WEBVTT

NOTE duration:"01:04:23"

NOTE recognizability:0.794

NOTE language:en-us

NOTE Confidence: 0.63331044

00:00:00.000 --> 00:00:03.396 Will. Occupy some time,

NOTE Confidence: 0.63331044

00:00:03.396 --> 00:00:05.630 which we don't have a lot of today.

NOTE Confidence: 0.63331044

00:00:05.630 --> 00:00:08.426 Uh, my name is Nicolai Podolski.

NOTE Confidence: 0.63331044

00:00:08.430 --> 00:00:09.754 If I'm associate Professor,

NOTE Confidence: 0.63331044

00:00:09.754 --> 00:00:11.750 Department of Medicine, Hematology section,

NOTE Confidence: 0.63331044

00:00:11.750 --> 00:00:14.750 and I'm joined by Doctor Amir

NOTE Confidence: 0.63331044

00:00:14.750 --> 00:00:17.709 Zadan and Doctor Lourdes Mendez.

NOTE Confidence: 0.63331044

00:00:17.710 --> 00:00:19.796 Today we will be talking about myeloid

NOTE Confidence: 0.63331044

00:00:19.796 --> 00:00:21.230 malignancies and acute leukemias.

NOTE Confidence: 0.63331044

00:00:21.230 --> 00:00:24.701 I will start by talking about ash

NOTE Confidence: 0.63331044

00:00:24.701 --> 00:00:27.407 presentations I have selected on the

NOTE Confidence: 0.63331044

00:00:27.407 --> 00:00:29.490 topic of myeloproliferative neoplasms.

NOTE Confidence: 0.63331044

00:00:29.490 --> 00:00:33.008 Amar will continue and we'll discuss. Mrs.

NOTE Confidence: 0.63331044

00:00:33.008 --> 00:00:35.336 Abstracts and finally Lordis will finish,

NOTE Confidence: 0.63331044

00:00:35.340 --> 00:00:38.160 uh this session, uh,

NOTE Confidence: 0.63331044

00:00:38.160 --> 00:00:41.262 by discussion of studies which

NOTE Confidence: 0.63331044

00:00:41.262 --> 00:00:44.208 were presented on the subject of

NOTE Confidence: 0.63331044

00:00:44.208 --> 00:00:46.669 acute myeloid leukemia and all.

NOTE Confidence: 0.63331044

00:00:46.670 --> 00:00:48.414 So without further ado,

NOTE Confidence: 0.63331044

00:00:48.414 --> 00:00:51.030 I will proceed with my presentations.

NOTE Confidence: 0.63331044

00:00:51.030 --> 00:00:52.822 Those who are joining late will be

NOTE Confidence: 0.63331044

00:00:52.822 --> 00:00:54.865 able to get benefit anyway because

NOTE Confidence: 0.63331044

00:00:54.865 --> 00:00:56.489 this presentation is structured

NOTE Confidence: 0.63331044

00:00:56.489 --> 00:00:58.489 and includes quite a few things.

NOTE Confidence: 0.63331044

00:00:58.490 --> 00:01:00.110 So hold on one second,

NOTE Confidence: 0.63331044

00:01:00.110 --> 00:01:02.476 let me just see here we go

NOTE Confidence: 0.63331044

00:01:02.476 --> 00:01:04.650 this off my disclosures.

NOTE Confidence: 0.63331044

00:01:04.650 --> 00:01:07.650 Uh, so I'm going to talk about UH-4,

NOTE Confidence: 0.63331044

00:01:07.650 --> 00:01:08.059 uh,

NOTE Confidence: 0.63331044

00:01:08.059 --> 00:01:09.695 different presentations on the

NOTE Confidence: 0.63331044

00:01:09.695 --> 00:01:12.153 subject of myelofibrosis and then uh

NOTE Confidence: 0.63331044

00:01:12.153 --> 00:01:14.217 I will finish with polycythemia Vera.

NOTE Confidence: 0.63331044

00:01:14.220 --> 00:01:15.870 It is interesting how many drugs

NOTE Confidence: 0.63331044

00:01:15.870 --> 00:01:18.178 are being developed in the area of

NOTE Confidence: 0.63331044

00:01:18.178 --> 00:01:19.718 myelofibrosis taking into consideration

NOTE Confidence: 0.63331044

00:01:19.718 --> 00:01:21.442 relatively low prevalence of the

NOTE Confidence: 0.63331044

00:01:21.442 --> 00:01:22.727 disease in the United States.

NOTE Confidence: 0.63331044

00:01:22.730 --> 00:01:23.654 At any given time,

NOTE Confidence: 0.63331044

00:01:23.654 --> 00:01:25.000 we have about 13,000 patients.

NOTE Confidence: 0.63331044

00:01:25.000 --> 00:01:25.650 Of course,

NOTE Confidence: 0.63331044

00:01:25.650 --> 00:01:27.600 PVR is much more prevalent because

NOTE Confidence: 0.63331044

00:01:27.659 --> 00:01:29.549 these patients survive a bit longer,

NOTE Confidence: 0.63331044

00:01:29.550 --> 00:01:31.866 so maybe 10 times more so,

NOTE Confidence: 0.63331044

00:01:31.870 --> 00:01:33.335 but of course development of

NOTE Confidence: 0.63331044

00:01:33.335 --> 00:01:34.800 this new drugs are benefiting.

NOTE Confidence: 0.63331044

00:01:34.800 --> 00:01:36.624 For patients and today I will

NOTE Confidence: 0.63331044

00:01:36.624 --> 00:01:37.840 be talking about four,

NOTE Confidence: 0.63331044

00:01:37.840 --> 00:01:39.424 four different medications and

NOTE Confidence: 0.63331044

00:01:39.424 --> 00:01:41.008 different stages of development.

NOTE Confidence: 0.63331044

00:01:41.010 --> 00:01:43.096 And I just wanna say that none

NOTE Confidence: 0.63331044

00:01:43.096 --> 00:01:45.704 of them are approved by FDA in

NOTE Confidence: 0.63331044

00:01:45.704 --> 00:01:47.340 myelofibrosis at this time.

NOTE Confidence: 0.63331044

00:01:47.340 --> 00:01:49.300 And you know some of them are in

NOTE Confidence: 0.63331044

00:01:49.300 --> 00:01:50.847 the pipeline closer to be approved

NOTE Confidence: 0.63331044

00:01:50.847 --> 00:01:52.800 to others is just at the beginning

NOTE Confidence: 0.63331044

00:01:52.800 --> 00:01:54.368 and phase one development.

NOTE Confidence: 0.63331044

00:01:54.370 --> 00:01:58.248 So this is the table which summarizes

NOTE Confidence: 0.63331044

00:01:58.248 --> 00:02:00.913 currently approved drugs which are

NOTE Confidence: 0.63331044

00:02:00.913 --> 00:02:04.920 Jack inhibitors as well as the drug which is.

NOTE Confidence: 0.63331044

00:02:04.920 --> 00:02:07.080 Uh in the pipeline for approval,

NOTE Confidence: 0.63331044

00:02:07.080 --> 00:02:09.462 new drug application was submitted by

NOTE Confidence: 0.63331044

00:02:09.462 --> 00:02:12.100 the company developing this drug to the FDA.

NOTE Confidence: 0.63331044

00:02:12.100 --> 00:02:12.961 This is monoethnic,

NOTE Confidence: 0.63331044

00:02:12.961 --> 00:02:14.970 the last and the table and the

NOTE Confidence: 0.63331044

00:02:15.034 --> 00:02:16.894 review is expected to end sometime

NOTE Confidence: 0.63331044

00:02:16.894 --> 00:02:18.600 at the beginning of summer.

NOTE Confidence: 0.63331044

00:02:18.600 --> 00:02:20.476 So very soon we'll know if this

NOTE Confidence: 0.63331044

00:02:20.476 --> 00:02:22.341 drug is going to be approved and

NOTE Confidence: 0.63331044

00:02:22.341 --> 00:02:24.202 it is expected to be so this

NOTE Confidence: 0.63331044

00:02:24.202 --> 00:02:25.586 drugs called Jack inhibitors,

NOTE Confidence: 0.63331044

00:02:25.586 --> 00:02:27.396 but they actually have slightly

NOTE Confidence: 0.63331044

00:02:27.396 --> 00:02:29.274 different mechanism of action and that's

NOTE Confidence: 0.63331044

00:02:29.274 --> 00:02:30.924 why they may have slightly different

NOTE Confidence: 0.63331044

00:02:30.978 --> 00:02:32.598 effectiveness as well as different

NOTE Confidence: 0.63331044

00:02:32.598 --> 00:02:34.250 side effects was approved in 2011.

NOTE Confidence: 0.63331044

00:02:34.250 --> 00:02:36.573 More than 10 years ago and it is Jack

NOTE Confidence: 0.63331044

00:02:36.573 --> 00:02:38.358 one Jack 2 inhibitor used in frontline

NOTE Confidence: 0.63331044

00:02:38.419 --> 00:02:40.324 treatment for high risk patients

NOTE Confidence: 0.63331044

00:02:40.324 --> 00:02:41.467 with myelofibrosis intermediate

NOTE Confidence: 0.63331044

00:02:41.467 --> 00:02:43.746 and high risk patients with main

NOTE Confidence: 0.63331044

00:02:43.746 --> 00:02:45.641 side effects related to cytopenias

NOTE Confidence: 0.63331044

00:02:45.641 --> 00:02:47.828 to drive them followed in 2019,

NOTE Confidence: 0.63331044

00:02:47.830 --> 00:02:48.592 eight years later.

NOTE Confidence: 0.63331044

00:02:48.592 --> 00:02:50.656 And this is the drug which can be

NOTE Confidence: 0.63331044

00:02:50.656 --> 00:02:52.287 used in frontline but most of us

NOTE Confidence: 0.63331044

00:02:52.287 --> 00:02:54.176 are using it in second line and it

NOTE Confidence: 0.63331044

00:02:54.176 --> 00:02:56.538 inhibits Jack 2 but also Jack one and

NOTE Confidence: 0.63331044

00:02:56.538 --> 00:02:58.348 some other tising kinase including

NOTE Confidence: 0.63331044

00:02:58.348 --> 00:03:00.466 fleet 3 enhanced GI side effects.

NOTE Confidence: 0.727097525

00:03:00.470 --> 00:03:02.442 Pacritinib approval was in

NOTE Confidence: 0.727097525

00:03:02.442 --> 00:03:04.850 February of 2022 for patients with.

NOTE Confidence: 0.727097525

00:03:04.850 --> 00:03:06.625 Myelofibrosis who have low platelet

NOTE Confidence: 0.727097525

00:03:06.625 --> 00:03:08.768 count less than 50 button second line

NOTE Confidence: 0.727097525

00:03:08.768 --> 00:03:11.123 NCC and recommends to use it uh for

NOTE Confidence: 0.727097525

00:03:11.123 --> 00:03:12.548 patients with any platelet count.

NOTE Confidence: 0.727097525

00:03:12.550 --> 00:03:14.888 Again GI side effects can be seen

NOTE Confidence: 0.727097525

00:03:14.888 --> 00:03:16.620 in patients using this drug.

NOTE Confidence: 0.727097525

00:03:16.620 --> 00:03:19.190 Finally momelotinib.

NOTE Confidence: 0.727097525

00:03:19.190 --> 00:03:21.350 Claims fame in the area of anemia which

NOTE Confidence: 0.727097525

00:03:21.350 --> 00:03:23.409 is one of the common manifestations

NOTE Confidence: 0.727097525

00:03:23.409 --> 00:03:25.593 of myelofibrosis and mostly it is

NOTE Confidence: 0.727097525

00:03:25.658 --> 00:03:28.232 expected to be beneficial for patients

NOTE Confidence: 0.727097525

00:03:28.232 --> 00:03:29.948 with myelofibrosis lavania because

NOTE Confidence: 0.727097525

00:03:29.950 --> 00:03:31.665 of its inhibition not only of Jack,

NOTE Confidence: 0.727097525

00:03:31.670 --> 00:03:33.704 not only Jack 2, Jack one, but acvr.

NOTE Confidence: 0.727097525

00:03:33.704 --> 00:03:35.606 In fact, inhibition of Jack two

NOTE Confidence: 0.727097525

00:03:35.606 --> 00:03:38.032 leads to anemia and acvr inhibition

NOTE Confidence: 0.727097525

00:03:38.032 --> 00:03:40.182 actually is beneficial for anemia.

NOTE Confidence: 0.727097525

00:03:40.190 --> 00:03:42.948 So this is the study momentum phase

NOTE Confidence: 0.727097525

00:03:42.948 --> 00:03:46.079 three study of MOMELOTINIB versus danazol

NOTE Confidence: 0.727097525

00:03:46.079 --> 00:03:49.184 in symptomatic patients with anemia.

NOTE Confidence: 0.727097525

00:03:49.190 --> 00:03:51.848 Who have uh intermediate or high

NOTE Confidence: 0.727097525

00:03:51.848 --> 00:03:53.620 risk myelofibrosis and previously

NOTE Confidence: 0.727097525

00:03:53.697 --> 00:03:55.577 treated with Jack inhibitor.

NOTE Confidence: 0.727097525

00:03:55.580 --> 00:03:58.149 So these are the patients mostly treated

NOTE Confidence: 0.727097525

00:03:58.149 --> 00:04:00.400 with ruxolitinib who then either were

NOTE Confidence: 0.727097525

00:04:00.400 --> 00:04:02.564 resistant or refractory to this drug

NOTE Confidence: 0.727097525

00:04:02.564 --> 00:04:04.688 and proceeded with the second line

NOTE Confidence: 0.727097525

00:04:04.688 --> 00:04:06.186 treatment which included monoethnic

NOTE Confidence: 0.727097525

00:04:06.186 --> 00:04:08.418 or danazol in this randomized study.

NOTE Confidence: 0.727097525

00:04:08.420 --> 00:04:11.178 So as I've mentioned inhibits Jack one,

NOTE Confidence: 0.727097525

00:04:11.180 --> 00:04:13.352 Jack two similar to ruxolitinib but

NOTE Confidence: 0.727097525

00:04:13.352 --> 00:04:16.849 also a CD R1 which is active in a

NOTE Confidence: 0.727097525

00:04:16.849 --> 00:04:19.419 receptor type one and signaling in ACR.

NOTE Confidence: 0.727097525

00:04:19.420 --> 00:04:22.060 One leads to increased production of

NOTE Confidence: 0.727097525

00:04:22.060 --> 00:04:24.661 hepcidin which limits access to iron

NOTE Confidence: 0.727097525

00:04:24.661 --> 00:04:27.349 for hematopoiesis and inhibition of C acvr.

NOTE Confidence: 0.727097525

00:04:27.350 --> 00:04:29.670 One actually decreases hepcidin and

NOTE Confidence: 0.727097525

00:04:29.670 --> 00:04:32.470 improves production of red blood cells.

NOTE Confidence: 0.727097525

00:04:32.470 --> 00:04:34.666 As the result it is expected

NOTE Confidence: 0.727097525

00:04:34.666 --> 00:04:36.130 that anemia can improve.

NOTE Confidence: 0.727097525

00:04:36.130 --> 00:04:38.531 So the phase three trial looked at

NOTE Confidence: 0.727097525

00:04:38.531 --> 00:04:40.396 patients who are Jack experienced

NOTE Confidence: 0.727097525

00:04:40.396 --> 00:04:42.694 and those who are symptomatic as

NOTE Confidence: 0.727097525

00:04:42.694 --> 00:04:44.987 well as an intermediate to high

NOTE Confidence: 0.727097525

00:04:44.987 --> 00:04:47.518 risk disease based on dips and have

NOTE Confidence: 0.727097525

00:04:47.518 --> 00:04:48.910 hemoglobin less than 10.

NOTE Confidence: 0.727097525

00:04:48.910 --> 00:04:49.620 So with all of this.

NOTE Confidence: 0.727097525

00:04:49.620 --> 00:04:51.666 Actions anemic to certain degree and

NOTE Confidence: 0.727097525

00:04:51.666 --> 00:04:54.347 platelet count should be more than 25,000.

NOTE Confidence: 0.727097525

00:04:54.347 --> 00:04:59.646 So the study randomized patients into to

NOTE Confidence: 0.727097525

00:04:59.646 --> 00:05:03.134 one fashion and the first group received

NOTE Confidence: 0.727097525

00:05:03.134 --> 00:05:04.964 more melatonin but 200 milligrams

NOTE Confidence: 0.727097525

00:05:04.964 --> 00:05:07.589 per day versus danazol placebo the.

NOTE Confidence: 0.727097525

00:05:07.589 --> 00:05:10.254 The group with Danazol received

NOTE Confidence: 0.727097525

00:05:10.254 --> 00:05:12.501 danazol 300 milligrams twice

NOTE Confidence: 0.727097525

00:05:12.501 --> 00:05:15.236 a day and monolithic placebo.

NOTE Confidence: 0.727097525

00:05:15.240 --> 00:05:18.649 So the key primary endpoint was told

NOTE Confidence: 0.727097525

00:05:18.649 --> 00:05:21.090 symptoms score response at Week 24,

NOTE Confidence: 0.727097525

00:05:21.090 --> 00:05:22.647 secondary endpoints transfusion

NOTE Confidence: 0.727097525

00:05:22.647 --> 00:05:25.242 independence at Week 24 and

NOTE Confidence: 0.727097525

00:05:25.242 --> 00:05:27.448 splenic response rate at week 24.

NOTE Confidence: 0.727097525

00:05:27.450 --> 00:05:29.898 This is the results which were

NOTE Confidence: 0.727097525

00:05:29.898 --> 00:05:30.844 presented AT-2022.

NOTE Confidence: 0.727097525

00:05:30.844 --> 00:05:35.650 So this the top line results at week 24.

NOTE Confidence: 0.727097525

00:05:35.650 --> 00:05:38.150 Also the results were published

NOTE Confidence: 0.727097525

00:05:38.150 --> 00:05:39.650 in Lancet climatology.

NOTE Confidence: 0.727097525

00:05:39.650 --> 00:05:43.136 This month, uh, so uh, as you can see,

NOTE Confidence: 0.727097525

00:05:43.136 --> 00:05:44.936 uh, I didn't start from primary endpoint,

NOTE Confidence: 0.727097525

00:05:44.940 --> 00:05:46.430 I started from transfusion independence

NOTE Confidence: 0.727097525

00:05:46.430 --> 00:05:48.837 here where you can see in the Red Square,

NOTE Confidence: 0.727097525

00:05:48.840 --> 00:05:51.366 the response rate for momelotinib group

NOTE Confidence: 0.727097525

00:05:51.366 --> 00:05:54.119 was higher than for danazol group,

NOTE Confidence: 0.727097525

00:05:54.120 --> 00:05:56.556 30% versus 20% of patients were

NOTE Confidence: 0.727097525

00:05:56.556 --> 00:05:58.504 transfusion independent at Week 24,

NOTE Confidence: 0.727097525

00:05:58.504 --> 00:06:00.448 it is actually impressive how well

NOTE Confidence: 0.727097525

00:06:00.448 --> 00:06:01.390 danazol did, 20%.

NOTE Confidence: 0.727097525

00:06:01.390 --> 00:06:03.420 So this drug certainly has role in

NOTE Confidence: 0.727097525

00:06:03.420 --> 00:06:04.834 management of anemia, myelofibrosis,

NOTE Confidence: 0.727097525

00:06:04.834 --> 00:06:07.198 but obviously one Molotov was better.

NOTE Confidence: 0.727097525

00:06:07.200 --> 00:06:09.314 So the other result, the primary endpoint,

NOTE Confidence: 0.727097525

00:06:09.320 --> 00:06:10.356 the symptoms.

NOTE Confidence: 0.727097525

00:06:10.356 --> 00:06:13.726 There are controlled in 25% of

NOTE Confidence: 0.727097525

00:06:13.726 --> 00:06:17.394 patients and splenic reduction by 35%

NOTE Confidence: 0.727097525

00:06:17.394 --> 00:06:19.744 was accomplished in 23% of patients.

NOTE Confidence: 0.727097525

00:06:19.744 --> 00:06:21.379 Certainly you wouldn't expect much

NOTE Confidence: 0.727097525

00:06:21.379 --> 00:06:22.360 of that happening

NOTE Confidence: 0.783701811538462

00:06:22.414 --> 00:06:24.518 in Danazol arm. So when the Lightning

NOTE Confidence: 0.783701811538462

00:06:24.518 --> 00:06:26.203 did reasonably well from the

NOTE Confidence: 0.783701811538462

00:06:26.203 --> 00:06:28.243 standpoint of symptoms and spleen size

NOTE Confidence: 0.783701811538462

00:06:28.243 --> 00:06:30.841 reduction in this group of patients

NOTE Confidence: 0.783701811538462

00:06:30.841 --> 00:06:33.030 previously treated with ruxolitinib.

NOTE Confidence: 0.783701811538462

00:06:33.030 --> 00:06:35.798 So the data was then looked at in

NOTE Confidence: 0.783701811538462

00:06:35.798 --> 00:06:37.535 different subgroups based on platelet

NOTE Confidence: 0.783701811538462

00:06:37.535 --> 00:06:40.410 count and it looks like it works as well.

