:58:18.286 --> 00:58:21.620 better afterwards that you heard of.
NOTE Confidence: 0.457523812

00:58:21.620 --> 00:58:24.470 Yeah, well, I mean so.
NOTE Confidence: 0.457523812

00:58:24.470 --> 00:58:28.649 So the humanizing party is 1 approach
NOTE Confidence: 0.457523812

00:58:28.649 --> 00:58:30.660 to for them to persist better.
NOTE Confidence: 0.457523812

00:58:30.660 --> 00:58:32.148 Again looking at the.
NOTE Confidence: 0.871919848

00:58:34.500 --> 00:58:37.640 Central memory phenotypes are using
NOTE Confidence: 0.871919848

00:58:37.640 --> 00:58:40.780 enriching for that particular patient
NOTE Confidence: 0.871919848

00:58:40.875 --> 00:58:43.715 population is another is another
NOTE Confidence: 0.871919848

00:58:43.715 --> 00:58:46.555 approach to to enhance retention.
NOTE Confidence: 0.871919848

00:58:46.560 --> 00:58:49.296 You know, the other thing is that they do
NOTE Confidence: 0.871919848

00:58:49.296 --> 00:58:52.116 have these Cortese that secrete cytokines,

NOTE Confidence: 0.871919848

00:58:52.120 --> 00:58:53.365 so that's another.

NOTE Confidence: 0.871919848

00:58:53.365 --> 00:58:54.610 That's another approach.

NOTE Confidence: 0.871919848

00:58:54.610 --> 00:58:56.970 And in fact there was actually an

NOTE Confidence: 0.871919848

00:58:56.970 --> 00:58:59.630 abstract at ASH that I didn't show,

NOTE Confidence: 0.871919848

00:58:59.630 --> 00:59:06.590 but I have a slide of with the BC MA therapy.

NOTE Confidence: 0.871919848

00:59:06.590 --> 00:59:10.598 Releasing, you know with AB Mccourtie

NOTE Confidence: 0.871919848

00:59:10.598 --> 00:59:13.147 releasing cytokines that enhance

NOTE Confidence: 0.871919848

00:59:13.147 --> 00:59:15.832 proliferation so so there are

NOTE Confidence: 0.871919848

00:59:15.832 --> 00:59:19.709 multiple approaches and actually.

NOTE Confidence: 0.871919848

00:59:19.710 --> 00:59:21.792 Come. You know, sometimes that can

NOTE Confidence: 0.871919848

00:59:21.792 --> 00:59:24.479 can be a double edged sword, right?

NOTE Confidence: 0.871919848

00:59:24.479 --> 00:59:26.424 Because these cells can proliferate

NOTE Confidence: 0.871919848

00:59:26.424 --> 00:59:28.872 very rapidly and then you have to

NOTE Confidence: 0.871919848

00:59:28.872 --> 00:59:31.164 think about a switch to turn them off

NOTE Confidence: 0.871919848

00:59:31.164 --> 00:59:33.348 because they can become a very toxic,

NOTE Confidence: 0.871919848

00:59:33.350 --> 00:59:34.910 but you can combine them.
NOTE Confidence: 0.871919848

00:59:34.910 --> 00:59:36.524 You can do basically like City
NOTE Confidence: 0.871919848

00:59:36.524 --> 00:59:37.950 Chen is doing at Yale,
NOTE Confidence: 0.871919848

00:59:37.950 --> 00:59:42.350 a dual knock in knockout, where you can.
NOTE Confidence: 0.871919848

00:59:42.350 --> 00:59:43.886 Knockout pretty one, so I mean,
NOTE Confidence: 0.871919848

00:59:43.890 --> 00:59:45.750 that's that's another approach, right?
NOTE Confidence: 0.871919848

00:59:45.750 --> 00:59:48.207 So so looking at the micro environment,
NOTE Confidence: 0.871919848

00:59:48.210 --> 00:59:53.226 can we actually can we actually.
NOTE Confidence: 0.871919848

00:59:53.230 --> 00:59:55.450 Get cells that are less exhausted
NOTE Confidence: 0.871919848

00:59:55.450 --> 00:59:57.959 by stimulating by by by affecting
NOTE Confidence: 0.871919848

00:59:57.959 --> 00:59:59.396 the micro environment.
NOTE Confidence: 0.871919848

00:59:59.400 --> 01:00:00.000 For example,
NOTE Confidence: 0.871919848

01:00:00.000 --> 01:00:02.100 those efforts are going on in CLL
NOTE Confidence: 0.871919848

01:00:02.100 --> 01:00:04.375 where there is a real problem with
NOTE Confidence: 0.871919848

01:00:04.375 --> 01:00:06.169 persistence of these court T cells,
NOTE Confidence: 0.871919848

01:00:06.170 --> 01:00:08.872 so those are all or or you

NOTE Confidence: 0.871919848

01:00:08.872 --> 01:00:10.979 know the other thing is.

