WEBVTT

NOTE duration:"01:03:14.9230000"

NOTE language:en-us

NOTE Confidence: 0.8286907

00:00:00.000 --> 00:00:02.598 Typically this is a CME event

NOTE Confidence: 0.8286907

00:00:02.598 --> 00:00:04.330 composed of six sessions.

NOTE Confidence: 0.8286907

00:00:04.330 --> 00:00:07.074 We already had the first session for

NOTE Confidence: 0.8286907

00:00:07.074 --> 00:00:10.161 multiple myeloma on January 15th and the

NOTE Confidence: 0.8286907

00:00:10.161 --> 00:00:12.456 lymphoid malignancy session last week.

NOTE Confidence: 0.8286907

00:00:12.460 --> 00:00:15.804 Today will be updating you on the myeloid

NOTE Confidence: 0.8286907

00:00:15.804 --> 00:00:18.702 malignancy and next week we have an

NOTE Confidence: 0.8286907

00:00:18.702 --> 00:00:21.357 update on pediatric leukemia and also

NOTE Confidence: 0.8286907

00:00:21.357 --> 00:00:23.749 adult acute lymphoblastic leukemia.

NOTE Confidence: 0.8286907

00:00:23.750 --> 00:00:26.216 February 12th will be classical or

NOTE Confidence: 0.8286907

00:00:26.216 --> 00:00:28.692 non benign hematology and we will

NOTE Confidence: 0.8286907

00:00:28.692 --> 00:00:30.954 conclude on February 19th with cell

NOTE Confidence: 0.8286907

00:00:30.954 --> 00:00:33.430 therapy and transplantation updates.

NOTE Confidence: 0.8444918

00:00:38.570 --> 00:00:40.280 So as you can tell,

NOTE Confidence: 0.8444918

00:00:40.280 --> 00:00:42.392 there are many great abstracts that

NOTE Confidence: 0.8444918

00:00:42.392 --> 00:00:44.709 are being presented in ash this year,

NOTE Confidence: 0.8444918

00:00:44.710 --> 00:00:46.335 and it's very difficult to

NOTE Confidence: 0.8444918

00:00:46.335 --> 00:00:48.460 try to cover all of these,

NOTE Confidence: 0.8444918

00:00:48.460 --> 00:00:50.160 especially with the time limitation.

NOTE Confidence: 0.8444918

00:00:50.160 --> 00:00:52.020 So here the abstracts that have

NOTE Confidence: 0.8444918

00:00:52.020 --> 00:00:54.001 been selected in this session and

NOTE Confidence: 0.8444918

00:00:54.001 --> 00:00:56.035 in the other sessions basically are

NOTE Confidence: 0.8444918

00:00:56.035 --> 00:00:58.010 chosen for their highest impact,

NOTE Confidence: 0.8444918

00:00:58.010 --> 00:01:00.056 and the ones that are most

NOTE Confidence: 0.8444918

00:01:00.056 --> 00:01:00.738 relevant clinically,

NOTE Confidence: 0.8444918

00:01:00.740 --> 00:01:02.828 especially in areas of unmet clinical

NOTE Confidence: 0.8444918

00:01:02.828 --> 00:01:04.951 need with decided to group them

NOTE Confidence: 0.8444918

00:01:04.951 --> 00:01:07.282 basically by the disease area AML MD's.

NOTE Confidence: 0.8444918

00:01:07.290 --> 00:01:09.747 And my love I almyra preffective neoplasms.

NOTE Confidence: 0.8444918

00:01:09.750 --> 00:01:11.964 Of course, that doesn't mean that

NOTE Confidence: 0.8444918

00:01:11.964 --> 00:01:13.828 the other abstracts that are

NOTE Confidence: 0.8444918

00:01:13.828 --> 00:01:15.736 not presented are not as great.

NOTE Confidence: 0.8444918

00:01:15.740 --> 00:01:17.500 It just as time limitation,

NOTE Confidence: 0.8444918

00:01:17.500 --> 00:01:19.292 and also important to remember that a

NOTE Confidence: 0.8444918

00:01:19.292 --> 00:01:21.556 lot of the abstracts contain preliminary

NOTE Confidence: 0.8444918

00:01:21.556 --> 00:01:23.476 information and preliminary data,

NOTE Confidence: 0.8444918

00:01:23.480 --> 00:01:25.388 and they have not been peer

NOTE Confidence: 0.8444918

00:01:25.388 --> 00:01:27.350 reviewed or finalize or published.

NOTE Confidence: 0.8444918

00:01:27.350 --> 00:01:29.541 So these results always have to be

NOTE Confidence: 0.8444918

00:01:29.541 --> 00:01:31.930 taken with that consideration in mind.

NOTE Confidence: 0.8444918

00:01:31.930 --> 00:01:34.079 We also like to thank all the

NOTE Confidence: 0.8444918

00:01:34.079 --> 00:01:35.506 authors of those abstracts

NOTE Confidence: 0.8444918

00:01:35.506 --> 00:01:37.676 who have shared their slides.

NOTE Confidence: 0.8444918

00:01:37.680 --> 00:01:39.626 With us for this presentation at the

NOTE Confidence: 0.8444918

00:01:39.626 --> 00:01:41.830 end of the entire Series A recording

NOTE Confidence: 0.8444918

00:01:41.830 --> 00:01:44.216 of this session and the other sessions

NOTE Confidence: 0.8444918

00:01:44.216 --> 00:01:46.806 will be available on the subsequent week.

NOTE Confidence: 0.8444918

00:01:46.810 --> 00:01:49.386 An slice of each presentation that will

NOTE Confidence: 0.8444918

00:01:49.386 --> 00:01:51.844 also be available for your review and

NOTE Confidence: 0.8444918

00:01:51.844 --> 00:01:54.560 for people who cannot make the live event.

NOTE Confidence: 0.8444918

00:01:54.560 --> 00:01:57.264 At the end of the six session series,

NOTE Confidence: 0.8444918

00:01:57.270 --> 00:01:58.965 CME Credit will be provided

NOTE Confidence: 0.8444918

00:01:58.965 --> 00:02:00.660 for those who claim it.

NOTE Confidence: 0.8444918

00:02:00.660 --> 00:02:05.079 You will have to fill a quick form and.

NOTE Confidence: 0.8444918

00:02:05.080 --> 00:02:07.660 Supply some feedback to claim the

NOTE Confidence: 0.8444918

00:02:07.660 --> 00:02:10.990 CME credit at the end of the series.

NOTE Confidence: 0.8444918

00:02:10.990 --> 00:02:12.630 So today we'll be covering

NOTE Confidence: 0.8444918

00:02:12.630 --> 00:02:13.614 the myeloid neoplasms.

NOTE Confidence: 0.8444918

00:02:13.620 --> 00:02:15.270 As you can see here,

NOTE Confidence: 0.8444918

00:02:15.270 --> 00:02:17.573 I will be updating you for Milo

NOTE Confidence: 0.8444918

00:02:17.573 --> 00:02:18.560 dysplastic syndromes then,

NOTE Confidence: 0.8444918

00:02:18.560 --> 00:02:20.786 Doctor Orish Alice will update us on

NOTE Confidence: 0.8444918

00:02:20.786 --> 00:02:22.829 acute myeloid leukemia and finally doctor,

NOTE Confidence: 0.8444918

00:02:22.830 --> 00:02:24.480 but also full update us

NOTE Confidence: 0.8444918

00:02:24.480 --> 00:02:25.140 on myeloproliferative.

NOTE Confidence: 0.8444918

00:02:25.140 --> 00:02:27.156 Neoplasm's will try to stick to

NOTE Confidence: 0.8444918

00:02:27.156 --> 00:02:29.727 the times that you can see here so

NOTE Confidence: 0.8444918

00:02:29.727 --> 00:02:31.886 that we can allow some time for

NOTE Confidence: 0.8444918

00:02:31.886 --> 00:02:34.016 questions in the last 10 minutes.

NOTE Confidence: 0.8444918

00:02:34.020 --> 00:02:36.644 We can stay a few minutes beyond one.

NOTE Confidence: 0.8444918

00:02:36.650 --> 00:02:39.922 For those of you who can stay if

NOTE Confidence: 0.8444918

00:02:39.922 --> 00:02:43.090 there are many questions as well.

NOTE Confidence: 0.8444918

00:02:43.090 --> 00:02:45.118 So I'll start with the updates

NOTE Confidence: 0.8444918

00:02:45.118 --> 00:02:47.220 on my latest ostick syndromes.

NOTE Confidence: 0.8444918

00:02:47.220 --> 00:02:50.410 So these are my disclosures.

NOTE Confidence: 0.8444918

00:02:50.410 --> 00:02:53.226 So I'm just as many of you know,

NOTE Confidence: 0.8444918

00:02:53.230 --> 00:02:54.985 their management is really highly

NOTE Confidence: 0.8444918

00:02:54.985 --> 00:02:55.687 risk adaptive.

NOTE Confidence: 0.8444918

00:02:55.690 --> 00:02:57.300 It's somewhat unusual compared to

NOTE Confidence: 0.8444918

00:02:57.300 --> 00:02:58.910 other malignancy's in which the

NOTE Confidence: 0.8444918

00:02:58.959 --> 00:03:00.108 interventions vary significantly

NOTE Confidence: 0.8444918

00:03:00.108 --> 00:03:02.023 all the way from observation.

NOTE Confidence: 0.8444918

00:03:02.030 --> 00:03:03.790 For patients with lower risk,

NOTE Confidence: 0.8444918

00:03:03.790 --> 00:03:05.904 MD S All the way to recommending

NOTE Confidence: 0.8444918

00:03:05.904 --> 00:03:07.660 a very aggressive intervention,

NOTE Confidence: 0.8444918

00:03:07.660 --> 00:03:08.968 like allogenic bone marrow

NOTE Confidence: 0.8444918

00:03:08.968 --> 00:03:10.276 transplantation for patients who

NOTE Confidence: 0.8444918

00:03:10.276 --> 00:03:11.879 have very aggressive disease,

NOTE Confidence: 0.8444918

00:03:11.880 --> 00:03:13.640 which have a prognosis almost

NOTE Confidence: 0.8444918

00:03:13.640 --> 00:03:15.048 like acute myeloid leukemia.

NOTE Confidence: 0.8444918

00:03:15.050 --> 00:03:17.507 In the most aggressive forms of Andy's,

NOTE Confidence: 0.8444918

00:03:17.510 --> 00:03:19.974 this is actually a schema from 2013,

NOTE Confidence: 0.8444918

00:03:19.980 --> 00:03:23.180 and the reason I'm showing you this one.

NOTE Confidence: 0.8444918

00:03:23.180 --> 00:03:26.618 From seven or eight years ago is be cause.

NOTE Confidence: 0.8444918

00:03:26.620 --> 00:03:28.744 Not much really has changed in

NOTE Confidence: 0.8444918

00:03:28.744 --> 00:03:31.011 the schema in the management of

NOTE Confidence: 0.8444918

00:03:31.011 --> 00:03:33.699 Andy as until last year until 2020

NOTE Confidence: 0.8444918

00:03:33.699 --> 00:03:36.898 and in 2020 we have the first 2

NOTE Confidence: 0.8444918

00:03:36.898 --> 00:03:38.071 approvers basically since

NOTE Confidence: 0.8375796

00:03:38.080 --> 00:03:40.936 2006 so we had 14 years without any

NOTE Confidence: 0.8375796

00:03:40.936 --> 00:03:43.557 approvals for Andy's until 2020 when we

NOTE Confidence: 0.8375796

00:03:43.557 --> 00:03:46.479 have two drugs that have been approved.

NOTE Confidence: 0.8375796

00:03:46.480 --> 00:03:49.014 One of them is last battleship which

NOTE Confidence: 0.8375796

00:03:49.014 --> 00:03:51.449 is a transforming growth factor beta,

NOTE Confidence: 0.8375796

00:03:51.450 --> 00:03:54.120 an inhibitor disinhibits. Elegant and.

NOTE Confidence: 0.8375796

00:03:54.120 --> 00:03:56.124 This is recommended for patients who

NOTE Confidence: 0.8375796

00:03:56.124 --> 00:03:58.543 have lower risk MD's who have any

NOTE Confidence: 0.8375796

00:03:58.543 --> 00:04:00.577 meandering senior class and other drug,

NOTE Confidence: 0.8375796

00:04:00.580 --> 00:04:01.940 was an oral decitabine.

NOTE Confidence: 0.8375796

00:04:01.940 --> 00:04:03.980 An oral version of this item,

NOTE Confidence: 0.8375796

00:04:03.980 --> 00:04:06.360 in that we will be talking about,

NOTE Confidence: 0.8375796

00:04:06.360 --> 00:04:09.237 but this was also approved in late

NOTE Confidence: 0.8375796

00:04:09.237 --> 00:04:11.719 2024 patients with high risk MD's.

NOTE Confidence: 0.8375796

00:04:11.720 --> 00:04:14.504 So I think it's important to start the

NOTE Confidence: 0.8375796

00:04:14.504 --> 00:04:16.454 presentation by highlighting that high

NOTE Confidence: 0.8375796

00:04:16.454 --> 00:04:19.599 unmet need for patients with high risk MD S.

NOTE Confidence: 0.8375796

00:04:19.600 --> 00:04:21.952 So these are some real life analysis

NOTE Confidence: 0.8375796

00:04:21.952 --> 00:04:23.934 that showed that despite the

NOTE Confidence: 0.8375796

00:04:23.934 --> 00:04:25.738 introduction of hypomethylating agents

NOTE Confidence: 0.8375796

00:04:25.738 --> 00:04:28.426 in for treatment for high risk MD

NOTE Confidence: 0.8375796

00:04:28.426 --> 00:04:30.697 as the outcomes or me and pull the

NOTE Confidence: 0.8375796

00:04:30.697 --> 00:04:33.196 overall responses is around 40 to 50%.

NOTE Confidence: 0.8375796

00:04:33.200 --> 00:04:33.557 However,

NOTE Confidence: 0.8375796

00:04:33.557 --> 00:04:35.699 the complete response rate is only

NOTE Confidence: 0.8375796

00:04:35.699 --> 00:04:38.295 around 15% and most of those responses

NOTE Confidence: 0.8375796

00:04:38.295 --> 00:04:40.675 are limited and most patients die

NOTE Confidence: 0.8375796

00:04:40.675 --> 00:04:42.865 from the disease relatively quickly.

NOTE Confidence: 0.8375796

00:04:42.870 --> 00:04:45.453 You can see here previous real life

NOTE Confidence: 0.8375796

00:04:45.453 --> 00:04:47.823 analysis that we conducted for patients

NOTE Confidence: 0.8375796

00:04:47.823 --> 00:04:50.602 who receive is cited in or decide

NOTE Confidence: 0.8375796

00:04:50.678 --> 00:04:53.423 to be in and you can see the median

NOTE Confidence: 0.8375796

00:04:53.423 --> 00:04:55.202 overall survival for older patients.

NOTE Confidence: 0.8375796

00:04:55.202 --> 00:04:57.410 And this was a serious Medicare

NOTE Confidence: 0.8375796

00:04:57.473 --> 00:04:59.753 analysis was eleven months while for

NOTE Confidence: 0.8375796

00:04:59.753 --> 00:05:01.988 patients who were younger and were

NOTE Confidence: 0.8375796

00:05:01.988 --> 00:05:03.938 referred to tertiary big centers in

NOTE Confidence: 0.8375796

00:05:03.938 --> 00:05:05.676 the MD's Clinical Research Consortium.

NOTE Confidence: 0.8375796

00:05:05.676 --> 00:05:08.210 The median overall survival was 17 months.

NOTE Confidence: 0.8375796

00:05:08.210 --> 00:05:10.807 So basically it's much lower than what

NOTE Confidence: 0.8375796

00:05:10.807 --> 00:05:13.079 is generally described in the literature.

NOTE Confidence: 0.8375796

00:05:13.080 --> 00:05:14.001 On 24 months,

NOTE Confidence: 0.8375796

00:05:14.001 --> 00:05:15.843 and for patients who progress after

NOTE Confidence: 0.8375796

00:05:15.843 --> 00:05:17.720 receiving those hypomethylating agents,

NOTE Confidence: 0.8375796

00:05:17.720 --> 00:05:19.510 their survival is even worse.

NOTE Confidence: 0.8375796

00:05:19.510 --> 00:05:21.448 This is an important study that

NOTE Confidence: 0.8375796

00:05:21.448 --> 00:05:23.430 was published by our colleague,

NOTE Confidence: 0.8375796

00:05:23.430 --> 00:05:24.838 Doctor to my Propay,

NOTE Confidence: 0.8375796

00:05:24.838 --> 00:05:26.598 showing that the median survival

NOTE Confidence: 0.8375796

00:05:26.598 --> 00:05:28.068 was only five months.

NOTE Confidence: 0.8375796

00:05:28.070 --> 00:05:29.840 Basically after failure of hypomethylating

NOTE Confidence: 0.8375796

00:05:29.840 --> 00:05:32.595 agents and I think all of this data

NOTE Confidence: 0.8375796

00:05:32.595 --> 00:05:34.145 highlight the significant unmet need

NOTE Confidence: 0.8375796

00:05:34.145 --> 00:05:36.471 that we should not just routinely

NOTE Confidence: 0.8375796

00:05:36.471 --> 00:05:37.707 use hypomethylating agents.

NOTE Confidence: 0.8375796

00:05:37.710 --> 00:05:40.392 But we should try to improve

NOTE Confidence: 0.8375796

00:05:40.392 --> 00:05:42.180 the outcomes of patients.

NOTE Confidence: 0.8375796

00:05:42.180 --> 00:05:44.329 So going to some of the major

NOTE Confidence: 0.8375796

00:05:44.329 --> 00:05:46.069 highlights from the ash meeting,

NOTE Confidence: 0.8375796

00:05:46.070 --> 00:05:48.008 I will start with this one.

NOTE Confidence: 0.8375796

00:05:48.010 --> 00:05:50.594 This is a drug that I just mentioned.

NOTE Confidence: 0.8375796

00:05:50.600 --> 00:05:52.721 Oral deci TB in that has just

NOTE Confidence: 0.8375796

00:05:52.721 --> 00:05:54.489 been approved in August 2020,

NOTE Confidence: 0.8375796

00:05:54.490 --> 00:05:56.770 so decide to be in the reason why

NOTE Confidence: 0.8375796

00:05:56.770 --> 00:05:59.288 you cannot give this ITB in orally

NOTE Confidence: 0.8375796

00:05:59.288 --> 00:06:01.168 is because it's highly metabolised

NOTE Confidence: 0.8375796

00:06:01.234 --> 00:06:02.920 in the gut by this enzyme.

NOTE Confidence: 0.8375796

00:06:02.920 --> 00:06:05.504 Citadine dominates as well as in the liver,

NOTE Confidence: 0.8375796

00:06:05.510 --> 00:06:07.778 so you have significant first pass effect.

NOTE Confidence: 0.8375796

00:06:07.780 --> 00:06:10.468 So what was done here in to develop

NOTE Confidence: 0.8375796

00:06:10.468 --> 00:06:13.007 this drug which is called in covi.

NOTE Confidence: 0.8375796

00:06:13.010 --> 00:06:15.873 Is to combine decided being with an

NOTE Confidence: 0.8375796

00:06:15.873 --> 00:06:18.474 inhibitor of this city in Germany

NOTE Confidence: 0.8375796

00:06:18.474 --> 00:06:21.066 is called sisters OR and the

NOTE Confidence: 0.8375796

00:06:21.066 --> 00:06:22.579 combination in phase one.

NOTE Confidence: 0.8375796

00:06:22.580 --> 00:06:25.572 Phase two trials was shown to result in

NOTE Confidence: 0.8375796

00:06:25.572 --> 00:06:27.570 similar pharmacodynamic and pharmacodynamic.

NOTE Confidence: 0.8306338

00:06:29.720 --> 00:06:32.216 Activities to the Ivy decided mean,

NOTE Confidence: 0.8306338

00:06:32.220 --> 00:06:35.172 so this combination was taken to a phase

NOTE Confidence: 0.8306338

00:06:35.172 --> 00:06:37.809 three trial that looked at pharmacokinetic

NOTE Confidence: 0.8306338

00:06:37.809 --> 00:06:40.539 equivalence as a final end point,

NOTE Confidence: 0.8306338

00:06:40.540 --> 00:06:43.578 and this trial was presented in 2019

NOTE Confidence: 0.8306338

00:06:43.578 --> 00:06:46.776 and you can see A at the bottom.

NOTE Confidence: 0.8306338

00:06:46.780 --> 00:06:49.685 The final conclusion, which you have 99%

NOTE Confidence: 0.8306338

00:06:49.690 --> 00:06:50.938 equivalence pharmacokinetic equivalence

NOTE Confidence: 0.8306338

00:06:50.938 --> 00:06:53.018 between oral and Ivy decitabine.

NOTE Confidence: 0.8306338

00:06:53.020 --> 00:06:56.748 However, the follow up from this study was

NOTE Confidence: 0.8306338

00:06:56.748 --> 00:06:59.659 somewhat limited and an important update.

NOTE Confidence: 0.8306338

00:06:59.660 --> 00:07:02.061 Was presented in the American side of

NOTE Confidence: 0.8306338

00:07:02.061 --> 00:07:04.078 hematology meeting this year by Doctor

NOTE Confidence: 0.8306338

00:07:04.078 --> 00:07:06.756 Savona, and this trial is actually a trial.

NOTE Confidence: 0.8306338

00:07:06.760 --> 00:07:08.310 We participated in an many

NOTE Confidence: 0.8306338

00:07:08.310 --> 00:07:10.480 of you in the care centers,

NOTE Confidence: 0.8306338

00:07:10.480 --> 00:07:12.170 have refer patients for us,

NOTE Confidence: 0.8306338

00:07:12.170 --> 00:07:14.186 so we thank you for that.

NOTE Confidence: 0.8306338

00:07:14.190 --> 00:07:16.374 So the update from the certain study

NOTE Confidence: 0.8306338

00:07:16.374 --> 00:07:18.116 showed that the complete response

NOTE Confidence: 0.8306338

00:07:18.116 --> 00:07:20.653 rate was around 22% and the median

NOTE Confidence: 0.8306338

00:07:20.653 --> 00:07:22.408 overall survival after median follow

NOTE Confidence: 0.8306338

00:07:22.408 --> 00:07:24.990 up of 24 months has not yet been

NOTE Confidence: 0.8306338

00:07:24.990 --> 00:07:26.614 reached and the median duration

NOTE Confidence: 0.8306338

00:07:26.614 --> 00:07:28.726 of best response was 12 months.

NOTE Confidence: 0.8306338

00:07:28.730 --> 00:07:31.350 So I think well.

NOTE Confidence: 0.8306338

00:07:31.350 --> 00:07:33.966 The follow up still needs to be longer.

NOTE Confidence: 0.8306338

00:07:33.970 --> 00:07:36.546 It's important to know that for now it

NOTE Confidence: 0.8306338

00:07:36.546 --> 00:07:38.974 seems that oral version of Decitabine is

NOTE Confidence: 0.8306338

00:07:38.974 --> 00:07:41.808 very similar to how we decide to be in,

NOTE Confidence: 0.8306338

00:07:41.810 --> 00:07:43.916 and I think we have a lot of data

NOTE Confidence: 0.8306338

00:07:43.916 --> 00:07:46.090 now suggesting that it can be

NOTE Confidence: 0.8306338

00:07:46.090 --> 00:07:47.960 completely replacing the IBD side

NOTE Confidence: 0.8306338

00:07:48.024 --> 00:07:49.989 been as monotherapy for Andy's.

NOTE Confidence: 0.8306338

00:07:49.990 --> 00:07:52.662 And on this note also I like to

NOTE Confidence: 0.8306338

00:07:52.662 --> 00:07:54.965 highlight that many of you are aware

NOTE Confidence: 0.8306338

00:07:54.965 --> 00:07:57.560 that there is an oral version of is

NOTE Confidence: 0.8306338

00:07:57.560 --> 00:08:00.210 cited in the CC-486 or on your leg.