NOTE Confidence: 0.783701811538462

00:06:40.410 --> 00:06:41.930 The patients got platelet count

NOTE Confidence: 0.783701811538462

00:06:41.930 --> 00:06:43.450 less than 50 uh hundred,

NOTE Confidence: 0.783701811538462

00:06:43.450 --> 00:06:45.368 less than 100 or less than 150

NOTE Confidence: 0.783701811538462

00:06:45.368 --> 00:06:47.835 with uh uh better results in

NOTE Confidence: 0.783701811538462

00:06:47.835 --> 00:06:49.407 MOMELOTINIB treated patients.

NOTE Confidence: 0.783701811538462

00:06:49.410 --> 00:06:51.138 So side effects, uh,

NOTE Confidence: 0.783701811538462

00:06:51.138 --> 00:06:54.070 there are not no surprises here uh.

NOTE Confidence: 0.783701811538462

00:06:54.070 --> 00:06:56.667 So the Grade 3 or higher adverse

NOTE Confidence: 0.783701811538462

00:06:56.667 --> 00:06:58.235 events happened with similar

NOTE Confidence: 0.783701811538462

00:06:58.235 --> 00:07:01.438 similarly in 49 and 46% of patients in

NOTE Confidence: 0.783701811538462

00:07:01.438 --> 00:07:03.548 Momelotinib Group and Danazol group,

NOTE Confidence: 0.783701811538462

00:07:03.550 --> 00:07:05.180 the rate of serious adverse

NOTE Confidence: 0.783701811538462

00:07:05.180 --> 00:07:06.484 events was very similar.

NOTE Confidence: 0.783701811538462

00:07:06.490 --> 00:07:09.114 So just want to highlight obviously you know

NOTE Confidence: 0.783701811538462

00:07:09.114 --> 00:07:11.148 cytopenia still a current myelofibrosis,

NOTE Confidence: 0.783701811538462

00:07:11.150 --> 00:07:13.418 there are some GI side effects which

NOTE Confidence: 0.783701811538462

00:07:13.418 --> 00:07:15.252 happened similarly in both groups

NOTE Confidence: 0.783701811538462

00:07:15.252 --> 00:07:17.262 of patients and peripheral sensory

NOTE Confidence: 0.783701811538462

00:07:17.262 --> 00:07:19.308 neuropathy is highlighted at the bottom.

NOTE Confidence: 0.783701811538462

00:07:19.310 --> 00:07:21.446 Was there was a signal in early phase

NOTE Confidence: 0.783701811538462

00:07:21.446 --> 00:07:23.731 studies that that may be an issue in

NOTE Confidence: 0.783701811538462

00:07:23.731 --> 00:07:25.205 more melodic treated patients but

NOTE Confidence: 0.783701811538462

00:07:25.205 --> 00:07:27.221 it didn't really seem to happen in

NOTE Confidence: 0.783701811538462

00:07:27.221 --> 00:07:29.120 this particular phase three trial?

NOTE Confidence: 0.783701811538462

00:07:29.120 --> 00:07:30.440 Moving on uh,

NOTE Confidence: 0.783701811538462

00:07:30.440 --> 00:07:32.708 so from Jack inhibitors to the drugs

NOTE Confidence: 0.783701811538462

00:07:32.708 --> 00:07:34.614 which uh have different mechanisms

NOTE Confidence: 0.783701811538462

00:07:34.614 --> 00:07:37.218 of action and still used and

NOTE Confidence: 0.783701811538462

00:07:37.218 --> 00:07:38.919 myelofibrosis and this particular

NOTE Confidence: 0.783701811538462

00:07:38.919 --> 00:07:41.593 drug is called navitoclax and in this

NOTE Confidence: 0.783701811538462

00:07:41.593 --> 00:07:44.263 study it was used together works with

NOTE Confidence: 0.783701811538462

00:07:44.263 --> 00:07:46.278 Jack inhibitor naive patients now.

NOTE Confidence: 0.783701811538462

00:07:46.280 --> 00:07:48.842 So it's a frontline treatment for

NOTE Confidence: 0.783701811538462

00:07:48.842 --> 00:07:51.044 patients with myelofibrosis who have

NOTE Confidence: 0.783701811538462

00:07:51.044 --> 00:07:53.179 intermediate to high risk disease.

NOTE Confidence: 0.783701811538462

00:07:53.180 --> 00:07:56.295 So and now the study highlights certain

NOTE Confidence: 0.783701811538462

00:07:56.295 --> 00:07:59.328 things which claim that the results are.

NOTE Confidence: 0.783701811538462

00:07:59.330 --> 00:08:00.942 Suggestive of disease modification.

NOTE Confidence: 0.783701811538462

00:08:00.942 --> 00:08:02.554 Let's look at uh,

NOTE Confidence: 0.783701811538462

00:08:02.560 --> 00:08:03.583 the navitoclax itself.

NOTE Confidence: 0.783701811538462

00:08:03.583 --> 00:08:06.429 So what does this drug so and why

NOTE Confidence: 0.783701811538462

00:08:06.429 --> 00:08:08.739 would we combine it with ruxolitinib?

NOTE Confidence: 0.783701811538462

00:08:08.740 --> 00:08:10.980 So rux lithium suppresses transcription

NOTE Confidence: 0.783701811538462

00:08:10.980 --> 00:08:13.760 through Jack inhibition of jackstadt pathway.

NOTE Confidence: 0.783701811538462

00:08:13.760 --> 00:08:16.504 You can see how it can suppress

NOTE Confidence: 0.783701811538462

00:08:16.504 --> 00:08:18.192 transcription of pro survival

NOTE Confidence: 0.783701811538462

00:08:18.192 --> 00:08:20.778 proteins MCL one and BCL Excel.

NOTE Confidence: 0.783701811538462

00:08:20.780 --> 00:08:23.786 So Navitoclax it's direct inhibitor of

NOTE Confidence: 0.783701811538462

00:08:23.786 --> 00:08:26.642 antiapoptotic activity of BCL XLS well

NOTE Confidence: 0.783701811538462

00:08:26.642 --> 00:08:29.337 as BCL two and in preclinical studies.

NOTE Confidence: 0.783701811538462

00:08:29.340 --> 00:08:29.732 Yeah,

NOTE Confidence: 0.783701811538462

00:08:29.732 --> 00:08:32.084 they showed this to drug showed

NOTE Confidence: 0.783701811538462

00:08:32.084 --> 00:08:33.738 synergistic synergism in inducing

NOTE Confidence: 0.783701811538462

00:08:33.738 --> 00:08:36.204 apoptosis in malignant cells that led

NOTE Confidence: 0.783701811538462

00:08:36.204 --> 00:08:38.770 to the development of this combination.

NOTE Confidence: 0.783701811538462

00:08:38.770 --> 00:08:42.532 And at ASH 2022 Cohort 3 of refined study

NOTE Confidence: 0.783701811538462

00:08:42.532 --> 00:08:46.043 phase two trial enrolling Jack Jack

NOTE Confidence: 0.783701811538462

00:08:46.043 --> 00:08:49.354 inhibitor naive patients was presented.

NOTE Confidence: 0.783701811538462

00:08:49.354 --> 00:08:54.718 So key criteria key endpoint was splenic

NOTE Confidence: 0.783701811538462

00:08:54.718 --> 00:08:59.380 volume reduction by 35% at week 24 measured.

NOTE Confidence: 0.783701811538462

00:08:59.380 --> 00:09:02.230 Grammarian cat scan and key secondary

NOTE Confidence: 0.783701811538462

00:09:02.230 --> 00:09:04.130 exploratory endpoints were changing

NOTE Confidence: 0.783701811538462

00:09:04.203 --> 00:09:06.373 bone marrow fibrosis grade from

NOTE Confidence: 0.783701811538462

00:09:06.373 --> 00:09:08.274 baseline reviewed locally as well

NOTE Confidence: 0.783701811538462

00:09:08.274 --> 00:09:10.104 as reduction variant frequency for

NOTE Confidence: 0.783701811538462

00:09:10.104 --> 00:09:12.248 driver mutations determined centrally.

NOTE Confidence: 0.783701811538462

00:09:12.250 --> 00:09:15.364 So as we are 35 was achieved in 80%

NOTE Confidence: 0.783701811538462

00:09:15.370 --> 00:09:17.926 of patients which is pretty good.

NOTE Confidence: 0.783701811538462

00:09:17.930 --> 00:09:19.850 So you can see that pretty much all

NOTE Confidence: 0.783701811538462

00:09:19.850 --> 00:09:21.789 of the patients had some splenic

NOTE Confidence: 0.783701811538462

00:09:21.789 --> 00:09:23.883 reduction and again among those who

NOTE Confidence: 0.783701811538462

00:09:23.945 --> 00:09:26.270 accomplish as CR35 response at 24

NOTE Confidence: 0.783701811538462

00:09:26.270 --> 00:09:29.390 weeks about third of patients had achieved.

NOTE Confidence: 0.783701811538462

00:09:29.390 --> 00:09:30.995 Reduction in marrow fibrosis by

NOTE Confidence: 0.783701811538462

00:09:30.995 --> 00:09:32.279 at least one grade.

NOTE Confidence: 0.783701811538462

00:09:32.280 --> 00:09:34.048 So the secondary endpoint

NOTE Confidence: 0.783701811538462

00:09:34.048 --> 00:09:35.816 looked at fibrosis itself.

NOTE Confidence: 0.783701811538462

00:09:35.820 --> 00:09:37.698 The reduction by one grade was

NOTE Confidence: 0.783701811538462

00:09:37.698 --> 00:09:39.880 observed in nine out of 32 patients

NOTE Confidence: 0.803785128

00:09:39.880 --> 00:09:41.610 28% and among nine patients,

NOTE Confidence: 0.803785128

00:09:41.610 --> 00:09:44.196 two had complete resolution of myelofibrosis.

NOTE Confidence: 0.803785128

00:09:44.200 --> 00:09:47.161 The mean time to resolution to reduction

NOTE Confidence: 0.803785128

00:09:47.161 --> 00:09:49.731 in bone marrow fibrosis was 12.3

NOTE Confidence: 0.803785128

00:09:49.731 --> 00:09:51.537 weeks and also there was reduction,

NOTE Confidence: 0.803785128

00:09:51.540 --> 00:09:53.850 significant reduction of Jack 2V617-F

NOTE Confidence: 0.803785128

00:09:53.850 --> 00:09:55.698 mutation very until frequency.

NOTE Confidence: 0.803785128

00:09:55.700 --> 00:09:59.861 So 36% of patients had 50% reduction or more.

NOTE Confidence: 0.803785128

00:09:59.861 --> 00:10:02.063 So this findings uh in improvement

NOTE Confidence: 0.803785128

00:10:02.063 --> 00:10:04.798 of fibrosis as well as reduction

NOTE Confidence: 0.803785128

00:10:04.798 --> 00:10:06.634 of varietal frequency objectives,

NOTE Confidence: 0.803785128

00:10:06.640 --> 00:10:09.015 617 mutations suggests disease modification

NOTE Confidence: 0.803785128

00:10:09.015 --> 00:10:12.270 with use of this medication combination.

NOTE Confidence: 0.803785128

00:10:12.270 --> 00:10:15.392 So next drug which also was tried

NOTE Confidence: 0.803785128

00:10:15.392 --> 00:10:17.590 in treatment naive patients.

NOTE Confidence: 0.803785128

00:10:17.590 --> 00:10:19.690 So together with ruxolitinib

NOTE Confidence: 0.803785128

00:10:19.690 --> 00:10:21.790 is called Palabra Zeb.

NOTE Confidence: 0.803785128

00:10:21.790 --> 00:10:24.009 So this is again a phase two

NOTE Confidence: 0.803785128

00:10:24.009 --> 00:10:26.843 study and first of all couple of

NOTE Confidence: 0.803785128

00:10:26.843 --> 00:10:28.647 words about collaborative itself.

NOTE Confidence: 0.803785128

00:10:28.650 --> 00:10:29.271 So it's better.

NOTE Confidence: 0.803785128

00:10:29.271 --> 00:10:30.720 Keep it and that is a family

NOTE Confidence: 0.803785128

00:10:30.767 --> 00:10:32.332 would be genetic proteins which

NOTE Confidence: 0.803785128

00:10:32.332 --> 00:10:33.584 are overexpressed in cancer.

NOTE Confidence: 0.803785128

00:10:33.590 --> 00:10:35.535 Collaborative is novel oral BET

NOTE Confidence: 0.803785128

00:10:35.535 --> 00:10:37.944 inhibitor which belongs to this class

NOTE Confidence: 0.803785128

00:10:37.944 --> 00:10:40.326 of drugs known as epigenetic modifiers.

NOTE Confidence: 0.803785128

00:10:40.330 --> 00:10:41.995 The lab razip selectively inhibits

NOTE Confidence: 0.803785128

00:10:41.995 --> 00:10:44.246 BD1 and D2 bromo domains of that

NOTE Confidence: 0.803785128

00:10:44.246 --> 00:10:46.101 proteins and you can see on the

NOTE Confidence: 0.803785128

00:10:46.101 --> 00:10:48.476 cartoon on the right that it can work

NOTE Confidence: 0.803785128

00:10:48.476 --> 00:10:49.892 concordantly with Jack inhibitors.

NOTE Confidence: 0.803785128

00:10:49.892 --> 00:10:52.552 So Jack inhibitors inhibitors jackstadt

NOTE Confidence: 0.803785128

00:10:52.552 --> 00:10:56.820 pathway that proteins are important in.

NOTE Confidence: 0.803785128

00:10:56.820 --> 00:10:58.568 Transcriptions which lead to

NOTE Confidence: 0.803785128

00:10:58.568 --> 00:11:01.660 production of TGF Beta NF, Kappa B,

NOTE Confidence: 0.803785128

00:11:01.660 --> 00:11:03.460 BCL two and cmic.

NOTE Confidence: 0.803785128

00:11:03.460 --> 00:11:05.740 Those are associated with aberrant

NOTE Confidence: 0.803785128

00:11:05.740 --> 00:11:06.724 mechanistic differentiation,

NOTE Confidence: 0.803785128

00:11:06.724 --> 00:11:07.708 increased cytokines,

NOTE Confidence: 0.803785128

00:11:07.708 --> 00:11:10.660 bone marrow fibrosis and cell survival.

NOTE Confidence: 0.803785128

00:11:10.660 --> 00:11:12.804 So if you inhibit Jack as well as

NOTE Confidence: 0.803785128

00:11:12.804 --> 00:11:15.178 better at the same time you decrease

NOTE Confidence: 0.803785128

00:11:15.178 --> 00:11:17.342 production of this site okines and

NOTE Confidence: 0.803785128

00:11:17.342 --> 00:11:19.610 this can lead to the improvement of

NOTE Confidence: 0.803785128

00:11:19.610 --> 00:11:21.538 symptoms and perhaps disease modification.

NOTE Confidence: 0.803785128

00:11:21.538 --> 00:11:24.917 So the study we're looking at is has

NOTE Confidence: 0.803785128

00:11:24.917 --> 00:11:26.780 four arms, but we're only looking at.

NOTE Confidence: 0.803785128

00:11:26.780 --> 00:11:29.820 Arm 3 which is a first line uh,

NOTE Confidence: 0.803785128

00:11:29.820 --> 00:11:31.600 uh treatment for patients not

NOTE Confidence: 0.803785128

00:11:31.600 --> 00:11:33.798 exposed to Jack inhibitors who have

NOTE Confidence: 0.803785128

00:11:33.798 --> 00:11:35.898 intermediate tool to high risk disease

NOTE Confidence: 0.803785128

00:11:35.898 --> 00:11:37.907 and there's all of these people

NOTE Confidence: 0.803785128

00:11:37.907 --> 00:11:39.986 were in this phase two trade study

NOTE Confidence: 0.803785128

00:11:39.990 --> 00:11:42.238 received collaborative and ruxolitinib.

NOTE Confidence: 0.803785128

00:11:42.238 --> 00:11:45.200 The primary endpoint was SVR 35,

NOTE Confidence: 0.803785128

00:11:45.200 --> 00:11:47.649 splenic volume reduction by 35% and total

NOTE Confidence: 0.803785128

00:11:47.649 --> 00:11:51.330 symptom score is actioned by 50% at week 24.

NOTE Confidence: 0.803785128

00:11:51.330 --> 00:11:54.896 So as you can see the SVR

NOTE Confidence: 0.803785128

00:11:54.896 --> 00:11:57.178 35 was at week 24 was 68.

NOTE Confidence: 0.803785128

00:11:57.180 --> 00:11:59.570 Some previous study actually 80% again

NOTE Confidence: 0.803785128

00:11:59.570 --> 00:12:02.030 we can't come cannot compare apples

NOTE Confidence: 0.803785128

00:12:02.030 --> 00:12:04.538 and oranges here and TSS 50 reduction

NOTE Confidence: 0.803785128

00:12:04.538 --> 00:12:07.180 was accomplished by 56% of patients.

NOTE Confidence: 0.803785128

00:12:07.180 --> 00:12:09.455 Interestingly at any given time as we

NOTE Confidence: 0.803785128

00:12:09.455 --> 00:12:11.775 are 35 was accomplished again by 80%

NOTE Confidence: 0.803785128

00:12:11.780 --> 00:12:13.670 of patients similar number to which

NOTE Confidence: 0.803785128

00:12:13.670 --> 00:12:15.940 was shown previous study I shared with you.

NOTE Confidence: 0.803785128

00:12:15.940 --> 00:12:18.682 So from the standpoint Ballmer of

NOTE Confidence: 0.803785128

00:12:18.682 --> 00:12:21.053 fibrosis again about 27% of patients

NOTE Confidence: 0.803785128

00:12:21.053 --> 00:12:23.846 here at had at least one great reduction

NOTE Confidence: 0.803785128

00:12:23.846 --> 00:12:26.674 in bone marrow fibrosis by Week 24.

NOTE Confidence: 0.803785128

00:12:26.680 --> 00:12:28.768 Clinical responses were connected

NOTE Confidence: 0.803785128

00:12:28.768 --> 00:12:31.378 to reduction of variable frequency

NOTE Confidence: 0.803785128

00:12:31.378 --> 00:12:32.664 inject 2V617-F mutations.

NOTE Confidence: 0.803785128

00:12:32.664 --> 00:12:34.956 Most adverse events here were low

NOTE Confidence: 0.803785128

00:12:34.956 --> 00:12:37.860 grade and 14% of patients had to

NOTE Confidence: 0.803785128

00:12:37.860 --> 00:12:39.572 discontinue the study participation

NOTE Confidence: 0.803785128

00:12:39.572 --> 00:12:41.318 due to adverse events.

NOTE Confidence: 0.803785128

00:12:41.320 --> 00:12:41.720 So uh,

NOTE Confidence: 0.803785128

00:12:41.720 --> 00:12:43.904 this is to me is one of the more

NOTE Confidence: 0.803785128

00:12:43.904 --> 00:12:45.980 exciting presentations plenary session.

NOTE Confidence: 0.803785128

00:12:45.980 --> 00:12:48.514 You can see this presentation #6 and

NOTE Confidence: 0.803785128

00:12:48.514 --> 00:12:50.913 it looks at completely different

NOTE Confidence: 0.803785128

00:12:50.913 --> 00:12:52.767 mechanism of action.

NOTE Confidence: 0.803785128

00:12:52.770 --> 00:12:54.960 This group of diseases and

NOTE Confidence: 0.803785128

00:12:54.960 --> 00:12:55.836 myeloproliferative neoplasms,

NOTE Confidence: 0.803785128

00:12:55.840 --> 00:12:58.090 so this is the presentation of

NOTE Confidence: 0.803785128

00:12:58.090 --> 00:12:59.590 preclinical data on monoclonal

NOTE Confidence: 0.865965874285714

00:12:59.660 --> 00:13:01.940 antibody against mutant calreticulin.

NOTE Confidence: 0.865965874285714

00:13:01.940 --> 00:13:05.594 So mutant calreticulin is so calreticulin

NOTE Confidence: 0.865965874285714

00:13:05.594 --> 00:13:10.279 as a protein is responsible for modification

NOTE Confidence: 0.865965874285714

00:13:10.279 --> 00:13:13.513 of thrombopoietin receptor before it moves

NOTE Confidence: 0.865965874285714

00:13:13.513 --> 00:13:17.605 to the surface of the cell and mutated

NOTE Confidence: 0.865965874285714

00:13:17.605 --> 00:13:19.995 calreticulin instead of just modifying

NOTE Confidence: 0.865965874285714

00:13:20.073 --> 00:13:23.076 it attaches itself to the TPO receptor.

NOTE Confidence: 0.865965874285714

00:13:23.080 --> 00:13:24.680 And moves together with the

NOTE Confidence: 0.865965874285714

00:13:24.680 --> 00:13:26.280 receptor to the surface uh,

NOTE Confidence: 0.865965874285714

00:13:26.280 --> 00:13:28.245 causing dimerization of the receptor

NOTE Confidence: 0.865965874285714

00:13:28.245 --> 00:13:29.817 and its activation uh,

NOTE Confidence: 0.865965874285714

00:13:29.820 --> 00:13:31.968 which doesn't require ligand.

NOTE Confidence: 0.865965874285714

00:13:31.968 --> 00:13:35.190 So what happens when antibody attacks

NOTE Confidence: 0.865965874285714

00:13:35.270 --> 00:13:37.510 and mutated color electrically and

NOTE Confidence: 0.865965874285714

00:13:37.510 --> 00:13:40.479 on the surface of the cell it?