NOTE Confidence: 0.871919848

01:00:10.980 --> 01:00:13.148 At CAR T cells like one of the

NOTE Confidence: 0.871919848

01:00:13.148 --> 01:00:15.619 labs is doing here with Sally Sue,

NOTE Confidence: 0.871919848

01:00:15.620 --> 01:00:16.804 you know,

NOTE Confidence: 0.871919848

01:00:16.804 --> 01:00:20.356 with the targeting low antigen density,

NOTE Confidence: 0.871919848

01:00:20.360 --> 01:00:22.364 for example T cells.

NOTE Confidence: 0.871919848

01:00:22.364 --> 01:00:24.869 So that's that's another approach

NOTE Confidence: 0.871919848

01:00:24.869 --> 01:00:27.577 so that once they they may.

NOTE Confidence: 0.871919848

01:00:27.580 --> 01:00:29.376 Progress after regular karty,

NOTE Confidence: 0.871919848

01:00:29.376 --> 01:00:32.960 or if you see decreased antigen expression,

NOTE Confidence: 0.871919848

01:00:32.960 --> 01:00:35.144 is to actually target them with the

NOTE Confidence: 0.871919848

01:00:35.144 --> 01:00:37.638 with the party that has higher avidity,

NOTE Confidence: 0.871919848

01:00:37.640 --> 01:00:39.976 so those are those are some of the

NOTE Confidence: 0.871919848

01:00:39.976 --> 01:00:42.131 approaches for to enhance the retention

NOTE Confidence: 0.871919848

01:00:42.131 --> 01:00:44.387 of these cells and continued response.

NOTE Confidence: 0.6548898125

01:00:47.070 --> 01:00:48.478 So so I have
NOTE Confidence: 0.689952899166667

01:00:48.490 --> 01:00:51.610 one question for you is that?
NOTE Confidence: 0.689952899166667

01:00:51.610 --> 01:00:53.870 Why it has come up in there has
NOTE Confidence: 0.689952899166667

01:00:53.870 --> 01:00:55.680 already been a trial, but given the
NOTE Confidence: 0.840418978

01:00:55.710 --> 01:00:56.898 the favorable results,
NOTE Confidence: 0.840418978

01:00:56.898 --> 01:00:59.293 at least from the Zuma 7 trial.
NOTE Confidence: 0.840418978

01:00:59.293 --> 01:01:02.258 Do you foresee a time
NOTE Confidence: 0.840418978

01:01:02.258 --> 01:01:05.380 when Carty are used even?
NOTE Confidence: 0.840418978

01:01:05.380 --> 01:01:06.804 In high risk patients,
NOTE Confidence: 0.840418978

01:01:06.804 --> 01:01:08.940 as part of their initial therapy,
NOTE Confidence: 0.840418978

01:01:08.940 --> 01:01:11.718 as opposed to waiting for disease,
NOTE Confidence: 0.840418978

01:01:11.720 --> 01:01:14.610 refractoriness or relapse.
NOTE Confidence: 0.720524061428572

01:01:17.400 --> 01:01:19.066 Well, I mean different from the Zuma.
NOTE Confidence: 0.720524061428572

01:01:19.070 --> 01:01:21.110 12 so Zuma 12. For example, right?
NOTE Confidence: 0.720524061428572

01:01:21.110 --> 01:01:23.270 They took really high risk patients
NOTE Confidence: 0.720524061428572

01:01:23.270 --> 01:01:26.170 and they stratified them by pet after

NOTE Confidence: 0.720524061428572
01:01:26.170 --> 01:01:29.116 two cycles and patients that were pet
NOTE Confidence: 0.720524061428572
01:01:29.116 --> 01:01:31.868 positive went on to get to get Carty
NOTE Confidence: 0.720524061428572
01:01:31.948 --> 01:01:34.546 and the outcomes were pretty good.
NOTE Confidence: 0.720524061428572
01:01:34.550 --> 01:01:38.474 You know the problem is I think we need to
NOTE Confidence: 0.720524061428572
01:01:38.474 --> 01:01:41.620 get a little bit longer follow-up because.
NOTE Confidence: 0.911926897666666
01:01:43.700 --> 01:01:46.052 You know patients who have a positive
NOTE Confidence: 0.911926897666666
01:01:46.052 --> 01:01:48.614 PET scan after two cycles you know may
NOTE Confidence: 0.911926897666666
01:01:48.614 --> 01:01:50.855 still go on to achieve complete remission
NOTE Confidence: 0.911926897666666
01:01:50.855 --> 01:01:53.591 at the end of 6 cycles of therapy,
NOTE Confidence: 0.911926897666666
01:01:53.600 --> 01:01:57.443 so I don't know if it's ever going to
NOTE Confidence: 0.911926897666666
01:01:57.443 --> 01:02:00.560 make it to to frontline it. It may.
NOTE Confidence: 0.911926897666666
01:02:00.560 --> 01:02:02.738 It's not. We're not there yet.
NOTE Confidence: 0.911926897666666
01:02:02.740 --> 01:02:05.436 I think that what companies are doing now,
NOTE Confidence: 0.911926897666666
01:02:05.440 --> 01:02:07.954 though they are sponsoring trials where
NOTE Confidence: 0.911926897666666
01:02:07.954 --> 01:02:11.121 they pay for the collection of T cells
NOTE Confidence: 0.911926897666666