NOTE Confidence: 0.8306338

00:08:00.210 --> 00:08:01.850 That has been approved,

NOTE Confidence: 0.8306338

00:08:01.850 --> 00:08:03.806 but this is was only approved

NOTE Confidence: 0.8306338

00:08:03.806 --> 00:08:06.009 in AML on your egg Aurora.

NOTE Confidence: 0.8306338

00:08:06.010 --> 00:08:08.439 Laser sighted in is very different in

NOTE Confidence: 0.8306338

00:08:08.439 --> 00:08:10.178 pharmacokinetics. Ann for Neko Dynamics.

NOTE Confidence: 0.8306338

00:08:10.178 --> 00:08:12.260 Then I be decided in an.

NOTE Confidence: 0.8306338

00:08:12.260 --> 00:08:13.078 I'm sorry.

NOTE Confidence: 0.8306338

00:08:13.078 --> 00:08:15.941 Then Ivy is exciting in and therefore

NOTE Confidence: 0.8306338

00:08:15.941 --> 00:08:18.920 should not be used in MD as its only

NOTE Confidence: 0.8306338

00:08:18.920 --> 00:08:21.445 approved for AML and I think it should

NOTE Confidence: 0.8306338

00:08:21.445 --> 00:08:23.708 be used only in that sitting and

NOTE Confidence: 0.8306338

00:08:23.708 --> 00:08:25.784 AML only in the maintenance setting.

NOTE Confidence: 0.8306338

00:08:25.790 --> 00:08:27.146 After achieving remission with

NOTE Confidence: 0.8306338

00:08:27.146 --> 00:08:28.841 intensive chemotherapy and not as

NOTE Confidence: 0.8306338

00:08:28.841 --> 00:08:30.777 a replacement as monotherapy or.

NOTE Confidence: 0.8306338

00:08:30.780 --> 00:08:32.495 In combination with Venator class

NOTE Confidence: 0.8306338

00:08:32.495 --> 00:08:34.580 so this is important to note.

NOTE Confidence: 0.8306338

00:08:34.580 --> 00:08:36.170 I think another combination that's

NOTE Confidence: 0.8306338

00:08:36.170 --> 00:08:38.152 attracting a lot of attention as

NOTE Confidence: 0.8306338

00:08:38.152 --> 00:08:39.500 a combination of hypomethylating

NOTE Confidence: 0.8306338

00:08:39.500 --> 00:08:40.848 agents with Veneto class.

NOTE Confidence: 0.8306338

00:08:40.850 --> 00:08:42.866 So this is an update that was

NOTE Confidence: 0.8306338

00:08:42.866 --> 00:08:44.913 presented by Doctor Garcia and her

NOTE Confidence: 0.8306338

00:08:44.913 --> 00:08:46.783 colleagues in the frontline setting,

NOTE Confidence: 0.8306338

00:08:46.790 --> 00:08:49.278 so this is a phase One piece study

NOTE Confidence: 0.8306338

00:08:49.278 --> 00:08:51.702 that looked at combination of SSI tied

NOTE Confidence: 0.8306338

00:08:51.702 --> 00:08:54.457 in with Veneto class and this is a

NOTE Confidence: 0.8306338

00:08:54.457 --> 00:08:56.683 single arm study and they provided an

NOTE Confidence: 0.8306338

00:08:56.690 --> 00:08:59.175 update here in around 78 patients and

NOTE Confidence: 0.8306338

00:08:59.175 --> 00:09:02.300 what you can see is a very high CR rates.

NOTE Confidence: 0.8306338

00:09:02.300 --> 00:09:05.135 So the CR rate is around 40%.

NOTE Confidence: 0.8306338

00:09:05.140 --> 00:09:08.479 Remember that the CR rate would is cited in.

NOTE Confidence: 0.8306338

00:09:08.480 --> 00:09:10.330 Monotherapy is only around 15%

NOTE Confidence: 0.8306338

00:09:10.330 --> 00:09:12.815 to 20% at best and the overall

NOTE Confidence: 0.8306338

00:09:12.815 --> 00:09:14.790 response rate is around 80%.

NOTE Confidence: 0.8306338

00:09:14.790 --> 00:09:15.530 The responses,

NOTE Confidence: 0.8306338

00:09:15.530 --> 00:09:17.010 as you can see,

NOTE Confidence: 0.8306338

00:09:17.010 --> 00:09:19.332 sorry for that responses were durable

NOTE Confidence: 0.8306338

00:09:19.332 --> 00:09:22.344 around 13 months and the median follow up

NOTE Confidence: 0.8306338

00:09:22.344 --> 00:09:25.169 on the study was somewhat short 16 months,

NOTE Confidence: 0.8306338

00:09:25.170 --> 00:09:27.030 but the survival so far,

NOTE Confidence: 0.8306338

00:09:27.030 --> 00:09:28.514 especially for those patients

NOTE Confidence: 0.8306338

00:09:28.514 --> 00:09:29.998 who have complete responses,

NOTE Confidence: 0.8676015

00:09:30.000 --> 00:09:31.245 appear quite significant.

NOTE Confidence: 0.8676015

00:09:31.245 --> 00:09:34.150 However, I think these data are important

NOTE Confidence: 0.8676015

00:09:34.213 --> 00:09:36.625 to take into consideration still early.

NOTE Confidence: 0.8676015

00:09:36.630 --> 00:09:38.842 A single arm. We don't have randomized

NOTE Confidence: 0.8676015

00:09:38.842 --> 00:09:41.464 data and we have many drugs that

NOTE Confidence: 0.8676015

00:09:41.464 --> 00:09:43.469 shown excellent data as monotherapy,

NOTE Confidence: 0.8676015

00:09:43.470 --> 00:09:45.474 but when they went to randomized

NOTE Confidence: 0.8676015

00:09:45.474 --> 00:09:47.675 setting they did not basically show

NOTE Confidence: 0.8676015

00:09:47.675 --> 00:09:49.660 improvement in overall survival and

NOTE Confidence: 0.8676015

00:09:49.660 --> 00:09:52.259 I think This is why it's important

NOTE Confidence: 0.8676015

00:09:52.259 --> 00:09:54.263 to wait for the randomized data

NOTE Confidence: 0.8676015

00:09:54.270 --> 00:09:56.790 before this could be used as a,

NOTE Confidence: 0.8676015

00:09:56.790 --> 00:10:00.669 you know a setting in like in routine clinic.

NOTE Confidence: 0.8676015

00:10:00.670 --> 00:10:03.030 Practice.

NOTE Confidence: 0.8676015

00:10:03.030 --> 00:10:05.571 Another I think important study is the

NOTE Confidence: 0.8676015

00:10:05.571 --> 00:10:08.755 one we conducted here at at at Yale in

NOTE Confidence: 0.8676015

00:10:08.755 --> 00:10:10.700 collaboration with many other centers.

NOTE Confidence: 0.8676015

00:10:10.700 --> 00:10:13.535 And we also provided an update from this data

NOTE Confidence: 0.8676015

00:10:13.535 --> 00:10:16.537 in the American Society of Hematology here.

NOTE Confidence: 0.8676015

00:10:16.540 --> 00:10:19.012 The other side in and venetoclax were used

NOTE Confidence: 0.8676015

00:10:19.012 --> 00:10:21.650 in the relapsed or refractory setting,

NOTE Confidence: 0.8676015

00:10:21.650 --> 00:10:23.470 and as you can see,

NOTE Confidence: 0.8676015

00:10:23.470 --> 00:10:26.025 the response rate is around 40% total.

NOTE Confidence: 0.8676015

00:10:26.025 --> 00:10:28.580 Around 7% of those have complete responses,

NOTE Confidence: 0.8676015

00:10:28.580 --> 00:10:30.463 but many of those who have more

NOTE Confidence: 0.8676015

00:10:30.463 --> 00:10:31.839 complete responses also achieved

NOTE Confidence: 0.8676015

00:10:31.839 --> 00:10:33.372 significant hematologic improvement

NOTE Confidence: 0.8676015

00:10:33.372 --> 00:10:34.905 transfusion independence of.

NOTE Confidence: 0.8676015

00:10:34.910 --> 00:10:35.891 Latest on blood.

NOTE Confidence: 0.8676015

00:10:35.891 --> 00:10:37.199 As you can see.

NOTE Confidence: 0.8676015

00:10:37.200 --> 00:10:39.156 So there are significant clinical benefits.

NOTE Confidence: 0.8676015

00:10:39.160 --> 00:10:42.430 But also as you can see on the right side,

NOTE Confidence: 0.8676015

00:10:42.430 --> 00:10:43.738 the median overall survival

NOTE Confidence: 0.8676015

00:10:43.738 --> 00:10:45.700 of all patients was 12 months,

NOTE Confidence: 0.8676015

00:10:45.700 --> 00:10:47.704 which compares favorably than the four

NOTE Confidence: 0.8676015

00:10:47.704 --> 00:10:50.467 to six months that I showed you earlier

NOTE Confidence: 0.8676015

00:10:50.467 --> 00:10:52.507 in the typical refractory relapsed MD

NOTE Confidence: 0.8676015

00:10:52.573 --> 00:10:54.624 S setting and even patients who have

NOTE Confidence: 0.8676015

00:10:54.624 --> 00:10:56.162 more OCR have significant survival.

NOTE Confidence: 0.8676015

00:10:56.162 --> 00:10:58.444 As you can see with 15 months.

NOTE Confidence: 0.8676015

00:10:58.450 --> 00:10:58.778 Again,

NOTE Confidence: 0.8676015

00:10:58.778 --> 00:11:00.418 this is single ARM study,

NOTE Confidence: 0.8676015

00:11:00.420 --> 00:11:01.056 not randomized,

NOTE Confidence: 0.8676015

00:11:01.056 --> 00:11:04.030 and I think we need more data before this

NOTE Confidence: 0.8676015

00:11:04.030 --> 00:11:06.599 could be used in routine clinical practice.

NOTE Confidence: 0.8676015

00:11:06.600 --> 00:11:07.988 There are important differences

NOTE Confidence: 0.8676015

00:11:07.988 --> 00:11:09.723 in how financial classes used

NOTE Confidence: 0.8676015

00:11:09.723 --> 00:11:11.689 in real life setting or for Andy

NOTE Confidence: 0.8676015

00:11:11.689 --> 00:11:13.439 as compared to AML for example.

NOTE Confidence: 0.8676015

00:11:13.440 --> 00:11:15.000 And both of those studies,

NOTE Confidence: 0.8676015

00:11:15.000 --> 00:11:17.488 Veneto class was given only for 14 days,

NOTE Confidence: 0.8676015

00:11:17.490 --> 00:11:20.280 not the 28 days that are given in AML.

NOTE Confidence: 0.8676015

00:11:20.280 --> 00:11:21.970 And that's important because MTS

NOTE Confidence: 0.8676015

00:11:21.970 --> 00:11:24.060 patients might not tolerate the same

NOTE Confidence: 0.8676015

00:11:24.060 --> 00:11:25.775 degree of myelosuppression that their

NOTE Confidence: 0.8676015

00:11:25.775 --> 00:11:28.109 male patients who tend to be somewhat

NOTE Confidence: 0.8676015

00:11:28.109 --> 00:11:30.216 younger than on average and MD's patients.

NOTE Confidence: 0.8676015

00:11:30.220 --> 00:11:32.884 So we have now around a nice face retrial.

NOTE Confidence: 0.8676015

00:11:32.890 --> 00:11:33.781 The Verona trial,

NOTE Confidence: 0.8676015

00:11:33.781 --> 00:11:34.969 which is looking at,

NOTE Confidence: 0.8676015

00:11:34.970 --> 00:11:37.290 is cited in versus cases cited in with

NOTE Confidence: 0.8676015

00:11:37.290 --> 00:11:38.916 venetoclax in the frontline setting

NOTE Confidence: 0.8676015

00:11:38.916 --> 00:11:41.219 among patients with high risk MBS and

NOTE Confidence: 0.8676015

00:11:41.280 --> 00:11:43.288 this study is going to open at Yale.

NOTE Confidence: 0.8676015

00:11:43.290 --> 00:11:45.618 We are also opening at a number of

NOTE Confidence: 0.8676015

00:11:45.618 --> 00:11:47.352 daycare centers and I encourage you

NOTE Confidence: 0.8676015

00:11:47.352 --> 00:11:49.683 to enroll patients on it to see if

NOTE Confidence: 0.8676015

00:11:49.683 --> 00:11:51.881 this setup we actually will change the

NOTE Confidence: 0.8676015

00:11:51.881 --> 00:11:54.950 standard management of high risk MD's.

NOTE Confidence: 0.8676015

00:11:54.950 --> 00:11:57.044 Another update that was prevent presented

NOTE Confidence: 0.8676015

00:11:57.044 --> 00:11:59.126 in the American state of Mythology

NOTE Confidence: 0.8676015

00:11:59.126 --> 00:12:00.998 meeting was on this drug people,

NOTE Confidence: 0.8676015

00:12:01.000 --> 00:12:03.368 and it is that which is the 1st

NOTE Confidence: 0.8676015

00:12:03.368 --> 00:12:05.369 in class need it inhibitor.

NOTE Confidence: 0.8676015

00:12:05.370 --> 00:12:07.698 So this this is an upstream of the

NOTE Confidence: 0.8676015

00:12:07.698 --> 00:12:09.629 proteasome and it was shown in

NOTE Confidence: 0.8676015

00:12:09.629 --> 00:12:11.234 early phase trials in combination

NOTE Confidence: 0.8676015

00:12:11.234 --> 00:12:13.587 with their society into lead to

NOTE Confidence: 0.8676015

00:12:13.587 --> 00:12:14.769 improvement and responses.

NOTE Confidence: 0.8676015

00:12:14.770 --> 00:12:16.226 This trial randomized patients,

NOTE Confidence: 0.8676015

00:12:16.226 --> 00:12:18.746 but this was a randomized phase two

NOTE Confidence: 0.8676015

00:12:18.746 --> 00:12:20.650 trial in which not only patients with

NOTE Confidence: 0.8676015

00:12:20.650 --> 00:12:23.509 MD as but also patients with illegal plastic,

NOTE Confidence: 0.8049437

00:12:23.510 --> 00:12:26.100 AML and CML were randomized to receive.

NOTE Confidence: 0.8049437

00:12:26.100 --> 00:12:28.989 Cited in alone or as a sighted in with

NOTE Confidence: 0.8049437

00:12:28.989 --> 00:12:31.692 people needed stat and this trial also

NOTE Confidence: 0.8049437

00:12:31.692 --> 00:12:34.697 was actually open here at at year and what

NOTE Confidence: 0.8049437

00:12:34.697 --> 00:12:37.206 you can see here or the subgroup analysis

NOTE Confidence: 0.8049437

00:12:37.206 --> 00:12:40.164 of the patients who had higher risk and

NOTE Confidence: 0.8049437

00:12:40.164 --> 00:12:42.747 the S which were a total of 67 patients.

NOTE Confidence: 0.8049437

00:12:42.750 --> 00:12:44.955 This paper this this was just also

NOTE Confidence: 0.8049437

00:12:44.955 --> 00:12:46.410 published in Leukemia Journal.

NOTE Confidence: 0.8049437

00:12:46.410 --> 00:12:48.950 What you can see is that there was like a

NOTE Confidence: 0.8049437

00:12:49.013 --> 00:12:51.737 marginal improvement in event free survival,

NOTE Confidence: 0.8049437

00:12:51.740 --> 00:12:54.169 But the primary endpoint of the study

NOTE Confidence: 0.8049437

00:12:54.169 --> 00:12:56.289 the overall survival was not improved.

NOTE Confidence: 0.8049437

00:12:56.290 --> 00:12:58.915 And I think most notable here is

NOTE Confidence: 0.8049437

00:12:58.915 --> 00:13:01.190 that the overall response rate,

NOTE Confidence: 0.8049437

00:13:01.190 --> 00:13:03.230 but especially the CR rate,

NOTE Confidence: 0.8049437

00:13:03.230 --> 00:13:05.466 was significantly higher with

NOTE Confidence: 0.8049437

00:13:05.466 --> 00:13:08.261 the combination compared to the

NOTE Confidence: 0.8049437

00:13:08.261 --> 00:13:10.509 monotherapy and was more durable.

NOTE Confidence: 0.8049437

00:13:10.510 --> 00:13:13.723 There is a phase three trial of the same.

NOTE Confidence: 0.8049437

00:13:13.730 --> 00:13:15.921 Basically, design of P1 is a sighted

NOTE Confidence: 0.8049437

00:13:15.921 --> 00:13:18.030 in compared to azacitidine alone.

NOTE Confidence: 0.8049437

00:13:18.030 --> 00:13:18.744 This trial,

NOTE Confidence: 0.8049437

00:13:18.744 --> 00:13:20.529 actually called the Panther trial,

NOTE Confidence: 0.8049437

00:13:20.530 --> 00:13:22.654 has fully accrued and we expect

NOTE Confidence: 0.8049437

00:13:22.654 --> 00:13:24.470 results from the study soon.

NOTE Confidence: 0.8049437

00:13:24.470 --> 00:13:27.599 So I think this also could potentially

NOTE Confidence: 0.8049437

00:13:27.599 --> 00:13:30.231 be a practice changing if the

NOTE Confidence: 0.8049437

00:13:30.231 --> 00:13:32.637 if there is us are posted.

NOTE Confidence: 0.8049437

00:13:32.640 --> 00:13:33.567 How about immunotherapy?

NOTE Confidence: 0.8049437

00:13:33.567 --> 00:13:35.421 Many of you use like immune

NOTE Confidence: 0.8049437

00:13:35.421 --> 00:13:37.109 checkpoint inhibitors such as anti PD,

NOTE Confidence: 0.8049437

00:13:37.110 --> 00:13:37.965 One PD, L1,

NOTE Confidence: 0.8049437

00:13:37.965 --> 00:13:39.390 CLU for routinely for management

NOTE Confidence: 0.8049437

00:13:39.390 --> 00:13:40.390 of solid tumors,

NOTE Confidence: 0.8049437

00:13:40.390 --> 00:13:42.532 we've been trying to use these drugs

NOTE Confidence: 0.8049437

00:13:42.532 --> 00:13:45.493 for some time now in high risk MD ASAN

NOTE Confidence: 0.8049437

00:13:45.493 --> 00:13:47.369 myeloid malignancy really and so far

NOTE Confidence: 0.8049437

00:13:47.369 --> 00:13:51.110 a lot of the data has been single arm and.

NOTE Confidence: 0.8049437

00:13:51.110 --> 00:13:52.394 A single center data.

NOTE Confidence: 0.8049437

00:13:52.394 --> 00:13:55.029 This is what I'm showing you is a

NOTE Confidence: 0.8049437

00:13:55.029 --> 00:13:56.955 presentation from ASH 2019 in which

NOTE Confidence: 0.8049437

00:13:56.955 --> 00:13:59.204 we showed with colleagues from other

NOTE Confidence: 0.8049437

00:13:59.204 --> 00:14:01.514 centers in a randomized phase two

NOTE Confidence: 0.8049437

00:14:01.520 --> 00:14:03.410 study that the combination of is

NOTE Confidence: 0.8049437

00:14:03.410 --> 00:14:05.998 cited in with the anti PDL one door

NOTE Confidence: 0.8049437

00:14:05.998 --> 00:14:07.888 volume app which is approved for

NOTE Confidence: 0.8049437

00:14:07.955 --> 00:14:10.337 several solid tumors did not improve

NOTE Confidence: 0.8049437

00:14:10.337 --> 00:14:12.444 outcomes compared to other sighting.

NOTE Confidence: 0.8049437

00:14:12.444 --> 00:14:15.528 However I think this is probably

NOTE Confidence: 0.8049437

00:14:15.528 --> 00:14:17.690 just related to PD L1.

NOTE Confidence: 0.8049437

00:14:17.690 --> 00:14:20.266 And does not extend necessarily to other

NOTE Confidence: 0.8049437

00:14:20.266 --> 00:14:22.830 classes of immune checkpoint inhibitors.

NOTE Confidence: 0.8049437

00:14:22.830 --> 00:14:25.086 And on that note,

NOTE Confidence: 0.8049437

00:14:25.086 --> 00:14:27.342 another immune checkpoint inhibitor

NOTE Confidence: 0.8049437

00:14:27.342 --> 00:14:29.759 called sabatella mob or MPG 453.

NOTE Confidence: 0.8049437

00:14:29.760 --> 00:14:31.630 Is basically being studied in

NOTE Confidence: 0.8049437

00:14:31.630 --> 00:14:33.126 combination with hypomethylating agents,

NOTE Confidence: 0.8049437

00:14:33.130 --> 00:14:35.368 not only for high risk MD's,

NOTE Confidence: 0.8049437

00:14:35.370 --> 00:14:37.918 but also for AML patients and the

NOTE Confidence: 0.8049437

00:14:37.918 --> 00:14:40.183 data from what was presented in

NOTE Confidence: 0.8049437

00:14:40.183 --> 00:14:43.191 in ash this year showed this is a

NOTE Confidence: 0.8049437

00:14:43.191 --> 00:14:45.465 single arm again phase one study,

NOTE Confidence: 0.8049437

00:14:45.470 --> 00:14:48.454 but it showed the CR rate of 23%

NOTE Confidence: 0.8049437

00:14:48.460 --> 00:14:50.330 which is slightly higher than

NOTE Confidence: 0.8049437

00:14:50.330 --> 00:14:52.200 what you expect with monotherapy,

NOTE Confidence: 0.8049437

00:14:52.200 --> 00:14:54.818 but the overall response rate was 64%,

NOTE Confidence: 0.8049437

00:14:54.820 --> 00:14:57.457 and what you can see on the right hand

NOTE Confidence: 0.8049437

00:14:57.457 --> 00:15:00.538 is that there was encouraging durability.

NOTE Confidence: 0.8049437

00:15:00.540 --> 00:15:01.653 Of the combination,

NOTE Confidence: 0.8049437

00:15:01.653 --> 00:15:03.508 especially with patients who have

NOTE Confidence: 0.8049437

00:15:03.508 --> 00:15:05.718 long or very high risk disease,

NOTE Confidence: 0.8049437

00:15:05.720 --> 00:15:07.988 and I would note the side effect

NOTE Confidence: 0.8049437

00:15:07.988 --> 00:15:11.021 profile here it does not seem to add

NOTE Confidence: 0.8049437

00:15:11.021 --> 00:15:13.490 myelosuppression to the exercise again alone,

NOTE Confidence: 0.8049437

00:15:13.490 --> 00:15:14.756 and also importantly,

NOTE Confidence: 0.8049437

00:15:14.756 --> 00:15:16.866 the incidence of immune related

NOTE Confidence: 0.8049437

00:15:16.866 --> 00:15:19.039 effects seems to be low with this.

NOTE Confidence: 0.8049437

00:15:19.040 --> 00:15:20.520 With this particular agent,

NOTE Confidence: 0.8049437

00:15:20.520 --> 00:15:22.370 so appears on this data.

NOTE Confidence: 0.8049437

00:15:22.370 --> 00:15:24.220 There are ongoing several study.

NOTE Confidence: 0.8049437

00:15:24.220 --> 00:15:27.444 We just completed a cruel to a randomized

NOTE Confidence: 0.8049437

00:15:27.444 --> 00:15:30.624 phase two study in higher risk MD S of.

NOTE Confidence: 0.82144034

00:15:30.630 --> 00:15:32.814 Is there with the battle map versus

NOTE Confidence: 0.82144034

00:15:32.814 --> 00:15:35.306 is alone and this study is completed

NOTE Confidence: 0.82144034

00:15:35.306 --> 00:15:37.532 accrual and we expect the results

NOTE Confidence: 0.82144034

00:15:37.601 --> 00:15:39.484 in the next one to two years.

NOTE Confidence: 0.82144034

00:15:39.490 --> 00:15:40.802 There's another face retrial

NOTE Confidence: 0.82144034

00:15:40.802 --> 00:15:42.770 that will open here as well.