NOTE Confidence: 0.865965874285714

00:13:40.480 --> 00:13:43.145 The reverses this dimerization and

NOTE Confidence: 0.865965874285714

00:13:43.145 --> 00:13:45.277 activation of jackstadt pathway.

NOTE Confidence: 0.865965874285714

00:13:45.280 --> 00:13:47.770 So this study used fully human

NOTE Confidence: 0.865965874285714

00:13:47.770 --> 00:13:51.072 FC silent IgG 1 antibody again

NOTE Confidence: 0.865965874285714

00:13:51.072 --> 00:13:53.400 against mutant calreticulin.

NOTE Confidence: 0.865965874285714

00:13:53.400 --> 00:13:56.418 The binding was selective to mutant

NOTE Confidence: 0.865965874285714

00:13:56.418 --> 00:13:57.927 calreticulin antagonized mutant

NOTE Confidence: 0.865965874285714

00:13:57.927 --> 00:14:00.578 calreticulin used signaling and congenic

NOTE Confidence: 0.865965874285714

00:14:00.578 --> 00:14:02.654 function inhibited cell proliferation.

NOTE Confidence: 0.865965874285714

00:14:02.660 --> 00:14:05.445 Start 5 phosphorylation in CD34

NOTE Confidence: 0.865965874285714

00:14:05.445 --> 00:14:07.116 mutant calreticulin cells.

NOTE Confidence: 0.865965874285714

00:14:07.120 --> 00:14:09.106 It caused apoptosis of those cells

NOTE Confidence: 0.865965874285714

00:14:09.106 --> 00:14:10.910 and didn't affect non mutant.

NOTE Confidence: 0.865965874285714

00:14:10.910 --> 00:14:12.998 Political in cells once again you

NOTE Confidence: 0.865965874285714

00:14:12.998 --> 00:14:15.858 know this is the uh preclinical data.

NOTE Confidence: 0.865965874285714

00:14:15.860 --> 00:14:19.577 The Phase One study is expected to

NOTE Confidence: 0.865965874285714

00:14:19.577 --> 00:14:22.939 be opened within next few months.

NOTE Confidence: 0.865965874285714

00:14:22.940 --> 00:14:26.420 So moving on to polycythemia Vera,

NOTE Confidence: 0.865965874285714

00:14:26.420 --> 00:14:28.435 much higher incidence and prevalence

NOTE Confidence: 0.865965874285714

00:14:28.435 --> 00:14:31.192 of this disease and the United States

NOTE Confidence: 0.865965874285714

00:14:31.192 --> 00:14:33.880 only one study and this is the study

NOTE Confidence: 0.865965874285714

00:14:33.948 --> 00:14:36.300 for patients with low risk disease.

NOTE Confidence: 0.865965874285714

00:14:36.300 --> 00:14:38.996 So low risk defined as age less

NOTE Confidence: 0.865965874285714

00:14:38.996 --> 00:14:41.234 than 60 and no history of.

NOTE Confidence: 0.865965874285714

00:14:41.240 --> 00:14:41.752 Thrombosis,

NOTE Confidence: 0.865965874285714

00:14:41.752 --> 00:14:43.800 so this patients historically

NOTE Confidence: 0.865965874285714

00:14:43.800 --> 00:14:46.360 treated with phlebotomies and aspirin

NOTE Confidence: 0.865965874285714

00:14:46.434 --> 00:14:48.653 and what this study looked at is

NOTE Confidence: 0.865965874285714

00:14:48.653 --> 00:14:51.498 addition of row peg interferon A2,

NOTE Confidence: 0.865965874285714

00:14:51.498 --> 00:14:53.706 B to this treatment.

NOTE Confidence: 0.865965874285714

00:14:53.710 --> 00:14:55.080 So the patients randomized in

NOTE Confidence: 0.865965874285714

00:14:55.080 --> 00:14:57.209 this phase two trial in one to one

NOTE Confidence: 0.865965874285714

00:14:57.209 --> 00:14:58.840 fashion standard of care is on the

NOTE Confidence: 0.865965874285714

00:14:58.895 --> 00:15:00.665 left phlebotomy plus aspirin and on

NOTE Confidence: 0.865965874285714

00:15:00.665 --> 00:15:02.580 the right is lobotomy plus aspirin

NOTE Confidence: 0.865965874285714

00:15:02.580 --> 00:15:04.770 as well as row peg interferon.

NOTE Confidence: 0.865965874285714

00:15:04.770 --> 00:15:07.598 It's at fixed dose of 100 micrograms

NOTE Confidence: 0.865965874285714

00:15:07.598 --> 00:15:08.810 every two weeks.

NOTE Confidence: 0.865965874285714

00:15:08.810 --> 00:15:11.340 Primary endpoint was response and.

NOTE Confidence: 0.865965874285714

00:15:11.340 --> 00:15:12.695 Response was defined as median

NOTE Confidence: 0.865965874285714

00:15:12.695 --> 00:15:14.793 chemical less than 45 in the absence

NOTE Confidence: 0.865965874285714

00:15:14.793 --> 00:15:15.828 of disease progression.

NOTE Confidence: 0.865965874285714

00:15:15.830 --> 00:15:17.558 Definition of disease progression

NOTE Confidence: 0.865965874285714

00:15:17.558 --> 00:15:20.150 for low risk HPV patients includes

NOTE Confidence: 0.865965874285714

00:15:20.218 --> 00:15:22.830 progressive symptoms and progressive

NOTE Confidence: 0.865965874285714

00:15:22.830 --> 00:15:24.170 symptomatic thrombocytosis,

NOTE Confidence: 0.865965874285714

00:15:24.170 --> 00:15:25.510 progressive Leukocytosis,

NOTE Confidence: 0.865965874285714

00:15:25.510 --> 00:15:27.890 vascular and major bleeding complications.

NOTE Confidence: 0.865965874285714

00:15:27.890 --> 00:15:29.426 So this is the primary endpoint.

NOTE Confidence: 0.865965874285714

00:15:29.430 --> 00:15:31.884 The study was published in 2021.

NOTE Confidence: 0.865965874285714

00:15:31.884 --> 00:15:34.082 So at that time the second interim

NOTE Confidence: 0.865965874285714

00:15:34.082 --> 00:15:35.670 analysis was presented at one

NOTE Confidence: 0.865965874285714

00:15:35.670 --> 00:15:37.749 year and this is a final results.

NOTE Confidence: 0.865965874285714

00:15:37.750 --> 00:15:39.526 So this is observation of patients

NOTE Confidence: 0.865965874285714

00:15:39.526 --> 00:15:41.349 over a period of two years.

NOTE Confidence: 0.865965874285714

00:15:41.350 --> 00:15:43.882 Study was stopped to accrual after

NOTE Confidence: 0.865965874285714

00:15:43.882 --> 00:15:46.737 uh second analysis uh because uh

NOTE Confidence: 0.865965874285714

00:15:46.737 --> 00:15:48.909 significantly better performance of

NOTE Confidence: 0.865965874285714

00:15:48.909 --> 00:15:51.873 patients who were treated with row

NOTE Confidence: 0.865965874285714

00:15:51.873 --> 00:15:53.938 peg interferon from the standoff

NOTE Confidence: 0.865965874285714

00:15:53.938 --> 00:15:55.177 composite primary endpoint.

NOTE Confidence: 0.865965874285714

00:15:55.180 --> 00:15:57.416 So you can see that this is

NOTE Confidence: 0.865965874285714

00:15:57.416 --> 00:15:59.128 schematically control lack of

NOTE Confidence: 0.865965874285714

00:15:59.128 --> 00:16:00.613 progression which was observed

NOTE Confidence: 0.865965874285714

00:16:00.613 --> 00:16:02.719 in much higher number of patients

NOTE Confidence: 0.865965874285714

00:16:02.719 --> 00:16:04.538 treated with row peg interferon.

NOTE Confidence: 0.865965874285714

00:16:04.540 --> 00:16:07.474 So the separate endpoints for hematocrit

NOTE Confidence: 0.865965874285714

00:16:07.474 --> 00:16:09.922 control and disease progression you

NOTE Confidence: 0.865965874285714

00:16:09.922 --> 00:16:12.424 can see that frequency of phlebotomies.

NOTE Confidence: 0.865965874285714

00:16:12.430 --> 00:16:15.664 Was less in experimental arm and uh,

NOTE Confidence: 0.865965874285714

00:16:15.670 --> 00:16:17.854 you can see that the disease

NOTE Confidence: 0.865965874285714

00:16:17.854 --> 00:16:19.851 progression was only observed in

NOTE Confidence: 0.865965874285714

00:16:19.851 --> 00:16:21.747 patients treated with phlebotomies

NOTE Confidence: 0.865965874285714

00:16:21.747 --> 00:16:23.643 plus aspirin without rollback.

NOTE Confidence: 0.865965874285714

00:16:23.650 --> 00:16:25.125 In six patients placed count

NOTE Confidence: 0.865965874285714

00:16:25.125 --> 00:16:27.050 increased to more than a million

NOTE Confidence: 0.865965874285714

00:16:27.050 --> 00:16:30.926 and baseline was lower than 602

NOTE Confidence: 0.865965874285714

00:16:30.926 --> 00:16:32.990 patients planning infarction and

NOTE Confidence: 0.865965874285714

00:16:32.990 --> 00:16:34.779 transient ischemic attack occurred.

NOTE Confidence: 0.865965874285714

00:16:34.779 --> 00:16:37.740 So the effect was reasonably durable as

NOTE Confidence: 0.822350579583333

00:16:37.814 --> 00:16:40.630 you can see and also there was improvement

NOTE Confidence: 0.822350579583333

00:16:40.630 --> 00:16:42.637 of symptoms as measured by MPN.

NOTE Confidence: 0.822350579583333

00:16:42.640 --> 00:16:45.442 Off TSS and P splenomegaly improved

NOTE Confidence: 0.822350579583333

00:16:45.442 --> 00:16:48.511 in ROBEC treated patients as well

NOTE Confidence: 0.822350579583333

00:16:48.511 --> 00:16:50.747 significantly when compared to

NOTE Confidence: 0.822350579583333

00:16:50.747 --> 00:16:52.983 patients treated without rollback.

NOTE Confidence: 0.822350579583333

00:16:52.990 --> 00:16:56.410 So Jack 2V617-F very until frequency

NOTE Confidence: 0.822350579583333

00:16:56.410 --> 00:16:58.210 decreased in ropek treated patients

NOTE Confidence: 0.822350579583333

00:16:58.210 --> 00:17:00.622 and slightly increased the 12 months in

NOTE Confidence: 0.822350579583333

00:17:00.622 --> 00:17:02.490 patients who didn't receive rollback.

NOTE Confidence: 0.822350579583333

00:17:02.490 --> 00:17:04.261 So I would like to also show

NOTE Confidence: 0.822350579583333

00:17:04.261 --> 00:17:05.430 the side effect table.

NOTE Confidence: 0.822350579583333

00:17:05.430 --> 00:17:08.160 Obviously people who are treated with row

NOTE Confidence: 0.822350579583333

00:17:08.160 --> 00:17:11.348 Peg had higher incidence of adverse events.

NOTE Confidence: 0.822350579583333

00:17:11.350 --> 00:17:13.178 This is included treatment.

NOTE Confidence: 0.822350579583333

00:17:13.178 --> 00:17:15.399 Related adverse events 55% versus 6%

NOTE Confidence: 0.822350579583333

00:17:15.399 --> 00:17:17.886 grade 3 or 4 adverse events were about

NOTE Confidence: 0.822350579583333

00:17:17.886 --> 00:17:20.945 the same and adverse events that caused

NOTE Confidence: 0.822350579583333

00:17:20.945 --> 00:17:22.734 treatment discontinuation were only

NOTE Confidence: 0.822350579583333

00:17:22.734 --> 00:17:24.844 revealed in rollback treated patients.

NOTE Confidence: 0.822350579583333

00:17:24.850 --> 00:17:25.446 In conclusion,

NOTE Confidence: 0.822350579583333

00:17:25.446 --> 00:17:27.234 I would like to summarize what

NOTE Confidence: 0.822350579583333

00:17:27.234 --> 00:17:28.250 I presented to you.

NOTE Confidence: 0.822350579583333

00:17:28.250 --> 00:17:30.175 Molotov may improve anemia in

NOTE Confidence: 0.822350579583333

00:17:30.175 --> 00:17:31.715 patients with myelofibrosis and

NOTE Confidence: 0.822350579583333

00:17:31.715 --> 00:17:33.510 acne due to acvr inhibition.

NOTE Confidence: 0.822350579583333

00:17:33.510 --> 00:17:34.968 Ruxolitinib and collaborative,

NOTE Confidence: 0.822350579583333

00:17:34.968 --> 00:17:37.398 the better inhibitor and light

NOTE Confidence: 0.822350579583333

00:17:37.398 --> 00:17:38.939 treatment associated with high

NOTE Confidence: 0.822350579583333

00:17:38.939 --> 00:17:40.782 SVR rates and TSS 50 reductions.

NOTE Confidence: 0.822350579583333

00:17:40.782 --> 00:17:43.642 Decrease fibrosis the clustering of

NOTE Confidence: 0.822350579583333

00:17:43.642 --> 00:17:46.300 megakaryocytes and decrease in Jack

NOTE Confidence: 0.822350579583333

00:17:46.300 --> 00:17:47.974 2V617 affair and total frequency may

NOTE Confidence: 0.822350579583333

00:17:47.974 --> 00:17:50.209 be a sign of disease modification and

NOTE Confidence: 0.822350579583333

00:17:50.209 --> 00:17:52.680 phase three trial which used the same

NOTE Confidence: 0.822350579583333

00:17:52.742 --> 00:17:55.268 model of combining roots lithium and

NOTE Confidence: 0.822350579583333

00:17:55.268 --> 00:17:56.952 collaborative just completed accrual.

NOTE Confidence: 0.822350579583333

00:17:56.960 --> 00:17:58.655 So waiting for the results

NOTE Confidence: 0.822350579583333

00:17:58.655 --> 00:18:00.350 Rubidium and Navitoclax and another

NOTE Confidence: 0.822350579583333

00:18:00.408 --> 00:18:02.160 combination frontline treatment.

NOTE Confidence: 0.822350579583333

00:18:02.160 --> 00:18:04.904 This BCL two BCL Excel inhibitor also

NOTE Confidence: 0.822350579583333

00:18:04.904 --> 00:18:07.001 was associated with a significant

NOTE Confidence: 0.822350579583333

00:18:07.001 --> 00:18:09.557 reduction in spleen volume as well

NOTE Confidence: 0.822350579583333

00:18:09.557 --> 00:18:11.718 as decreasing fibrosis and Jack.

NOTE Confidence: 0.822350579583333

00:18:11.720 --> 00:18:13.974 Will be six months S there until

NOTE Confidence: 0.822350579583333

00:18:13.974 --> 00:18:15.469 frequency phase three transform

NOTE Confidence: 0.822350579583333

00:18:15.469 --> 00:18:17.794 one study is ongoing monoclonal

NOTE Confidence: 0.822350579583333

00:18:17.794 --> 00:18:19.654 antibody against mutant calreticulin

NOTE Confidence: 0.822350579583333

00:18:19.720 --> 00:18:21.810 is effective in preclinical models.

NOTE Confidence: 0.822350579583333

00:18:21.810 --> 00:18:24.090 We are looking forward to see how this

NOTE Confidence: 0.822350579583333

00:18:24.090 --> 00:18:26.328 drug will perform in clinical trials.

NOTE Confidence: 0.822350579583333

00:18:26.330 --> 00:18:26.658 Finally,

NOTE Confidence: 0.822350579583333

00:18:26.658 --> 00:18:28.626 row Peg interferon can be considered

NOTE Confidence: 0.822350579583333

00:18:28.626 --> 00:18:30.200 for selected patients with low

NOTE Confidence: 0.822350579583333

00:18:30.200 --> 00:18:31.545 risk polycythemia Vera based on

NOTE Confidence: 0.822350579583333

00:18:31.545 --> 00:18:33.189 the results of phase two study.

NOTE Confidence: 0.827960139473684

00:18:39.040 --> 00:18:41.740 Thank you, Nikolai. So I'm going

NOTE Confidence: 0.827960139473684

00:18:41.740 --> 00:18:44.637 to be talking about MD S right

NOTE Confidence: 0.827960139473684

00:18:44.637 --> 00:18:47.610 now and let me share my. Slides.

NOTE Confidence: 0.7744013

00:18:51.740 --> 00:18:52.210 OK.

NOTE Confidence: 0.879195086666667

00:19:04.560 --> 00:19:07.599 OK. Thanks everyone.

NOTE Confidence: 0.879195086666667

00:19:07.600 --> 00:19:09.694 So I decided actually talk a

NOTE Confidence: 0.879195086666667

00:19:09.694 --> 00:19:11.902 little bit more in general about

NOTE Confidence: 0.879195086666667

00:19:11.902 --> 00:19:14.450 some of the main updates and on

NOTE Confidence: 0.879195086666667

00:19:14.450 --> 00:19:16.760 the management of MSDS in 2022

NOTE Confidence: 0.879195086666667

00:19:16.760 --> 00:19:18.560 integrating some of the ASH abstracts.

NOTE Confidence: 0.879195086666667

00:19:18.560 --> 00:19:19.888 These are my disclosures.

NOTE Confidence: 0.879195086666667

00:19:19.888 --> 00:19:22.343 So I'm going to talk about updates

NOTE Confidence: 0.879195086666667

00:19:22.343 --> 00:19:23.958 in the diagnosis, classification,

NOTE Confidence: 0.879195086666667

00:19:23.958 --> 00:19:25.630 prognostication and response assessment

NOTE Confidence: 0.879195086666667

00:19:25.630 --> 00:19:27.720 and then management to flower.

NOTE Confidence: 0.879195086666667

00:19:27.720 --> 00:19:29.700 On higher risk MD S.

NOTE Confidence: 0.879195086666667

00:19:29.700 --> 00:19:32.356 So I think the first important thing to

NOTE Confidence: 0.879195086666667

00:19:32.356 --> 00:19:34.679 know is that the diagnostic criteria

NOTE Confidence: 0.879195086666667

00:19:34.679 --> 00:19:37.410 for MDS were updated by The Who.

NOTE Confidence: 0.879195086666667

00:19:37.410 --> 00:19:39.306 So right now rather than requiring

NOTE Confidence: 0.879195086666667

00:19:39.306 --> 00:19:41.683 a hemoglobin of less than 10 and a

NOTE Confidence: 0.879195086666667

00:19:41.683 --> 00:19:43.267 platelet count of less than 100,

NOTE Confidence: 0.879195086666667

00:19:43.270 --> 00:19:44.607 as you can see to the left,

NOTE Confidence: 0.879195086666667

00:19:44.610 --> 00:19:46.370 the thresholds were a little

NOTE Confidence: 0.879195086666667

00:19:46.370 --> 00:19:47.426 bit less restrictive.

NOTE Confidence: 0.879195086666667

00:19:47.430 --> 00:19:49.272 So any anemia which is hemoglobin

NOTE Confidence: 0.879195086666667

00:19:49.272 --> 00:19:52.408 less than 12 in women and 13 in men

NOTE Confidence: 0.879195086666667

00:19:52.408 --> 00:19:53.884 or thrombocytopenia platelet count

NOTE Confidence: 0.879195086666667

00:19:53.884 --> 00:19:56.072 less than 150 can diagnose MSDS

NOTE Confidence: 0.879195086666667

00:19:56.072 --> 00:19:58.300 once you exclude other things that

NOTE Confidence: 0.879195086666667

00:19:58.300 --> 00:20:00.650 can cause MSDS but importantly.

NOTE Confidence: 0.879195086666667

00:20:00.650 --> 00:20:02.522 Certain genetic alterations such

NOTE Confidence: 0.879195086666667

00:20:02.522 --> 00:20:06.670 as as after B1 and B53 one could

NOTE Confidence: 0.879195086666667

00:20:06.670 --> 00:20:09.070 potentially lead to diagnosis

NOTE Confidence: 0.879195086666667

00:20:09.070 --> 00:20:11.598 of MDS in the right context.

NOTE Confidence: 0.879195086666667

00:20:11.598 --> 00:20:13.936 So that will probably mean that you

NOTE Confidence: 0.879195086666667

00:20:13.936 --> 00:20:15.628 are going to see more diagnosis

NOTE Confidence: 0.879195086666667

00:20:15.628 --> 00:20:17.788 on the as among your patients.

NOTE Confidence: 0.879195086666667

00:20:17.790 --> 00:20:20.567 The second I think major change in 2022.

NOTE Confidence: 0.879195086666667

00:20:20.567 --> 00:20:24.326 Is the update of The Who classification.

NOTE Confidence: 0.879195086666667

00:20:24.330 --> 00:20:26.070 We have two different classifications

NOTE Confidence: 0.879195086666667

00:20:26.070 --> 00:20:27.114 right now for

NOTE Confidence: 0.8667911825

00:20:29.350 --> 00:20:33.612 MDDS WHO 20222020 and ICC 2022 and

NOTE Confidence: 0.8667911825

00:20:33.612 --> 00:20:36.096 this is important because you there

NOTE Confidence: 0.8667911825

00:20:36.096 --> 00:20:39.295 are some differences between these two

NOTE Confidence: 0.8667911825

00:20:39.295 --> 00:20:43.017 classifications and you are going to start

NOTE Confidence: 0.8667911825

00:20:43.017 --> 00:20:45.856 seeing in your pathology reports some

NOTE Confidence: 0.8667911825

00:20:45.856 --> 00:20:48.386 discrepancies between the two diagnosis.