01:02:11.121 --> 01:02:13.492 early on in somebody's presentation.
NOTE Confidence: 0.911926897666666

01:02:13.492 --> 01:02:18.248 And they saved them in the event that
NOTE Confidence: 0.911926897666666

01:02:18.248 --> 01:02:23.298 patients do relapse and they will probably.
NOTE Confidence: 0.911926897666666

01:02:23.300 --> 01:02:24.539 Sell that information.
NOTE Confidence: 0.911926897666666

01:02:24.539 --> 01:02:27.017 Sell those to pharmaceutical companies that
NOTE Confidence: 0.911926897666666

01:02:27.017 --> 01:02:31.108 are designing that are designing trials.
NOTE Confidence: 0.911926897666666

01:02:31.110 --> 01:02:32.250 That's interesting, so so,
NOTE Confidence: 0.911926897666666

01:02:32.250 --> 01:02:34.315 so that's going on because I think
NOTE Confidence: 0.911926897666666

01:02:34.315 --> 01:02:35.795 it's really important to collect
NOTE Confidence: 0.911926897666666

01:02:35.795 --> 01:02:37.966 the cells as early as possible when
NOTE Confidence: 0.911926897666666

01:02:37.966 --> 01:02:39.521 they're when they're fit before
NOTE Confidence: 0.911926897666666

01:02:39.521 --> 01:02:42.790 people have a lot of chemotherapy.
NOTE Confidence: 0.911926897666666

01:02:42.790 --> 01:02:45.220 So so you know there may.
NOTE Confidence: 0.911926897666666

01:02:45.220 --> 01:02:45.832 I mean,
NOTE Confidence: 0.911926897666666

01:02:45.832 --> 01:02:48.088 the FDA hasn't even approved yet, right?
NOTE Confidence: 0.911926897666666

01:02:48.088 --> 01:02:50.596 For they haven't even approved access

NOTE Confidence: 0.911926897666666

01:02:50.596 --> 01:02:53.636 L or based on or Lisle based on

NOTE Confidence: 0.911926897666666

01:02:53.636 --> 01:02:56.030 the Zuma 7 and transform results.

NOTE Confidence: 0.911926897666666

01:02:56.030 --> 01:02:58.316 I think that's the next step.

NOTE Confidence: 0.911926897666666

01:02:58.320 --> 01:02:59.930 Because I think it should be approved,

NOTE Confidence: 0.911926897666666

01:02:59.930 --> 01:03:03.283 'cause clearly there's a PFS benefit in

NOTE Confidence: 0.911926897666666

01:03:03.283 --> 01:03:06.020 that patient population over transplant,

NOTE Confidence: 0.911926897666666

01:03:06.020 --> 01:03:07.763 so I think that's going to be

NOTE Confidence: 0.911926897666666

01:03:07.763 --> 01:03:09.030 probably the first approval,

NOTE Confidence: 0.911926897666666

01:03:09.030 --> 01:03:10.830 and then after that you know

NOTE Confidence: 0.911926897666666

01:03:10.830 --> 01:03:11.730 we're looking at.

NOTE Confidence: 0.911926897666666

01:03:11.730 --> 01:03:12.183 Yeah,

NOTE Confidence: 0.911926897666666

01:03:12.183 --> 01:03:13.995 potentially incorporating it in

NOTE Confidence: 0.911926897666666

01:03:13.995 --> 01:03:16.260 people with double hit lymphomas

NOTE Confidence: 0.911926897666666

01:03:16.327 --> 01:03:18.267 or primary refractory disease.

NOTE Confidence: 0.911926897666666

01:03:18.270 --> 01:03:20.370 Incorporating it early on.

NOTE Confidence: 0.605640722

01:03:22.250 --> 01:03:23.522 Alright, well we're a we're a

NOTE Confidence: 0.605640722

01:03:23.522 --> 01:03:24.747 few minutes after the hour,

NOTE Confidence: 0.605640722

01:03:24.747 --> 01:03:26.118 so, great presentations,

NOTE Confidence: 0.93276105

01:03:26.130 --> 01:03:29.082 great questions and discussion.

NOTE Confidence: 0.93276105

01:03:29.082 --> 01:03:30.558 Thanks everybody.

NOTE Confidence: 0.93276105

01:03:30.560 --> 01:03:32.430 Have a good weekend.

NOTE Confidence: 0.93276105

01:03:32.430 --> 01:03:33.999 Thank you everyone.