NOTE Confidence: 0.82144034

00:15:42.770 --> 00:15:44.410 Called the stimulus MD S2,

NOTE Confidence: 0.82144034

00:15:44.410 --> 00:15:46.714 which is a randomized phase three

NOTE Confidence: 0.82144034

00:15:46.714 --> 00:15:48.939 of the same combination is with

NOTE Confidence: 0.82144034

00:15:48.939 --> 00:15:51.109 the battle map versus Asia and we

NOTE Confidence: 0.82144034

00:15:51.109 --> 00:15:53.143 have our as well a frontline study

NOTE Confidence: 0.82144034

00:15:53.143 --> 00:15:55.390 with a 7 is events a battle map.

NOTE Confidence: 0.82144034

00:15:55.390 --> 00:15:57.572 All of those are open at at

NOTE Confidence: 0.82144034

00:15:57.572 --> 00:15:59.192 yet another interesting immune

NOTE Confidence: 0.82144034

00:15:59.192 --> 00:16:01.480 checkpoint inhibitor is the CD 47.

NOTE Confidence: 0.82144034

00:16:01.480 --> 00:16:03.965 Anti CD 47. They don't eat me.

NOTE Confidence: 0.82144034

00:16:03.970 --> 00:16:05.690 Signal inhibitor mag rolling up

NOTE Confidence: 0.82144034

00:16:05.690 --> 00:16:07.778 what was presented in ash this

NOTE Confidence: 0.82144034

00:16:07.778 --> 00:16:09.892 year was an update and what the

NOTE Confidence: 0.82144034

00:16:09.892 --> 00:16:11.851 authors shown the significant plus

NOTE Confidence: 0.82144034

00:16:11.851 --> 00:16:13.575 reduction among all patients.

NOTE Confidence: 0.82144034

00:16:13.580 --> 00:16:16.002 But the data was most impressive in

NOTE Confidence: 0.82144034

00:16:16.002 --> 00:16:18.251 patients who have TP 53 mutations

NOTE Confidence: 0.82144034

00:16:18.251 --> 00:16:20.525 in which the median overall survival

NOTE Confidence: 0.82144034

00:16:20.525 --> 00:16:22.480 among patients who had TP 50.

NOTE Confidence: 0.82144034

00:16:22.480 --> 00:16:23.792 Three was 12 months,

NOTE Confidence: 0.82144034

00:16:23.792 --> 00:16:25.760 which is higher than what we

NOTE Confidence: 0.82144034

00:16:25.833 --> 00:16:28.179 typically expect it to nine months.

NOTE Confidence: 0.82144034

00:16:28.180 --> 00:16:30.665 Generally in patients who have this mutation.

NOTE Confidence: 0.82144034

00:16:30.670 --> 00:16:33.267 So this drug now is being studied.

NOTE Confidence: 0.82144034

00:16:33.270 --> 00:16:35.015 In a randomized trial called

NOTE Confidence: 0.82144034

00:16:35.015 --> 00:16:37.131 the enhance in high risk MD's

NOTE Confidence: 0.82144034

00:16:37.131 --> 00:16:39.210 whether they have TP 53 or not,

NOTE Confidence: 0.82144034

00:16:39.210 --> 00:16:41.520 magherally map with laser versus is alone,

NOTE Confidence: 0.82144034

00:16:41.520 --> 00:16:44.067 but also there are efforts to study it in

NOTE Confidence: 0.82144034

00:16:44.067 --> 00:16:46.468 acute myeloid leukemia patients as well,

NOTE Confidence: 0.82144034

00:16:46.470 --> 00:16:49.270 especially those with TP 53.

NOTE Confidence: 0.82144034

00:16:49.270 --> 00:16:50.538 This is a transplant

NOTE Confidence: 0.82144034

00:16:50.538 --> 00:16:52.123 abstract and as I mentioned,

NOTE Confidence: 0.82144034

00:16:52.130 --> 00:16:53.875 there is a separate transplant

NOTE Confidence: 0.82144034

00:16:53.875 --> 00:16:55.271 presentation that will happen

NOTE Confidence: 0.82144034

00:16:55.271 --> 00:16:56.900 at the end of the series,

NOTE Confidence: 0.82144034

00:16:56.900 --> 00:16:58.928 but I just wanted to highlight

NOTE Confidence: 0.82144034

00:16:58.928 --> 00:17:00.624 this the conclusion from this

NOTE Confidence: 0.82144034

00:17:00.624 --> 00:17:02.310 because this is in my view,

NOTE Confidence: 0.82144034

00:17:02.310 --> 00:17:04.254 one of the most important abstracts

NOTE Confidence: 0.82144034

00:17:04.254 --> 00:17:06.207 from this ash becausw it showed

NOTE Confidence: 0.82144034

00:17:06.207 --> 00:17:07.707 in a randomized trial data,

NOTE Confidence: 0.82144034

00:17:07.710 --> 00:17:09.300 so here this was randomized.

NOTE Confidence: 0.82144034

00:17:09.300 --> 00:17:11.548 All the data that we have about MD's

NOTE Confidence: 0.82144034

00:17:11.548 --> 00:17:13.540 improving survival in high risk MD's

NOTE Confidence: 0.82144034

00:17:13.540 --> 00:17:14.912 patients compared to hypomethylating

NOTE Confidence: 0.82144034

00:17:14.912 --> 00:17:16.930 agents alone is based on Markov

NOTE Confidence: 0.82144034

00:17:16.930 --> 00:17:18.210 decision analysis and modeling,

NOTE Confidence: 0.82144034

00:17:18.210 --> 00:17:20.148 but this is the first randomized

NOTE Confidence: 0.82144034

00:17:20.148 --> 00:17:21.440 trial to actually show.

NOTE Confidence: 0.82144034

00:17:21.440 --> 00:17:23.285 An absolute improvement in overall

NOTE Confidence: 0.82144034

00:17:23.285 --> 00:17:25.520 survival and the three year survival

NOTE Confidence: 0.82144034

00:17:25.520 --> 00:17:27.506 for donor versus no donor arm.

NOTE Confidence: 0.82144034

00:17:27.510 --> 00:17:31.236 And I think what is very important is this

NOTE Confidence: 0.82144034

00:17:31.236 --> 00:17:34.935 study allowed patients after the age of 75.

NOTE Confidence: 0.82144034

00:17:34.940 --> 00:17:37.276 And this is important to get out there,

NOTE Confidence: 0.82144034

00:17:37.280 --> 00:17:39.198 that because we still see patients who

NOTE Confidence: 0.82144034

00:17:39.198 --> 00:17:41.655 are like 72 who come to us very later

NOTE Confidence: 0.82144034

00:17:41.655 --> 00:17:43.769 there and their scores and being told

NOTE Confidence: 0.82144034

00:17:43.769 --> 00:17:45.779 they were not candidates for transplant.

NOTE Confidence: 0.82144034

00:17:45.780 --> 00:17:47.936 So I think it's important to know

NOTE Confidence: 0.82144034

00:17:47.936 --> 00:17:50.203 that even patients up to the age of

NOTE Confidence: 0.82144034

00:17:50.203 --> 00:17:51.843 75 could be considered for curative

NOTE Confidence: 0.82144034

00:17:51.843 --> 00:17:53.957 therapy and they should be re ferd

NOTE Confidence: 0.82144034

00:17:53.957 --> 00:17:55.802 for big Centers for clinical trials

NOTE Confidence: 0.82144034

00:17:55.802 --> 00:17:57.342 as well as transplant consideration

NOTE Confidence: 0.82144034

00:17:57.342 --> 00:17:58.966 in the last couple of minutes.

NOTE Confidence: 0.82144034

00:17:58.970 --> 00:18:00.958 I will talk about lower risk MD's

NOTE Confidence: 0.82144034

00:18:00.958 --> 00:18:03.023 as I mentioned was partnership has

NOTE Confidence: 0.82144034

00:18:03.023 --> 00:18:04.943 been approved after ESA failure.

NOTE Confidence: 0.82144034

00:18:04.950 --> 00:18:06.790 For patients who have RingCentral

NOTE Confidence: 0.82144034

00:18:06.790 --> 00:18:09.210 plastic anemia from lower risk MD's now,

NOTE Confidence: 0.82144034

00:18:09.210 --> 00:18:11.569 this drug is being studied in the

NOTE Confidence: 0.82144034

00:18:11.569 --> 00:18:13.829 frontline setting in the commands trial,

NOTE Confidence: 0.82144034

00:18:13.830 --> 00:18:16.161 so this is it's being studied compared

NOTE Confidence: 0.82144034

00:18:16.161 --> 00:18:18.266 to low Earth roelle powerton and

NOTE Confidence: 0.82144034

00:18:18.266 --> 00:18:20.688 this or a potent procrit and this

NOTE Confidence: 0.7745304

00:18:20.756 --> 00:18:23.360 is in the frontline setting and regardless

NOTE Confidence: 0.7745304

00:18:23.360 --> 00:18:26.610 so whether you have ringstad or plus or not,

NOTE Confidence: 0.7745304

00:18:26.610 --> 00:18:29.165 you could be randomized to either a

NOTE Confidence: 0.7745304

00:18:29.165 --> 00:18:32.046 proton or low spatter set and this trial

NOTE Confidence: 0.7745304

00:18:32.046 --> 00:18:35.029 is open in the care centers as well.

NOTE Confidence: 0.7745304

00:18:35.030 --> 00:18:38.500 So many of you will be able to enroll in it.

NOTE Confidence: 0.7745304

00:18:38.500 --> 00:18:40.698 Another interesting drug is the emitted step,

NOTE Confidence: 0.7745304

00:18:40.700 --> 00:18:42.625 which is the 1st in class telomerase

NOTE Confidence: 0.7745304

00:18:42.625 --> 00:18:44.598 inhibitor which has been shown also

NOTE Confidence: 0.7745304

00:18:44.598 --> 00:18:46.058 to improve transfusion independence.

NOTE Confidence: 0.7745304

00:18:46.060 --> 00:18:47.920 Regardless of having RingCentral Plus or

NOTE Confidence: 0.7745304

00:18:47.920 --> 00:18:50.156 not and some of those responses which

NOTE Confidence: 0.7745304

00:18:50.156 --> 00:18:52.670 occur in 42% of patients were at durable.

NOTE Confidence: 0.7745304

00:18:52.670 --> 00:18:55.190 Now we have actually an open study here.

NOTE Confidence: 0.7745304

00:18:55.190 --> 00:18:57.388 The High Merge study the phase three

NOTE Confidence: 0.7745304

00:18:57.388 --> 00:18:59.848 so this is a randomized study after

NOTE Confidence: 0.7745304

00:18:59.848 --> 00:19:02.689 he has a failure so frontline we have

NOTE Confidence: 0.7745304

00:19:02.689 --> 00:19:05.097 the commands in lower risk and be as.

NOTE Confidence: 0.7745304

00:19:05.100 --> 00:19:07.524 Refractory, we have the Hymer study

NOTE Confidence: 0.7745304

00:19:07.524 --> 00:19:09.891 for patients after failure of PSA

NOTE Confidence: 0.7745304

00:19:09.891 --> 00:19:11.925 in which patients are randomized to

NOTE Confidence: 0.7745304

00:19:11.925 --> 00:19:14.110 him until a stat versus placebo.

NOTE Confidence: 0.7745304

00:19:14.110 --> 00:19:16.886 In the last minute I wanna show you

NOTE Confidence: 0.7745304

00:19:16.886 --> 00:19:18.877 another like non interventional study

NOTE Confidence: 0.7745304

00:19:18.877 --> 00:19:22.415 that we did in patients with MD S who

NOTE Confidence: 0.7745304

00:19:22.415 --> 00:19:24.903 have lower who have anemia and as you

NOTE Confidence: 0.7745304

00:19:24.910 --> 00:19:27.790 know one of the open questions in MDSS.

NOTE Confidence: 0.7745304

00:19:27.790 --> 00:19:29.746 When do you transfuse patients with

NOTE Confidence: 0.7745304

00:19:29.746 --> 00:19:32.281 MD S and many people use different

NOTE Confidence: 0.7745304

00:19:32.281 --> 00:19:34.983 cut off seven or eight of hemoglobin?

NOTE Confidence: 0.7745304

00:19:34.990 --> 00:19:37.293 Here we used verified quality of life

NOTE Confidence: 0.7745304

00:19:37.293 --> 00:19:39.120 instrument in a investigator initiated

NOTE Confidence: 0.7745304

00:19:39.120 --> 00:19:41.822 effort led by Doctor Go in Table.

NOTE Confidence: 0.7745304

00:19:41.830 --> 00:19:43.082 Go on Dana Farber.

NOTE Confidence: 0.7745304

00:19:43.082 --> 00:19:45.835 And we looked at the quality of life

NOTE Confidence: 0.7745304

00:19:45.835 --> 00:19:47.835 improvement before and after transfusion

NOTE Confidence: 0.7745304

00:19:47.835 --> 00:19:50.843 and what we have shown is that most

NOTE Confidence: 0.7745304

00:19:50.843 --> 00:19:52.889 patients 2/3 of patients did not

NOTE Confidence: 0.7745304

00:19:52.889 --> 00:19:54.434 experience an improvement in their

NOTE Confidence: 0.7745304

00:19:54.434 --> 00:19:56.340 quality of life after transfusion.

NOTE Confidence: 0.7745304

00:19:56.340 --> 00:19:58.755 So I think that puts into question

NOTE Confidence: 0.7745304

00:19:58.755 --> 00:20:00.210 our practice of Troy.

NOTE Confidence: 0.7745304

00:20:00.210 --> 00:20:01.880 Using patients based on hemoglobin

NOTE Confidence: 0.7745304

00:20:01.880 --> 00:20:03.216 cut offs of aid,

NOTE Confidence: 0.7745304

00:20:03.220 --> 00:20:05.306 and I think it's important to try

NOTE Confidence: 0.7745304

00:20:05.306 --> 00:20:07.282 to study this in more extensive

NOTE Confidence: 0.7745304

00:20:07.282 --> 00:20:09.641 sitting about what is the right cut

NOTE Confidence: 0.7745304

00:20:09.704 --> 00:20:11.228 off for transfusions in,

NOTE Confidence: 0.7745304

00:20:11.230 --> 00:20:12.900 especially in the outpatient setting.

NOTE Confidence: 0.7745304

00:20:12.900 --> 00:20:14.808 For patients with ambius rather than

NOTE Confidence: 0.7745304

00:20:14.808 --> 00:20:16.909 using random cut offs of hemoglobin.

NOTE Confidence: 0.7745304

00:20:16.910 --> 00:20:19.295 So this is my last slide and I will

NOTE Confidence: 0.7745304

00:20:19.295 --> 00:20:21.735 give the floor now to my colleague

NOTE Confidence: 0.7745304

00:20:21.735 --> 00:20:23.987 Doctor Rory Challis who will update

NOTE Confidence: 0.7745304

00:20:23.987 --> 00:20:25.927 us on acute myeloid leukemia.

NOTE Confidence: 0.7745304

00:20:25.930 --> 00:20:27.302 Updates from the ash.

NOTE Confidence: 0.7745304

00:20:27.302 --> 00:20:29.778 Thank you and we'll be happy all

NOTE Confidence: 0.7745304

00:20:29.778 --> 00:20:31.836 of us will be taking questions.

NOTE Confidence: 0.7745304

00:20:31.840 --> 00:20:34.280 At the end of that seminar at 12:50,

NOTE Confidence: 0.7745304

00:20:34.280 --> 00:20:34.590 thanks.

NOTE Confidence: 0.78832996

00:20:52.070 --> 00:20:53.700 OK, How are we looking?

NOTE Confidence: 0.78832996

00:20:53.700 --> 00:20:55.646 Every seeing a full slide who

NOTE Confidence: 0.78832996

00:20:55.646 --> 00:21:00.100 screens two screens again? Sorry.

NOTE Confidence: 0.78832996

00:21:00.100 --> 00:21:01.828 Standard technical difficulties.

NOTE Confidence: 0.80935025

00:21:07.370 --> 00:21:09.786 Yeah, I think you need to swap your

NOTE Confidence: 0.80935025

00:21:09.790 --> 00:21:11.310 screens. Let's try this again.

NOTE Confidence: 0.8119342

00:21:15.390 --> 00:21:18.156 Yep. How's that? That looks good,

NOTE Confidence: 0.7934169

00:21:18.160 --> 00:21:19.240 not yet ticket.

NOTE Confidence: 0.9394388

00:21:20.540 --> 00:21:21.070 Yes.

NOTE Confidence: 0.88221246

00:21:22.750 --> 00:21:23.310 Looks good.

NOTE Confidence: 0.8302369

00:21:25.320 --> 00:21:27.272 You're seeing one. Yes, one scream.

NOTE Confidence: 0.8302369

00:21:27.272 --> 00:21:30.290 You're good to go alright? Do this by then.

NOTE Confidence: 0.8640053

00:21:32.410 --> 00:21:33.379 Sorry bout that.

NOTE Confidence: 0.88886964

00:21:35.390 --> 00:21:36.220 OK.

NOTE Confidence: 0.85143447

00:21:38.370 --> 00:21:43.258 Alright one screen we're good to go so.

NOTE Confidence: 0.85143447

00:21:43.260 --> 00:21:45.200 Thanks for the introduction.

NOTE Confidence: 0.85143447

00:21:45.200 --> 00:21:47.625 I'll be specifically focusing on

NOTE Confidence: 0.85143447

00:21:47.625 --> 00:21:50.032 the highlights presented this past

NOTE Confidence: 0.85143447

00:21:50.032 --> 00:21:52.804 meeting as they pertain to AML.

NOTE Confidence: 0.85143447

00:21:52.810 --> 00:21:57.470 I have no disclosures, so.

NOTE Confidence: 0.85143447

00:21:57.470 --> 00:22:00.720 Again, you're still seeing one screen, right?

NOTE Confidence: 0.85143447

00:22:00.720 --> 00:22:03.200 OK, it's a bit hard to really focus

NOTE Confidence: 0.85143447

00:22:03.200 --> 00:22:05.935 in on really a select few updates

NOTE Confidence: 0.85143447

00:22:05.935 --> 00:22:08.280 from an entire years worth of.

NOTE Confidence: 0.85143447

00:22:08.280 --> 00:22:12.186 I would say progress in the field.

NOTE Confidence: 0.85143447

00:22:12.190 --> 00:22:14.598 So I'll try to really focus on agents

NOTE Confidence: 0.85143447

00:22:14.598 --> 00:22:16.991 with which we already have some

NOTE Confidence: 0.85143447

00:22:16.991 --> 00:22:18.715 familiar that Phillip familiarity,

NOTE Confidence: 0.85143447

00:22:18.720 --> 00:22:21.268 but also some new combinations or regiments,

NOTE Confidence: 0.85143447

00:22:21.270 --> 00:22:23.692 some of which you can guess we're

NOTE Confidence: 0.85143447

00:22:23.692 --> 00:22:25.934 going to include the BCL two

NOTE Confidence: 0.85143447

00:22:25.934 --> 00:22:27.438 inhibitor of medical acts.

NOTE Confidence: 0.85143447

00:22:27.440 --> 00:22:29.820 All of these are all the studies

NOTE Confidence: 0.85143447

00:22:29.820 --> 00:22:32.302 I'll be discussing are going to be

NOTE Confidence: 0.85143447

00:22:32.302 --> 00:22:34.384 interventional of only really try to

NOTE Confidence: 0.85143447

00:22:34.455 --> 00:22:36.777 give some minimal background so it's

NOTE Confidence: 0.85143447

00:22:36.777 --> 00:22:39.052 really focused on the updates themselves.

NOTE Confidence: 0.85143447

00:22:39.052 --> 00:22:40.496 So jump right in.

NOTE Confidence: 0.85143447

00:22:40.500 --> 00:22:42.720 As many of you are.

NOTE Confidence: 0.85143447

00:22:42.720 --> 00:22:44.460 Aware Gilteritinib is a

NOTE Confidence: 0.85143447

00:22:44.460 --> 00:22:45.765 flip through inhibitor,

NOTE Confidence: 0.85143447

00:22:45.770 --> 00:22:48.724 which in the Admiral trial was shown

NOTE Confidence: 0.85143447

00:22:48.724 --> 00:22:51.244 to improve survival when compared

NOTE Confidence: 0.85143447

00:22:51.244 --> 00:22:53.596 with classical salvage chemotherapy

NOTE Confidence: 0.85143447

00:22:53.596 --> 00:22:55.948 in their refractory setting.

NOTE Confidence: 0.85143447

00:22:55.950 --> 00:22:57.876 So its approval for such over

NOTE Confidence: 0.85143447

00:22:57.876 --> 00:22:59.654 the outcomes for these patients

NOTE Confidence: 0.85143447

00:22:59.654 --> 00:23:00.950 treated with guilt,

NOTE Confidence: 0.85143447

00:23:00.950 --> 00:23:03.798 or it never guilt are still quite poor.

NOTE Confidence: 0.85143447

00:23:03.800 --> 00:23:05.825 The preclinical data does support

NOTE Confidence: 0.85143447

00:23:05.825 --> 00:23:07.850 some synergy when Gilteritinib is

NOTE Confidence: 0.85143447

00:23:07.915 --> 00:23:09.979 combined with a BCL two inhibitor

NOTE Confidence: 0.85143447

00:23:09.979 --> 00:23:12.348 and those data prompted the launch of

NOTE Confidence: 0.85143447

00:23:12.348 --> 00:23:14.504 the trial that I'll be talking about.

NOTE Confidence: 0.85143447

00:23:14.510 --> 00:23:16.658 In brief, you can see here,

NOTE Confidence: 0.85143447

00:23:16.660 --> 00:23:19.164 so this was done in the context of

NOTE Confidence: 0.85143447

00:23:19.164 --> 00:23:21.299 the following trial schema patients,

NOTE Confidence: 0.85143447

00:23:21.300 --> 00:23:22.724 as you guessed it,

NOTE Confidence: 0.85143447

00:23:22.724 --> 00:23:24.148 had relapsed refractory disease,

NOTE Confidence: 0.85143447

00:23:24.150 --> 00:23:25.734 including wild type patients.

NOTE Confidence: 0.85143447

00:23:25.734 --> 00:23:27.714 In the dose escalation phase,

NOTE Confidence: 0.85143447

00:23:27.720 --> 00:23:30.177 without you know, a low white counts.

NOTE Confidence: 0.85143447

00:23:30.180 --> 00:23:31.940 They really had controlled proliferation.

NOTE Confidence: 0.85143447

00:23:31.940 --> 00:23:33.820 They received standard phonetic lacks

NOTE Confidence: 0.85143447

00:23:33.820 --> 00:23:35.700 4 milligrams in combination with

NOTE Confidence: 0.85143447

00:23:35.754 --> 00:23:37.578 either guilt 80 or 120 milligrams,

NOTE Confidence: 0.85143447

00:23:37.580 --> 00:23:39.995 which the latter of which is the

NOTE Confidence: 0.85143447

00:23:39.995 --> 00:23:42.507 standard dose that was studied in Phase

NOTE Confidence: 0.85143447

00:23:42.507 --> 00:23:44.970 3 testing, and this was later expanded,

NOTE Confidence: 0.85143447

00:23:44.970 --> 00:23:46.374 so the demographics were,

NOTE Confidence: 0.85143447

00:23:46.374 --> 00:23:48.836 for the most part, I would say,

NOTE Confidence: 0.85143447

00:23:48.836 --> 00:23:50.596 expected with regards to age,

NOTE Confidence: 0.85143447

00:23:50.600 --> 00:23:52.819 set of genetic risk given the inclusion

NOTE Confidence: 0.85143447

00:23:52.819 --> 00:23:54.819 criteria that I mentioned before,

NOTE Confidence: 0.85143447

00:23:54.820 --> 00:23:56.684 a majority of patients.

NOTE Confidence: 0.85143447

00:23:56.684 --> 00:23:58.548 Did have ITD mutations?