NOTE Confidence: 0.8667911825

00:20:48.390 --> 00:20:50.256 In some cases a patient could

NOTE Confidence: 0.8667911825

00:20:50.256 --> 00:20:51.189 be diagnosed with.

NOTE Confidence: 0.8667911825

00:20:51.190 --> 00:20:55.465 Animal by one category and MDS by the other.

NOTE Confidence: 0.8667911825

00:20:55.470 --> 00:20:57.350 For the sake of time today I'm not going to

NOTE Confidence: 0.8667911825

00:20:57.394 --> 00:20:59.230 be able to go through the details of this,

NOTE Confidence: 0.8667911825

00:20:59.230 --> 00:21:01.687 but the main updates is that certain

NOTE Confidence: 0.8667911825

00:21:01.687 --> 00:21:03.529 genetic alteration as I mentioned,

NOTE Confidence: 0.8667911825

00:21:03.530 --> 00:21:07.646 such as 3B1 and TB53 mutated

NOTE Confidence: 0.8667911825

00:21:07.646 --> 00:21:10.390 now can define genetically.

NOTE Confidence: 0.8667911825

00:21:10.390 --> 00:21:16.033 And the and also the category of 10 to

NOTE Confidence: 0.8667911825

00:21:16.040 --> 00:21:19.322 19% blast in the ICC classification

NOTE Confidence: 0.8667911825

00:21:19.322 --> 00:21:21.092 is called M DS/AMD.

NOTE Confidence: 0.8667911825

00:21:21.092 --> 00:21:23.780 So I think this is important to remember

NOTE Confidence: 0.8667911825

00:21:23.855 --> 00:21:26.167 as you look at your path reports and

NOTE Confidence: 0.8667911825

00:21:26.167 --> 00:21:28.839 one of the ASH abstracts actually

NOTE Confidence: 0.8667911825

00:21:28.839 --> 00:21:30.859 compared the two classifications.

NOTE Confidence: 0.8667911825

00:21:30.860 --> 00:21:33.233 This was a large effort on behalf

NOTE Confidence: 0.8667911825

00:21:33.233 --> 00:21:35.199 of the International Consortium for

NOTE Confidence: 0.8667911825

00:21:35.200 --> 00:21:37.624 MDS and I'm not going to go again

NOTE Confidence: 0.8667911825

00:21:37.624 --> 00:21:39.954 through all these results, but what?

NOTE Confidence: 0.8667911825

00:21:39.954 --> 00:21:42.453 Was found is that certain aspects of

NOTE Confidence: 0.8667911825

00:21:42.453 --> 00:21:44.826 each classification seem to function

NOTE Confidence: 0.8667911825

00:21:44.826 --> 00:21:47.730 well and therefore ideally this these

NOTE Confidence: 0.8667911825

00:21:47.803 --> 00:21:50.608 two classification should be harmonized,

NOTE Confidence: 0.8667911825

00:21:50.610 --> 00:21:53.786 which is an effort that is currently ongoing.

NOTE Confidence: 0.8667911825

00:21:53.790 --> 00:21:55.146 But until that happens,

NOTE Confidence: 0.8667911825

00:21:55.146 --> 00:21:58.323 feel free to reach out to us and to

NOTE Confidence: 0.8667911825

00:21:58.323 --> 00:22:00.412 the pathologist to discuss any aspects

NOTE Confidence: 0.8667911825

00:22:00.412 --> 00:22:02.729 of the path report that does confuse

NOTE Confidence: 0.8667911825

00:22:02.729 --> 00:22:05.003 you a little bit because it's going

NOTE Confidence: 0.8667911825

00:22:05.003 --> 00:22:07.912 to be a confusing gear in terms of

NOTE Confidence: 0.8667911825

00:22:07.912 --> 00:22:09.504 the diagnosis and classification.

NOTE Confidence: 0.8667911825

00:22:09.510 --> 00:22:10.966 Now going to prognostication

NOTE Confidence: 0.8667911825

00:22:10.966 --> 00:22:13.150 where things a little bit easier.

NOTE Confidence: 0.8667911825

00:22:13.150 --> 00:22:15.490 So we still think about MDS in two big

NOTE Confidence: 0.8667911825

00:22:15.490 --> 00:22:17.020 groups, lower risk and higher risk.

NOTE Confidence: 0.8667911825

00:22:17.020 --> 00:22:19.747 Lower risk quality of life is the main goal.

NOTE Confidence: 0.8667911825

00:22:19.750 --> 00:22:21.130 Higher risk you generally would

NOTE Confidence: 0.8667911825

00:22:21.130 --> 00:22:22.936 treat with the goal of changing

NOTE Confidence: 0.8667911825

00:22:22.936 --> 00:22:24.049 the Natural History,

NOTE Confidence: 0.8667911825

00:22:24.050 --> 00:22:27.840 often requiring bone marrow transplantation.

NOTE Confidence: 0.8667911825

00:22:27.840 --> 00:22:30.899 So this is the classical scoring systems,

NOTE Confidence: 0.8667911825

00:22:30.900 --> 00:22:32.372 IPS and revised ipss,

NOTE Confidence: 0.8667911825

00:22:32.372 --> 00:22:34.580 the two most commonly used ones.

NOTE Confidence: 0.8667911825

00:22:34.580 --> 00:22:38.550 And based on the adding of the blast count,

NOTE Confidence: 0.8667911825

00:22:38.550 --> 00:22:41.040 cytogenetics and cytopenias you classify the

NOTE Confidence: 0.8667911825

00:22:41.040 --> 00:22:43.597 patient into these lower and higher risk.

NOTE Confidence: 0.8667911825

00:22:43.600 --> 00:22:45.980 And one of the main developments of

NOTE Confidence: 0.8667911825

00:22:45.980 --> 00:22:49.557 2022 was the publication of the ISM.

NOTE Confidence: 0.8667911825

00:22:49.560 --> 00:22:52.520 So this finally and formally

NOTE Confidence: 0.8667911825

00:22:52.520 --> 00:22:55.174 integrated molecular IPS into the

NOTE Confidence: 0.8667911825

00:22:55.174 --> 00:22:57.796 prognostic picture you can see here.

NOTE Confidence: 0.8667911825

00:22:57.800 --> 00:22:59.288 On this table a list of the genes.

NOTE Confidence: 0.8667911825

00:22:59.290 --> 00:23:01.690 So there are 17 or sorry,

NOTE Confidence: 0.8667911825

00:23:01.690 --> 00:23:03.797 there are 31 different genes that are

NOTE Confidence: 0.8667911825

00:23:03.797 --> 00:23:05.572 part of the molecular classification

NOTE Confidence: 0.8667911825

00:23:05.572 --> 00:23:08.002 and this is becoming the standard

NOTE Confidence: 0.8667911825

00:23:08.002 --> 00:23:10.170 of care risk tool assessment.

NOTE Confidence: 0.8667911825

00:23:10.170 --> 00:23:10.532 Again,

NOTE Confidence: 0.8667911825

00:23:10.532 --> 00:23:13.066 why is that important for your practice

NOTE Confidence: 0.8667911825

00:23:13.066 --> 00:23:15.834 is now it's having the molecular

NOTE Confidence: 0.8667911825

00:23:15.834 --> 00:23:18.294 data affects both the diagnosis

NOTE Confidence: 0.8667911825

00:23:18.294 --> 00:23:20.118 classification as well as prognostication

NOTE Confidence: 0.8667911825

00:23:20.118 --> 00:23:23.054 of MD S and I still see many path

NOTE Confidence: 0.8667911825

00:23:23.054 --> 00:23:25.790 reports or when the World Cup for Ms.

NOTE Confidence: 0.8667911825

00:23:25.790 --> 00:23:27.940 is done in Community settings.

NOTE Confidence: 0.8667911825

00:23:27.940 --> 00:23:29.632 Many times people are just sending

NOTE Confidence: 0.8667911825

00:23:29.632 --> 00:23:31.503 karyotype and fish and they are

NOTE Confidence: 0.8667911825

00:23:31.503 --> 00:23:32.887 not sending molecular assessment.

NOTE Confidence: 0.8667911825

00:23:32.890 --> 00:23:34.725 So it's really important that

NOTE Confidence: 0.8667911825

00:23:34.725 --> 00:23:35.826 an exigency sequencing,

NOTE Confidence: 0.8667911825

00:23:35.830 --> 00:23:38.959 which is readily available in our impact

NOTE Confidence: 0.8667911825

00:23:38.959 --> 00:23:41.476 department should be run on those

NOTE Confidence: 0.8667911825

00:23:41.476 --> 00:23:44.560 patients because it can affect all of these.

NOTE Confidence: 0.8667911825

00:23:44.560 --> 00:23:46.414 Assessments which subsequently

NOTE Confidence: 0.8667911825

00:23:46.414 --> 00:23:48.268 can influence therapy.

NOTE Confidence: 0.8667911825

00:23:48.270 --> 00:23:51.258 The ISM now uses 6 categories

NOTE Confidence: 0.8667911825

00:23:51.258 --> 00:23:53.250 rather than five categories,

NOTE Confidence: 0.794596277777778

00:23:53.250 --> 00:23:55.698 3 lower risk ones and three high risk ones.

NOTE Confidence: 0.794596277777778

00:23:55.700 --> 00:23:57.700 And the good news is that this good

NOTE Confidence: 0.794596277777778

00:23:57.700 --> 00:23:59.582 thread of the intermediate ISR,

NOTE Confidence: 0.794596277777778

00:23:59.582 --> 00:24:02.832 which used to be a problem because it

NOTE Confidence: 0.794596277777778

00:24:02.832 --> 00:24:04.386 it was never clear whether you treat

NOTE Confidence: 0.794596277777778

00:24:04.386 --> 00:24:06.169 it as lower risk or higher risk.

NOTE Confidence: 0.794596277777778

00:24:06.170 --> 00:24:08.284 There are different ways to do that,

NOTE Confidence: 0.794596277777778

00:24:08.290 --> 00:24:10.509 but in the molecular IPS the patient

NOTE Confidence: 0.794596277777778

00:24:10.509 --> 00:24:12.630 is either lower risk or high risk,

NOTE Confidence: 0.794596277777778

00:24:12.630 --> 00:24:14.990 and I think that makes it somewhat easier.

NOTE Confidence: 0.794596277777778

00:24:14.990 --> 00:24:17.982 Now this model is a bit complex and

NOTE Confidence: 0.794596277777778

00:24:17.982 --> 00:24:20.858 it's not easy to clearly remember

NOTE Confidence: 0.794596277777778

00:24:20.858 --> 00:24:22.711 all the different variables,

NOTE Confidence: 0.794596277777778

00:24:22.711 --> 00:24:24.958 but the good news is that you

NOTE Confidence: 0.794596277777778

00:24:24.958 --> 00:24:26.180 have this website.

NOTE Confidence: 0.794596277777778

00:24:26.180 --> 00:24:29.930 And the as riskmodel.com you can see to

NOTE Confidence: 0.794596277777778

00:24:29.930 --> 00:24:32.284 the left side and all what you need to

NOTE Confidence: 0.794596277777778

00:24:32.284 --> 00:24:34.400 do is just enter the variables plus count,

NOTE Confidence: 0.794596277777778

00:24:34.400 --> 00:24:35.368 age, hemoglobin,

NOTE Confidence: 0.794596277777778

00:24:35.368 --> 00:24:37.788 platelet count and what molecular

NOTE Confidence: 0.794596277777778

00:24:37.788 --> 00:24:39.580 alteration the patient has.

NOTE Confidence: 0.794596277777778

00:24:39.580 --> 00:24:42.219 And then you can see that the

NOTE Confidence: 0.794596277777778

00:24:42.219 --> 00:24:44.304 ISM score for example for this

NOTE Confidence: 0.794596277777778

00:24:44.304 --> 00:24:46.053 patient was .24 moderate high.

NOTE Confidence: 0.794596277777778

00:24:46.053 --> 00:24:49.040 Also, this gives you the revised ISS score,

NOTE Confidence: 0.794596277777778

00:24:49.040 --> 00:24:51.776 so you can get both the molecular and

NOTE Confidence: 0.794596277777778

00:24:51.776 --> 00:24:54.274 the revised IPS in the same in the

NOTE Confidence: 0.794596277777778

00:24:54.274 --> 00:24:56.703 same snapshot when you enter the data.

NOTE Confidence: 0.794596277777778

00:24:56.710 --> 00:24:59.020 So one of the important presentations

NOTE Confidence: 0.794596277777778

00:24:59.020 --> 00:25:01.306 from ASH 2022 was comparing the

NOTE Confidence: 0.794596277777778

00:25:01.306 --> 00:25:03.580 molecular IPS which was just published

NOTE Confidence: 0.794596277777778

00:25:03.646 --> 00:25:07.706 in 2022 again against the revised IPS.

NOTE Confidence: 0.794596277777778

00:25:07.710 --> 00:25:09.334 And what you can see here is that

NOTE Confidence: 0.794596277777778

00:25:09.334 --> 00:25:10.110 the C index,

NOTE Confidence: 0.794596277777778

00:25:10.110 --> 00:25:12.567 which is a measure of the prognostic

NOTE Confidence: 0.794596277777778

00:25:12.567 --> 00:25:14.765 utility or the model accuracy is

NOTE Confidence: 0.794596277777778

00:25:14.765 --> 00:25:16.913 better for the molecular IPS as

NOTE Confidence: 0.794596277777778

00:25:16.913 --> 00:25:19.197 in this large European cohort.

NOTE Confidence: 0.794596277777778

00:25:19.200 --> 00:25:21.132 There were a number several presentations

NOTE Confidence: 0.794596277777778

00:25:21.132 --> 00:25:23.057 looking at this from different cohorts

NOTE Confidence: 0.794596277777778

00:25:23.057 --> 00:25:25.385 and all of them showing the same thing

NOTE Confidence: 0.794596277777778

00:25:25.438 --> 00:25:27.307 is that the molecular IPS is better.

NOTE Confidence: 0.794596277777778

00:25:27.310 --> 00:25:29.934 And therefore I think we should really try

NOTE Confidence: 0.794596277777778

00:25:29.934 --> 00:25:33.139 to get it calculated on all of our patients,

NOTE Confidence: 0.794596277777778

00:25:33.140 --> 00:25:35.079 but of course that's going to require

NOTE Confidence: 0.794596277777778

00:25:35.079 --> 00:25:37.100 you to give them molecular data.

NOTE Confidence: 0.794596277777778

00:25:37.100 --> 00:25:39.752 So we talked about diagnosis classification

NOTE Confidence: 0.794596277777778

00:25:39.752 --> 00:25:42.160 prognosis and the response criteria.

NOTE Confidence: 0.794596277777778

00:25:42.160 --> 00:25:44.200 And response criteria have been

NOTE Confidence: 0.794596277777778

00:25:44.200 --> 00:25:46.695 somewhat problematic in MD S because

NOTE Confidence: 0.794596277777778

00:25:46.695 --> 00:25:49.017 they have contributed to some of

NOTE Confidence: 0.794596277777778

00:25:49.017 --> 00:25:51.144 the delayed drug development in

NOTE Confidence: 0.794596277777778

00:25:51.144 --> 00:25:53.374 my opinion by introducing data,

NOTE Confidence: 0.794596277777778

00:25:53.380 --> 00:25:55.056 molecular response responses that

NOTE Confidence: 0.794596277777778

00:25:55.056 --> 00:25:57.570 are sub optimal such as model.

NOTE Confidence: 0.794596277777778

00:25:57.570 --> 00:26:00.069 PR which has never been correlated with

NOTE Confidence: 0.794596277777778

00:26:00.069 --> 00:26:02.621 long term survival and at the same time

NOTE Confidence: 0.794596277777778

00:26:02.621 --> 00:26:04.780 used very high cutoff for hemoglobin,

NOTE Confidence: 0.794596277777778

00:26:04.780 --> 00:26:07.307 for example of 11 to denoise donate

NOTE Confidence: 0.794596277777778

00:26:07.307 --> 00:26:09.020 complete response which is very

NOTE Confidence: 0.794596277777778

00:26:09.020 --> 00:26:10.718 difficult to obtain in an Ms.

NOTE Confidence: 0.794596277777778

00:26:10.720 --> 00:26:11.080 patient.

NOTE Confidence: 0.794596277777778

00:26:11.080 --> 00:26:13.960 And there's this is beyond the scope of

NOTE Confidence: 0.794596277777778

00:26:13.960 --> 00:26:16.038 discussion today about all the issues

NOTE Confidence: 0.794596277777778

00:26:16.038 --> 00:26:18.300 that come with the response criteria.

NOTE Confidence: 0.794596277777778

00:26:18.300 --> 00:26:20.280 But finally an international panel,

NOTE Confidence: 0.794596277777778

00:26:20.280 --> 00:26:24.168 the IWG has revised the criteria so we

NOTE Confidence: 0.794596277777778

00:26:24.168 --> 00:26:27.760 have a new criteria for higher risk.

NOTE Confidence: 0.794596277777778

00:26:27.760 --> 00:26:28.150 Mrs.

NOTE Confidence: 0.794596277777778

00:26:28.150 --> 00:26:31.985 and I think this is going to address several

NOTE Confidence: 0.794596277777778

00:26:31.985 --> 00:26:36.630 of the shortcomings of the 2006 criteria.

NOTE Confidence: 0.794596277777778

00:26:36.630 --> 00:26:39.666 How about some of the clinical

NOTE Confidence: 0.794596277777778

00:26:39.666 --> 00:26:40.678 development abstracts?

NOTE Confidence: 0.794596277777778

00:26:40.680 --> 00:26:42.095 There were several important ones

NOTE Confidence: 0.794596277777778

00:26:42.095 --> 00:26:44.159 for both lower risk and higher risk.

NOTE Confidence: 0.794596277777778

00:26:44.160 --> 00:26:46.582 For lower risk MD as the treatment

NOTE Confidence: 0.794596277777778

00:26:46.582 --> 00:26:48.672 continues to be ESA erythropoiesis

NOTE Confidence: 0.794596277777778

00:26:48.672 --> 00:26:50.636 stimulating agents for most

NOTE Confidence: 0.794596277777778

00:26:50.636 --> 00:26:53.020 patients with lower risk MD S.

NOTE Confidence: 0.794596277777778

00:26:53.020 --> 00:26:54.840 How about for patients who have deletion?

NOTE Confidence: 0.794596277777778

00:26:54.840 --> 00:26:59.046 5Q Lenalidomide is an important drug.

NOTE Confidence: 0.74674568

00:26:59.050 --> 00:27:00.718 Lenalidomide is currently approved

NOTE Confidence: 0.74674568

00:27:00.718 --> 00:27:03.572 for lower risk deletion 5Q DS patients

NOTE Confidence: 0.74674568

00:27:03.572 --> 00:27:05.148 who are transfusion dependent.

NOTE Confidence: 0.74674568

00:27:05.150 --> 00:27:06.766 So this important abstract,

NOTE Confidence: 0.74674568

00:27:06.766 --> 00:27:09.190 this is a randomized phase three

NOTE Confidence: 0.74674568

00:27:09.263 --> 00:27:11.453 trial looked at giving Lenalidomide

NOTE Confidence: 0.74674568

00:27:11.453 --> 00:27:14.090 in patients with Delphi Q lower risk

NOTE Confidence: 0.74674568

00:27:14.090 --> 00:27:16.070 who are not yet transfusion dependent.

NOTE Confidence: 0.74674568

00:27:16.070 --> 00:27:18.032 As you can see the criteria

NOTE Confidence: 0.74674568

00:27:18.032 --> 00:27:19.889 eligibility anemia of less than 12.

NOTE Confidence: 0.74674568

00:27:19.890 --> 00:27:21.318 So if you have a hemoglobin of

NOTE Confidence: 0.74674568

00:27:21.318 --> 00:27:23.240 10 or 11 and you are symptomatic.

NOTE Confidence: 0.74674568

00:27:23.240 --> 00:27:25.109 Even if you are not needing transfusions,

NOTE Confidence: 0.74674568

00:27:25.110 --> 00:27:26.909 you would be eligible for this trial.

NOTE Confidence: 0.74674568

00:27:26.910 --> 00:27:28.574 Patients were randomized to

NOTE Confidence: 0.74674568

00:27:28.574 --> 00:27:31.070 Lenalidomide in a time limited fashion,

NOTE Confidence: 0.74674568

00:27:31.070 --> 00:27:32.060 meaning that you are getting

NOTE Confidence: 0.74674568

00:27:32.060 --> 00:27:33.330 the drug only for two years,

NOTE Confidence: 0.74674568

00:27:33.330 --> 00:27:36.170 it's not continuous versus placebo.

NOTE Confidence: 0.74674568

00:27:36.170 --> 00:27:38.347 And then the patient who are monitored

NOTE Confidence: 0.74674568

00:27:38.347 --> 00:27:41.027 and this is the top line result of

NOTE Confidence: 0.74674568

00:27:41.027 --> 00:27:43.201 this study is that Lenalidomide has

NOTE Confidence: 0.74674568

00:27:43.201 --> 00:27:45.346 significantly lower the chance of

NOTE Confidence: 0.74674568

00:27:45.346 --> 00:27:47.554 needing regular transfusions as well

NOTE Confidence: 0.74674568

00:27:47.554 --> 00:27:50.458 as delayed the time to transition

NOTE Confidence: 0.74674568

00:27:50.458 --> 00:27:53.050 dependency significantly more than six years.