NOTE Confidence: 0.85143447

00:23:58.550 --> 00:23:59.304 Of note,

NOTE Confidence: 0.85143447

00:23:59.304 --> 00:24:01.189 65% of patients received prior

NOTE Confidence: 0.85143447

00:24:01.189 --> 00:24:03.521 therapy with the flip three inhibitor

NOTE Confidence: 0.85143447

00:24:03.521 --> 00:24:05.783 and a third enrolled after they

NOTE Confidence: 0.85143447

00:24:05.783 --> 00:24:08.419 had a relapse after allogeneic

NOTE Confidence: 0.85143447

00:24:08.419 --> 00:24:10.607 metaplastic stem cell transplantation.

NOTE Confidence: 0.85143447

00:24:10.610 --> 00:24:12.445 All patients experienced an adverse

NOTE Confidence: 0.85143447

00:24:12.445 --> 00:24:14.710 event in nearly all grade three,

NOTE Confidence: 0.85143447

00:24:14.710 --> 00:24:16.580 with unsurprisingly, was being cytopenias.

NOTE Confidence: 0.85143447

00:24:16.580 --> 00:24:17.324 You know,

NOTE Confidence: 0.85143447

00:24:17.324 --> 00:24:19.556 given the combination with medical access,

NOTE Confidence: 0.85143447

00:24:19.560 --> 00:24:22.115 you know a very well known Milo

NOTE Confidence: 0.85143447

00:24:22.115 --> 00:24:23.670 toxic amount suppressive agent,

NOTE Confidence: 0.85143447

00:24:23.670 --> 00:24:25.896 but perhaps some contribution of guilt.

NOTE Confidence: 0.85143447

00:24:25.900 --> 00:24:27.046 And as well,

NOTE Confidence: 0.85143447

00:24:27.046 --> 00:24:29.338 three patients were reported as having

NOTE Confidence: 0.85143447

00:24:29.338 --> 00:24:31.245 laboratory tumor lysis syndrome with

NOTE Confidence: 0.85143447

00:24:31.245 --> 00:24:33.740 only one of these having clinical TLS,

NOTE Confidence: 0.85143447

00:24:33.740 --> 00:24:35.232 only 60% of patients,

NOTE Confidence: 0.85143447

00:24:35.232 --> 00:24:37.470 at least as of last follow-up,

NOTE Confidence: 0.85143447

00:24:37.470 --> 00:24:40.746 discontinued the drug due to adverse events.

NOTE Confidence: 0.85143447

00:24:40.750 --> 00:24:41.430 Of note,

NOTE Confidence: 0.85143447

00:24:41.430 --> 00:24:44.150 no patients died within a month of dosing,

NOTE Confidence: 0.85143447

00:24:44.150 --> 00:24:49.199 but six died with up to 60 days out.

NOTE Confidence: 0.85143447

00:24:49.200 --> 00:24:51.960 Amongst 41 amongst 41 adult patients,

NOTE Confidence: 0.85143447

00:24:51.960 --> 00:24:55.149 only three achieved CR or 7% specifically.

NOTE Confidence: 0.85143447

00:24:55.149 --> 00:24:55.578 However,

NOTE Confidence: 0.85143447

00:24:55.578 --> 00:24:57.723 27% of patients achieved a

NOTE Confidence: 0.85143447

00:24:57.723 --> 00:24:59.780 less than CR remission,

NOTE Confidence: 0.8010021

00:24:59.780 --> 00:25:04.487 which here was inclusive of CR or CR P.

NOTE Confidence: 0.8010021

00:25:04.490 --> 00:25:06.650 Half of patients achieved MFS or

NOTE Confidence: 0.8010021

00:25:06.650 --> 00:25:08.490 morphologic leukemia Free State again,

NOTE Confidence: 0.8010021

00:25:08.490 --> 00:25:11.088 in the context of the Netflix

NOTE Confidence: 0.8010021

00:25:11.088 --> 00:25:12.387 related mileage suppression.

NOTE Confidence: 0.8010021

00:25:12.390 --> 00:25:13.096 Amongst responders,

NOTE Confidence: 0.8010021

00:25:13.096 --> 00:25:15.920 the median time to response was one month,

NOTE Confidence: 0.8010021

00:25:15.920 --> 00:25:17.332 but best responses were

NOTE Confidence: 0.8010021

00:25:17.332 --> 00:25:19.450 observed up to four months out.

NOTE Confidence: 0.8010021

00:25:19.450 --> 00:25:21.005 No more could differences in

NOTE Confidence: 0.8010021

00:25:21.005 --> 00:25:23.009 response or the types of response

NOTE Confidence: 0.8010021

00:25:23.009 --> 00:25:25.301 for that matter were apparent after

NOTE Confidence: 0.8010021

00:25:25.301 --> 00:25:27.216 accounting for prior flip three

NOTE Confidence: 0.8010021

00:25:27.216 --> 00:25:28.981 inhibitor exposure other than maybe

NOTE Confidence: 0.8010021

00:25:28.981 --> 00:25:31.452 a little less or chance of CR.

NOTE Confidence: 0.8010021

00:25:31.452 --> 00:25:33.217 As you can see here,

NOTE Confidence: 0.8010021

00:25:33.220 --> 00:25:37.030 7.3 versus one quote versus 3.6%.

NOTE Confidence: 0.8010021

00:25:37.030 --> 00:25:38.655 The median overall survival for

NOTE Confidence: 0.8010021

00:25:38.655 --> 00:25:40.740 the overall cohort was 12.3 months

NOTE Confidence: 0.8010021

00:25:40.740 --> 00:25:42.328 and specifically not reached,

NOTE Confidence: 0.8010021

00:25:42.330 --> 00:25:44.442 including an unreached lower limit of

NOTE Confidence: 0.8010021

00:25:44.442 --> 00:25:46.910 the 95% confidence interval for ITD patients.

NOTE Confidence: 0.8010021

00:25:46.910 --> 00:25:48.585 Clear differences in survival were

NOTE Confidence: 0.8010021

00:25:48.585 --> 00:25:50.800 noted based on prior filter exposure,

NOTE Confidence: 0.8010021

00:25:50.800 --> 00:25:53.455 so I would say in some the addition of

NOTE Confidence: 0.8010021

00:25:53.455 --> 00:25:55.674 attacks appears to augment the efficacy

NOTE Confidence: 0.8010021

00:25:55.674 --> 00:25:58.560 of of guilt monotherapy in this situation,

NOTE Confidence: 0.8010021

00:25:58.560 --> 00:26:00.325 which based on the Admiral

NOTE Confidence: 0.8010021

00:26:00.325 --> 00:26:02.090 trial I had mentioned before,

NOTE Confidence: 0.8010021

00:26:02.090 --> 00:26:03.742 predicts a median survival

NOTE Confidence: 0.8010021

00:26:03.742 --> 00:26:06.870 around 9 nine and a half months.

NOTE Confidence: 0.8010021

00:26:06.870 --> 00:26:09.054 This is at the expense of near

NOTE Confidence: 0.8010021

00:26:09.054 --> 00:26:09.990 double hematologic toxicity,

NOTE Confidence: 0.8010021

00:26:09.990 --> 00:26:12.358 which I think we can all agree is

NOTE Confidence: 0.8010021

00:26:12.358 --> 00:26:14.049 attributable to the phonetic LAX,

NOTE Confidence: 0.8010021

00:26:14.050 --> 00:26:14.968 but of course.

NOTE Confidence: 0.8010021

00:26:14.968 --> 00:26:16.804 Just heating some caution and saying

NOTE Confidence: 0.8010021

00:26:16.804 --> 00:26:19.017 it appears to increase the efficacy

NOTE Confidence: 0.8010021

00:26:19.017 --> 00:26:21.260 outside of a randomized clinical trial,

NOTE Confidence: 0.8010021

00:26:21.260 --> 00:26:22.994 so this isn't of course need

NOTE Confidence: 0.8010021

00:26:22.994 --> 00:26:24.520 to at least confirm this.

NOTE Confidence: 0.8010021

00:26:24.520 --> 00:26:25.708 This likely benefit here.

NOTE Confidence: 0.77116615

00:26:27.760 --> 00:26:29.490 Jump into the next update.

NOTE Confidence: 0.77116615

00:26:29.490 --> 00:26:33.819 I have 40 or so older patients with AML.

NOTE Confidence: 0.77116615

00:26:33.820 --> 00:26:35.590 Have generally a poor outcomes,

NOTE Confidence: 0.77116615

00:26:35.590 --> 00:26:37.564 but there there is some variance

NOTE Confidence: 0.77116615

00:26:37.564 --> 00:26:39.480 noted to improve these outcomes.

NOTE Confidence: 0.77116615

00:26:39.480 --> 00:26:41.610 Ventures like the following are underway,

NOTE Confidence: 0.77116615

00:26:41.610 --> 00:26:43.794 so next I'd like to discuss the

NOTE Confidence: 0.77116615

00:26:43.794 --> 00:26:45.989 interim results of a striking study

NOTE Confidence: 0.77116615

00:26:45.989 --> 00:26:47.979 of cladribine and lodosa Terrapin,

NOTE Confidence: 0.77116615

00:26:47.980 --> 00:26:49.750 which is essentially a double

NOTE Confidence: 0.77116615

00:26:49.750 --> 00:26:51.166 nucleoside backbone and Aza,

NOTE Confidence: 0.77116615

00:26:51.170 --> 00:26:53.994 both with the addition of an ethics course.

NOTE Confidence: 0.77116615

00:26:54.000 --> 00:26:56.124 The double clad plus Ldac backbone

NOTE Confidence: 0.77116615

00:26:56.124 --> 00:26:57.890 has been previously studied this.

NOTE Confidence: 0.77116615

00:26:57.890 --> 00:27:00.122 This isn't showing here in this

NOTE Confidence: 0.77116615

00:27:00.122 --> 00:27:02.349 slide with alternating decide to be

NOTE Confidence: 0.77116615

00:27:02.349 --> 00:27:04.044 as treatment for newly diagnosed.

NOTE Confidence: 0.77116615

00:27:04.050 --> 00:27:07.490 Older patients with AML and this led to

NOTE Confidence: 0.77116615

00:27:07.490 --> 00:27:10.561 a composite CR of 68%, including CR 50%.

NOTE Confidence: 0.77116615

00:27:10.561 --> 00:27:13.123 Quite quite nice with a median

NOTE Confidence: 0.77116615

00:27:13.123 --> 00:27:15.310 OS of well over a year.

NOTE Confidence: 0.77116615

00:27:15.310 --> 00:27:18.222 It appears 14.8 months with quite low

NOTE Confidence: 0.77116615

00:27:18.222 --> 00:27:21.738 for an 8 week rates of mortality.

NOTE Confidence: 0.77116615

00:27:21.740 --> 00:27:23.726 So this is the actual trial.

NOTE Confidence: 0.77116615

00:27:23.730 --> 00:27:25.716 This scheme is a little complex,

NOTE Confidence: 0.77116615

00:27:25.720 --> 00:27:27.380 but essentially like I mentioned,

NOTE Confidence: 0.77116615

00:27:27.380 --> 00:27:27.730 older,

NOTE Confidence: 0.77116615

00:27:27.730 --> 00:27:29.480 newly diagnosed patients with AML

NOTE Confidence: 0.77116615

00:27:29.480 --> 00:27:31.699 received clad plus ldac with van with.

NOTE Confidence: 0.77116615

00:27:31.700 --> 00:27:33.360 As you can see here,

NOTE Confidence: 0.77116615

00:27:33.360 --> 00:27:35.035 the standard dose reductions for

NOTE Confidence: 0.77116615

00:27:35.035 --> 00:27:37.089 CYP 3A four inhibitor use receive

NOTE Confidence: 0.77116615

00:27:37.089 --> 00:27:38.337 this for cycle one,

NOTE Confidence: 0.77116615

00:27:38.340 --> 00:27:40.384 with cycle to being the same three

NOTE Confidence: 0.77116615

00:27:40.384 --> 00:27:42.872 drugs but less clad and a little bit

NOTE Confidence: 0.77116615

00:27:42.872 --> 00:27:44.864 less fanatical acts with cycle three

NOTE Confidence: 0.77116615

00:27:44.864 --> 00:27:46.388 switching the nucleoside backbone

NOTE Confidence: 0.77116615

00:27:46.388 --> 00:27:48.632 for Asia on the standard schedule,

NOTE Confidence: 0.77116615

00:27:48.632 --> 00:27:50.956 again with phonetic lacks for 14 days,

NOTE Confidence: 0.77116615

00:27:50.960 --> 00:27:52.488 similar to cycle two.

NOTE Confidence: 0.77116615

00:27:52.488 --> 00:27:54.016 So basically patients received.

NOTE Confidence: 0.77116615

00:27:54.020 --> 00:27:54.542 Part A,

NOTE Confidence: 0.77116615

00:27:54.542 --> 00:27:57.030 as you can see here and they can move.

NOTE Confidence: 0.77116615

00:27:57.030 --> 00:27:57.542 I don't.

NOTE Confidence: 0.77116615

00:27:57.542 --> 00:27:59.334 I don't know how to use a

NOTE Confidence: 0.77116615

00:27:59.334 --> 00:28:00.319 highlighter or whatever,

NOTE Confidence: 0.77116615

00:28:00.320 --> 00:28:02.318 but patients received a * 2 then

NOTE Confidence: 0.77116615

00:28:02.318 --> 00:28:05.304 B * 2 and then back and forth back

NOTE Confidence: 0.77116615

00:28:05.304 --> 00:28:07.978 and forth for up to 18 cycles.

NOTE Confidence: 0.77116615

00:28:07.980 --> 00:28:10.225 So here the patient characteristics

NOTE Confidence: 0.77116615

00:28:10.225 --> 00:28:13.440 as of the first day to cut of

NOTE Confidence: 0.77116615

00:28:13.440 --> 00:28:15.638 note 40% of patients for older.

NOTE Confidence: 0.77116615

00:28:15.638 --> 00:28:17.648 Sorry older than 70 years,

NOTE Confidence: 0.77116615

00:28:17.650 --> 00:28:19.665 25% were had disease characterized

NOTE Confidence: 0.77116615

00:28:19.665 --> 00:28:20.874 by porous I,

NOTE Confidence: 0.77116615

00:28:20.880 --> 00:28:23.100 genetics ANAN would be would be

NOTE Confidence: 0.77116615

00:28:23.100 --> 00:28:25.310 generally expected given this population,

NOTE Confidence: 0.77116615

00:28:25.310 --> 00:28:27.675 although nearly half were ellenor

NOTE Confidence: 0.77116615

00:28:27.675 --> 00:28:30.040 European leukemia net poor risk

NOTE Confidence: 0.77116615

00:28:30.121 --> 00:28:32.381 after accounting for the relevant

NOTE Confidence: 0.77116615

00:28:32.381 --> 00:28:35.370 molecular features on top of genetics.

NOTE Confidence: 0.77116615

00:28:35.370 --> 00:28:37.510 Amongst the 54 patients that

NOTE Confidence: 0.77116615

00:28:37.510 --> 00:28:40.105 today have been accrued and are

NOTE Confidence: 0.77116615

00:28:40.105 --> 00:28:42.349 in fact invaluable with a median

NOTE Confidence: 0.77116615

00:28:42.349 --> 00:28:45.008 one cycle or month to responses,

NOTE Confidence: 0.77116615

00:28:45.010 --> 00:28:47.908 striking 78% achieved CR and basically all

NOTE Confidence: 0.77116615

00:28:47.908 --> 00:28:50.450 except three achieved MFC MRD negativity.

NOTE Confidence: 0.77116615

00:28:50.450 --> 00:28:50.923 Basically,

NOTE Confidence: 0.77116615

00:28:50.923 --> 00:28:53.288 MRD negativity negativity by flow

NOTE Confidence: 0.77116615

00:28:53.288 --> 00:28:55.180 centric analysis including CRIA

NOTE Confidence: 0.77116615

00:28:55.245 --> 00:28:57.190 composite CR rate of 93% was

NOTE Confidence: 0.77116615

00:28:57.190 --> 00:28:59.890 rendered which is simply amazing and

NOTE Confidence: 0.77116615

00:28:59.890 --> 00:29:02.536 perhaps I really should have saved

NOTE Confidence: 0.77116615

00:29:02.536 --> 00:29:05.357 this safest route for the end so.

NOTE Confidence: 0.77116615

00:29:05.360 --> 00:29:07.810 One of the more striking updates from

NOTE Confidence: 0.77116615

00:29:07.810 --> 00:29:10.359 ASH with regards to the response rates.

NOTE Confidence: 0.77116615

00:29:10.360 --> 00:29:10.716 However,

NOTE Confidence: 0.77116615

00:29:10.716 --> 00:29:12.852 it's not all about response rates

NOTE Confidence: 0.77116615

00:29:12.852 --> 00:29:14.678 for the patient not proceeding

NOTE Confidence: 0.77116615

00:29:14.678 --> 00:29:16.070 to cure to therapy,

NOTE Confidence: 0.77116615

00:29:16.070 --> 00:29:18.350 really care bout event based outcomes

NOTE Confidence: 0.77116615

00:29:18.350 --> 00:29:20.249 like survival in evaluating survival

NOTE Confidence: 0.77116615

00:29:20.249 --> 00:29:22.496 and a medium median of 14.2 months.

NOTE Confidence: 0.77116615

00:29:22.500 --> 00:29:24.636 The OS and RFS curves were

NOTE Confidence: 0.77116615

00:29:24.636 --> 00:29:25.704 essentially the same,

NOTE Confidence: 0.77116615

00:29:25.710 --> 00:29:28.209 meaning OS was reached was not reached.

NOTE Confidence: 0.77116615

00:29:28.210 --> 00:29:28.521 Sorry,

NOTE Confidence: 0.77116615

00:29:28.521 --> 00:29:31.009 and 60% of patients were still alive at

NOTE Confidence: 0.77116615

00:29:31.009 --> 00:29:33.558 two years after starting therapy again.

NOTE Confidence: 0.77116615

00:29:33.560 --> 00:29:35.052 Quite amazing considering the

NOTE Confidence: 0.77116615

00:29:35.052 --> 00:29:37.290 fact that half of patients were.

NOTE Confidence: 0.64456517

00:29:37.290 --> 00:29:38.994 Yellen adverse risk. Sorry

NOTE Confidence: 0.64456517

00:29:38.994 --> 00:29:40.698 hadelin adverse risk disease.

NOTE Confidence: 0.8340789

00:29:42.750 --> 00:29:44.610 However, this is just some.

NOTE Confidence: 0.8340789

00:29:44.610 --> 00:29:46.460 You know, some smaller kind

NOTE Confidence: 0.8340789

00:29:46.460 --> 00:29:47.570 of subpopulation analysis.

NOTE Confidence: 0.8340789

00:29:47.570 --> 00:29:50.146 You can see that when accounting for

NOTE Confidence: 0.8340789

00:29:50.146 --> 00:29:52.770 set of genetic risk and Dylan risk,

NOTE Confidence: 0.8340789

00:29:52.770 --> 00:29:53.880 not surprising differences

NOTE Confidence: 0.8340789

00:29:53.880 --> 00:29:55.360 are in fact observed.

NOTE Confidence: 0.8340789

00:29:55.360 --> 00:29:57.586 I would note that 11 patients

NOTE Confidence: 0.8340789

00:29:57.586 --> 00:29:59.862 or 2524% of the 45 responding.

NOTE Confidence: 0.8340789

00:29:59.862 --> 00:30:01.011 Patients proceeding to

NOTE Confidence: 0.8340789

00:30:01.011 --> 00:30:02.740 transplant with these patients,

NOTE Confidence: 0.8340789

00:30:02.740 --> 00:30:04.112 patients really enjoying more

NOTE Confidence: 0.8340789

00:30:04.112 --> 00:30:06.168 than 90% survival at one year,

NOTE Confidence: 0.8340789

00:30:06.168 --> 00:30:07.878 which when compared with the

NOTE Confidence: 0.8340789

00:30:07.878 --> 00:30:09.634 folks not getting to transform

NOTE Confidence: 0.8340789

00:30:09.634 --> 00:30:11.339 with 69% but a difference,

NOTE Confidence: 0.8340789

00:30:11.339 --> 00:30:13.054 did not reach statistical significance.

NOTE Confidence: 0.8340789

00:30:13.060 --> 00:30:15.118 Likely in the setting of just,

NOTE Confidence: 0.8340789

00:30:15.120 --> 00:30:15.806 you know,

NOTE Confidence: 0.8340789

00:30:15.806 --> 00:30:17.864 obviously a small early phase study.

NOTE Confidence: 0.7932578

00:30:20.240 --> 00:30:21.825 So just going to switch

NOTE Confidence: 0.7932578

00:30:21.825 --> 00:30:23.750 gears a little bit with AML,

NOTE Confidence: 0.7932578

00:30:23.750 --> 00:30:25.750 one of the first decision we have to

NOTE Confidence: 0.7932578

00:30:25.750 --> 00:30:28.218 make is whether patient is quote unquote

NOTE Confidence: 0.7932578

00:30:28.218 --> 00:30:30.123 intensive therapy eligible or not.

NOTE Confidence: 0.7932578

00:30:30.130 --> 00:30:32.062 The first 2 trials I mentioned were

NOTE Confidence: 0.7932578

00:30:32.062 --> 00:30:33.707 really geared towards patients that

NOTE Confidence: 0.7932578

00:30:33.707 --> 00:30:35.227 are intensive therapy ineligible.

NOTE Confidence: 0.7932578

00:30:35.230 --> 00:30:36.980 But what about patients receiving

NOTE Confidence: 0.7932578

00:30:36.980 --> 00:30:39.034 intensive therapy generally felt to be

NOTE Confidence: 0.7932578

00:30:39.034 --> 00:30:41.058 the standard of care for those who are

NOTE Confidence: 0.7932578

00:30:41.058 --> 00:30:42.888 eligible with some specific exceptions?

NOTE Confidence: 0.7932578

00:30:42.890 --> 00:30:44.480 Of course if prompted debate,

NOTE Confidence: 0.7932578

00:30:44.480 --> 00:30:46.400 but that's a discussion for another.

NOTE Confidence: 0.7932578

00:30:46.400 --> 00:30:47.052 Another presentation.

NOTE Confidence: 0.7932578

00:30:47.052 --> 00:30:49.660 Here is the schema for a trial also

NOTE Confidence: 0.7932578

00:30:49.718 --> 00:30:51.674 out of MD Anderson and evaluating

NOTE Confidence: 0.7932578

00:30:51.674 --> 00:30:53.380 the addition of genetic lacks.

NOTE Confidence: 0.7932578

00:30:53.380 --> 00:30:56.084 To CPX, 3/5 one or the brand name

NOTE Confidence: 0.7932578

00:30:56.084 --> 00:30:58.851 being fix EOS which is standard of

NOTE Confidence: 0.7932578

00:30:58.851 --> 00:31:01.886 care for patients with AML MRC and

NOTE Confidence: 0.7932578

00:31:01.886 --> 00:31:04.246 therapy quote unquote related AML.

NOTE Confidence: 0.7932578

00:31:04.250 --> 00:31:06.924 The design included cohort for adults with

NOTE Confidence: 0.7932578

00:31:06.924 --> 00:31:09.188 newly diagnosed AML as well as looks.

NOTE Confidence: 0.7932578

00:31:09.190 --> 00:31:10.955 Factory disease, with the latter

NOTE Confidence: 0.7932578

00:31:10.955 --> 00:31:12.367 allowing prior phonetics exposure.

NOTE Confidence: 0.7932578

00:31:12.370 --> 00:31:13.375 Quite important criterion.

NOTE Confidence: 0.7932578

00:31:13.375 --> 00:31:15.385 A dose escalation phase or safety

NOTE Confidence: 0.7932578

00:31:15.385 --> 00:31:16.250 run included.