NOTE Confidence: 0.74674568

00:27:53.050 --> 00:27:54.910 For patients who are only related

NOTE Confidence: 0.74674568

00:27:54.910 --> 00:27:57.143 to mild compared to patients who are

NOTE Confidence: 0.74674568

00:27:57.143 --> 00:27:59.003 getting a placebo and also induced

NOTE Confidence: 0.74674568

00:27:59.003 --> 00:28:01.352 a lot of cytogenetic responses and

NOTE Confidence: 0.74674568

00:28:01.352 --> 00:28:02.537 their safety profile,

NOTE Confidence: 0.74674568

00:28:02.540 --> 00:28:05.275 both hematological and and non

NOTE Confidence: 0.74674568

00:28:05.275 --> 00:28:08.010 hematological was generally well tolerated.

NOTE Confidence: 0.74674568

00:28:08.010 --> 00:28:09.564 So I think this could potentially

NOTE Confidence: 0.74674568

00:28:09.564 --> 00:28:12.027 lead to a major change in practice in

NOTE Confidence: 0.74674568

00:28:12.027 --> 00:28:13.399 earlier initiation of Lenalidomide

NOTE Confidence: 0.74674568

00:28:13.399 --> 00:28:15.729 and this is one thing that I think

NOTE Confidence: 0.74674568

00:28:15.729 --> 00:28:17.604 is important to consider in patients

NOTE Confidence: 0.74674568

00:28:17.604 --> 00:28:20.453 with deletion 5Q who are anemic but

NOTE Confidence: 0.74674568

00:28:20.453 --> 00:28:23.019 not yet transfusion dependent.

NOTE Confidence: 0.74674568

00:28:23.020 --> 00:28:25.456 The Middle East trial which many of

NOTE Confidence: 0.74674568

00:28:25.456 --> 00:28:29.220 you have contributed to when it was ongoing.

NOTE Confidence: 0.74674568

00:28:29.220 --> 00:28:31.901 This trial led to the approval of

NOTE Confidence: 0.74674568

00:28:31.901 --> 00:28:33.758 Los Battleship the transforming

NOTE Confidence: 0.74674568

00:28:33.758 --> 00:28:36.654 growth factor pathway drug that is

NOTE Confidence: 0.74674568

00:28:36.654 --> 00:28:39.020 illegal trap that has been shown in

NOTE Confidence: 0.74674568

00:28:39.093 --> 00:28:41.628 patients with RingCentral Plast Mrs.

NOTE Confidence: 0.74674568

00:28:41.630 --> 00:28:44.190 with ring sideroblasts to improve

NOTE Confidence: 0.74674568

00:28:44.190 --> 00:28:45.214 transition independence.

NOTE Confidence: 0.74674568

00:28:45.220 --> 00:28:46.781 You can see this is the New

NOTE Confidence: 0.74674568

00:28:46.781 --> 00:28:47.940 England Journal of Medicine,

NOTE Confidence: 0.74674568

00:28:47.940 --> 00:28:50.369 a paper that led to the approval

NOTE Confidence: 0.74674568

00:28:50.370 --> 00:28:52.346 38% transfusion independence we.

NOTE Confidence: 0.74674568

00:28:52.346 --> 00:28:54.816 Published an update from that

NOTE Confidence: 0.74674568

00:28:54.816 --> 00:28:56.978 study in 2022 showing that the

NOTE Confidence: 0.74674568

00:28:56.978 --> 00:28:58.788 responses would lose better ship,

NOTE Confidence: 0.74674568

00:28:58.790 --> 00:29:00.722 were long lasting and not only

NOTE Confidence: 0.74674568

00:29:00.722 --> 00:29:02.010 limited to transfusion dependence,

NOTE Confidence: 0.74674568

00:29:02.010 --> 00:29:04.873 but there was a lot of improvement

NOTE Confidence: 0.74674568

00:29:04.873 --> 00:29:07.272 in hematologic parameters as well as

NOTE Confidence: 0.74674568

00:29:07.272 --> 00:29:09.480 significant reduction in the red blood

NOTE Confidence: 0.74674568

00:29:09.480 --> 00:29:12.472 cell transfusion among those who did

NOTE Confidence: 0.74674568

00:29:12.472 --> 00:29:15.027 not fully achieve transfusion independence.

NOTE Confidence: 0.74674568

00:29:15.030 --> 00:29:15.484 However,

NOTE Confidence: 0.74674568

00:29:15.484 --> 00:29:18.208 the approval was after SF failure

NOTE Confidence: 0.74674568

00:29:18.210 --> 00:29:19.750 for patients who have Ms.

NOTE Confidence: 0.74674568

00:29:19.750 --> 00:29:20.974 with ring sideroblasts,

NOTE Confidence: 0.74674568

00:29:20.974 --> 00:29:23.630 so the commands trial this is a phase three.

NOTE Confidence: 0.74674568

00:29:23.630 --> 00:29:24.017 Well,

NOTE Confidence: 0.74674568

00:29:24.017 --> 00:29:26.339 uh of less partnership versus ESA,

NOTE Confidence: 0.74674568

00:29:26.340 --> 00:29:28.308 so this is a frontline treatment

NOTE Confidence: 0.74674568

00:29:28.308 --> 00:29:30.037 where patients were randomized to

NOTE Confidence: 0.74674568

00:29:30.037 --> 00:29:31.832 receive either lose partnership or

NOTE Confidence: 0.74674568

00:29:31.832 --> 00:29:33.268 erythropoietin in the frontline

NOTE Confidence: 0.74674568

00:29:33.330 --> 00:29:35.364 setting first treatment and not only

NOTE Confidence: 0.74674568

00:29:35.364 --> 00:29:36.995 in patients with RingCentral Press,

NOTE Confidence: 0.74674568

00:29:36.995 --> 00:29:38.920 but also in patients without ring syndrome.

NOTE Confidence: 0.74674568

00:29:38.920 --> 00:29:42.028 Last and this trial was a large

NOTE Confidence: 0.74674568

00:29:42.028 --> 00:29:42.916 international trial,

NOTE Confidence: 0.74674568

00:29:42.920 --> 00:29:45.560 more than 350 patients were enrolled

NOTE Confidence: 0.74674568

00:29:45.560 --> 00:29:48.454 including here at TL and data were

NOTE Confidence: 0.74674568

00:29:48.454 --> 00:29:51.100 not presented from this trial in ASH,

NOTE Confidence: 0.74674568

00:29:51.100 --> 00:29:53.662 but there was a press release from

NOTE Confidence: 0.74674568

00:29:53.662 --> 00:29:54.394 the manufacturer.

NOTE Confidence: 0.74674568

00:29:54.400 --> 00:29:54.892 Uh,

NOTE Confidence: 0.74674568

00:29:54.892 --> 00:29:56.368 basically declaring positive

NOTE Confidence: 0.74674568

00:29:56.368 --> 00:29:58.828 results for the primary endpoint.

NOTE Confidence: 0.74674568

00:29:58.830 --> 00:30:00.950 So this is I think could be an

NOTE Confidence: 0.74674568

00:30:00.950 --> 00:30:01.980 important development in the

NOTE Confidence: 0.74674568

00:30:01.980 --> 00:30:03.829 management of lower risk MD S in 2023.

NOTE Confidence: 0.74674568

00:30:03.829 --> 00:30:06.520 We are hoping to see the data later this

NOTE Confidence: 0.838432266190476

00:30:06.587 --> 00:30:08.963 year describing the impact of Los

NOTE Confidence: 0.838432266190476

00:30:08.963 --> 00:30:11.140 leadership in the frontline setting.

NOTE Confidence: 0.838432266190476

00:30:11.140 --> 00:30:14.467 Another free trial that. Was open here.

NOTE Confidence: 0.838432266190476

00:30:14.467 --> 00:30:16.210 TL is the trial that looked at

NOTE Confidence: 0.838432266190476

00:30:16.271 --> 00:30:18.155 the imetelstat which is a first

NOTE Confidence: 0.838432266190476

00:30:18.155 --> 00:30:19.517 in class telomerase inhibitor.

NOTE Confidence: 0.838432266190476

00:30:19.517 --> 00:30:22.853 This is an IV drug that's given every

NOTE Confidence: 0.838432266190476

00:30:22.853 --> 00:30:26.189 four weeks and phase two data single arm.

NOTE Confidence: 0.838432266190476

00:30:26.190 --> 00:30:28.275 Phase two data previously published

NOTE Confidence: 0.838432266190476

00:30:28.275 --> 00:30:30.844 have shown that among patients who

NOTE Confidence: 0.838432266190476

00:30:30.844 --> 00:30:32.504 are heavily transfused without

NOTE Confidence: 0.838432266190476

00:30:32.504 --> 00:30:35.580 deletion 5Q but had lower risk.

NOTE Confidence: 0.838432266190476

00:30:35.580 --> 00:30:38.115 MD S 38 patients have higher

NOTE Confidence: 0.838432266190476

00:30:38.115 --> 00:30:39.695 rates of transfusion independence.

NOTE Confidence: 0.838432266190476

00:30:39.700 --> 00:30:42.160 With this drug 40% achieve

NOTE Confidence: 0.838432266190476

00:30:42.160 --> 00:30:43.144 transfusion independence.

NOTE Confidence: 0.838432266190476

00:30:43.150 --> 00:30:44.602 This was previously published.

NOTE Confidence: 0.838432266190476

00:30:44.602 --> 00:30:47.217 What was presented in ASH is an

NOTE Confidence: 0.838432266190476

00:30:47.217 --> 00:30:49.467 update on the patients who had

NOTE Confidence: 0.838432266190476

00:30:49.467 --> 00:30:51.210 transfusion independence on the drug,

NOTE Confidence: 0.838432266190476

00:30:51.210 --> 00:30:52.812 which lasted more than one year

NOTE Confidence: 0.838432266190476

00:30:52.812 --> 00:30:54.439 and there were eleven out of the

NOTE Confidence: 0.918951911

00:30:56.830 --> 00:31:00.086 3829%. And you can see here that among

NOTE Confidence: 0.918951911

00:31:00.086 --> 00:31:02.634 those patients there was significant

NOTE Confidence: 0.918951911

00:31:02.634 --> 00:31:05.524 durability of the transition independence,

NOTE Confidence: 0.918951911

00:31:05.530 --> 00:31:07.490 92 weeks of transfusion independence,

NOTE Confidence: 0.918951911

00:31:07.490 --> 00:31:09.401 but also the mean change in the

NOTE Confidence: 0.918951911

00:31:09.401 --> 00:31:10.850 hemoglobin was quite impressive.

NOTE Confidence: 0.918951911

00:31:10.850 --> 00:31:13.566 The median increase was almost 3 grams.

NOTE Confidence: 0.918951911

00:31:13.570 --> 00:31:14.800 So those are not patients.

NOTE Confidence: 0.918951911

00:31:14.800 --> 00:31:16.288 Going from hemoglobin 8 to 9,

NOTE Confidence: 0.918951911

00:31:16.290 --> 00:31:18.546 this is someone going from 8 to 11.

NOTE Confidence: 0.918951911

00:31:18.550 --> 00:31:22.288 So that's certainly is a meaningful benefit.

NOTE Confidence: 0.918951911

00:31:22.290 --> 00:31:24.670 But importantly there was a press release

NOTE Confidence: 0.918951911

00:31:24.670 --> 00:31:27.306 also this was a year of press releases,

NOTE Confidence: 0.918951911

00:31:27.310 --> 00:31:29.130 all our risk and bias,

NOTE Confidence: 0.918951911

00:31:29.130 --> 00:31:31.590 the Imerge phase three trial,

NOTE Confidence: 0.918951911

00:31:31.590 --> 00:31:33.792 the top line results also confirmed

NOTE Confidence: 0.918951911

00:31:33.792 --> 00:31:36.702 that advantage of the phase two showing

NOTE Confidence: 0.918951911

00:31:36.702 --> 00:31:38.530 transition independence with the

NOTE Confidence: 0.918951911

00:31:38.530 --> 00:31:41.190 loss would initially start in 40% of

NOTE Confidence: 0.918951911

00:31:41.190 --> 00:31:43.290 patients who have received this drug

NOTE Confidence: 0.918951911

00:31:43.290 --> 00:31:45.946 and this drug is now in front of the.

NOTE Confidence: 0.918951911

00:31:45.950 --> 00:31:48.414 They are also in consideration for approval.

NOTE Confidence: 0.918951911

00:31:48.420 --> 00:31:50.366 We are hoping to see the data

NOTE Confidence: 0.918951911

00:31:50.366 --> 00:31:51.580 also later this year.

NOTE Confidence: 0.918951911

00:31:51.580 --> 00:31:53.100 But between these two drugs,

NOTE Confidence: 0.918951911

00:31:53.100 --> 00:31:54.976 I think there could be a significant

NOTE Confidence: 0.918951911

00:31:54.976 --> 00:31:56.970 change in the landscape of management of

NOTE Confidence: 0.918951911

00:31:56.970 --> 00:32:00.640 lower risk MD S about higher risk MD S.

NOTE Confidence: 0.918951911

00:32:00.640 --> 00:32:03.209 So at Jamies have been a significant.

NOTE Confidence: 0.846365137272727

00:32:05.290 --> 00:32:07.796 Basically in terms of helping patients with

NOTE Confidence: 0.846365137272727

00:32:07.796 --> 00:32:10.782 high risk MD S but real life data such as

NOTE Confidence: 0.846365137272727

00:32:10.782 --> 00:32:13.232 the one I'm showing you here showed that

NOTE Confidence: 0.846365137272727

00:32:13.232 --> 00:32:15.800 the benefit from HM is is suboptimal.

NOTE Confidence: 0.846365137272727

00:32:15.800 --> 00:32:18.302 The median survival is only 11 to 17 months.

NOTE Confidence: 0.846365137272727

00:32:18.310 --> 00:32:19.482 Once they stop working,

NOTE Confidence: 0.846365137272727

00:32:19.482 --> 00:32:21.730 the survival is 5 to six months.

NOTE Confidence: 0.846365137272727

00:32:21.730 --> 00:32:23.970 So we certainly need improvements.

NOTE Confidence: 0.846365137272727

00:32:23.970 --> 00:32:26.392 However, many of the drugs that were

NOTE Confidence: 0.846365137272727

00:32:26.392 --> 00:32:29.602 added to HMA's have not unfortunately

NOTE Confidence: 0.846365137272727

00:32:29.602 --> 00:32:31.486 shown any benefit.

NOTE Confidence: 0.846365137272727

00:32:31.490 --> 00:32:33.289 We have a big graveyard of drugs.

NOTE Confidence: 0.846365137272727

00:32:33.290 --> 00:32:35.634 You can see some of them listed here.

NOTE Confidence: 0.846365137272727

00:32:35.640 --> 00:32:37.761 That once combined with HM is initially

NOTE Confidence: 0.846365137272727

00:32:37.761 --> 00:32:40.140 they showed good data in single arm trials,

NOTE Confidence: 0.846365137272727

00:32:40.140 --> 00:32:42.068 but once you have the phase three trials

NOTE Confidence: 0.846365137272727

00:32:42.068 --> 00:32:44.039 or the randomized phase two trials,

NOTE Confidence: 0.846365137272727

00:32:44.040 --> 00:32:46.248 the results were negative.

NOTE Confidence: 0.846365137272727

00:32:46.248 --> 00:32:48.225 However, we have other drugs that

NOTE Confidence: 0.846365137272727

00:32:48.225 --> 00:32:50.713 are now in phase three trials and we

NOTE Confidence: 0.846365137272727

00:32:50.713 --> 00:32:52.699 are optimistic about some of those.

NOTE Confidence: 0.846365137272727

00:32:52.700 --> 00:32:55.430 You can see here 6 randomized phase

NOTE Confidence: 0.846365137272727

00:32:55.430 --> 00:32:58.039 three trials ongoing in the high risk

NOTE Confidence: 0.846365137272727

00:32:58.039 --> 00:33:00.440 MD S sitting in combination with HMS.

NOTE Confidence: 0.846365137272727

00:33:00.440 --> 00:33:02.337 The two trials that you see the

NOTE Confidence: 0.846365137272727

00:33:02.337 --> 00:33:04.093 drug listed in black people need

NOTE Confidence: 0.846365137272727

00:33:04.093 --> 00:33:05.648 to start and APR 246.

NOTE Confidence: 0.846365137272727

00:33:05.648 --> 00:33:05.982 Unfortunately,

NOTE Confidence: 0.846365137272727

00:33:05.982 --> 00:33:08.320 those two threads have read out as

NOTE Confidence: 0.846365137272727

00:33:08.387 --> 00:33:10.347 negative for the primary endpoint.

NOTE Confidence: 0.846365137272727

00:33:10.350 --> 00:33:12.380 But the other four trials with venetoclax,

NOTE Confidence: 0.846365137272727

00:33:12.380 --> 00:33:13.234 sabatelli map,

NOTE Confidence: 0.846365137272727

00:33:13.234 --> 00:33:15.369 negroli Mab and Tammy paroxetine,

NOTE Confidence: 0.846365137272727

00:33:15.370 --> 00:33:16.962 all of those are ongoing and I'm going

NOTE Confidence: 0.846365137272727

00:33:16.962 --> 00:33:18.625 to tell you a little bit about them.

NOTE Confidence: 0.846365137272727

00:33:18.630 --> 00:33:19.030 However,

NOTE Confidence: 0.846365137272727

00:33:19.030 --> 00:33:22.230 none of those four trials have yet reported.

NOTE Confidence: 0.846365137272727

00:33:22.230 --> 00:33:24.294 But I think those are trials

NOTE Confidence: 0.846365137272727

00:33:24.294 --> 00:33:26.690 that are important for the field

NOTE Confidence: 0.846365137272727

00:33:26.690 --> 00:33:28.109 because they potentially,

NOTE Confidence: 0.846365137272727

00:33:28.110 --> 00:33:29.256 if any of them are positive,

NOTE Confidence: 0.846365137272727

00:33:29.260 --> 00:33:31.720 it could change the landscape of

NOTE Confidence: 0.846365137272727

00:33:31.720 --> 00:33:34.635 treatment of high risk MD S so

NOTE Confidence: 0.846365137272727

00:33:34.635 --> 00:33:36.635 another important reminder is that.

NOTE Confidence: 0.846365137272727

00:33:36.640 --> 00:33:38.225 Patients with MDD should be

NOTE Confidence: 0.846365137272727

00:33:38.225 --> 00:33:39.493 considered for transplant when

NOTE Confidence: 0.846365137272727

00:33:39.493 --> 00:33:41.118 they have higher risk disease.

NOTE Confidence: 0.846365137272727

00:33:41.120 --> 00:33:43.604 If you just keep the patient on HMA alone

NOTE Confidence: 0.846365137272727

00:33:43.604 --> 00:33:45.919 the long term survival is very poor,

NOTE Confidence: 0.846365137272727

00:33:45.920 --> 00:33:47.767 4% for higher risk Ms. patients.

NOTE Confidence: 0.846365137272727

00:33:47.767 --> 00:33:50.089 And now we have randomized data.

NOTE Confidence: 0.846365137272727

00:33:50.090 --> 00:33:52.640 This is biological assignment trial.

NOTE Confidence: 0.846365137272727

00:33:52.640 --> 00:33:55.322 If you have a donor versus no donor and

NOTE Confidence: 0.846365137272727

00:33:55.322 --> 00:33:58.020 that showed up to the age of 75 that

NOTE Confidence: 0.846365137272727

00:33:58.020 --> 00:34:00.330 your overall survival could be doubled.

NOTE Confidence: 0.846365137272727

00:34:00.330 --> 00:34:02.130 The three-year survival for patients

NOTE Confidence: 0.846365137272727

00:34:02.130 --> 00:34:04.458 who had a donor was 50% compared

NOTE Confidence: 0.846365137272727

00:34:04.458 --> 00:34:06.334 to 26% and again this is up.

NOTE Confidence: 0.846365137272727

00:34:06.340 --> 00:34:08.030 At the age of 75,

NOTE Confidence: 0.846365137272727

00:34:08.030 --> 00:34:10.221 many patients are being told they are

NOTE Confidence: 0.846365137272727

00:34:10.221 --> 00:34:11.853 not candidate for transplant because

NOTE Confidence: 0.846365137272727

00:34:11.853 --> 00:34:14.065 they are late 60s or early 70s.

NOTE Confidence: 0.846365137272727

00:34:14.070 --> 00:34:16.630 But if the patient is otherwise good shape,

NOTE Confidence: 0.846365137272727

00:34:16.630 --> 00:34:18.646 I would strongly recommend that you

NOTE Confidence: 0.846365137272727

00:34:18.646 --> 00:34:21.840 refer them to discuss transplant.

NOTE Confidence: 0.846365137272727

00:34:21.840 --> 00:34:23.640 Venetoclax is approved for all

NOTE Confidence: 0.846365137272727

00:34:23.640 --> 00:34:25.440 their unfit patients with AML.

NOTE Confidence: 0.846365137272727

00:34:25.440 --> 00:34:25.752 However,

NOTE Confidence: 0.846365137272727

00:34:25.752 --> 00:34:27.624 the data in frontline in high

NOTE Confidence: 0.846365137272727

00:34:27.624 --> 00:34:29.858 risk MD S has been promising.