NOTE Confidence: 0.7932578

00:31:16.250 --> 00:31:18.020 Of course, all the patients,

NOTE Confidence: 0.7932578

00:31:18.020 --> 00:31:19.428 irrespective of whether they

NOTE Confidence: 0.7932578

00:31:19.428 --> 00:31:20.484 were Dinovo slash,

NOTE Confidence: 0.7932578

00:31:20.490 --> 00:31:23.850 newly diagnosed or realtor factory.

NOTE Confidence: 0.7932578

00:31:23.850 --> 00:31:26.013 Of note CPX 3/5 one was given

NOTE Confidence: 0.7932578

00:31:26.013 --> 00:31:27.969 at the standard dose on label.

NOTE Confidence: 0.7932578

00:31:27.970 --> 00:31:29.402 Essentially event began fairly

NOTE Confidence: 0.7932578

00:31:29.402 --> 00:31:32.158 quickly on day two with a three day

NOTE Confidence: 0.7932578

00:31:32.158 --> 00:31:34.310 ramp up to a target dose of 400,

NOTE Confidence: 0.7932578

00:31:34.310 --> 00:31:35.775 again with the standard dose

NOTE Confidence: 0.7932578

00:31:35.775 --> 00:31:37.620 reductions you would expect or should

NOTE Confidence: 0.7932578

00:31:37.620 --> 00:31:39.235 be considering with concurrency 3A

NOTE Confidence: 0.7932578

00:31:39.235 --> 00:31:41.230 four inhibition as well as toxicities

NOTE Confidence: 0.7932578

00:31:41.230 --> 00:31:42.522 prompted prompting dropping to

NOTE Confidence: 0.7932578

00:31:42.522 --> 00:31:44.741 lower dose levels as they came up.

NOTE Confidence: 0.7932578

00:31:44.741 --> 00:31:46.890 Essentially this was then was given for

NOTE Confidence: 0.7932578

00:31:46.957 --> 00:31:48.769 three weeks during induction as well

NOTE Confidence: 0.7932578

00:31:48.769 --> 00:31:51.428 As for 20 three weeks during each cycle.

NOTE Confidence: 0.7932578

00:31:51.430 --> 00:31:51.808 Consolidation.

NOTE Confidence: 0.7932578

00:31:51.808 --> 00:31:55.210 In this case they allowed up to four cycles.

NOTE Confidence: 0.7932578

00:31:55.210 --> 00:31:56.202 Of consolidation,

NOTE Confidence: 0.7932578

00:31:56.202 --> 00:32:00.600 in contrast to the standard on label CPX 351.

NOTE Confidence: 0.7932578

00:32:00.600 --> 00:32:02.950 Monotherapy consolidation.

NOTE Confidence: 0.7932578

00:32:02.950 --> 00:32:04.570 Here the characteristics of the

NOTE Confidence: 0.7932578

00:32:04.570 --> 00:32:06.554 patients who had a broad range

NOTE Confidence: 0.7932578

00:32:06.554 --> 00:32:08.384 of age instead of genetic risk,

NOTE Confidence: 0.7932578

00:32:08.390 --> 00:32:10.707 I'll call your attention to the right

NOTE Confidence: 0.7932578

00:32:10.707 --> 00:32:13.202 where you can see that 30% of patients

NOTE Confidence: 0.7932578

00:32:13.202 --> 00:32:14.832 had disease characterized by the

NOTE Confidence: 0.7932578

00:32:14.832 --> 00:32:17.308 presence of a TP 53 mutation and after

NOTE Confidence: 0.7932578

00:32:17.308 --> 00:32:19.590 including ASL one and runx one mutations,

NOTE Confidence: 0.7932578

00:32:19.590 --> 00:32:21.753 the majority of patients did in fact

NOTE Confidence: 0.7932578

00:32:21.753 --> 00:32:23.429 have guillain adverse risk disease.

NOTE Confidence: 0.79286337

00:32:25.610 --> 00:32:27.956 Only 6% of patients achieved CR,

NOTE Confidence: 0.79286337

00:32:27.960 --> 00:32:31.080 but CR CRA was the rate of CRC.

NOTE Confidence: 0.79286337

00:32:31.080 --> 00:32:33.912 I was 39% still fairly low with a

NOTE Confidence: 0.79286337

00:32:33.912 --> 00:32:36.558 median one cycle time to response.

NOTE Confidence: 0.79286337

00:32:36.560 --> 00:32:39.128 The most common reason for coming off of

NOTE Confidence: 0.79286337

00:32:39.128 --> 00:32:42.030 study was actually proceeding to transplant.

NOTE Confidence: 0.79286337

00:32:42.030 --> 00:32:44.599 This occurred in 31 patients were but

NOTE Confidence: 0.79286337

00:32:44.599 --> 00:32:47.508 generally 50 half of the patient population.

NOTE Confidence: 0.79286337

00:32:47.510 --> 00:32:49.814 The most common grade 3 plus

NOTE Confidence: 0.79286337

00:32:49.814 --> 00:32:52.199 ease were human logic in nature,

NOTE Confidence: 0.79286337

00:32:52.200 --> 00:32:55.160 pneumonia amongst other infections didn't.

NOTE Confidence: 0.79286337

00:32:55.160 --> 00:32:58.086 Did also occur 30 and 60 day

NOTE Confidence: 0.79286337

00:32:58.086 --> 00:32:59.878 mortality were weren't nominal

NOTE Confidence: 0.79286337

00:32:59.878 --> 00:33:03.678 10% at 30 days and 20% at 60 days,

NOTE Confidence: 0.79286337

00:33:03.678 --> 00:33:06.450 so a fairly toxic regimen with again

NOTE Confidence: 0.79286337

00:33:06.540 --> 00:33:09.185 relatively limited efficacy in comparison

NOTE Confidence: 0.79286337

00:33:09.185 --> 00:33:12.740 to the other guys I've presented.

NOTE Confidence: 0.79286337

00:33:12.740 --> 00:33:15.323 The median overall survival was six months

NOTE Confidence: 0.79286337

00:33:15.323 --> 00:33:18.468 with a 6 month OS rate of about 53%.

NOTE Confidence: 0.79286337

00:33:18.470 --> 00:33:21.691 Just to be specific and 46% at one year.

NOTE Confidence: 0.79286337

00:33:21.691 --> 00:33:23.119 So not terribly different.

NOTE Confidence: 0.79286337

00:33:23.120 --> 00:33:25.268 6 versus 12 months among responders,

NOTE Confidence: 0.79286337

00:33:25.270 --> 00:33:28.126 the median OS and RFS were not reached,

NOTE Confidence: 0.79286337

00:33:28.130 --> 00:33:30.552 and the six month OS and RFS

NOTE Confidence: 0.79286337

00:33:30.552 --> 00:33:32.070 were essentially about 8590%.

NOTE Confidence: 0.79286337

00:33:32.070 --> 00:33:34.152 You can see that patients without

NOTE Confidence: 0.79286337

00:33:34.152 --> 00:33:36.010 prior medical exposure did better.

NOTE Confidence: 0.79286337

00:33:36.010 --> 00:33:38.158 However, again, given the small numbers,

NOTE Confidence: 0.79286337

00:33:38.160 --> 00:33:42.240 this did not reach statistical significance.

NOTE Confidence: 0.79286337

00:33:42.240 --> 00:33:44.478 Sticking with this is another trial.

NOTE Confidence: 0.79286337

00:33:44.480 --> 00:33:45.972 Sticking with intensive therapy

NOTE Confidence: 0.79286337

00:33:45.972 --> 00:33:46.718 eligible patients.

NOTE Confidence: 0.79286337

00:33:46.720 --> 00:33:48.994 What about adding then to other

NOTE Confidence: 0.79286337

00:33:48.994 --> 00:33:50.820 intensive backbones beyond CPX 351,

NOTE Confidence: 0.79286337

00:33:50.820 --> 00:33:52.878 here's a schema which demonstrates that

NOTE Confidence: 0.79286337

00:33:52.878 --> 00:33:54.708 patients with both newly diagnosed

NOTE Confidence: 0.79286337

00:33:54.708 --> 00:33:56.718 disease and relapse refractory disease

NOTE Confidence: 0.79286337

00:33:56.718 --> 00:33:58.650 received a fairly standard flag.

NOTE Confidence: 0.79286337

00:33:58.650 --> 00:34:01.634 Ida regimen and dosing with Medical X added,

NOTE Confidence: 0.79286337

00:34:01.640 --> 00:34:03.228 especially specifically during days

NOTE Confidence: 0.79286337

00:34:03.228 --> 00:34:06.004 one through 14 at a target dose

NOTE Confidence: 0.79286337

00:34:06.004 --> 00:34:07.978 of 400 in standard target dose,

NOTE Confidence: 0.79286337

00:34:07.980 --> 00:34:10.761 but not without a ramp up and then high

NOTE Confidence: 0.79286337

00:34:10.761 --> 00:34:13.679 debt consolidation had been incorporated.

NOTE Confidence: 0.79286337

00:34:13.680 --> 00:34:15.988 Days one through 14.

NOTE Confidence: 0.79286337

00:34:15.990 --> 00:34:17.534 So a complex slide,

NOTE Confidence: 0.79286337

00:34:17.534 --> 00:34:20.359 but hopefully that kind of summed it up.

NOTE Confidence: 0.79286337

00:34:20.360 --> 00:34:22.908 Here are the patient demographics or sorry

NOTE Confidence: 0.79286337

00:34:22.908 --> 00:34:24.000 patient characteristics specifically,

NOTE Confidence: 0.79286337

00:34:24.000 --> 00:34:25.700 noting that the relapse refractory

NOTE Confidence: 0.79286337

00:34:25.700 --> 00:34:27.863 cohorts were a bit more enriched

NOTE Confidence: 0.79286337

00:34:27.863 --> 00:34:29.459 for adverse risk disease.

NOTE Confidence: 0.79286337

00:34:29.460 --> 00:34:32.001 And as you would otherwise expect and

NOTE Confidence: 0.79286337

00:34:32.001 --> 00:34:33.826 38% had received prior allogeneic

NOTE Confidence: 0.79286337

00:34:33.826 --> 00:34:35.646 Amanda poetic stem cell transplant.

NOTE Confidence: 0.79211825

00:34:37.970 --> 00:34:40.328 The toxicity was what you would

NOTE Confidence: 0.79211825

00:34:40.328 --> 00:34:42.303 expect with intensive therapy and

NOTE Confidence: 0.79211825

00:34:42.303 --> 00:34:44.313 addition of class including based on

NOTE Confidence: 0.79211825

00:34:44.313 --> 00:34:48.838 what I just presented. For C PX351.

NOTE Confidence: 0.79211825

00:34:48.840 --> 00:34:52.701 CRC is 90% and in the newly diagnosed cohort

NOTE Confidence: 0.79211825

00:34:52.701 --> 00:34:55.830 60 to 75% in the roaster factory cohorts.

NOTE Confidence: 0.79211825

00:34:55.830 --> 00:35:00.998 So and fairly good rates of MRD negativity.

NOTE Confidence: 0.79211825

00:35:01.000 --> 00:35:04.664 And this is essentially just looking at at.

NOTE Confidence: 0.79211825

00:35:04.670 --> 00:35:06.390 Based on their their disease,

NOTE Confidence: 0.79211825

00:35:06.390 --> 00:35:07.834 the disease cohort specifically.

NOTE Confidence: 0.79211825

00:35:07.834 --> 00:35:10.689 So I'll just kind of wrap it up

NOTE Confidence: 0.79211825

00:35:10.689 --> 00:35:12.555 with just promise two more slides.

NOTE Confidence: 0.79211825

00:35:12.560 --> 00:35:14.270 So those updates for therapies

NOTE Confidence: 0.79211825

00:35:14.270 --> 00:35:15.296 we already had.

NOTE Confidence: 0.79211825

00:35:15.300 --> 00:35:17.190 But what about just one update

NOTE Confidence: 0.79211825

00:35:17.190 --> 00:35:19.080 on an agent or regimen?

NOTE Confidence: 0.79211825

00:35:19.080 --> 00:35:21.126 We do not yet really have.

NOTE Confidence: 0.79211825

00:35:21.130 --> 00:35:23.545 This is Google Map or the this

NOTE Confidence: 0.79211825

00:35:23.545 --> 00:35:25.249 is the humanized anti CD.

NOTE Confidence: 0.79211825

00:35:25.250 --> 00:35:26.965 47 IgG, four monoclonal antibody

NOTE Confidence: 0.79211825

00:35:26.965 --> 00:35:28.680 product from from Gilead Sciences,

NOTE Confidence: 0.79211825

00:35:28.680 --> 00:35:29.988 relevant as tumor expression

NOTE Confidence: 0.79211825

00:35:29.988 --> 00:35:31.950 of CD 47 prompts evasion from

NOTE Confidence: 0.79211825

00:35:32.012 --> 00:35:33.480 an 80 minute survaillance.

NOTE Confidence: 0.79211825

00:35:33.480 --> 00:35:34.509 Specifically macrophage mediated.

NOTE Confidence: 0.79211825

00:35:34.509 --> 00:35:36.224 Microcytosis and in fact pre

NOTE Confidence: 0.79211825

00:35:36.224 --> 00:35:37.729 clinical data support that AML,

NOTE Confidence: 0.79211825

00:35:37.730 --> 00:35:38.878 leukemic blast doing factor,

NOTE Confidence: 0.79211825

00:35:38.878 --> 00:35:41.200 or enriched for CD 47 Express expression.

NOTE Confidence: 0.79211825

00:35:41.200 --> 00:35:43.054 So this was studied in combination

NOTE Confidence: 0.79211825

00:35:43.054 --> 00:35:44.980 with Asia and a phase one.

NOTE Confidence: 0.79211825

00:35:44.980 --> 00:35:48.102 B2 trial that armored actually touched on

NOTE Confidence: 0.79211825

00:35:48.102 --> 00:35:51.199 earlier most in the context of high risk

NOTE Confidence: 0.79211825

00:35:51.199 --> 00:35:54.837 MD S but I'll just focus on the AML cohort.

NOTE Confidence: 0.79211825

00:35:54.840 --> 00:35:55.230 Specifically,

NOTE Confidence: 0.79211825

00:35:55.230 --> 00:35:56.400 90 except sorry,

NOTE Confidence: 0.79211825

00:35:56.400 --> 00:35:58.550 70% porous surgeon attics 70% P

NOTE Confidence: 0.79211825

00:35:58.550 --> 00:36:00.310 three mutations with a robust

NOTE Confidence: 0.79211825

00:36:00.371 --> 00:36:02.466 median vaf which would otherwise

NOTE Confidence: 0.79211825

00:36:02.466 --> 00:36:04.561 predict biallelic loss of function.

NOTE Confidence: 0.79211825

00:36:04.570 --> 00:36:06.122 So essentially a very,

NOTE Confidence: 0.79211825

00:36:06.122 --> 00:36:06.510 very,

NOTE Confidence: 0.79211825

00:36:06.510 --> 00:36:09.210 very poorest population and not the

NOTE Confidence: 0.79211825

00:36:09.210 --> 00:36:11.450 toxicity profile was generally what

NOTE Confidence: 0.79211825

00:36:11.450 --> 00:36:14.026 you would expect with as a monotherapy

NOTE Confidence: 0.79211825

00:36:14.026 --> 00:36:16.506 other than I'd say a mild transient

NOTE Confidence: 0.79211825

00:36:16.506 --> 00:36:18.595 on targeting me that was reversible.

NOTE Confidence: 0.79211825

00:36:18.595 --> 00:36:21.085 Know whether grade 3/4 plus 80s

NOTE Confidence: 0.79211825

00:36:21.085 --> 00:36:23.844 and no immune related AE's given

NOTE Confidence: 0.79211825

00:36:23.844 --> 00:36:25.760 macros mechanism of action.

NOTE Confidence: 0.79211825

00:36:25.760 --> 00:36:27.884 This is a slide hammer showed

NOTE Confidence: 0.79211825

00:36:27.884 --> 00:36:30.250 you this is the AML cohort,

NOTE Confidence: 0.79211825

00:36:30.250 --> 00:36:32.770 essentially a 20% rate of see better

NOTE Confidence: 0.79211825

00:36:32.770 --> 00:36:34.740 in comparison to generate 20%

NOTE Confidence: 0.79211825

00:36:34.740 --> 00:36:36.978 rate of expected as a monotherapy.

NOTE Confidence: 0.79211825

00:36:36.980 --> 00:36:38.102 60 ish percent,

NOTE Confidence: 0.79211825

00:36:38.102 --> 00:36:39.224 essentially with essentially

NOTE Confidence: 0.79211825

00:36:39.224 --> 00:36:40.720 in the waterfall plot.

NOTE Confidence: 0.79211825

00:36:40.720 --> 00:36:42.590 Here nearly all patients experiencing

NOTE Confidence: 0.79211825

00:36:42.590 --> 00:36:44.086 Meryl Blast percentage reduction

NOTE Confidence: 0.79211825

00:36:44.086 --> 00:36:45.957 with many being robust reductions.

NOTE Confidence: 0.79211825

00:36:45.960 --> 00:36:48.352 The median OS at last day to cut

NOTE Confidence: 0.79211825

00:36:48.352 --> 00:36:51.025 off of patients in the trial was

NOTE Confidence: 0.79211825

00:36:51.025 --> 00:36:53.557 18.9 months and even after isolating

NOTE Confidence: 0.79211825

00:36:53.557 --> 00:36:56.317 patients that had a P3 mutation.

NOTE Confidence: 0.79211825

00:36:56.320 --> 00:36:57.940 And we still 12.9 months,

NOTE Confidence: 0.79211825

00:36:57.940 --> 00:36:59.781 which to be honest is the longest

NOTE Confidence: 0.79211825

00:36:59.781 --> 00:37:01.867 median OS I believe ever reported

NOTE Confidence: 0.79211825

00:37:01.867 --> 00:37:03.097 for this population,

NOTE Confidence: 0.79211825

00:37:03.100 --> 00:37:05.354 so quite striking as you can see,

NOTE Confidence: 0.79211825

00:37:05.360 --> 00:37:07.274 four or five patients are still

NOTE Confidence: 0.79211825

00:37:07.274 --> 00:37:09.240 alive more than two years out,

NOTE Confidence: 0.79211825

00:37:09.240 --> 00:37:10.143 so quite impressive.

NOTE Confidence: 0.79211825

00:37:10.143 --> 00:37:12.674 So I am a little bit over and

NOTE Confidence: 0.79211825

00:37:12.674 --> 00:37:14.090 I apologize to Nikolai.

NOTE Confidence: 0.79211825

00:37:14.090 --> 00:37:15.410 Mostly this is raw,

NOTE Confidence: 0.79211825

00:37:15.410 --> 00:37:17.060 conclude my section and look

NOTE Confidence: 0.79211825

00:37:17.060 --> 00:37:18.929 forward any questions at the end.

NOTE Confidence: 0.79211825

00:37:18.930 --> 00:37:20.850 So next I'd like to introduce

NOTE Confidence: 0.79211825

00:37:20.850 --> 00:37:22.130 Doctor Nikolai Pedulla civilly

NOTE Confidence: 0.79211825

00:37:22.187 --> 00:37:23.787 discussing the ash 2020 updates

NOTE Confidence: 0.79211825

00:37:23.787 --> 00:37:25.387 in there almost perfect NPS.

NOTE Confidence: 0.8451901

00:37:29.040 --> 00:37:31.374 Alright, thank you Oriel let

NOTE Confidence: 0.8451901

00:37:31.374 --> 00:37:34.260 me share my slides with you.

NOTE Confidence: 0.89198864

00:37:34.260 --> 00:37:35.228 How does it look?

NOTE Confidence: 0.89198864

00:37:35.228 --> 00:37:36.680 Does it look like one screen?

NOTE Confidence: 0.72244483

00:37:40.950 --> 00:37:42.830 We don't see slides head.

NOTE Confidence: 0.72244483

00:37:42.830 --> 00:37:45.080 Sadly you don't see slides OK,

NOTE Confidence: 0.72244483

00:37:45.080 --> 00:37:48.244 just a second. We just see you.

NOTE Confidence: 0.72244483

00:37:48.244 --> 00:37:49.905 Oh interesting. Alright,

NOTE Confidence: 0.72244483

00:37:49.905 --> 00:37:52.825 so hold on let me escape from here.

NOTE Confidence: 0.72244483

00:37:52.830 --> 00:37:57.949 And so I'll do this. How about now?

NOTE Confidence: 0.72244483

00:37:57.950 --> 00:38:01.950 Do you see two right and I need to swap?

NOTE Confidence: 0.72244483

00:38:01.950 --> 00:38:03.558 No, we still don't see them.

NOTE Confidence: 0.72244483

00:38:03.558 --> 00:38:04.630 You don't see them.

NOTE Confidence: 0.71176875

00:38:14.660 --> 00:38:18.670 Did you share a video girl OK?

NOTE Confidence: 0.71176875

00:38:18.670 --> 00:38:20.916 Yep, now we see alright.

NOTE Confidence: 0.71176875

00:38:20.916 --> 00:38:23.604 You see this one slide right?

NOTE Confidence: 0.71176875

00:38:23.610 --> 00:38:24.766 Alright, OK,

NOTE Confidence: 0.71176875

00:38:24.766 --> 00:38:28.234 alright so I'll be talking about.

NOTE Confidence: 0.71176875

00:38:28.240 --> 00:38:30.844 Milo proliferative neoplasms and I had to

NOTE Confidence: 0.71176875

00:38:30.844 --> 00:38:33.108 be selective because of the time frame,

NOTE Confidence: 0.71176875

00:38:33.110 --> 00:38:35.510 so this are my disclosures.

NOTE Confidence: 0.71176875

00:38:35.510 --> 00:38:37.830 I'll go over 4 studies and the first

NOTE Confidence: 0.71176875

00:38:37.830 --> 00:38:40.552 one was presented as a late breaking

NOTE Confidence: 0.71176875

00:38:40.552 --> 00:38:43.076 abstract is not the interventional study

NOTE Confidence: 0.71176875

00:38:43.076 --> 00:38:45.729 I thought would be important to mention.

NOTE Confidence: 0.71176875

00:38:45.730 --> 00:38:48.285 I just have one slide about it.

NOTE Confidence: 0.71176875

00:38:48.290 --> 00:38:50.110 This is about driver mutation,

NOTE Confidence: 0.71176875

00:38:50.110 --> 00:38:51.940 acquisition in pH, negative MPs,

NOTE Confidence: 0.71176875

00:38:51.940 --> 00:38:54.716 and this study managed to show that this

NOTE Confidence: 0.71176875

00:38:54.716 --> 00:38:57.676 mutations are quite as early as in utero

NOTE Confidence: 0.71176875

00:38:57.676 --> 00:38:59.600 until disease develops decades later.

NOTE Confidence: 0.71176875

00:38:59.600 --> 00:39:02.155 So the goal of the study was

NOTE Confidence: 0.71176875

00:39:02.155 --> 00:39:03.705 timing of driver, mutation,

NOTE Confidence: 0.71176875

00:39:03.705 --> 00:39:04.160 acquisition,

NOTE Confidence: 0.71176875

00:39:04.160 --> 00:39:05.980 and clonal expansion evolution

NOTE Confidence: 0.71176875

00:39:05.980 --> 00:39:07.800 dynamics of the clones.

NOTE Confidence: 0.71176875

00:39:07.800 --> 00:39:10.494 The methods used by UK investigators

NOTE Confidence: 0.71176875

00:39:10.494 --> 00:39:13.039 included studying 10 patients with Jack.

NOTE Confidence: 0.71176875

00:39:13.040 --> 00:39:15.662 Two mutations of this is Jack

NOTE Confidence: 0.71176875

00:39:15.662 --> 00:39:17.410 two mutation for Stevens.

NOTE Confidence: 0.71176875

00:39:17.410 --> 00:39:20.469 This patients were between H20 and 76.

NOTE Confidence: 0.71176875

00:39:20.470 --> 00:39:22.142 The single cell derived

NOTE Confidence: 0.71176875

00:39:22.142 --> 00:39:23.814 hematopoietic colonies were studied

NOTE Confidence: 0.71176875

00:39:23.814 --> 00:39:25.719 using whole exome sequencing.