NOTE Confidence: 0.846365137272727

00:34:29.860 --> 00:34:31.900 But this is single arm trial.

NOTE Confidence: 0.846365137272727

00:34:31.900 --> 00:34:34.144 We have previously published a trial

NOTE Confidence: 0.846365137272727

00:34:34.144 --> 00:34:36.492 that Yale participated in in the

NOTE Confidence: 0.846365137272727

00:34:36.492 --> 00:34:38.060 relapse refractory setting where

NOTE Confidence: 0.846365137272727

00:34:38.060 --> 00:34:40.337 venetoclax has been added after HMA

NOTE Confidence: 0.846365137272727

00:34:40.337 --> 00:34:42.257 failure and the Verona trial which

NOTE Confidence: 0.846365137272727

00:34:42.257 --> 00:34:44.380 also was open at TL randomized

NOTE Confidence: 0.846365137272727

00:34:44.380 --> 00:34:46.600 patients to receive Asia versus Asia

NOTE Confidence: 0.846365137272727

00:34:46.668 --> 00:34:48.840 when this trial has fully accrued.

NOTE Confidence: 0.846365137272727

00:34:48.840 --> 00:34:50.751 And we are waiting for the results

NOTE Confidence: 0.846365137272727

00:34:50.751 --> 00:34:51.800 of this trial to.

NOTE Confidence: 0.846365137272727

00:34:51.800 --> 00:34:53.720 Look at the role of venetoclax

NOTE Confidence: 0.846365137272727

00:34:53.720 --> 00:34:55.000 in high risk MD

NOTE Confidence: 0.783587409090909

00:34:55.071 --> 00:34:56.842 S. Another I think interesting

NOTE Confidence: 0.783587409090909

00:34:56.842 --> 00:34:58.882 molecule that we've been part

NOTE Confidence: 0.783587409090909

00:34:58.882 --> 00:35:01.265 of is sabatelli map and item 3.

NOTE Confidence: 0.783587409090909

00:35:01.270 --> 00:35:04.063 So tem three basically is an inhibitory

NOTE Confidence: 0.783587409090909

00:35:04.063 --> 00:35:07.468 receptor that is not only present on T

NOTE Confidence: 0.783587409090909

00:35:07.468 --> 00:35:09.603 cells like regular immune checkpoints,

NOTE Confidence: 0.783587409090909

00:35:09.610 --> 00:35:11.810 but this is also present on some of

NOTE Confidence: 0.783587409090909

00:35:11.810 --> 00:35:13.859 the leukemia stem cells and the blast.

NOTE Confidence: 0.783587409090909

00:35:13.860 --> 00:35:17.328 So Sabato Lima could basically be

NOTE Confidence: 0.783587409090909

00:35:17.328 --> 00:35:19.456 targeting both the immune system

NOTE Confidence: 0.783587409090909

00:35:19.456 --> 00:35:21.066 as an immune checkpoint inhibitor,

NOTE Confidence: 0.783587409090909

00:35:21.070 --> 00:35:23.140 but also directly attacking the

NOTE Confidence: 0.783587409090909

00:35:23.140 --> 00:35:25.710 plus and the leukemia stem cells.

NOTE Confidence: 0.783587409090909

00:35:25.710 --> 00:35:27.725 Early data have suggested activity

NOTE Confidence: 0.783587409090909

00:35:27.725 --> 00:35:30.139 in the clinical setting and based

NOTE Confidence: 0.783587409090909

00:35:30.139 --> 00:35:32.414 on this around the phase two trial

NOTE Confidence: 0.783587409090909

00:35:32.420 --> 00:35:34.135 which we had open here at TL,

NOTE Confidence: 0.783587409090909

00:35:34.140 --> 00:35:37.040 the stimulus MS1 randomized patients

NOTE Confidence: 0.783587409090909

00:35:37.040 --> 00:35:40.502 to receive Sabato Lima with HMA

NOTE Confidence: 0.783587409090909

00:35:40.502 --> 00:35:43.328 versus HMA alone and the primary

NOTE Confidence: 0.783587409090909

00:35:43.328 --> 00:35:45.559 endpoint was CR and PFS.

NOTE Confidence: 0.783587409090909

00:35:45.560 --> 00:35:48.157 We presented this data in in ASH.

NOTE Confidence: 0.783587409090909

00:35:48.160 --> 00:35:50.320 This was the only randomized phase

NOTE Confidence: 0.783587409090909

00:35:50.320 --> 00:35:52.495 two trial presented in ASH 2022.

NOTE Confidence: 0.783587409090909

00:35:52.495 --> 00:35:54.395 Unfortunately the primary endpoint

NOTE Confidence: 0.783587409090909

00:35:54.395 --> 00:35:55.820 on this randomized.

NOTE Confidence: 0.783587409090909

00:35:55.820 --> 00:35:57.150 This too was not reached.

NOTE Confidence: 0.783587409090909

00:35:57.150 --> 00:35:59.020 There was still no significant

NOTE Confidence: 0.783587409090909

00:35:59.020 --> 00:36:00.890 difference in CR and PFS.

NOTE Confidence: 0.783587409090909

00:36:00.890 --> 00:36:02.498 But what I attract your attention

NOTE Confidence: 0.783587409090909

00:36:02.498 --> 00:36:04.412 to is that there was late separation

NOTE Confidence: 0.783587409090909

00:36:04.412 --> 00:36:06.644 of the curves and the PFS was eleven

NOTE Confidence: 0.783587409090909

00:36:06.644 --> 00:36:08.666 months compared to 8.5 months,

NOTE Confidence: 0.783587409090909

00:36:08.666 --> 00:36:11.206 which would be potentially consistent

NOTE Confidence: 0.783587409090909

00:36:11.206 --> 00:36:14.185 with delayed onset of action seen

NOTE Confidence: 0.783587409090909

00:36:14.185 --> 00:36:16.510 with immune checkpoint inhibitors and

NOTE Confidence: 0.783587409090909

00:36:16.510 --> 00:36:19.330 importantly among patients who achieve CR.

NOTE Confidence: 0.783587409090909

00:36:19.330 --> 00:36:20.947 So the CR rate was not increased,

NOTE Confidence: 0.783587409090909

00:36:20.950 --> 00:36:22.790 but those who achieved CR,

NOTE Confidence: 0.783587409090909

00:36:22.790 --> 00:36:24.659 the duration of the CR was doubled

NOTE Confidence: 0.783587409090909

00:36:24.659 --> 00:36:26.109 for the combination compared to.

NOTE Confidence: 0.783587409090909

00:36:26.110 --> 00:36:28.784 I mean one of therapy again suggesting

NOTE Confidence: 0.783587409090909

00:36:28.784 --> 00:36:31.068 potentially that there could be a

NOTE Confidence: 0.783587409090909

00:36:31.068 --> 00:36:32.853 deeper response and more durable

NOTE Confidence: 0.783587409090909

00:36:32.853 --> 00:36:34.950 response with with the combination.

NOTE Confidence: 0.783587409090909

00:36:34.950 --> 00:36:38.548 But of course these are exploratory analysis.

NOTE Confidence: 0.783587409090909

00:36:38.550 --> 00:36:41.581 The phase three trial is already also

NOTE Confidence: 0.783587409090909

00:36:41.581 --> 00:36:43.590 fully accrued. It was open at Yale.

NOTE Confidence: 0.783587409090909

00:36:43.590 --> 00:36:45.390 Some of the care centers have

NOTE Confidence: 0.783587409090909

00:36:45.390 --> 00:36:47.610 contributed patients to this royal

NOTE Confidence: 0.783587409090909

00:36:47.610 --> 00:36:49.830 which randomized patients to receive

NOTE Confidence: 0.783587409090909

00:36:49.894 --> 00:36:51.674 Sabathia versus sorry Sabato Lima

NOTE Confidence: 0.783587409090909

00:36:51.674 --> 00:36:54.146 with HM versus is alone and this

NOTE Confidence: 0.783587409090909

00:36:54.146 --> 00:36:56.018 trial is fully accrued and we

NOTE Confidence: 0.783587409090909

00:36:56.018 --> 00:36:57.829 are waiting for the results.

NOTE Confidence: 0.783587409090909

00:36:57.829 --> 00:37:00.580 Negroli Mab is another drug that had

NOTE Confidence: 0.783587409090909

00:37:00.663 --> 00:37:02.945 attracted a lot of attention in AML

NOTE Confidence: 0.783587409090909

00:37:02.945 --> 00:37:05.980 and MD S This is this works on the on

NOTE Confidence: 0.783587409090909

00:37:05.980 --> 00:37:09.267 the CD 47 but don't Eat Me Signal CD

NOTE Confidence: 0.783587409090909

00:37:09.267 --> 00:37:12.554 47 is expressed in MDR cells and it.

NOTE Confidence: 0.783587409090909

00:37:12.554 --> 00:37:15.074 Can evade phagocytosis so inhibiting

NOTE Confidence: 0.783587409090909

00:37:15.074 --> 00:37:19.160 it with the anti CD 47 agent can

NOTE Confidence: 0.783587409090909

00:37:19.160 --> 00:37:21.140 lead to increased phagocytosis

NOTE Confidence: 0.783587409090909

00:37:21.140 --> 00:37:24.079 of blasts and clinical benefit.

NOTE Confidence: 0.783587409090909

00:37:24.080 --> 00:37:26.974 This is a phase two study of

NOTE Confidence: 0.783587409090909

00:37:26.974 --> 00:37:28.882 margaroli map with azacitidine

NOTE Confidence: 0.783587409090909

00:37:28.882 --> 00:37:30.313 showing promising responses,

NOTE Confidence: 0.783587409090909

00:37:30.320 --> 00:37:32.560 but this was a single arm trial.

NOTE Confidence: 0.783587409090909

00:37:32.560 --> 00:37:34.816 They are ongoing phase three trials

NOTE Confidence: 0.783587409090909

00:37:34.816 --> 00:37:36.640 with this drug margaroli map.

NOTE Confidence: 0.783587409090909

00:37:36.640 --> 00:37:39.772 And we also have a study coming ATL where

NOTE Confidence: 0.783587409090909

00:37:39.772 --> 00:37:43.157 oral HMA is being combined with Negroli map.

NOTE Confidence: 0.783587409090909

00:37:43.160 --> 00:37:45.827 This is a trial in progress abstract

NOTE Confidence: 0.783587409090909

00:37:45.827 --> 00:37:47.865 presented in ASH that discusses

NOTE Confidence: 0.783587409090909

00:37:47.865 --> 00:37:49.920 the design of this trial.

NOTE Confidence: 0.783587409090909

00:37:49.920 --> 00:37:52.769 And we have another anti CD 47

NOTE Confidence: 0.783587409090909

00:37:52.769 --> 00:37:58.261 agent that is being tested and for

NOTE Confidence: 0.783587409090909

00:37:58.261 --> 00:38:03.187 MSDS and AML after HMA failure.

NOTE Confidence: 0.783587409090909

00:38:03.190 --> 00:38:05.398 So a lot of drugs are being tested

NOTE Confidence: 0.783587409090909

00:38:05.398 --> 00:38:07.848 in MD S This is showing them of

NOTE Confidence: 0.783587409090909

00:38:07.848 --> 00:38:10.514 some of the trials that we had open

NOTE Confidence: 0.783587409090909

00:38:10.514 --> 00:38:12.584 or are in activation process that

NOTE Confidence: 0.508897156666667

00:38:12.590 --> 00:38:15.788 Tammy protein which is Arara agonist,

NOTE Confidence: 0.508897156666667

00:38:15.790 --> 00:38:18.070 super agonist.

NOTE Confidence: 0.508897156666667

00:38:18.070 --> 00:38:20.020 Aurora is basically over expressed in

NOTE Confidence: 0.508897156666667

00:38:20.020 --> 00:38:22.428 around half of the patients with MDS.

NOTE Confidence: 0.508897156666667

00:38:22.430 --> 00:38:24.705 So this is a phase three trial

NOTE Confidence: 0.508897156666667

00:38:24.705 --> 00:38:26.449 that randomizes patients to Asia

NOTE Confidence: 0.508897156666667

00:38:26.449 --> 00:38:27.865 Tami paroxetine versus Asia.

NOTE Confidence: 0.508897156666667

00:38:27.870 --> 00:38:29.994 This is an activation in addition

NOTE Confidence: 0.508897156666667

00:38:29.994 --> 00:38:32.190 to the single arm oral decitabine

NOTE Confidence: 0.508897156666667

00:38:32.190 --> 00:38:34.668 with macro for higher risk MD S

NOTE Confidence: 0.508897156666667

00:38:34.668 --> 00:38:37.051 and then for the lower risk we

NOTE Confidence: 0.508897156666667

00:38:37.051 --> 00:38:39.042 have an extension of the imetelstat

NOTE Confidence: 0.508897156666667

00:38:39.042 --> 00:38:41.429 sub study that I mentioned to you.

NOTE Confidence: 0.508897156666667

00:38:41.430 --> 00:38:44.302 So this is a single arm study that

NOTE Confidence: 0.508897156666667

00:38:44.302 --> 00:38:46.440 gives patients initially stat and

NOTE Confidence: 0.508897156666667

00:38:46.440 --> 00:38:47.990 this includes patients with HMA.

NOTE Confidence: 0.508897156666667

00:38:47.990 --> 00:38:49.642 Earlier or Lenalidomide failure.

NOTE Confidence: 0.508897156666667

00:38:49.642 --> 00:38:52.629 So I encourage you to refer patients

NOTE Confidence: 0.508897156666667

00:38:52.629 --> 00:38:54.829 who are transfusion dependent who

NOTE Confidence: 0.508897156666667

00:38:54.829 --> 00:38:57.100 have not responded or benefited

NOTE Confidence: 0.508897156666667

00:38:57.100 --> 00:38:59.280 from standard of care drugs.

NOTE Confidence: 0.508897156666667

00:38:59.280 --> 00:39:01.128 So this is my last slide and I'm

NOTE Confidence: 0.508897156666667

00:39:01.128 --> 00:39:03.058 happy to take any questions later.

NOTE Confidence: 0.508897156666667

00:39:03.060 --> 00:39:03.800 Thank you so much.

NOTE Confidence: 0.88455987

00:39:14.110 --> 00:39:16.868 OK, this will present now

NOTE Confidence: 0.88455987

00:39:16.868 --> 00:39:18.556 updates on acute leukemias.

NOTE Confidence: 0.831800535

00:39:20.060 --> 00:39:22.832 OK. So I'm going to start with

NOTE Confidence: 0.831800535

00:39:22.832 --> 00:39:25.320 AML and then move to a LL.

NOTE Confidence: 0.831800535

00:39:25.320 --> 00:39:27.268 I have no disclosures.

NOTE Confidence: 0.831800535

00:39:27.268 --> 00:39:29.703 So AML remains a disease

NOTE Confidence: 0.831800535

00:39:29.703 --> 00:39:32.160 with suboptimal outcomes.

NOTE Confidence: 0.831800535

00:39:32.160 --> 00:39:35.406 The five year relative survival is 30.5%

NOTE Confidence: 0.831800535

00:39:35.406 --> 00:39:38.814 and this is a disease of older adults.

NOTE Confidence: 0.831800535

00:39:38.820 --> 00:39:40.292 Median age at diagnosis

NOTE Confidence: 0.831800535

00:39:40.292 --> 00:39:43.672 is 68 and at death is 73.

NOTE Confidence: 0.831800535

00:39:43.672 --> 00:39:46.932 And so treatments that are

NOTE Confidence: 0.831800535

00:39:46.932 --> 00:39:49.980 efficacious either new agents or.

NOTE Confidence: 0.831800535

00:39:49.980 --> 00:39:51.026 New combinations,

NOTE Confidence: 0.831800535

00:39:51.026 --> 00:39:53.118 particularly that are tolerated

NOTE Confidence: 0.831800535

00:39:53.118 --> 00:39:56.149 by this age group are needed.

NOTE Confidence: 0.831800535

00:39:56.150 --> 00:39:59.041 The addition of an edit flex to

NOTE Confidence: 0.831800535

00:39:59.041 --> 00:40:00.588 hypomethylating agents improved CR

NOTE Confidence: 0.831800535

00:40:00.588 --> 00:40:04.610 rates to 65 to 70% in the frontline

NOTE Confidence: 0.831800535

00:40:04.610 --> 00:40:07.560 setting and older unfit AML.

NOTE Confidence: 0.831800535

00:40:07.560 --> 00:40:09.420 However.

NOTE Confidence: 0.831800535

00:40:09.420 --> 00:40:12.206 Longer term data from the Viale study

NOTE Confidence: 0.831800535

00:40:12.206 --> 00:40:15.425 has shown that only a minority of

NOTE Confidence: 0.831800535

00:40:15.425 --> 00:40:17.268 patients experience durable remission

NOTE Confidence: 0.831800535

00:40:17.268 --> 00:40:20.306 and survival such as it two years

NOTE Confidence: 0.831800535

00:40:20.306 --> 00:40:23.380 and in high risk groups such as TP53,

NOTE Confidence: 0.831800535

00:40:23.380 --> 00:40:24.220 mutant JML,

NOTE Confidence: 0.831800535

00:40:24.220 --> 00:40:26.740 but also flip three mutant AML.

NOTE Confidence: 0.831800535

00:40:26.740 --> 00:40:30.674 Particularly in older and unfit AML patients,

NOTE Confidence: 0.831800535

00:40:30.680 --> 00:40:35.356 they're continued to be very poor outcomes.

NOTE Confidence: 0.831800535

00:40:35.360 --> 00:40:38.160 As an example, in TP53 mutant AML,

NOTE Confidence: 0.831800535

00:40:38.160 --> 00:40:41.505 the median overall survival is 5 to 7 months.

NOTE Confidence: 0.831800535

00:40:41.505 --> 00:40:43.935 With our standard of care therapies,

NOTE Confidence: 0.831800535

00:40:43.940 --> 00:40:46.502 there's also a great need in

NOTE Confidence: 0.831800535

00:40:46.502 --> 00:40:48.693 relapsed refractory AML where the

NOTE Confidence: 0.831800535

00:40:48.693 --> 00:40:50.718 median overall survival and the

NOTE Confidence: 0.831800535

00:40:50.718 --> 00:40:53.298 unfit subgroup is 3 to 7 months.

NOTE Confidence: 0.827654426

00:40:57.430 --> 00:41:01.378 And so turning to the TP 53 mutated group,

NOTE Confidence: 0.827654426

00:41:01.378 --> 00:41:05.010 it is occurring this mutation in five

NOTE Confidence: 0.827654426

00:41:05.010 --> 00:41:08.170 to 10% of patients with the Novo AML

NOTE Confidence: 0.827654426

00:41:08.170 --> 00:41:10.926 and its enriched in therapy related

NOTE Confidence: 0.827654426

00:41:10.926 --> 00:41:14.240 AML and as noted before with standard

NOTE Confidence: 0.827654426

00:41:14.240 --> 00:41:18.219 of care the survival is poor less than

NOTE Confidence: 0.827654426

00:41:18.219 --> 00:41:20.754 one year including post transplant.

NOTE Confidence: 0.827654426

00:41:20.760 --> 00:41:24.090 And so doctor Zaiden discussed this

NOTE Confidence: 0.827654426

00:41:24.090 --> 00:41:27.699 agent Mike Roll Amab which targets

NOTE Confidence: 0.827654426

00:41:27.700 --> 00:41:30.916 CD-47 which has been called amyloid

NOTE Confidence: 0.827654426

00:41:30.920 --> 00:41:35.357 checkpoint and is a do not eat me signal

NOTE Confidence: 0.827654426

00:41:35.357 --> 00:41:39.050 and naval daver presented results from

NOTE Confidence: 0.827654426

00:41:39.050 --> 00:41:41.970 the phase one two study of the triplet

NOTE Confidence: 0.827654426

00:41:42.048 --> 00:41:44.694 of megola map on the venetta claxson,

NOTE Confidence: 0.827654426

00:41:44.700 --> 00:41:47.520 azacitidine backbone and

NOTE Confidence: 0.827654426

00:41:47.520 --> 00:41:50.102 newly diagnosed patients with.

NOTE Confidence: 0.827654426

00:41:50.102 --> 00:41:53.457 AML, a group of in in a group of

NOTE Confidence: 0.827654426

00:41:53.457 --> 00:41:55.792 patients that was heavily enriched

NOTE Confidence: 0.827654426

00:41:55.792 --> 00:41:58.860 for TP53 mutated AML and still

NOTE Confidence: 0.827654426

00:41:58.860 --> 00:42:02.712 what's being shown here and what was

NOTE Confidence: 0.827654426

00:42:02.712 --> 00:42:05.597 presented was a frontline cohort

NOTE Confidence: 0.827654426

00:42:05.597 --> 00:42:09.665 and separated into de Novo AML and

NOTE Confidence: 0.827654426

00:42:09.665 --> 00:42:12.455 secondary AML that was untreated

NOTE Confidence: 0.827654426

00:42:12.455 --> 00:42:16.620 secondary meaning having antecedent

NOTE Confidence: 0.827654426

00:42:16.620 --> 00:42:21.568 hematologic malignancy that could have been.

NOTE Confidence: 0.827654426

00:42:21.568 --> 00:42:24.753 Treated but not with hypomethylating

NOTE Confidence: 0.827654426

00:42:24.753 --> 00:42:28.771 agent and so you can see the age

NOTE Confidence: 0.827654426

00:42:28.771 --> 00:42:31.670 is older individuals and almost

NOTE Confidence: 0.827654426

00:42:31.670 --> 00:42:34.932 exclusively I'm heavily weighed in

NOTE Confidence: 0.827654426

00:42:34.932 --> 00:42:37.764 terms of being adverse risk group

NOTE Confidence: 0.827654426

00:42:37.770 --> 00:42:42.538 ELN 2017 classification system.

NOTE Confidence: 0.827654426

00:42:42.540 --> 00:42:45.486 And further separated into by the

NOTE Confidence: 0.827654426

00:42:45.486 --> 00:42:49.104 TP 53 status mutant versus wild type

NOTE Confidence: 0.827654426

00:42:49.104 --> 00:42:52.218 and as I mentioned heavily enriched

NOTE Confidence: 0.827654426

00:42:52.218 --> 00:42:55.020 for TP53 mutated patients given

NOTE Confidence: 0.827654426

00:42:55.020 --> 00:42:58.969 that there's hope for a grolla mab

NOTE Confidence: 0.827654426

00:42:58.969 --> 00:43:01.723 for the subtype of AML and.

NOTE Confidence: 0.827654426

00:43:01.723 --> 00:43:05.461 These are the response rates again

NOTE Confidence: 0.827654426

00:43:05.461 --> 00:43:09.959 separated into the de Novo group and

NOTE Confidence: 0.827654426

00:43:09.959 --> 00:43:13.653 the untreated secondary AML group and

NOTE Confidence: 0.827654426

00:43:13.653 --> 00:43:18.460 separated by the status of TP53 mutation.

NOTE Confidence: 0.827654426

00:43:18.460 --> 00:43:24.810 And so there is a CR CRI rate of

NOTE Confidence: 0.827654426

00:43:24.810 --> 00:43:30.545 63% with TP53 mutated patients in

NOTE Confidence: 0.827654426

00:43:30.545 --> 00:43:33.020 de Novo and untreated secondary.

NOTE Confidence: 0.827654426

00:43:33.020 --> 00:43:35.960 In a higher CRI CRI rate in in the wild

NOTE Confidence: 0.827654426

00:43:36.042 --> 00:43:40.990 type patients ranging from 80 to 90%.

NOTE Confidence: 0.827654426

00:43:40.990 --> 00:43:45.199 And on the left is the are the survival

NOTE Confidence: 0.827654426

00:43:45.199 --> 00:43:48.440 curves for the de Novo population alone.

NOTE Confidence: 0.827654426

00:43:48.440 --> 00:43:50.554 You can see a separation in the

NOTE Confidence: 0.827654426

00:43:50.554 --> 00:43:53.340 curves between TP53 wild type and

NOTE Confidence: 0.827654426

00:43:53.340 --> 00:43:54.975 TP53 mutant patients.

NOTE Confidence: 0.827654426

00:43:54.980 --> 00:43:58.184 The 12 month overall survival of

NOTE Confidence: 0.827654426

00:43:58.184 --> 00:44:01.620 the TP53 mutant patients was 53%

NOTE Confidence: 0.827654426

00:44:01.620 --> 00:44:07.380 which compared to historical data is

NOTE Confidence: 0.827654426

00:44:07.380 --> 00:44:09.580 encouraging because I'll remind you

NOTE Confidence: 0.827654426

00:44:09.580 --> 00:44:11.780 that the median overall survival.

NOTE Confidence: 0.827654426

00:44:11.780 --> 00:44:14.300 Is on the order of six months.

NOTE Confidence: 0.827654426

00:44:14.300 --> 00:44:16.533 On the right is the median overall

NOTE Confidence: 0.827654426

00:44:16.533 --> 00:44:19.218 survival in the combined frontline groups,

NOTE Confidence: 0.827654426

00:44:19.220 --> 00:44:22.526 which is less favorable because the

NOTE Confidence: 0.827654426

00:44:22.526 --> 00:44:25.940 secondary AML patients did not respond

NOTE Confidence: 0.827654426

00:44:25.940 --> 00:44:30.980 as well and had short responses as well.

NOTE Confidence: 0.827654426

00:44:30.980 --> 00:44:35.336 So moving on to a separate high risk group,

NOTE Confidence: 0.827654426

00:44:35.340 --> 00:44:40.400 the FLIP 3 mutated group.

NOTE Confidence: 0.827654426

00:44:40.400 --> 00:44:42.676 Nicholas Short reported updated

NOTE Confidence: 0.827654426

00:44:42.676 --> 00:44:46.781 results from a phase one two study

NOTE Confidence: 0.827654426

00:44:46.781 --> 00:44:48.560 of another triplet,

NOTE Confidence: 0.827654426

00:44:48.560 --> 00:44:51.446 gilteritinib added on to the backbone

NOTE Confidence: 0.827654426

00:44:51.446 --> 00:44:53.830 of venetoclax and azacitidine for

NOTE Confidence: 0.827654426

00:44:53.830 --> 00:44:56.110 patients with FLIP 3 mutated AML.

NOTE Confidence: 0.899006091428571

00:44:58.130 --> 00:45:00.426 And there were two groups of patients,

NOTE Confidence: 0.899006091428571

00:45:00.430 --> 00:45:02.035 those who were newly diagnosed

NOTE Confidence: 0.899006091428571

00:45:02.035 --> 00:45:03.934 with split three mutated AML and

NOTE Confidence: 0.899006091428571

00:45:03.934 --> 00:45:05.806 this could be ITD or TKD who were

NOTE Confidence: 0.899006091428571

00:45:05.806 --> 00:45:07.568 unfit for intensive chemotherapy.

NOTE Confidence: 0.899006091428571

00:45:07.570 --> 00:45:10.516 And then there was also a

NOTE Confidence: 0.899006091428571

00:45:10.516 --> 00:45:11.989 relapsed refractory group.

NOTE Confidence: 0.899006091428571

00:45:11.990 --> 00:45:14.654 And in the middle you see the schedule

NOTE Confidence: 0.899006091428571

00:45:14.654 --> 00:45:16.845 of treatment notably with triplets

NOTE Confidence: 0.899006091428571

00:45:16.845 --> 00:45:18.785 myelosuppression is a concern.

NOTE Confidence: 0.899006091428571

00:45:18.790 --> 00:45:21.940 And so built into the treatment schedule

NOTE Confidence: 0.899006091428571

00:45:21.940 --> 00:45:25.803 is a day 14 mayoral that informs

NOTE Confidence: 0.899006091428571

00:45:25.803 --> 00:45:28.818 the subsequent continuation or not.

NOTE Confidence: 0.899006091428571

00:45:28.820 --> 00:45:29.730 Of venetoclax,

NOTE Confidence: 0.899006091428571

00:45:29.730 --> 00:45:32.460 Gilteritinib was given at one of

NOTE Confidence: 0.899006091428571

00:45:32.460 --> 00:45:35.404 two doses and the recommended phase

NOTE Confidence: 0.899006091428571

00:45:35.404 --> 00:45:38.326 two dose was ultimately selected to

NOTE Confidence: 0.899006091428571

00:45:38.412 --> 00:45:41.047 be 80 milligrams of gilteritinib.

NOTE Confidence: 0.899006091428571

00:45:41.050 --> 00:45:44.109 And on the right you see the

NOTE Confidence: 0.899006091428571

00:45:44.109 --> 00:45:45.420 consolidation treatment plan.

NOTE Confidence: 0.882014708461538

00:45:48.320 --> 00:45:50.875 So these are the responses for the

NOTE Confidence: 0.882014708461538

00:45:50.875 --> 00:45:53.799 frontline and the relapse refractory group.

NOTE Confidence: 0.882014708461538

00:45:53.800 --> 00:45:55.670 You can see the composite

NOTE Confidence: 0.882014708461538

00:45:55.670 --> 00:45:57.540 CR rates are quite high,

NOTE Confidence: 0.882014708461538

00:45:57.540 --> 00:45:59.920 100% in the frontline group and 70%

NOTE Confidence: 0.882014708461538

00:45:59.920 --> 00:46:02.332 in the relapse refractory group and

NOTE Confidence: 0.882014708461538

00:46:02.332 --> 00:46:05.210 there were no early deaths and it

NOTE Confidence: 0.882014708461538

00:46:05.210 --> 00:46:07.460 was considered to be well tolerated.

NOTE Confidence: 0.882014708461538

00:46:07.460 --> 00:46:10.106 These are the overall the relapse rate

NOTE Confidence: 0.882014708461538

00:46:10.106 --> 00:46:13.060 survival on the on the left and the

NOTE Confidence: 0.882014708461538

00:46:13.060 --> 00:46:15.552 overall survival curves on the right and

NOTE Confidence: 0.882014708461538

00:46:15.552 --> 00:46:18.240 you can see that the one year overall.

NOTE Confidence: 0.882014708461538

00:46:18.240 --> 00:46:20.648 Survival rate is 85%,

NOTE Confidence: 0.882014708461538

00:46:20.648 --> 00:46:26.380 which is again very encouraging and.

NOTE Confidence: 0.882014708461538

00:46:26.380 --> 00:46:31.365 Umm, sorry, Umm compares favorably

NOTE Confidence: 0.882014708461538

00:46:31.365 --> 00:46:34.130 with historical results.

NOTE Confidence: 0.847792006111111

00:46:36.230 --> 00:46:39.037 So I just briefly want to touch

NOTE Confidence: 0.847792006111111

00:46:39.037 --> 00:46:42.210 on men and inhibitors and the

NOTE Confidence: 0.847792006111111

00:46:42.210 --> 00:46:45.320 concept behind these these drugs.

NOTE Confidence: 0.847792006111111

00:46:45.320 --> 00:46:47.605 There are several minute inhibitors

NOTE Confidence: 0.847792006111111

00:46:47.605 --> 00:46:51.225 under development and the men in KMT

NOTE Confidence: 0.847792006111111

00:46:51.225 --> 00:46:54.506 2A previously known as ML interaction.

NOTE Confidence: 0.847792006111111

00:46:54.506 --> 00:46:57.962 Is it critical dependency in ML

NOTE Confidence: 0.847792006111111

00:46:57.962 --> 00:47:00.669 mutated rearranged leukemias as well

NOTE Confidence: 0.847792006111111

00:47:00.669 --> 00:47:03.363 as interestingly in NPM 1 mutated

NOTE Confidence: 0.847792006111111

00:47:03.363 --> 00:47:05.690 leukemias where it's responsible?

NOTE Confidence: 0.847792006111111

00:47:05.690 --> 00:47:08.696 Um for enacting an aberrant leukemia

NOTE Confidence: 0.847792006111111

00:47:08.696 --> 00:47:11.674 genic gene expression program so the

NOTE Confidence: 0.847792006111111

00:47:11.674 --> 00:47:14.596 inhibitors bind a well defined pocket

NOTE Confidence: 0.847792006111111

00:47:14.596 --> 00:47:17.990 and this disrupts the interaction between

NOTE Confidence: 0.847792006111111

00:47:17.990 --> 00:47:22.420 ML and MENNEN and causes an abnormal

NOTE Confidence: 0.847792006111111

00:47:22.420 --> 00:47:25.460 transcription complex to disassemble

NOTE Confidence: 0.847792006111111

00:47:25.460 --> 00:47:30.278 and through down regulation of Hawks,

NOTE Confidence: 0.847792006111111

00:47:30.280 --> 00:47:33.420 A and mice, mice,

NOTE Confidence: 0.847792006111111

00:47:33.420 --> 00:47:36.560 transcription and other targets.

NOTE Confidence: 0.847792006111111

00:47:36.560 --> 00:47:38.308 Allows differentiation of the

NOTE Confidence: 0.847792006111111

00:47:38.308 --> 00:47:41.440 leukemia cells as well as apoptosis.

NOTE Confidence: 0.900019746

00:47:44.340 --> 00:47:46.170 And so as I mentioned,

NOTE Confidence: 0.900019746

00:47:46.170 --> 00:47:48.576 there's more than one of these

NOTE Confidence: 0.900019746

00:47:48.576 --> 00:47:51.408 inhibitors that's being developed and.

NOTE Confidence: 0.900019746

00:47:51.408 --> 00:47:56.320 Doctor Isa reported results

NOTE Confidence: 0.900019746

00:47:56.320 --> 00:48:01.036 from the Phase one study of the

NOTE Confidence: 0.900019746

00:48:01.036 --> 00:48:04.108 men and inhibitor review Munib

NOTE Confidence: 0.900019746

00:48:04.108 --> 00:48:06.354 in patients with KM22KMT2A

NOTE Confidence: 0.900019746

00:48:06.354 --> 00:48:08.538 rearranged or MPM One mutant AML.

NOTE Confidence: 0.853216424545454

00:48:10.860 --> 00:48:13.252 And for the sake of time that trial

NOTE Confidence: 0.853216424545454

00:48:13.252 --> 00:48:16.066 is the AUGMENT 101 trial and what was

NOTE Confidence: 0.853216424545454

00:48:16.066 --> 00:48:19.037 notable in terms of adverse events were

NOTE Confidence: 0.853216424545454

00:48:19.037 --> 00:48:21.372 frequent QTC prolongations and there

NOTE Confidence: 0.853216424545454

00:48:21.372 --> 00:48:24.460 were two dose limiting toxicities because

NOTE Confidence: 0.853216424545454

00:48:24.460 --> 00:48:27.109 of QTC prolongation, but there was.

NOTE Confidence: 0.820616738333333

00:48:29.420 --> 00:48:31.132 Lesser rate of grade,

NOTE Confidence: 0.820616738333333

00:48:31.132 --> 00:48:33.700 three or more QTC prolongation and

NOTE Confidence: 0.820616738333333

00:48:33.784 --> 00:48:36.514 in a heavily pretreated group with a

NOTE Confidence: 0.820616738333333

00:48:36.514 --> 00:48:39.678 median of four prior lines of treatment,

NOTE Confidence: 0.820616738333333

00:48:39.680 --> 00:48:41.612 there was encouraging activity

NOTE Confidence: 0.820616738333333

00:48:41.612 --> 00:48:45.048 with 30% CRC RH meaning incomplete

NOTE Confidence: 0.820616738333333

00:48:45.048 --> 00:48:46.899 hematologic recovery rate.

NOTE Confidence: 0.820616738333333

00:48:46.900 --> 00:48:49.650 In these genetic subgroups and

NOTE Confidence: 0.820616738333333

00:48:49.650 --> 00:48:53.042 MLL rearranged and NPM 1 mutated

NOTE Confidence: 0.820616738333333

00:48:53.042 --> 00:48:56.022 leukemias and the response rates

NOTE Confidence: 0.820616738333333

00:48:56.022 --> 00:48:59.309 were different by each genotype.

NOTE Confidence: 0.820616738333333

00:48:59.310 --> 00:49:02.410 Doctor Harry Erba presented on

NOTE Confidence: 0.820616738333333

00:49:02.410 --> 00:49:05.155 another minute inhibitor Dominic

NOTE Confidence: 0.820616738333333

00:49:05.155 --> 00:49:10.378 in the same type of AML and also in

NOTE Confidence: 0.820616738333333

00:49:10.378 --> 00:49:12.090 the relapsed refractory setting,

NOTE Confidence: 0.820616738333333

00:49:12.090 --> 00:49:16.677 the comment 001 trial and.

NOTE Confidence: 0.820616738333333

00:49:16.677 --> 00:49:18.378 Here differentiation syndrome

NOTE Confidence: 0.820616738333333

00:49:18.378 --> 00:49:22.381 was observed as was and with the

NOTE Confidence: 0.820616738333333

00:49:22.381 --> 00:49:24.397 prior men and inhibitor,

NOTE Confidence: 0.820616738333333

00:49:24.400 --> 00:49:27.652 but there were no drug induced

NOTE Confidence: 0.820616738333333

00:49:27.652 --> 00:49:30.830 QT or QTC Prolongations reported.

NOTE Confidence: 0.820616738333333

00:49:30.830 --> 00:49:31.934 And again,

NOTE Confidence: 0.820616738333333

00:49:31.934 --> 00:49:35.246 particularly at the 600 milligrams dose,

NOTE Confidence: 0.820616738333333

00:49:35.250 --> 00:49:38.957 which was the recommended phase two dose,

NOTE Confidence: 0.820616738333333

00:49:38.957 --> 00:49:41.992 there was in heavily pretreated

NOTE Confidence: 0.820616738333333

00:49:41.992 --> 00:49:44.420 population evidence of encouraging

NOTE Confidence: 0.820616738333333

00:49:44.507 --> 00:49:48.045 activity with a 30% CR rate in

NOTE Confidence: 0.820616738333333

00:49:48.045 --> 00:49:51.270 the NPM 1 mutated group.

NOTE Confidence: 0.820616738333333

00:49:51.270 --> 00:49:53.390 The CR rate was much lower in the

NOTE Confidence: 0.820616738333333

00:49:53.390 --> 00:49:55.775 in the ML group and it remains to

NOTE Confidence: 0.820616738333333

00:49:55.775 --> 00:49:58.134 be seen whether in fact there's

NOTE Confidence: 0.820616738333333

00:49:58.134 --> 00:50:00.879 differential activity in different genotypes.

NOTE Confidence: 0.820616738333333

00:50:00.880 --> 00:50:02.869 With these agents.

NOTE Confidence: 0.820616738333333

00:50:02.870 --> 00:50:05.649 So in conclusion for the for this

NOTE Confidence: 0.820616738333333

00:50:05.649 --> 00:50:06.443 AML section,

NOTE Confidence: 0.820616738333333

00:50:06.450 --> 00:50:08.475 men and inhibitors are showing

NOTE Confidence: 0.820616738333333

00:50:08.475 --> 00:50:10.500 promising activities and relapsed NPM

NOTE Confidence: 0.820616738333333

00:50:10.565 --> 00:50:13.127 one and MLL rearranged or mutated patients.

NOTE Confidence: 0.820616738333333

00:50:13.130 --> 00:50:15.954 And the two triplets that I I touched

NOTE Confidence: 0.820616738333333

00:50:15.954 --> 00:50:18.904 on with gilteritinib on a backbone

NOTE Confidence: 0.820616738333333

00:50:18.904 --> 00:50:21.609 of azacitidine and venetoclax also

NOTE Confidence: 0.820616738333333

00:50:21.609 --> 00:50:24.145 showing promising safety and efficacy

NOTE Confidence: 0.820616738333333

00:50:24.145 --> 00:50:27.466 in the upfront but also relapse setting.

NOTE Confidence: 0.820616738333333

00:50:27.466 --> 00:50:30.142 Whereas Megola map added to azacitidine

NOTE Confidence: 0.820616738333333

00:50:30.142 --> 00:50:32.780 and venetoclax shows promising activity.

NOTE Confidence: 0.820616738333333

00:50:32.780 --> 00:50:37.238 And TP 53 mutated AML's and

NOTE Confidence: 0.820616738333333

00:50:37.238 --> 00:50:40.210 their randomized trials ongoing.

NOTE Confidence: 0.820616738333333

00:50:40.210 --> 00:50:42.628 For magala map.

NOTE Confidence: 0.820616738333333

00:50:42.630 --> 00:50:47.195 So turning to ALAL is evenly split in

NOTE Confidence: 0.820616738333333

00:50:47.195 --> 00:50:50.347 the in between the pediatric and the

NOTE Confidence: 0.820616738333333

00:50:50.347 --> 00:50:53.358 adult groups, roughly half and half.

NOTE Confidence: 0.820616738333333

00:50:53.358 --> 00:50:53.890 However,

NOTE Confidence: 0.820616738333333

00:50:53.890 --> 00:50:56.274 whereas the median age at diagnosis is 17,

NOTE Confidence: 0.820616738333333

00:50:56.280 --> 00:50:58.648 the median age at death is 58 and

NOTE Confidence: 0.820616738333333

00:50:58.648 --> 00:51:00.774 so the outcomes are far inferior

NOTE Confidence: 0.820616738333333

00:51:00.774 --> 00:51:03.552 in adults and this is a particular

NOTE Confidence: 0.820616738333333

00:51:03.552 --> 00:51:05.628 problem in older adults.

NOTE Confidence: 0.820616738333333

00:51:05.630 --> 00:51:09.504 And here you see a summary of overall

NOTE Confidence: 0.820616738333333

00:51:09.504 --> 00:51:12.600 survival at the three and five year marks.

NOTE Confidence: 0.820616738333333

00:51:12.600 --> 00:51:14.580 Which on average is about 20%.

NOTE Confidence: 0.820616738333333

00:51:14.580 --> 00:51:16.330 And if you consider individuals

NOTE Confidence: 0.820616738333333

00:51:16.330 --> 00:51:18.540 that are elderly 70 or above,

NOTE Confidence: 0.820616738333333

00:51:18.540 --> 00:51:21.738 they're really dismal rates and

NOTE Confidence: 0.820616738333333

00:51:21.738 --> 00:51:24.251 outcomes and just as a kind of

NOTE Confidence: 0.820616738333333

00:51:24.251 --> 00:51:27.798 a reminder of the importance of

NOTE Confidence: 0.820616738333333

00:51:27.798 --> 00:51:29.658 measurable residual disease.