NOTE Confidence: 0.71176875

00:39:25.720 --> 00:39:28.210 There was targeted resequencing of

NOTE Confidence: 0.71176875

00:39:28.210 --> 00:39:30.700 longitudinal blood samples from the

NOTE Confidence: 0.71176875

00:39:30.781 --> 00:39:32.811 stem patients and something which

NOTE Confidence: 0.71176875

00:39:32.811 --> 00:39:35.770 is still not clear very clear to me,

NOTE Confidence: 0.71176875

00:39:35.770 --> 00:39:39.046 but they were able to create those.

NOTE Confidence: 0.71176875

00:39:39.050 --> 00:39:41.400 Polygenetic trees or of hematopoiesis,

NOTE Confidence: 0.71176875

00:39:41.400 --> 00:39:43.980 allowing them to understand when

NOTE Confidence: 0.71176875

00:39:43.980 --> 00:39:46.044 initial driver mutation occurred

NOTE Confidence: 0.71176875

00:39:46.044 --> 00:39:49.229 as the result it was found that

NOTE Confidence: 0.71176875

00:39:49.229 --> 00:39:50.957 mpanza originate from driver

NOTE Confidence: 0.71176875

00:39:51.039 --> 00:39:53.619 mutation quite very early in life,

NOTE Confidence: 0.71176875

00:39:53.620 --> 00:39:55.000 including before birth,

NOTE Confidence: 0.71176875

00:39:55.000 --> 00:39:57.300 and then there is lifelong

NOTE Confidence: 0.71176875

00:39:57.300 --> 00:39:59.259 clonal expansion and evolution.

NOTE Confidence: 0.71176875

00:39:59.260 --> 00:40:00.064 So this.

NOTE Confidence: 0.71176875

00:40:00.064 --> 00:40:02.476 Results are quite amazing because they

NOTE Confidence: 0.71176875

00:40:02.476 --> 00:40:05.410 tell us that this Jack two mutation,

NOTE Confidence: 0.71176875

00:40:05.410 --> 00:40:06.974 which eventually leads to

NOTE Confidence: 0.71176875

00:40:06.974 --> 00:40:09.320 development of MPN late at life,

NOTE Confidence: 0.71176875

00:40:09.320 --> 00:40:12.704 is present in utero and perhaps if we can

NOTE Confidence: 0.71176875

00:40:12.704 --> 00:40:15.186 understand how it develops and evolves,

NOTE Confidence: 0.71176875

00:40:15.190 --> 00:40:17.746 we may use some preventative strategies

NOTE Confidence: 0.71176875

00:40:17.746 --> 00:40:20.462 in the future to prevent expansion

NOTE Confidence: 0.71176875

00:40:20.462 --> 00:40:23.258 of this clone or its evolution.

NOTE Confidence: 0.71176875

00:40:23.260 --> 00:40:25.300 Moving onto interventional studies,

NOTE Confidence: 0.71176875

00:40:25.300 --> 00:40:26.830 first of all,

NOTE Confidence: 0.71176875

00:40:26.830 --> 00:40:30.071 I will talk about CML and again

NOTE Confidence: 0.71176875

00:40:30.071 --> 00:40:32.949 another late breaking abstract second.

NOTE Confidence: 0.71176875

00:40:32.950 --> 00:40:35.995 I will talk about one study using

NOTE Confidence: 0.71176875

00:40:35.995 --> 00:40:39.580 new drug for Milo fibrosis patients,

NOTE Confidence: 0.71176875

00:40:39.580 --> 00:40:42.130 and finally I'll finish with

NOTE Confidence: 0.71176875

00:40:42.130 --> 00:40:44.680 the study for PVR patients.

NOTE Confidence: 0.71176875

00:40:44.680 --> 00:40:47.746 So the second study I would

NOTE Confidence: 0.71176875

00:40:47.746 --> 00:40:51.500 like to talk about looked at a

NOTE Confidence: 0.71176875

00:40:51.500 --> 00:40:54.686 synonym also known as able 001.

NOTE Confidence: 0.71176875

00:40:54.690 --> 00:40:58.078 This is the first class stamp inhibitor.

NOTE Confidence: 0.71176875

00:40:58.080 --> 00:41:01.014 An stamp is specifically targeting the

NOTE Confidence: 0.71176875

00:41:01.014 --> 00:41:04.848 Belmira stole pork it so its allosteric BSL,

NOTE Confidence: 0.71176875

00:41:04.850 --> 00:41:07.466 one BSL BCR ABL one inhibitor

NOTE Confidence: 0.71176875

00:41:07.466 --> 00:41:09.882 which is different to advertising

NOTE Confidence: 0.71176875

00:41:09.882 --> 00:41:12.210 kinese inhibitors which targeting

NOTE Confidence: 0.71176875

00:41:12.210 --> 00:41:15.120 ATP pocket on April 1.

NOTE Confidence: 0.71176875

00:41:15.120 --> 00:41:17.624 So as you can see on the cartoon

NOTE Confidence: 0.71176875

00:41:17.624 --> 00:41:19.961 from New England Journal Medicine

NOTE Confidence: 0.71176875

00:41:19.961 --> 00:41:22.133 article discussing Phase One

NOTE Confidence: 0.71176875

00:41:22.133 --> 00:41:24.680 results with this medication.

NOTE Confidence: 0.71176875

00:41:24.680 --> 00:41:27.344 There is Mr Lated and terminal

NOTE Confidence: 0.71176875

00:41:27.344 --> 00:41:29.668 which auto inhibits able one

NOTE Confidence: 0.71176875

00:41:29.668 --> 00:41:31.958 an with BCR ABL translocation.

NOTE Confidence: 0.71176875

00:41:31.960 --> 00:41:35.920 This N terminal piece of.

NOTE Confidence: 0.71176875

00:41:35.920 --> 00:41:37.066 Peace is gone,

NOTE Confidence: 0.71176875

00:41:37.066 --> 00:41:40.362 so you have PCR and now there is

NOTE Confidence: 0.71176875

00:41:40.362 --> 00:41:43.542 no auto inhibition and there is

NOTE Confidence: 0.71176875

00:41:43.542 --> 00:41:46.091 constitutive activation of ABL kinase

NOTE Confidence: 0.71176875

00:41:46.091 --> 00:41:49.129 Aciman app targets that fork it and

NOTE Confidence: 0.71176875

00:41:49.129 --> 00:41:51.706 can allosterically inhibit PCR able?

NOTE Confidence: 0.71176875

00:41:51.706 --> 00:41:54.376 So as you can see,

NOTE Confidence: 0.71176875

00:41:54.380 --> 00:41:57.418 the other tiki eyes we have currently

NOTE Confidence: 0.71176875

00:41:57.418 --> 00:41:59.941 in practice and use in practice

NOTE Confidence: 0.71176875

00:41:59.941 --> 00:42:02.580 go to ATP binding site and the

NOTE Confidence: 0.78682363

00:42:02.666 --> 00:42:05.166 Aciman app actually affects able

NOTE Confidence: 0.78682363

00:42:05.166 --> 00:42:08.111 one kinase inhibits able one kinase

NOTE Confidence: 0.78682363

00:42:08.111 --> 00:42:10.316 using this mirror style pocket,

NOTE Confidence: 0.78682363

00:42:10.320 --> 00:42:12.092 hence the name specifically

NOTE Confidence: 0.78682363

00:42:12.092 --> 00:42:14.750 targeting the able Morris to pocket.

NOTE Confidence: 0.78682363

00:42:14.750 --> 00:42:17.750 So it works even when mutations

NOTE Confidence: 0.78682363

00:42:17.750 --> 00:42:20.635 like T315Y inhibit ability of the

NOTE Confidence: 0.78682363

00:42:20.635 --> 00:42:23.023 tiki eyes to inhibit able one.

NOTE Confidence: 0.78682363

00:42:23.030 --> 00:42:24.840 Like in this particular situation,

NOTE Confidence: 0.78682363

00:42:24.840 --> 00:42:27.094 in the cartoon you can see that

NOTE Confidence: 0.78682363

00:42:27.094 --> 00:42:28.480 the teising kinase inhibitor

NOTE Confidence: 0.78682363

00:42:28.480 --> 00:42:30.568 cannot attach to the pocket due

NOTE Confidence: 0.78682363

00:42:30.568 --> 00:42:32.779 to change of its confirmation,

NOTE Confidence: 0.78682363

00:42:32.780 --> 00:42:35.404 but a synonym still able to attach to

NOTE Confidence: 0.78682363

00:42:35.404 --> 00:42:37.830 Bristol Pocket inhibiting able one kinase.

NOTE Confidence: 0.78682363

00:42:37.830 --> 00:42:40.486 So this is a phase three study was

NOTE Confidence: 0.78682363

00:42:40.486 --> 00:42:42.861 Simonette versus Design IP in patients

NOTE Confidence: 0.78682363

00:42:42.861 --> 00:42:44.911 with chronic phase CML previously

NOTE Confidence: 0.78682363

00:42:44.911 --> 00:42:47.218 treated with at least two tiki eyes,

NOTE Confidence: 0.78682363

00:42:47.220 --> 00:42:49.422 two different guys and this is

NOTE Confidence: 0.78682363

00:42:49.422 --> 00:42:51.308 an important study because the

NOTE Confidence: 0.78682363

00:42:51.308 --> 00:42:53.048 drug is now undergoing review

NOTE Confidence: 0.78682363

00:42:53.048 --> 00:42:55.280 for approval and I'm hoping that.

NOTE Confidence: 0.78682363

00:42:55.280 --> 00:42:57.782 It will be available as yet

NOTE Confidence: 0.78682363

00:42:57.782 --> 00:43:00.047 another medication to treat chronic

NOTE Confidence: 0.78682363

00:43:00.047 --> 00:43:02.637 myeloid leukemia later this year.

NOTE Confidence: 0.78682363

00:43:02.640 --> 00:43:05.502 So the selection criteria listed and

NOTE Confidence: 0.78682363

00:43:05.502 --> 00:43:07.902 patients were included had chronic

NOTE Confidence: 0.78682363

00:43:07.902 --> 00:43:10.765 phase two or more GIS used before

NOTE Confidence: 0.78682363

00:43:10.765 --> 00:43:13.571 and patients have to change treatment

NOTE Confidence: 0.78682363

00:43:13.571 --> 00:43:15.956 either because they were intolerant

NOTE Confidence: 0.78682363

00:43:15.956 --> 00:43:18.530 or resistant to treatment and so

NOTE Confidence: 0.78682363

00:43:18.530 --> 00:43:21.212 the patients was 2315 I mutation

NOTE Confidence: 0.78682363

00:43:21.212 --> 00:43:23.737 or V299L mutations were excluded

NOTE Confidence: 0.78682363

00:43:23.737 --> 00:43:26.160 because pursuit Nip is not.

NOTE Confidence: 0.78682363

00:43:26.160 --> 00:43:27.900 Active against this mutation.

NOTE Confidence: 0.78682363

00:43:27.900 --> 00:43:31.094 So this is specifically the study which

NOTE Confidence: 0.78682363

00:43:31.094 --> 00:43:33.629 didn't include T315I mutated patients.

NOTE Confidence: 0.78682363

00:43:33.630 --> 00:43:36.546 This particular group of patients was

NOTE Confidence: 0.78682363

00:43:36.546 --> 00:43:39.745 addressed by the Phase One study and

NOTE Confidence: 0.78682363

00:43:39.745 --> 00:43:42.468 the drug is active against the BCR

NOTE Confidence: 0.78682363

00:43:42.552 --> 00:43:45.307 ABL with this particular mutation,

NOTE Confidence: 0.78682363

00:43:45.310 --> 00:43:47.146 so patients were randomized.

NOTE Confidence: 0.78682363

00:43:47.146 --> 00:43:51.380 As you can see in two to one fashion,

NOTE Confidence: 0.78682363

00:43:51.380 --> 00:43:53.530 and the demographics were slightly

NOTE Confidence: 0.78682363

00:43:53.530 --> 00:43:56.620 different in two groups I highlighted.

NOTE Confidence: 0.78682363

00:43:56.620 --> 00:43:59.350 In yellow here that a similar patients

NOTE Confidence: 0.78682363

00:43:59.350 --> 00:44:01.679 there were more men than women.

NOTE Confidence: 0.78682363

00:44:01.680 --> 00:44:03.620 Also in a similar patients,

NOTE Confidence: 0.78682363

00:44:03.620 --> 00:44:06.077 the switch of therapy was less likely

NOTE Confidence: 0.78682363

00:44:06.077 --> 00:44:09.227 to be due to lack of efficacy and more

NOTE Confidence: 0.78682363

00:44:09.227 --> 00:44:12.041 likely due to be taller ability and

NOTE Confidence: 0.78682363

00:44:12.041 --> 00:44:14.356 that basically is characteristic of

NOTE Confidence: 0.78682363

00:44:14.356 --> 00:44:17.510 a group of patients which may be more

NOTE Confidence: 0.78682363

00:44:17.510 --> 00:44:20.348 responsive to the next line of treatment.

NOTE Confidence: 0.78682363

00:44:20.350 --> 00:44:23.010 And finally also in a similar barm

NOTE Confidence: 0.78682363

00:44:23.010 --> 00:44:25.020 less patience than in pursuit.

NOTE Confidence: 0.78682363

00:44:25.020 --> 00:44:27.768 Newbomb received three or more tikis.

NOTE Confidence: 0.78682363

00:44:27.770 --> 00:44:30.087 So this is the primary endpoint of

NOTE Confidence: 0.78682363

00:44:30.087 --> 00:44:31.934 this study which showed improved

NOTE Confidence: 0.78682363

00:44:31.934 --> 00:44:33.884 major molecular response rate at

NOTE Confidence: 0.78682363

00:44:33.884 --> 00:44:35.840 24 weeks at six months,

NOTE Confidence: 0.78682363

00:44:35.840 --> 00:44:38.505 and the difference between two

NOTE Confidence: 0.78682363

00:44:38.505 --> 00:44:41.170 groups was twelve point 2%.

NOTE Confidence: 0.78682363

00:44:41.170 --> 00:44:42.965 So taking into consideration the

NOTE Confidence: 0.78682363

00:44:42.965 --> 00:44:44.760 differences between two groups I

NOTE Confidence: 0.78682363

00:44:44.819 --> 00:44:47.003 showed on previous slide that the

NOTE Confidence: 0.78682363

00:44:47.003 --> 00:44:48.843 logistic regression analysis was done

NOTE Confidence: 0.78682363

00:44:48.843 --> 00:44:50.763 and showed that odds ratios adjusted

NOTE Confidence: 0.78682363

00:44:50.763 --> 00:44:52.681 for those things which were different

NOTE Confidence: 0.78682363

00:44:52.681 --> 00:44:54.583 in two groups were quite similar

NOTE Confidence: 0.78682363

00:44:54.583 --> 00:44:56.310 towards ratios without adjustment,

NOTE Confidence: 0.78682363

00:44:56.310 --> 00:44:58.690 which gives us hope that the improved

NOTE Confidence: 0.78682363

00:44:58.690 --> 00:45:01.008 outcome in a similar treated patients

NOTE Confidence: 0.78682363

00:45:01.008 --> 00:45:03.456 is not related to the difference

NOTE Confidence: 0.78682363

00:45:03.456 --> 00:45:04.960 in the population.

NOTE Confidence: 0.78682363

00:45:04.960 --> 00:45:07.584 So the side effect profiles a lot of

NOTE Confidence: 0.78682363

00:45:07.584 --> 00:45:09.858 patients get different side effects,

NOTE Confidence: 0.78682363

00:45:09.860 --> 00:45:12.198 but overall a similar patients have less

NOTE Confidence: 0.78682363

00:45:12.198 --> 00:45:14.758 side effects than positive treated patients.

NOTE Confidence: 0.78682363

00:45:14.760 --> 00:45:16.944 One thing I would like to highlight

NOTE Confidence: 0.78682363

00:45:16.944 --> 00:45:19.229 here that a similar group there

NOTE Confidence: 0.78682363

00:45:19.229 --> 00:45:21.779 were two deaths related to arterial

NOTE Confidence: 0.78682363

00:45:21.779 --> 00:45:23.807 embolism won an ischemic stroke.

NOTE Confidence: 0.78682363

00:45:23.810 --> 00:45:25.298 Another Iman positive patients.

NOTE Confidence: 0.78682363

00:45:25.298 --> 00:45:27.530 One patient died due to septic

NOTE Confidence: 0.800081

00:45:27.599 --> 00:45:30.222 shock, so the side effect profile was

NOTE Confidence: 0.800081

00:45:30.222 --> 00:45:33.140 different, so anemia and thrombo cytopenia.

NOTE Confidence: 0.800081

00:45:33.140 --> 00:45:35.450 Sorry, Trump said opinion neutropenia were

NOTE Confidence: 0.800081

00:45:35.450 --> 00:45:38.352 similar in both groups and then GI side

NOTE Confidence: 0.800081

00:45:38.352 --> 00:45:40.302 effects in the left abnormalities were

NOTE Confidence: 0.800081

00:45:40.371 --> 00:45:42.855 more common in bosutinib treated patients.

NOTE Confidence: 0.800081

00:45:42.860 --> 00:45:45.120 So in conclusion, this assemble

NOTE Confidence: 0.800081

00:45:45.120 --> 00:45:48.012 study was the first control study

NOTE Confidence: 0.800081

00:45:48.012 --> 00:45:50.220 comparing tikis for treatment.

NOTE Confidence: 0.800081

00:45:50.220 --> 00:45:51.753 Assistant Intolerant CML

NOTE Confidence: 0.800081

00:45:51.753 --> 00:45:53.286 population and assimilate,

NOTE Confidence: 0.800081

00:45:53.290 --> 00:45:56.356 which is first class stamp inhibitor,

NOTE Confidence: 0.800081

00:45:56.360 --> 00:45:58.875 showed superior efficacy compared with

NOTE Confidence: 0.800081

00:45:58.875 --> 00:46:02.000 bosutinib with favorable side effect profile,

NOTE Confidence: 0.800081

00:46:02.000 --> 00:46:06.130 so this is upcoming hopefully.

NOTE Confidence: 0.800081

00:46:06.130 --> 00:46:08.040 Approved in the near future

NOTE Confidence: 0.800081

00:46:08.040 --> 00:46:09.950 treatment option for CML patients,

NOTE Confidence: 0.800081

00:46:09.950 --> 00:46:11.474 particularly with resistant and

NOTE Confidence: 0.800081

00:46:11.474 --> 00:46:12.236 intolerant disease.

NOTE Confidence: 0.800081

00:46:12.240 --> 00:46:14.526 After treatment with two different guys.

NOTE Confidence: 0.800081

00:46:14.530 --> 00:46:16.690 Also, the drug is effective in

NOTE Confidence: 0.800081

00:46:16.690 --> 00:46:18.740 treating patients with T315I mutation,

NOTE Confidence: 0.800081

00:46:18.740 --> 00:46:21.407 so moving on to the next study.

NOTE Confidence: 0.800081

00:46:21.410 --> 00:46:24.466 I wanted to present today you will understand

NOTE Confidence: 0.800081

00:46:24.466 --> 00:46:27.518 towards the end why pick this particular one?

NOTE Confidence: 0.800081

00:46:27.520 --> 00:46:29.912 There are a number of drugs where there

NOTE Confidence: 0.800081

00:46:29.912 --> 00:46:32.914 are a number of drugs being developed

NOTE Confidence: 0.800081

00:46:32.914 --> 00:46:34.778 in patients with myelofibrosis.

NOTE Confidence: 0.800081

00:46:34.780 --> 00:46:37.558 I think they're up to 10.

NOTE Confidence: 0.800081

00:46:37.560 --> 00:46:40.110 A phase three randomized phase

NOTE Confidence: 0.800081

00:46:40.110 --> 00:46:42.660 three studies in this field.

NOTE Confidence: 0.800081

00:46:42.660 --> 00:46:45.255 So this particular study presented

NOTE Confidence: 0.800081

00:46:45.255 --> 00:46:48.270 by John Mascarenhas is about CPI,

NOTE Confidence: 0.800081

00:46:48.270 --> 00:46:48.763 0610.

NOTE Confidence: 0.800081

00:46:48.763 --> 00:46:50.735 Bromodomain angusta terminal domain

NOTE Confidence: 0.800081

00:46:50.735 --> 00:46:53.813 protein or BET inhibitor in combination

NOTE Confidence: 0.800081

00:46:53.813 --> 00:46:57.029 with reflective for Jack inhibitor naive

NOTE Confidence: 0.800081

00:46:57.029 --> 00:47:00.000 Milo fibrosis patients or manifest study.

NOTE Confidence: 0.800081

00:47:00.000 --> 00:47:04.216 So one word about bet so bromodomain and

NOTE Confidence: 0.800081

00:47:04.216 --> 00:47:07.568 extra terminal domain protein promote.

NOTE Confidence: 0.800081

00:47:07.570 --> 00:47:09.755 Symptoms of Milo fibrosis by

NOTE Confidence: 0.800081

00:47:09.755 --> 00:47:11.940 activating bet targeted genes leading

NOTE Confidence: 0.800081

00:47:12.011 --> 00:47:14.701 to increase production of cytokines

NOTE Confidence: 0.800081

00:47:14.701 --> 00:47:16.315 responsible for inflammation,

NOTE Confidence: 0.800081

00:47:16.320 --> 00:47:17.290 extramental hematopoiesis,

NOTE Confidence: 0.800081

00:47:17.290 --> 00:47:19.230 and bone marrow fibrosis.

NOTE Confidence: 0.800081

00:47:19.230 --> 00:47:21.980 All manifestations of patients with

NOTE Confidence: 0.800081

00:47:21.980 --> 00:47:24.730 primary myelofibrosis as well as

NOTE Confidence: 0.800081

00:47:24.819 --> 00:47:28.251 modify process after PD and 80 so the

NOTE Confidence: 0.800081

00:47:28.251 --> 00:47:31.037 other influence of bat is activations

NOTE Confidence: 0.800081

00:47:31.037 --> 00:47:33.803 of target genes leading to aberrant

NOTE Confidence: 0.800081

00:47:33.810 --> 00:47:36.465 erythroid differentiation as well as

NOTE Confidence: 0.800081

00:47:36.465 --> 00:47:38.058 aberrant megakaryocytic differentiation.

NOTE Confidence: 0.800081

00:47:38.060 --> 00:47:40.440 And this patients may have an email.

NOTE Confidence: 0.800081

00:47:40.440 --> 00:47:40.762 Thrombocytopenia,

NOTE Confidence: 0.800081

00:47:40.762 --> 00:47:41.728 as you know.

NOTE Confidence: 0.800081

00:47:41.728 --> 00:47:44.578 So CPI 610 inhibits bat and may suppress

NOTE Confidence: 0.800081

00:47:44.578 --> 00:47:47.146 cytokine production as well as promote

NOTE Confidence: 0.800081

00:47:47.146 --> 00:47:49.535 erythroid differentiation as well as

NOTE Confidence: 0.800081

00:47:49.535 --> 00:47:51.008 normalized megakaryocytic differentiation.

NOTE Confidence: 0.800081

00:47:51.010 --> 00:47:53.176 So let's see how this drug

NOTE Confidence: 0.800081

00:47:53.176 --> 00:47:55.689 did in this phase two studies.

NOTE Confidence: 0.800081

00:47:55.690 --> 00:47:57.250 So first of all,

NOTE Confidence: 0.800081

00:47:57.250 --> 00:47:59.200 the study had three arms,

NOTE Confidence: 0.800081

00:47:59.200 --> 00:48:01.540 so they are mine going present.

NOTE Confidence: 0.800081

00:48:01.540 --> 00:48:04.480 Today's I'm three which looked at Jack

NOTE Confidence: 0.800081

00:48:04.480 --> 00:48:06.856 inhibitor naive patients and use the

NOTE Confidence: 0.800081

00:48:06.856 --> 00:48:08.944 combination of CPI 610 and Rosslyn.

NOTE Confidence: 0.800081

00:48:08.950 --> 00:48:12.460 If the other two arms were add on CPI,

NOTE Confidence: 0.800081

00:48:12.460 --> 00:48:14.064 six dental clinic patients

NOTE Confidence: 0.800081

00:48:14.064 --> 00:48:16.069 who didn't have full benefit.

NOTE Confidence: 0.800081

00:48:16.070 --> 00:48:17.810 From Brooklyn balloon treatment

NOTE Confidence: 0.800081

00:48:17.810 --> 00:48:19.550 and monotherapy with CPI,

NOTE Confidence: 0.800081

00:48:19.550 --> 00:48:19.972 0610,

NOTE Confidence: 0.800081

00:48:19.972 --> 00:48:22.926 this study was also presented as an

NOTE Confidence: 0.800081

00:48:22.926 --> 00:48:26.080 abstract as a poster during ash meeting,

NOTE Confidence: 0.800081

00:48:26.080 --> 00:48:27.385 so I'm three,

NOTE Confidence: 0.800081

00:48:27.385 --> 00:48:29.560 basically Jack inhibitor naive Milo

NOTE Confidence: 0.800081

00:48:29.560 --> 00:48:31.729 fibrosis patients who need treatment.

NOTE Confidence: 0.800081

00:48:31.730 --> 00:48:33.418 They received two drugs,

NOTE Confidence: 0.800081

00:48:33.418 --> 00:48:36.476 rock Solid Nap standard of care but

NOTE Confidence: 0.800081

00:48:36.476 --> 00:48:39.128 in additional CPI 0610 better hitter.

NOTE Confidence: 0.800081

00:48:39.130 --> 00:48:41.746 So this drug better hitter was

NOTE Confidence: 0.800081

00:48:41.746 --> 00:48:44.349 administered two weeks on two weeks,

NOTE Confidence: 0.800081

00:48:44.350 --> 00:48:46.546 one week off and.

NOTE Confidence: 0.800081

00:48:46.546 --> 00:48:50.690 The endpoints which we were looked at was.

NOTE Confidence: 0.800081

00:48:50.690 --> 00:48:52.825 Spleen volume response 35% spleen

NOTE Confidence: 0.800081

00:48:52.825 --> 00:48:55.811 world in response at 24 weeks as

NOTE Confidence: 0.800081

00:48:55.811 --> 00:48:58.115 well as total symptom score 50%.

NOTE Confidence: 0.800081

00:48:58.120 --> 00:49:00.598 Reduction of symptoms by 24 weeks.

NOTE Confidence: 0.800081

00:49:00.600 --> 00:49:03.258 So this is primary endpoint which

NOTE Confidence: 0.800081

00:49:03.258 --> 00:49:05.559 basically it was achieved by 67%

NOTE Confidence: 0.800081

00:49:05.560 --> 00:49:08.062 of patients so again the drug

NOTE Confidence: 0.800081

00:49:08.062 --> 00:49:09.730 probably worked a little

NOTE Confidence: 0.8362344

00:49:09.808 --> 00:49:13.075 bit better for patients who are low risk but

NOTE Confidence: 0.8362344

00:49:13.075 --> 00:49:16.296 it was compatible 7273% for intermediate 160.

NOTE Confidence: 0.8362344

00:49:16.296 --> 00:49:19.275 Four 66% for intermediate to high risk

NOTE Confidence: 0.8362344

00:49:19.275 --> 00:49:22.869 based on the IP SS and IP address.

NOTE Confidence: 0.8362344

00:49:22.870 --> 00:49:25.016 Most of the patients cadres, reduction

NOTE Confidence: 0.8362344

00:49:25.016 --> 00:49:27.508 of spleen volume only one had increased.

NOTE Confidence: 0.8362344

00:49:27.510 --> 00:49:30.009 This is out of 70 patients studied,

NOTE Confidence: 0.8362344

00:49:30.010 --> 00:49:32.152 so the second endpoint at the

NOTE Confidence: 0.8362344

00:49:32.152 --> 00:49:33.580 symptoms decreased by 50%.

NOTE Confidence: 0.8362344

00:49:33.580 --> 00:49:36.522 Again, this was seen in 57% of patients.

NOTE Confidence: 0.8362344

00:49:36.522 --> 00:49:39.329 Most of the patients get this clinical

NOTE Confidence: 0.8362344

00:49:39.329 --> 00:49:41.425 benefit in the study at week 24,

NOTE Confidence: 0.8362344

00:49:41.430 --> 00:49:43.789 so one of the interesting finding when

NOTE Confidence: 0.8362344

00:49:43.789 --> 00:49:46.213 you start looks lit up in patients

NOTE Confidence: 0.8362344

00:49:46.213 --> 00:49:48.235 with myelofibrosis you expect a dip

NOTE Confidence: 0.8362344

00:49:48.299 --> 00:49:50.359 in hemoglobin about three points,

NOTE Confidence: 0.8362344

00:49:50.360 --> 00:49:53.400 so here the dip was not as deep.

NOTE Confidence: 0.8362344

00:49:53.400 --> 00:49:55.278 And then, as you can see,

NOTE Confidence: 0.8362344

00:49:55.280 --> 00:49:56.222 hemoglobin improved overtime.

NOTE Confidence: 0.8362344

00:49:56.222 --> 00:49:58.106 In fact, baseline increased a little

NOTE Confidence: 0.8362344

00:49:58.106 --> 00:50:00.430 bit higher than the baseline, so this.

NOTE Confidence: 0.8362344

00:50:00.430 --> 00:50:03.055 Awful actually looks at patients who had

NOTE Confidence: 0.8362344

00:50:03.055 --> 00:50:05.370 hemoglobin more than 10 and less than 10,

NOTE Confidence: 0.8362344

00:50:05.370 --> 00:50:06.698 but didn't require transfusions.

NOTE Confidence: 0.8362344

00:50:06.698 --> 00:50:08.358 And as you can see,

NOTE Confidence: 0.8362344

00:50:08.360 --> 00:50:10.565 after initial small dip there is improvement

NOTE Confidence: 0.8362344

00:50:10.565 --> 00:50:13.007 in anemia in this subgroup of patients,

NOTE Confidence: 0.8362344

00:50:13.010 --> 00:50:14.334 which is quite impressive.

NOTE Confidence: 0.8362344

00:50:14.334 --> 00:50:15.658 So one other thing,

NOTE Confidence: 0.8362344

00:50:15.660 --> 00:50:16.904 at the bone marrow's,

NOTE Confidence: 0.8362344

00:50:16.904 --> 00:50:18.770 their biopsies were done at the

NOTE Confidence: 0.8362344

00:50:18.834 --> 00:50:20.927 beginning as well as during the study

NOTE Confidence: 0.8362344

00:50:20.927 --> 00:50:23.300 and there was improvement in fibrosis.

NOTE Confidence: 0.8362344

00:50:23.300 --> 00:50:25.844 Great in 1/3 of patients and most of

NOTE Confidence: 0.8362344

00:50:25.844 --> 00:50:27.704 the improvements observed were observed

NOTE Confidence: 0.8362344

00:50:27.704 --> 00:50:30.399 during the first six months of treatment.

NOTE Confidence: 0.8362344

00:50:30.400 --> 00:50:32.764 Only two patients get worsening of

NOTE Confidence: 0.8362344

00:50:32.764 --> 00:50:35.338 fibrosis and you can see that there

NOTE Confidence: 0.8362344

00:50:35.338 --> 00:50:38.292 is also a sign that there is improved

NOTE Confidence: 0.8362344

00:50:38.292 --> 00:50:41.188 air throughout differentiation and

NOTE Confidence: 0.8362344

00:50:41.188 --> 00:50:43.360 normalization of megakaryocytic

NOTE Confidence: 0.8362344

00:50:43.360 --> 00:50:44.084 histopathology.

NOTE Confidence: 0.8362344

00:50:44.090 --> 00:50:47.418 So the side effects the CPI 16 in

NOTE Confidence: 0.8362344

00:50:47.418 --> 00:50:50.036 combination with Link was generally

NOTE Confidence: 0.8362344

00:50:50.036 --> 00:50:51.168 well tolerated.

NOTE Confidence: 0.8362344

00:50:51.170 --> 00:50:54.002 So 87% reported at least one

NOTE Confidence: 0.8362344

00:50:54.002 --> 00:50:55.890 treatment emergent adverse event.

NOTE Confidence: 0.8362344

00:50:55.890 --> 00:50:57.934 44% reported, one grade,

NOTE Confidence: 0.8362344

00:50:57.934 --> 00:51:00.489 three treatment emergent adverse event.

NOTE Confidence: 0.8362344

00:51:00.490 --> 00:51:02.386 So the most common ones were

NOTE Confidence: 0.8362344

00:51:02.386 --> 00:51:04.025 haematological and now this was

NOTE Confidence: 0.8362344

00:51:04.025 --> 00:51:05.580 an email from both cytopenia.

NOTE Confidence: 0.8362344

00:51:05.580 --> 00:51:07.488 Of course this may be manifestations

NOTE Confidence: 0.8362344

00:51:07.488 --> 00:51:08.760 of the disease itself,

NOTE Confidence: 0.8362344

00:51:08.760 --> 00:51:11.658 the most common and non human to

NOTE Confidence: 0.8362344

00:51:11.658 --> 00:51:14.115 logic was diarrhea or which was

NOTE Confidence: 0.8362344

00:51:14.115 --> 00:51:16.383 mild moderate Grade 1 two so.

NOTE Confidence: 0.8362344

00:51:16.390 --> 00:51:18.250 Great five were two events.

NOTE Confidence: 0.8362344

00:51:18.250 --> 00:51:20.110 Multiorgan failure with due to

NOTE Confidence: 0.8362344

00:51:20.110 --> 00:51:21.226 sepsis times two.

NOTE Confidence: 0.8362344

00:51:21.230 --> 00:51:23.456 So overall the drug was pretty

NOTE Confidence: 0.8362344

00:51:23.456 --> 00:51:24.569 reasonably well tolerated.

NOTE Confidence: 0.8362344

00:51:24.570 --> 00:51:26.550 The combination of drugs I have

NOTE Confidence: 0.8362344

00:51:26.550 --> 00:51:28.702 to say because we're looking at

NOTE Confidence: 0.8362344

00:51:28.702 --> 00:51:30.988 the side effect profile of two

NOTE Confidence: 0.8362344

00:51:30.988 --> 00:51:32.390 drugs administered together.

NOTE Confidence: 0.8362344

00:51:32.390 --> 00:51:34.562 So finally conclusions 67% of patients

NOTE Confidence: 0.8362344

00:51:34.562 --> 00:51:37.219 achieve CVR 35 comparing to historical phase,

NOTE Confidence: 0.8362344

00:51:37.220 --> 00:51:39.080 three studies simplifying comfort studies.

NOTE Confidence: 0.8362344

00:51:39.080 --> 00:51:41.530 This is looks better even though we

NOTE Confidence: 0.8362344

00:51:41.530 --> 00:51:43.818 cannot compare apples to oranges in

NOTE Confidence: 0.8362344

00:51:43.818 --> 00:51:45.773 those studies with ruxolitinib alone,

NOTE Confidence: 0.8362344

00:51:45.780 --> 00:51:48.318 the response was 28 to 42%.

NOTE Confidence: 0.8362344

00:51:48.320 --> 00:51:50.630 57% in the study achieved improvement

NOTE Confidence: 0.8362344

00:51:50.630 --> 00:51:51.400 and symptoms.

NOTE Confidence: 0.8362344

00:51:51.400 --> 00:51:53.332 50% reduction of symptoms and there

NOTE Confidence: 0.8362344

00:51:53.332 --> 00:51:55.609 were improvement in bone marrow findings

NOTE Confidence: 0.8362344

00:51:55.609 --> 00:51:57.944 suggestive of potential disease modification.

NOTE Confidence: 0.8362344

00:51:57.950 --> 00:52:00.631 So it was well tolerated combination an

NOTE Confidence: 0.8362344

00:52:00.631 --> 00:52:03.227 phase three study is planned and this

NOTE Confidence: 0.8362344

00:52:03.227 --> 00:52:06.030 would be a randomized study for treatment.

NOTE Confidence: 0.8362344

00:52:06.030 --> 00:52:07.955 Naive patients looks lit up

NOTE Confidence: 0.8362344

00:52:07.955 --> 00:52:09.110 against ruxolitinib Sir,

NOTE Confidence: 0.8362344

00:52:09.110 --> 00:52:11.420 plus CPI six 110 versus wrestling

NOTE Confidence: 0.8362344

00:52:11.420 --> 00:52:12.190 plus placebo,

NOTE Confidence: 0.8362344

00:52:12.190 --> 00:52:14.500 which allows crossover down the road.

NOTE Confidence: 0.8362344

00:52:14.500 --> 00:52:18.770 We are planning to open it at Yale this year.

NOTE Confidence: 0.8362344

00:52:18.770 --> 00:52:22.220 So the final study I want to present is PG

NOTE Confidence: 0.7385071

00:52:22.310 --> 00:52:25.516 300 study hepcidin mimetic as you know,

NOTE Confidence: 0.7385071

00:52:25.520 --> 00:52:28.299 hepcidin was discovered about 20 years ago,

NOTE Confidence: 0.7385071

00:52:28.300 --> 00:52:30.495 master regulator why and metabolism

NOTE Confidence: 0.7385071

00:52:30.495 --> 00:52:33.096 with high hepcidin level shutting down

NOTE Confidence: 0.7385071

00:52:33.096 --> 00:52:35.434 for a port and transport of ferritin.

NOTE Confidence: 0.7385071

00:52:35.440 --> 00:52:38.563 And so the reason to use it in polycythemia

NOTE Confidence: 0.7385071

00:52:38.563 --> 00:52:41.378 Vera is of course this patient need

NOTE Confidence: 0.7385071

00:52:41.378 --> 00:52:44.350 phlebotomies as the main part of their

NOTE Confidence: 0.7385071

00:52:44.350 --> 00:52:46.954 treatment which lead to iron deficiency.

NOTE Confidence: 0.7385071

00:52:46.960 --> 00:52:49.396 Perhaps keep citing analog PG 300?

NOTE Confidence: 0.7385071

00:52:49.400 --> 00:52:51.892 Can do this instead by shutting down

NOTE Confidence: 0.7385071

00:52:51.892 --> 00:52:55.084 availability of iron to every throw pesis so

NOTE Confidence: 0.7385071

00:52:55.084 --> 00:52:57.144 eligibility requirement PV diagnosed based

NOTE Confidence: 0.7385071

00:52:57.211 --> 00:52:59.710 on most recent to double check criteria,

NOTE Confidence: 0.7385071

00:52:59.710 --> 00:53:01.672 three phlebotomies in the last six

NOTE Confidence: 0.7385071

00:53:01.672 --> 00:53:03.888 months or more necessary primary endpoint

NOTE Confidence: 0.7385071

00:53:03.888 --> 00:53:06.018 is proportion of patients randomized

NOTE Confidence: 0.7385071

00:53:06.018 --> 00:53:08.504 withdrawal period whose cymatic Rick is

NOTE Confidence: 0.7385071

00:53:08.504 --> 00:53:10.409 maintained without need for phlebotomy.

NOTE Confidence: 0.7385071

00:53:10.410 --> 00:53:12.395 Secondary endpoint response at Week

NOTE Confidence: 0.7385071

00:53:12.395 --> 00:53:15.123 29 as well as improvement in symptoms

NOTE Confidence: 0.7385071

00:53:15.123 --> 00:53:17.328 using MP NTSS. So complicated schema.

NOTE Confidence: 0.7385071

00:53:17.328 --> 00:53:19.704 What we're looking at is just

NOTE Confidence: 0.7385071

00:53:19.704 --> 00:53:21.489 initial phase of this study.

NOTE Confidence: 0.7385071

00:53:21.490 --> 00:53:22.190 First 18.

NOTE Confidence: 0.7385071

00:53:22.190 --> 00:53:23.940 Patients enrolled who went through

NOTE Confidence: 0.7385071

00:53:23.940 --> 00:53:25.828 the first part of the study.

NOTE Confidence: 0.7385071

00:53:25.830 --> 00:53:27.400 Those finding at 28 weeks.

NOTE Confidence: 0.7385071

00:53:27.400 --> 00:53:28.450 There's those escalation,

NOTE Confidence: 0.7385071

00:53:28.450 --> 00:53:30.200 trying to identify how much

NOTE Confidence: 0.7385071

00:53:30.200 --> 00:53:31.499 subcutaneous injections once a week.

NOTE Confidence: 0.7385071

00:53:31.500 --> 00:53:33.010 You need to control phlebotomy

NOTE Confidence: 0.7385071

00:53:33.010 --> 00:53:35.280 and you know when you identify it.

NOTE Confidence: 0.7385071

00:53:35.280 --> 00:53:37.478 You kind of continue with that dose.

NOTE Confidence: 0.7385071

00:53:37.480 --> 00:53:39.440 Then you reach the second part of

NOTE Confidence: 0.7385071

00:53:39.440 --> 00:53:40.950 the study blinded withdrawal.

NOTE Confidence: 0.7385071

00:53:40.950 --> 00:53:42.870 Some patients continue real thing others

NOTE Confidence: 0.7385071

00:53:42.870 --> 00:53:45.419 and switch to placebo to see how it's

NOTE Confidence: 0.7385071

00:53:45.419 --> 00:53:47.243 going to affect the phlebotomy requirement.

NOTE Confidence: 0.7385071

00:53:47.250 --> 00:53:47.940 And finally,

NOTE Confidence: 0.7385071

00:53:47.940 --> 00:53:50.010 there is open label extension so

NOTE Confidence: 0.7385071

00:53:50.010 --> 00:53:52.041 that the report only dealt with

NOTE Confidence: 0.7385071

00:53:52.041 --> 00:53:53.955 this red part of the study.

NOTE Confidence: 0.7385071

00:53:53.960 --> 00:53:55.976 And as you can see in the red

NOTE Confidence: 0.7385071

00:53:55.976 --> 00:53:58.150 dots are phlebotomy requirements.

NOTE Confidence: 0.7385071

00:53:58.150 --> 00:53:59.890 Before initiation of the study,

NOTE Confidence: 0.7385071

00:53:59.890 --> 00:54:01.920 before the 1st dose and then after

NOTE Confidence: 0.7385071

00:54:01.920 --> 00:54:04.132 the first was only three patients

NOTE Confidence: 0.7385071

00:54:04.132 --> 00:54:05.828 required one phlebotomy Chen,

NOTE Confidence: 0.7385071

00:54:05.830 --> 00:54:08.382 those were getting the low level of the

NOTE Confidence: 0.7385071

00:54:08.382 --> 00:54:10.707 medication with which was further escalated.

NOTE Confidence: 0.7385071

00:54:10.710 --> 00:54:12.102 So pretty impressive effectiveness.

NOTE Confidence: 0.7385071

00:54:12.102 --> 00:54:13.494 As you can see,

NOTE Confidence: 0.7385071

00:54:13.500 --> 00:54:14.550 ferritin increasing significantly,

NOTE Confidence: 0.7385071

00:54:14.550 --> 00:54:16.650 showing that iron deficiency is gone.

NOTE Confidence: 0.7385071

00:54:16.650 --> 00:54:18.738 Total symptom score improving with time.

NOTE Confidence: 0.7385071

00:54:18.740 --> 00:54:20.784 And this is subset you know you

NOTE Confidence: 0.7385071

00:54:20.784 --> 00:54:22.580 can see improved concentration,

NOTE Confidence: 0.7385071

00:54:22.580 --> 00:54:24.188 fatigue, itching for writers,

NOTE Confidence: 0.7385071

00:54:24.188 --> 00:54:25.796 and though this is.

NOTE Confidence: 0.7385071

00:54:25.800 --> 00:54:27.912 The scoring system used to assess

NOTE Confidence: 0.7385071

00:54:27.912 --> 00:54:29.320 MPN scores MPN symptoms.

NOTE Confidence: 0.7385071

00:54:29.320 --> 00:54:31.848 We can say that perhaps some of it

NOTE Confidence: 0.7385071

00:54:31.848 --> 00:54:34.318 is related to the fact that iron

NOTE Confidence: 0.7385071

00:54:34.318 --> 00:54:36.522 deficiency is gone because I am

NOTE Confidence: 0.7385071

00:54:36.522 --> 00:54:38.387 deficiency can cause the symptoms

NOTE Confidence: 0.7385071

00:54:38.387 --> 00:54:40.232 as well was well tolerated.

NOTE Confidence: 0.7385071

00:54:40.232 --> 00:54:42.696 More than 90% had drug related adverse

NOTE Confidence: 0.7385071

00:54:42.696 --> 00:54:45.156 events, but all of them were sorry,

NOTE Confidence: 0.7385071

00:54:45.160 --> 00:54:47.920 not more than 90% of those who had

NOTE Confidence: 0.7385071

00:54:47.920 --> 00:54:49.739 adverse events were great one,

NOTE Confidence: 0.7385071

00:54:49.740 --> 00:54:52.204 so I would like to conclude by

NOTE Confidence: 0.7385071

00:54:52.204 --> 00:54:53.260 summarizing this study.

NOTE Confidence: 0.7385071

00:54:53.260 --> 00:54:55.015 It was PG 300 subcutaneously

NOTE Confidence: 0.7385071

00:54:55.015 --> 00:54:56.419 administered once a week,

NOTE Confidence: 0.7385071

00:54:56.420 --> 00:54:59.509 was safe and well tolerated, no Grade 3/4.

NOTE Confidence: 0.7385071

00:54:59.509 --> 00:55:01.724 Adverse events related to treatment.

NOTE Confidence: 0.7385071

00:55:01.730 --> 00:55:04.145 It was effective in eliminating

NOTE Confidence: 0.7385071

00:55:04.145 --> 00:55:06.077 the therapeutic phlebotomy's and

NOTE Confidence: 0.7385071

00:55:06.077 --> 00:55:08.405 reversing iron deficiency impact on

NOTE Confidence: 0.7385071

00:55:08.405 --> 00:55:10.620 previous symptoms is being studied,

NOTE Confidence: 0.7385071

00:55:10.620 --> 00:55:13.380 and this study is also planned

NOTE Confidence: 0.7385071

00:55:13.380 --> 00:55:16.239 for opening at Yell this year.

NOTE Confidence: 0.7385071

00:55:16.240 --> 00:55:17.170 Thank you.

NOTE Confidence: 0.8375762

00:55:19.670 --> 00:55:21.806 Thank you Nikolaj and Rory great

NOTE Confidence: 0.8375762

00:55:21.806 --> 00:55:24.299 talks and I think very important

NOTE Confidence: 0.8375762

00:55:24.300 --> 00:55:26.232 updates from from the meeting

NOTE Confidence: 0.8375762

00:55:26.232 --> 00:55:28.548 since we're a little bit overtime,

NOTE Confidence: 0.8375762

00:55:28.550 --> 00:55:30.300 will actually take 10 minutes

NOTE Confidence: 0.8375762

00:55:30.300 --> 00:55:32.790 beyond 1:00 PM for any questions,

NOTE Confidence: 0.8375762

00:55:32.790 --> 00:55:36.264 but I will start with a question for Doctor.

NOTE Confidence: 0.8375762

00:55:36.270 --> 00:55:38.918 But also as he needs to go out

NOTE Confidence: 0.8375762

00:55:38.918 --> 00:55:41.667 at 1:00 PM for another meeting.

NOTE Confidence: 0.8375762

00:55:41.670 --> 00:55:42.828 Actually two questions.

NOTE Confidence: 0.8375762

00:55:42.828 --> 00:55:44.758 So one of them is.

NOTE Confidence: 0.8375762

00:55:44.760 --> 00:55:47.460 Are there any immediately practice changing

NOTE Confidence: 0.8375762

00:55:47.460 --> 00:55:50.790 updates you take from from the ash meeting?

NOTE Confidence: 0.8375762

00:55:50.790 --> 00:55:54.040 In terms of what we do day today and the

NOTE Confidence: 0.8375762

00:55:54.128 --> 00:55:57.140 second question is from Doctor Isufi,

NOTE Confidence: 0.8375762

00:55:57.140 --> 00:55:59.185 she's asking whether the ampion

NOTE Confidence: 0.8375762

00:55:59.185 --> 00:56:00.821 driver mutations were acquired

NOTE Confidence: 0.8375762

00:56:00.821 --> 00:56:02.699 that were acquired in nutri,

NOTE Confidence: 0.8375762

00:56:02.700 --> 00:56:04.460 worthy, germline or somatic.

NOTE Confidence: 0.8375762

00:56:04.460 --> 00:56:07.100 Also please free to type your

NOTE Confidence: 0.8375762

00:56:07.179 --> 00:56:09.183 questions and if you want to

NOTE Confidence: 0.8375762

00:56:09.183 --> 00:56:11.429 ask live or any can unmute,

NOTE Confidence: 0.8375762

00:56:11.430 --> 00:56:13.018 you just just indicating

NOTE Confidence: 0.7818602

00:56:13.020 --> 00:56:15.402 the chat Nikolai so no immediate

NOTE Confidence: 0.7818602

00:56:15.402 --> 00:56:16.593 practice changing presentations.

NOTE Confidence: 0.7818602

00:56:16.600 --> 00:56:19.060 I think a similar but the

NOTE Confidence: 0.7818602

00:56:19.060 --> 00:56:21.090 drug for CML will be.

NOTE Confidence: 0.7818602

00:56:21.090 --> 00:56:22.835 Changing our practice when the

NOTE Confidence: 0.7818602

00:56:22.835 --> 00:56:25.479 drug and if the drug is approved,

NOTE Confidence: 0.7818602

00:56:25.480 --> 00:56:27.694 which I think should be you

NOTE Confidence: 0.7818602

00:56:27.694 --> 00:56:29.870 know towards the end of 2021,

NOTE Confidence: 0.7818602

00:56:29.870 --> 00:56:32.250 so you know I presented two studies

NOTE Confidence: 0.7818602

00:56:32.250 --> 00:56:34.506 where the drugs are very interesting

NOTE Confidence: 0.7818602

00:56:34.506 --> 00:56:37.215 and for that reason this studies will

NOTE Confidence: 0.7818602

00:56:37.288 --> 00:56:39.759 be available to our patients at Yale.

NOTE Confidence: 0.7818602

00:56:39.760 --> 00:56:43.046 So in regards to the mutations in utero, no.

NOTE Confidence: 0.7818602

00:56:43.046 --> 00:56:44.510 Those are somatic mutations.

NOTE Confidence: 0.7818602

00:56:44.510 --> 00:56:46.340 Those are not germline mutations.

NOTE Confidence: 0.7818602

00:56:46.340 --> 00:56:48.536 This is somatic mutations which acquired.

NOTE Confidence: 0.8318645

00:56:49.530 --> 00:56:51.666 So Doctor God actually follows up on on

NOTE Confidence: 0.8318645

00:56:51.666 --> 00:56:53.695 the CML presentation and he's asking

NOTE Confidence: 0.8318645

00:56:53.695 --> 00:56:55.843 if this drug is actually approved.

NOTE Confidence: 0.8318645

00:56:55.850 --> 00:56:58.124 Does that change your calculation and

NOTE Confidence: 0.8318645

00:56:58.124 --> 00:56:59.993 whether you transplant patients would

NOTE Confidence: 0.8318645

00:56:59.993 --> 00:57:02.030 would CML as they go through multiple

NOTE Confidence: 0.8318645

00:57:02.030 --> 00:57:04.375 tiki eyes and maybe to follow up on that?

NOTE Confidence: 0.8318645

00:57:04.380 --> 00:57:06.876 Like would you put this drug ahead of

NOTE Confidence: 0.8318645

00:57:06.876 --> 00:57:09.438 assertive in your kind of lines of therapy?

NOTE Confidence: 0.8318645

00:57:09.440 --> 00:57:11.020 If the drug is approved?

NOTE Confidence: 0.8318645

00:57:11.020 --> 00:57:12.910 Or how would you approach it?

NOTE Confidence: 0.8318645

00:57:12.910 --> 00:57:14.178 Yeah, so you know,

NOTE Confidence: 0.8318645

00:57:14.180 --> 00:57:16.452 I, I think it's too early to say

NOTE Confidence: 0.8318645

00:57:16.452 --> 00:57:18.735 if this is going to eliminate

NOTE Confidence: 0.8318645

00:57:18.735 --> 00:57:21.201 transplant for some of our patients.

NOTE Confidence: 0.8318645

00:57:21.210 --> 00:57:23.020 So, but yes, you know,

NOTE Confidence: 0.8318645

00:57:23.020 --> 00:57:25.916 based on the study which I presented today,

NOTE Confidence: 0.8318645

00:57:25.920 --> 00:57:28.020 it may be before positive for

NOTE Confidence: 0.8318645

00:57:28.020 --> 00:57:30.620 patients who had two tiki eyes prior.

NOTE Confidence: 0.8318645

00:57:30.620 --> 00:57:33.154 You know, looking at the results here.

NOTE Confidence: 0.7883626

00:57:35.170 --> 00:57:37.290 So unless there are other

NOTE Confidence: 0.7883626

00:57:37.290 --> 00:57:38.990 questions for doctor adults,

NOTE Confidence: 0.7883626

00:57:38.990 --> 00:57:41.944 if I will go to Doctor Challace.

NOTE Confidence: 0.7883626

00:57:41.950 --> 00:57:44.674 So Rory, any immediate practice changing

NOTE Confidence: 0.7883626

00:57:44.674 --> 00:57:47.318 abstracts for what people do to

NOTE Confidence: 0.7883626

00:57:47.318 --> 00:57:49.586 leukemia in their practices right now,

NOTE Confidence: 0.7883626

00:57:49.590 --> 00:57:52.248 whether in the community or in

NOTE Confidence: 0.7883626

00:57:52.248 --> 00:57:54.484 the academic centers that you

NOTE Confidence: 0.7883626

00:57:54.484 --> 00:57:56.788 take out from the ash meeting.

NOTE Confidence: 0.7030181

00:57:58.250 --> 00:57:59.228 Great question. Thanks

NOTE Confidence: 0.7030181

00:57:59.230 --> 00:58:01.528 amarum. I guess I'll kind of piggyback,

NOTE Confidence: 0.7030181

00:58:01.530 --> 00:58:03.532 but Nikolai said I mean at the

NOTE Confidence: 0.7030181

00:58:03.532 --> 00:58:05.790 moment I would say nothing imminent.

NOTE Confidence: 0.7030181

00:58:05.790 --> 00:58:07.434 Clearly some interesting interim data,

NOTE Confidence: 0.7030181

00:58:07.434 --> 00:58:09.069 although not yet practice changing.

NOTE Confidence: 0.7030181

00:58:09.070 --> 00:58:11.697 I'm most interested in the data for Kinetic

NOTE Confidence: 0.7030181

00:58:11.697 --> 00:58:13.988 lacks added to the dual nucleoside therapy.

NOTE Confidence: 0.7030181

00:58:13.990 --> 00:58:14.980 Cladribine motive sutera

NOTE Confidence: 0.7030181

00:58:14.980 --> 00:58:16.700 been alternating with visa.

NOTE Confidence: 0.7030181

00:58:16.700 --> 00:58:18.874 You know, it's hard to argue with 93%

NOTE Confidence: 0.7030181

00:58:18.874 --> 00:58:21.256 CRC or I rate with you know meeting one

NOTE Confidence: 0.7030181

00:58:21.256 --> 00:58:23.630 cycle response and meeting OS not reached.

NOTE Confidence: 0.7030181

00:58:23.630 --> 00:58:25.370 This compares very favorably with you.

NOTE Confidence: 0.7030181

00:58:25.370 --> 00:58:27.980 Know that the data phrase event you know 15

NOTE Confidence: 0.7030181

00:58:27.980 --> 00:58:31.480 months OS on the median OS on Bailey a trial.

NOTE Confidence: 0.7030181

00:58:31.480 --> 00:58:31.805 However,

NOTE Confidence: 0.7030181

00:58:31.805 --> 00:58:34.410 we've learned this year a few times over.

NOTE Confidence: 0.7030181

00:58:34.410 --> 00:58:34.740 Unfortunately,

NOTE Confidence: 0.7030181

00:58:34.740 --> 00:58:36.695 that single arm studies of agents,

NOTE Confidence: 0.7030181

00:58:36.695 --> 00:58:37.670 despite great clinical

NOTE Confidence: 0.7212018

00:58:37.670 --> 00:58:38.978 preclinical rationale, a priority.

NOTE Confidence: 0.733859

00:58:40.400 --> 00:58:41.946 Or excellent similar data can

NOTE Confidence: 0.733859

00:58:41.946 --> 00:58:43.800 fall short, so this needs to

NOTE Confidence: 0.733859

00:58:43.800 --> 00:58:45.650 be confirmed in a randomized study.

NOTE Confidence: 0.733859

00:58:45.650 --> 00:58:47.506 The same goes for Magnolia Map,

NOTE Confidence: 0.733859

00:58:47.506 --> 00:58:49.046 which is currently being evaluated

NOTE Confidence: 0.733859

00:58:49.046 --> 00:58:50.907 in phase three in comparison days,

NOTE Confidence: 0.733859

00:58:50.907 --> 00:58:52.760 amount of therapy, but the double

NOTE Confidence: 0.733859

00:58:52.760 --> 00:58:55.538 edged sword you know, pretty

NOTE Confidence: 0.733859

00:58:54.310 --> 00:58:55.540 exciting preclinical data is

NOTE Confidence: 0.733859

00:58:55.540 --> 00:58:56.156 very exciting.

NOTE Confidence: 0.733859

00:58:56.156 --> 00:58:57.696 Single arm data begets more.

NOTE Confidence: 0.733859

00:58:57.700 --> 00:58:59.560 Add on therapy notes with Phase

NOTE Confidence: 0.733859

00:58:59.560 --> 00:59:01.408 one trial of triplet with days

NOTE Confidence: 0.733859

00:59:01.410 --> 00:59:02.956 of medical acts makrolon map.

NOTE Confidence: 0.733859

00:59:02.956 --> 00:59:03.880 Now Aizen Gilteritinib

NOTE Confidence: 0.733859

00:59:03.880 --> 00:59:05.430 phonetic lacks, so I mean

NOTE Confidence: 0.733859

00:59:05.430 --> 00:59:06.970 there's kind of divergent goals

NOTE Confidence: 0.733859

00:59:06.970 --> 00:59:07.900 here. But to

NOTE Confidence: 0.733859

00:59:07.900 --> 00:59:09.140 answer your question directly,

NOTE Confidence: 0.733859

00:59:09.140 --> 00:59:10.740 I'd say nothing that's immediately

NOTE Confidence: 0.733859

00:59:10.740 --> 00:59:11.850 practice changing, but.

NOTE Confidence: 0.733859

00:59:11.850 --> 00:59:13.960 Excited for this to be a

NOTE Confidence: 0.733859

00:59:13.960 --> 00:59:14.640 different conversation,

NOTE Confidence: 0.8116402

00:59:14.640 --> 00:59:17.027 maybe a few months to a year.

NOTE Confidence: 0.8116402

00:59:17.030 --> 00:59:19.070 Yeah, look a lot of exciting

NOTE Confidence: 0.8116402

00:59:19.070 --> 00:59:20.090 agents in development.

NOTE Confidence: 0.8116402

00:59:20.090 --> 00:59:22.136 This is a question from Doctor

NOTE Confidence: 0.8116402

00:59:22.136 --> 00:59:23.500 Isufi about Sabbato Lima.

NOTE Confidence: 0.8116402

00:59:23.500 --> 00:59:25.470 Basically, she's asking whether this

NOTE Confidence: 0.8116402

00:59:25.470 --> 00:59:28.052 targets the leukemia stem cell or does

NOTE Confidence: 0.8116402

00:59:28.052 --> 00:59:29.984 it work as an immune activator and

NOTE Confidence: 0.8116402

00:59:29.984 --> 00:59:32.029 this is a great question arrested.

NOTE Confidence: 0.8116402

00:59:32.030 --> 00:59:33.735 There's there's a lot of

NOTE Confidence: 0.8116402

00:59:33.735 --> 00:59:35.440 ongoing research on this issue,

NOTE Confidence: 0.8116402

00:59:35.440 --> 00:59:37.130 but currently the thinking is

NOTE Confidence: 0.8116402

00:59:37.130 --> 00:59:39.190 that it's a dual targeting drug,

NOTE Confidence: 0.8116402

00:59:39.190 --> 00:59:41.122 meaning that there is direct evidence

NOTE Confidence: 0.8116402

00:59:41.122 --> 00:59:42.852 that it affects the leukemia

NOTE Confidence: 0.8116402

00:59:42.852 --> 00:59:44.737 stem cells by interfering with.

NOTE Confidence: 0.8116402

00:59:44.740 --> 00:59:47.314 One of the leg and that is important for

NOTE Confidence: 0.8116402

00:59:47.314 --> 00:59:49.885 self renewal of the leukemic stem cells,

NOTE Confidence: 0.8116402

00:59:49.890 --> 00:59:51.843 and I think this is an interesting

NOTE Confidence: 0.8116402

00:59:51.843 --> 00:59:52.680 differentiator from other

NOTE Confidence: 0.8116402

00:59:52.730 --> 00:59:54.080 immune checkpoint activators,

NOTE Confidence: 0.8116402

00:59:54.080 --> 00:59:56.593 but there is also clearly data that

NOTE Confidence: 0.8116402

00:59:56.593 --> 00:59:58.391 also activates the immune response

NOTE Confidence: 0.8116402

00:59:58.391 --> 01:00:00.666 at the level of the T cells.

NOTE Confidence: 0.8116402

01:00:00.670 --> 01:00:02.854 How do we dissect the clinical

NOTE Confidence: 0.8116402

01:00:02.854 --> 01:00:05.083 efficacy in terms of being related

NOTE Confidence: 0.8116402

01:00:05.083 --> 01:00:06.818 to one or the other?

NOTE Confidence: 0.8116402

01:00:06.820 --> 01:00:08.812 I think it's a question that

NOTE Confidence: 0.8116402

01:00:08.812 --> 01:00:10.622 we are currently exploring and

NOTE Confidence: 0.8116402

01:00:10.622 --> 01:00:11.888 ongoing clinical trials,

NOTE Confidence: 0.8116402

01:00:11.890 --> 01:00:14.062 but I think this would be

NOTE Confidence: 0.8116402

01:00:14.062 --> 01:00:15.510 very important to explore.

NOTE Confidence: 0.8176035

01:00:17.930 --> 01:00:20.410 I think there's a question here

NOTE Confidence: 0.8176035

01:00:20.410 --> 01:00:22.888 from Doctor Gowda about CD 447.

NOTE Confidence: 0.8176035

01:00:22.890 --> 01:00:25.711 Inhibition is asking whether CD 47 inhibition

NOTE Confidence: 0.8176035

01:00:25.711 --> 01:00:28.670 does not cause many immune side effects.

NOTE Confidence: 0.8176035

01:00:28.670 --> 01:00:31.554 Thoughts, this is actually a good question.

NOTE Confidence: 0.8176035

01:00:31.560 --> 01:00:35.277 I will let also really give his his insight.

NOTE Confidence: 0.8176035

01:00:35.280 --> 01:00:38.815 I think this is one of the

NOTE Confidence: 0.8176035

01:00:38.815 --> 01:00:41.978 important things in terms of like.

NOTE Confidence: 0.8176035

01:00:41.980 --> 01:00:44.746 Issue related to like single arm

NOTE Confidence: 0.8176035

01:00:44.746 --> 01:00:47.883 studies and needing to know more data

NOTE Confidence: 0.8176035

01:00:47.883 --> 01:00:51.178 so CD 47 is actually expressed in most

NOTE Confidence: 0.8176035

01:00:51.178 --> 01:00:54.306 of their cells in in the normal body.

NOTE Confidence: 0.8176035

01:00:54.310 --> 01:00:56.872 However, they seem to be overexpressed

NOTE Confidence: 0.8176035

01:00:56.872 --> 01:01:00.247 by the leukemia cells and the idea here

NOTE Confidence: 0.8176035

01:01:00.247 --> 01:01:02.635 is that you're exploring a therapeutic

NOTE Confidence: 0.8176035

01:01:02.715 --> 01:01:06.187 window where using the CD 47 you are

NOTE Confidence: 0.8176035

01:01:06.187 --> 01:01:08.449 preferentially targeting the leukemia cells.

NOTE Confidence: 0.8176035

01:01:08.449 --> 01:01:11.227 However, because City 47 is also

NOTE Confidence: 0.8176035

01:01:11.227 --> 01:01:13.040 expressed on. Red blood cells.

NOTE Confidence: 0.8176035

01:01:13.040 --> 01:01:14.790 We do see hemolytic anemia,

NOTE Confidence: 0.8176035

01:01:14.790 --> 01:01:16.878 and some of those patients which

NOTE Confidence: 0.8176035

01:01:16.878 --> 01:01:19.373 can be actually quite severe and it

NOTE Confidence: 0.8176035

01:01:19.373 --> 01:01:21.437 has to be managed quite carefully,

NOTE Confidence: 0.8176035

01:01:21.440 --> 01:01:23.190 especially during the initial phases.

NOTE Confidence: 0.8176035

01:01:23.190 --> 01:01:25.654 And This is why they prime this drug

NOTE Confidence: 0.8176035

01:01:25.654 --> 01:01:28.002 and carefully monitor patients, it, etc.

NOTE Confidence: 0.8176035

01:01:28.002 --> 01:01:30.450 But I think it's a very good question

NOTE Confidence: 0.8176035

01:01:30.517 --> 01:01:32.827 about why no activity against other

NOTE Confidence: 0.8176035

01:01:32.827 --> 01:01:35.438 CD 47 expressing cells are being seen.

NOTE Confidence: 0.8176035

01:01:35.440 --> 01:01:37.890 I think what's gonna tell us really?

NOTE Confidence: 0.8176035

01:01:37.890 --> 01:01:40.634 The answer is once we see randomized

NOTE Confidence: 0.8176035

01:01:40.634 --> 01:01:42.130 data and try to.

NOTE Confidence: 0.8176035

01:01:42.130 --> 01:01:42.706 You know,

NOTE Confidence: 0.8176035

01:01:42.706 --> 01:01:44.434 explore whether some of the things

NOTE Confidence: 0.8176035

01:01:44.434 --> 01:01:46.478 that get attributed to the disease,

NOTE Confidence: 0.8176035

01:01:46.480 --> 01:01:47.032 for example,

NOTE Confidence: 0.8176035

01:01:47.032 --> 01:01:48.964 are really disease related or some kind

NOTE Confidence: 0.8176035

01:01:48.964 --> 01:01:51.147 of subtle immune related adverse events.

NOTE Confidence: 0.8176035

01:01:51.150 --> 01:01:53.658 But I think what is clear.

NOTE Confidence: 0.8176035

01:01:53.660 --> 01:01:55.879 Is we are not seeing the typical

NOTE Confidence: 0.8176035

01:01:55.879 --> 01:01:57.569 immune adverse effects that are seen

NOTE Confidence: 0.8176035

01:01:57.569 --> 01:01:59.896 with the PD one or CTL A4 type of

NOTE Confidence: 0.8176035

01:01:59.896 --> 01:02:01.626 drugs such as pneumonitis colitis.

NOTE Confidence: 0.8176035

01:02:01.630 --> 01:02:03.590 It doesn't seem that this is commonly

NOTE Confidence: 0.8176035

01:02:03.590 --> 01:02:06.006 seen or or do you have any additional

NOTE Confidence: 0.8176035

01:02:06.006 --> 01:02:08.410 insights on this that was very well said?

NOTE Confidence: 0.8176035

01:02:08.410 --> 01:02:09.000 I mean,

NOTE Confidence: 0.8176035

01:02:09.000 --> 01:02:10.180 I think the key

NOTE Confidence: 0.80842

01:02:10.180 --> 01:02:11.360 points are the transient,

NOTE Confidence: 0.80842

01:02:11.360 --> 01:02:12.835 presumed immune mediated hemolytic anemia,

NOTE Confidence: 0.80842

01:02:12.840 --> 01:02:15.200 which really is why do you know the

NOTE Confidence: 0.80842

01:02:15.200 --> 01:02:16.968 priming dose is sort of incorporated,

NOTE Confidence: 0.80842

01:02:16.968 --> 01:02:18.438 but I think you're right.

NOTE Confidence: 0.80842

01:02:18.440 --> 01:02:20.210 I mean, there's some element of

NOTE Confidence: 0.80842

01:02:20.210 --> 01:02:21.853 specificity for those cells on

NOTE Confidence: 0.80842

01:02:21.853 --> 01:02:23.959 which CD 47 is just enriched.

NOTE Confidence: 0.80842

01:02:23.960 --> 01:02:25.716 Which happens to be within cells,

NOTE Confidence: 0.80842

01:02:25.716 --> 01:02:28.060 and I mean outside of like you said,

NOTE Confidence: 0.80842

01:02:28.060 --> 01:02:29.524 subtle or maybe even delayed

NOTE Confidence: 0.80842

01:02:29.524 --> 01:02:31.868 immune IR A ES that sort of thing.

NOTE Confidence: 0.80842

01:02:31.870 --> 01:02:33.998 And I think we have what median

NOTE Confidence: 0.80842

01:02:33.998 --> 01:02:35.678 fourteen 1516 months of follow up?

NOTE Confidence: 0.80842

01:02:35.678 --> 01:02:37.439 I mean, maybe there are delayed

NOTE Confidence: 0.80842

01:02:37.439 --> 01:02:39.197 events that did not yet occurred,

NOTE Confidence: 0.80842

01:02:39.200 --> 01:02:41.321 but I think it comes down to

NOTE Confidence: 0.80842

01:02:41.321 --> 01:02:43.004 specificity and more of a different

NOTE Confidence: 0.80842

01:02:43.004 --> 01:02:44.173 mechanism of action comparison.

NOTE Confidence: 0.80842

01:02:44.173 --> 01:02:45.638 So you know more of

NOTE Confidence: 0.7841068

01:02:45.640 --> 01:02:46.808 a direct cell effect.

NOTE Confidence: 0.8520811

01:02:48.170 --> 01:02:50.168 Thank you so much for a

NOTE Confidence: 0.8520811

01:02:50.168 --> 01:02:51.500 few minutes past hour.

NOTE Confidence: 0.8520811

01:02:51.500 --> 01:02:53.498 Be very cognizant of the time.

NOTE Confidence: 0.8520811

01:02:53.500 --> 01:02:54.792 On a Friday afternoon,

NOTE Confidence: 0.8520811

01:02:54.792 --> 01:02:56.730 I'd like to thank everybody who

NOTE Confidence: 0.8520811

01:02:56.791 --> 01:02:59.039 joined us for for this session and if

NOTE Confidence: 0.8520811

01:02:59.039 --> 01:03:01.158 there are any additional questions,

NOTE Confidence: 0.8520811

01:03:01.160 --> 01:03:03.158 feel free how to free to

NOTE Confidence: 0.8520811

01:03:03.158 --> 01:03:04.490 email their speakers directly.

NOTE Confidence: 0.8520811

01:03:04.490 --> 01:03:06.356 Thank you so much and looking

NOTE Confidence: 0.8520811

01:03:06.356 --> 01:03:08.721 forward to seeing you next week with

NOTE Confidence: 0.8520811

01:03:08.721 --> 01:03:10.476 their next session next Friday.

NOTE Confidence: 0.8520811

01:03:10.480 --> 01:03:12.150 Have a great weekend everyone.

NOTE Confidence: 0.8520811

01:03:12.150 --> 01:03:12.810 Thank you.