NOTE Confidence: 0.820616738333333

00:51:29.660 --> 00:51:33.308 In L, the two two outcomes,

NOTE Confidence: 0.820616738333333

00:51:33.310 --> 00:51:35.560 event free survival and overall survival,

NOTE Confidence: 0.820616738333333

00:51:35.560 --> 00:51:37.100 you see, you know,

NOTE Confidence: 0.820616738333333

00:51:37.100 --> 00:51:38.640 dramatic split between those

NOTE Confidence: 0.820616738333333

00:51:38.640 --> 00:51:40.616 patients who have no measurable

NOTE Confidence: 0.820616738333333

00:51:40.616 --> 00:51:42.884 residual disease and those who do.

NOTE Confidence: 0.820616738333333

00:51:42.890 --> 00:51:43.982 But importantly,

NOTE Confidence: 0.820616738333333

00:51:43.982 --> 00:51:46.712 there's also relapse and mortality

NOTE Confidence: 0.820616738333333

00:51:46.712 --> 00:51:50.342 even in the situation of no

NOTE Confidence: 0.820616738333333

00:51:50.342 --> 00:51:52.247 measurable residual disease.

NOTE Confidence: 0.820616738333333

00:51:52.250 --> 00:51:54.357 And so one of the strategies that's

NOTE Confidence: 0.820616738333333

00:51:54.357 --> 00:51:56.870 been taken to try and improve outcomes,

NOTE Confidence: 0.820616738333333

00:51:56.870 --> 00:51:58.778 particularly in older adults,

NOTE Confidence: 0.820616738333333

00:51:58.778 --> 00:52:01.640 is the integration of novel agents

NOTE Confidence: 0.820616738333333

00:52:01.717 --> 00:52:03.729 into the frontline setting,

NOTE Confidence: 0.820616738333333

00:52:03.730 --> 00:52:07.190 focusing on blinatumomab and inotuzumab.

NOTE Confidence: 0.820616738333333

00:52:07.190 --> 00:52:09.830 Inotuzumab is an antibody drug

NOTE Confidence: 0.820616738333333

00:52:09.830 --> 00:52:11.694 conjugate against CD22 Lina.

NOTE Confidence: 0.820616738333333

00:52:11.694 --> 00:52:14.910 Tuma Mab is a bi functional T cell

NOTE Confidence: 0.820616738333333

00:52:15.003 --> 00:52:17.227 engaging antibody that directs

NOTE Confidence: 0.820616738333333

00:52:17.227 --> 00:52:21.188 cytotoxic T cells to CD19 expressing cells.

NOTE Confidence: 0.820616738333333

00:52:21.188 --> 00:52:22.366 And notably,

NOTE Confidence: 0.820616738333333

00:52:22.366 --> 00:52:26.760 the trials that led to the approval

NOTE Confidence: 0.820616738333333

00:52:26.760 --> 00:52:30.495 of Blinatumomab and Inotuzumab in

NOTE Confidence: 0.820616738333333

00:52:30.495 --> 00:52:33.090 relapse refractory Bal demonstrated

NOTE Confidence: 0.820616738333333

00:52:33.090 --> 00:52:35.190 that I Natuzzi Mob has activity

NOTE Confidence: 0.820616738333333

00:52:35.190 --> 00:52:36.240 across all levels

NOTE Confidence: 0.774469366923077

00:52:36.302 --> 00:52:38.014 of disease burden, suggesting that

NOTE Confidence: 0.774469366923077

00:52:38.014 --> 00:52:40.096 it could be suitable for induction,

NOTE Confidence: 0.774469366923077

00:52:40.100 --> 00:52:41.684 whereas blinatumomab has higher

NOTE Confidence: 0.774469366923077

00:52:41.684 --> 00:52:44.060 efficacy with lower burden of disease.

NOTE Confidence: 0.774469366923077

00:52:44.060 --> 00:52:46.720 I'm suggesting that its role may be

NOTE Confidence: 0.774469366923077

00:52:46.720 --> 00:52:49.419 primarily in a setting where there's

NOTE Confidence: 0.774469366923077

00:52:49.419 --> 00:52:51.889 already been side a reduction.

NOTE Confidence: 0.774469366923077

00:52:51.890 --> 00:52:54.575 So there's multiple trials that

NOTE Confidence: 0.774469366923077

00:52:54.575 --> 00:52:56.723 are studying the combinations

NOTE Confidence: 0.774469366923077

00:52:56.723 --> 00:52:59.789 of inotuzumab with chemotherapy.

NOTE Confidence: 0.774469366923077

00:52:59.790 --> 00:53:02.855 Particularly in older individuals and

NOTE Confidence: 0.774469366923077

00:53:02.855 --> 00:53:07.868 this is one that Gmall initial one trial.

NOTE Confidence: 0.774469366923077

00:53:07.870 --> 00:53:10.012 And in this trial it's the sequential

NOTE Confidence: 0.774469366923077

00:53:10.012 --> 00:53:12.051 strategy and the choose amab is

NOTE Confidence: 0.774469366923077

00:53:12.051 --> 00:53:13.811 given for three cycles followed

NOTE Confidence: 0.774469366923077

00:53:13.811 --> 00:53:15.269 by conventional chemotherapy and

NOTE Confidence: 0.774469366923077

00:53:15.269 --> 00:53:17.698 patients greater than 55 years of age.

NOTE Confidence: 0.774469366923077

00:53:17.700 --> 00:53:20.458 In this trial a primary event free,

NOTE Confidence: 0.774469366923077

00:53:20.460 --> 00:53:22.476 the primary endpoint was 12 month

NOTE Confidence: 0.774469366923077

00:53:22.476 --> 00:53:24.418 event free survival with a goal

NOTE Confidence: 0.774469366923077

00:53:24.418 --> 00:53:26.322 of seeing better than 60% and and

NOTE Confidence: 0.774469366923077

00:53:26.322 --> 00:53:28.578 you can see on the left that this

NOTE Confidence: 0.774469366923077

00:53:28.578 --> 00:53:30.994 was met at one year it was 88% and

NOTE Confidence: 0.774469366923077

00:53:30.994 --> 00:53:32.681 the two years it was 73%.

NOTE Confidence: 0.774469366923077

00:53:32.681 --> 00:53:34.186 But you'll also note though

NOTE Confidence: 0.774469366923077

00:53:34.186 --> 00:53:36.084 is the downward slope of this

NOTE Confidence: 0.774469366923077

00:53:36.084 --> 00:53:37.674 curve indicating that there are.

NOTE Confidence: 0.774469366923077

00:53:37.680 --> 00:53:40.350 Ongoing events after year one suggesting

NOTE Confidence: 0.774469366923077

00:53:40.350 --> 00:53:44.047 that there may be a need to improve

NOTE Confidence: 0.774469366923077

00:53:44.047 --> 00:53:45.887 on the consolidation strategy.

NOTE Confidence: 0.774469366923077

00:53:45.890 --> 00:53:50.774 There was a similar in terms of

NOTE Confidence: 0.774469366923077

00:53:50.774 --> 00:53:54.734 approach study that was presented by

NOTE Confidence: 0.774469366923077

00:53:54.734 --> 00:53:57.072 Chevalier the result of the Ewal Ino

NOTE Confidence: 0.774469366923077

00:53:57.072 --> 00:54:00.127 study and here I know choose Amab is

NOTE Confidence: 0.774469366923077

00:54:00.127 --> 00:54:01.967 intercalated with chemotherapy from

NOTE Confidence: 0.774469366923077

00:54:01.967 --> 00:54:04.295 the beginning and these are only two

NOTE Confidence: 0.774469366923077

00:54:04.295 --> 00:54:08.238 of a number of of such studies the the.

NOTE Confidence: 0.774469366923077

00:54:08.238 --> 00:54:10.846 Presentation that perhaps received

NOTE Confidence: 0.774469366923077

00:54:10.846 --> 00:54:14.448 the most notoriety at ASH 2022 was

NOTE Confidence: 0.774469366923077

00:54:14.448 --> 00:54:17.291 by in the space of L was by Mark

NOTE Confidence: 0.774469366923077

00:54:17.291 --> 00:54:20.080 Lizzo reporting the results of

NOTE Confidence: 0.774469366923077

00:54:20.080 --> 00:54:22.935 E1910A phase three randomized trial

NOTE Confidence: 0.774469366923077

00:54:22.935 --> 00:54:25.790 of BLINATUMOMAB for newly diagnosed

NOTE Confidence: 0.774469366923077

00:54:25.877 --> 00:54:27.967 pH negative Bal in adults.

NOTE Confidence: 0.774469366923077

00:54:27.970 --> 00:54:32.506 And these adults were age ages ranging

NOTE Confidence: 0.774469366923077

00:54:32.506 --> 00:54:37.359 from 30 to 70 and they received.

NOTE Confidence: 0.774469366923077

00:54:37.360 --> 00:54:39.990 Two cycles of induction intensification

NOTE Confidence: 0.774469366923077

00:54:39.990 --> 00:54:43.393 and were then randomized either to the

NOTE Confidence: 0.774469366923077

00:54:43.393 --> 00:54:45.774 experimental arm or to the standard

NOTE Confidence: 0.774469366923077

00:54:45.774 --> 00:54:47.676 consolidation chemotherapy arm.

NOTE Confidence: 0.774469366923077

00:54:47.676 --> 00:54:51.480 The experimental arm had four cycles

NOTE Confidence: 0.774469366923077

00:54:51.568 --> 00:54:54.778 of blood and blinatumomab intercalated

NOTE Confidence: 0.774469366923077

00:54:54.778 --> 00:54:56.704 with chemotherapy consolidation

NOTE Confidence: 0.774469366923077

00:54:56.704 --> 00:54:59.722 and MRD of course was it.

NOTE Confidence: 0.774469366923077

00:54:59.722 --> 00:55:02.428 It was actually the outcomes in

NOTE Confidence: 0.774469366923077

00:55:02.428 --> 00:55:05.161 MRD negative patients was the focus

NOTE Confidence: 0.774469366923077

00:55:05.161 --> 00:55:06.897 of the study and.

NOTE Confidence: 0.774469366923077

00:55:06.900 --> 00:55:08.982 MRD was defined as greater than

NOTE Confidence: 0.774469366923077

00:55:08.982 --> 00:55:12.124 or equal to 1 in 10,000 cells as

NOTE Confidence: 0.774469366923077

00:55:12.124 --> 00:55:14.626 assessed by 6 color flow cytometry.

NOTE Confidence: 0.774469366923077

00:55:14.630 --> 00:55:18.956 And so these are the the results.

NOTE Confidence: 0.774469366923077

00:55:18.960 --> 00:55:21.834 These are this is overall survival

NOTE Confidence: 0.774469366923077

00:55:21.834 --> 00:55:24.790 and MRD negative patients and you can

NOTE Confidence: 0.774469366923077

00:55:24.790 --> 00:55:27.086 see a very clear survival advantage

NOTE Confidence: 0.774469366923077

00:55:27.086 --> 00:55:29.626 with the addition of BLINATUMOMAB.

NOTE Confidence: 0.774469366923077

00:55:29.630 --> 00:55:32.045 The median overall survival is 71 months.

NOTE Confidence: 0.774469366923077

00:55:32.050 --> 00:55:34.479 It with chemotherapy alone and with the

NOTE Confidence: 0.774469366923077

00:55:34.479 --> 00:55:37.080 addition of Lena Tuma Mab is not reached.

NOTE Confidence: 0.774469366923077

00:55:37.080 --> 00:55:39.224 And so this was,

NOTE Confidence: 0.774469366923077

00:55:39.224 --> 00:55:42.440 this is a landmark study and.

NOTE Confidence: 0.774469366923077

00:55:42.440 --> 00:55:46.336 Showed for the first time a benefit of

NOTE Confidence: 0.774469366923077

00:55:46.336 --> 00:55:49.358 blinatumomab and MRD negative patients.

NOTE Confidence: 0.774469366923077

00:55:49.360 --> 00:55:50.750 Not I'm not showing here,

NOTE Confidence: 0.774469366923077

00:55:50.750 --> 00:55:52.282 but MRD positive patients.

NOTE Confidence: 0.774469366923077

00:55:52.282 --> 00:55:54.580 There's also a separation in the

NOTE Confidence: 0.774469366923077

00:55:54.652 --> 00:55:57.262 curves that did not reach statistical

NOTE Confidence: 0.774469366923077

00:55:57.262 --> 00:55:59.992 significance and it's unclear if this is

NOTE Confidence: 0.774469366923077

00:55:59.992 --> 00:56:04.068 due to smaller numbers or for other reasons.

NOTE Confidence: 0.774469366923077

00:56:04.068 --> 00:56:07.640 So very briefly for pH positive,

NOTE Confidence: 0.774469366923077

00:56:07.640 --> 00:56:09.990 AL.

NOTE Confidence: 0.774469366923077

00:56:09.990 --> 00:56:14.048 Nicholas Short presented for upfront

NOTE Confidence: 0.774469366923077

00:56:14.048 --> 00:56:18.122 treatment the combination of panic and

NOTE Confidence: 0.774469366923077

00:56:18.122 --> 00:56:21.224 blinatumomab and here the rationale

NOTE Confidence: 0.774469366923077

00:56:21.224 --> 00:56:24.309 is that with second generation

NOTE Confidence: 0.774469366923077

00:56:24.309 --> 00:56:26.777 tyrosine kinase inhibitors the

NOTE Confidence: 0.774469366923077

00:56:26.777 --> 00:56:29.909 majority of patients will relapse with

NOTE Confidence: 0.619180544705882

00:56:29.910 --> 00:56:33.138 T315I mutated BCR able which put

NOTE Confidence: 0.619180544705882

00:56:33.138 --> 00:56:36.729 that nib is active against and

NOTE Confidence: 0.619180544705882

00:56:36.729 --> 00:56:40.044 in pH positive AML chemotherapy.

NOTE Confidence: 0.619180544705882

00:56:40.050 --> 00:56:43.643 Free induction has been pioneered with

NOTE Confidence: 0.619180544705882

00:56:43.643 --> 00:56:46.058 publications on dissent and Prednisone,

NOTE Confidence: 0.619180544705882

00:56:46.060 --> 00:56:49.180 ponatinib and Prednisone and the Dealba

NOTE Confidence: 0.619180544705882

00:56:49.180 --> 00:56:52.320 trial reporting Dasatinib and BLINATUMOMAB.

NOTE Confidence: 0.619180544705882

00:56:52.320 --> 00:56:54.760 And just very briefly,

NOTE Confidence: 0.619180544705882

00:56:54.760 --> 00:56:57.200 they're very striking results

NOTE Confidence: 0.619180544705882

00:56:57.200 --> 00:57:00.398 in 40 patients in the frontline

NOTE Confidence: 0.619180544705882

00:57:00.398 --> 00:57:03.716 setting CR CRI rates of 96%,

NOTE Confidence: 0.619180544705882

00:57:03.716 --> 00:57:09.152 complete molecular response of 87% with an.

NOTE Confidence: 0.619180544705882

00:57:09.152 --> 00:57:12.372 Equally striking event free survival

NOTE Confidence: 0.619180544705882

00:57:12.372 --> 00:57:16.214 and overall survival curves with a

NOTE Confidence: 0.619180544705882

00:57:16.214 --> 00:57:20.590 medium follow-up of 18 months with the

NOTE Confidence: 0.619180544705882

00:57:20.590 --> 00:57:26.460 two year overall survival being 95%.

NOTE Confidence: 0.619180544705882

00:57:26.460 --> 00:57:27.321 So in summary,

NOTE Confidence: 0.619180544705882

00:57:27.321 --> 00:57:29.790 for the abstract shown for ALS into choose,

NOTE Confidence: 0.619180544705882

00:57:29.790 --> 00:57:32.286 the map is an effective induction

NOTE Confidence: 0.619180544705882

00:57:32.286 --> 00:57:35.568 agent with acceptable low toxicity and

NOTE Confidence: 0.619180544705882

00:57:35.568 --> 00:57:38.016 promising early survival outcomes.

NOTE Confidence: 0.619180544705882

00:57:38.020 --> 00:57:41.218 And in the late breaking abstract

NOTE Confidence: 0.619180544705882

00:57:41.218 --> 00:57:43.350 presented by Doctor Litzow,

NOTE Confidence: 0.619180544705882

00:57:43.350 --> 00:57:46.205 the addition of Blinatumomab to

NOTE Confidence: 0.619180544705882

00:57:46.205 --> 00:57:48.489 chemotherapy consolidation in adult

NOTE Confidence: 0.619180544705882

00:57:48.489 --> 00:57:51.024 patients with MRD negative Bal has

NOTE Confidence: 0.619180544705882

00:57:51.024 --> 00:57:54.310 shown for the first time in overall and

NOTE Confidence: 0.619180544705882

00:57:54.310 --> 00:57:57.411 relapse free survival in a randomized study.

NOTE Confidence: 0.619180544705882

00:57:57.420 --> 00:58:00.108 And so blinatumomab as a part of post

NOTE Confidence: 0.619180544705882

00:58:00.108 --> 00:58:01.783 remission therapy represents a new

NOTE Confidence: 0.619180544705882

00:58:01.783 --> 00:58:04.580 standard of care for this group of patients.

NOTE Confidence: 0.619180544705882

00:58:04.580 --> 00:58:07.572 And one of the challenges in the field

NOTE Confidence: 0.619180544705882

00:58:07.572 --> 00:58:10.848 will be how to incorporate this in

NOTE Confidence: 0.619180544705882

00:58:10.848 --> 00:58:15.084 regiments in addition to E 1910 since

NOTE Confidence: 0.619180544705882

00:58:15.084 --> 00:58:17.808 that is not too frequently used.

NOTE Confidence: 0.619180544705882

00:58:17.810 --> 00:58:19.910 And the combination of Panaginip

NOTE Confidence: 0.619180544705882

00:58:19.910 --> 00:58:22.010 and Blinatumomab is a promising

NOTE Confidence: 0.619180544705882

00:58:22.083 --> 00:58:24.079 chemotherapy free potentially transplant

NOTE Confidence: 0.619180544705882

00:58:24.079 --> 00:58:27.073 sparing regimen for pH positive AL.

NOTE Confidence: 0.904009388333333

00:58:32.140 --> 00:58:35.356 Alright, so we're open for questions.

NOTE Confidence: 0.904009388333333

00:58:35.360 --> 00:58:37.748 Um, uh, please go ahead. We will

NOTE Confidence: 0.904009388333333

00:58:37.748 --> 00:58:40.296 stay a few minutes late if necessary.

NOTE Confidence: 0.904009388333333

00:58:40.300 --> 00:58:42.324 I know it's end of the hour already.

NOTE Confidence: 0.89197285

00:58:50.430 --> 00:58:51.190 Any questions?

NOTE Confidence: 0.82241168375

00:58:53.220 --> 00:58:56.116 I probably can ask question while we are

NOTE Confidence: 0.82241168375

00:58:56.116 --> 00:58:58.999 waiting for people like to to poor Mendez,

NOTE Confidence: 0.82241168375

00:58:59.000 --> 00:59:02.060 so for for ALS treatment,

NOTE Confidence: 0.82241168375

00:59:02.060 --> 00:59:05.420 do you foresee moving away to

NOTE Confidence: 0.82241168375

00:59:05.420 --> 00:59:08.768 chemo free regimens even in younger

NOTE Confidence: 0.82241168375

00:59:08.768 --> 00:59:11.553 patients in the near future?

NOTE Confidence: 0.82241168375

00:59:11.560 --> 00:59:14.140 Clearly the progress has been quite

NOTE Confidence: 0.82241168375

00:59:14.140 --> 00:59:16.678 impressive with those novel novel agents.

NOTE Confidence: 0.843237201304348

00:59:17.710 --> 00:59:20.587 I think so, especially I mean one

NOTE Confidence: 0.843237201304348

00:59:20.587 --> 00:59:23.113 of the hesitancies in terms of

NOTE Confidence: 0.843237201304348

00:59:23.113 --> 00:59:25.128 bringing ponatinib to the front

NOTE Confidence: 0.843237201304348

00:59:25.128 --> 00:59:27.680 line is its toxicity profile,

NOTE Confidence: 0.843237201304348

00:59:27.680 --> 00:59:29.913 which I didn't have a chance to

NOTE Confidence: 0.843237201304348

00:59:29.913 --> 00:59:32.098 discuss and the concern for that

NOTE Confidence: 0.843237201304348

00:59:32.098 --> 00:59:34.408 would be less in younger patients.

NOTE Confidence: 0.843237201304348

00:59:34.410 --> 00:59:36.839 And the efficacy at least that we're

NOTE Confidence: 0.843237201304348

00:59:36.839 --> 00:59:39.686 seeing is so high that I think that

NOTE Confidence: 0.843237201304348

00:59:39.686 --> 00:59:42.130 that would be a reasonable approach,

NOTE Confidence: 0.843237201304348

00:59:42.130 --> 00:59:45.106 I think one of especially I mean in

NOTE Confidence: 0.843237201304348

00:59:45.106 --> 00:59:47.170 combination with BLINATUMOMAB so.

NOTE Confidence: 0.843237201304348

00:59:47.170 --> 00:59:49.070 One can envision a chemotherapy

NOTE Confidence: 0.843237201304348

00:59:49.070 --> 00:59:51.623 free approach there and I think the

NOTE Confidence: 0.843237201304348

00:59:51.623 --> 00:59:53.877 difficult question is the role of stem

NOTE Confidence: 0.843237201304348

00:59:53.944 --> 00:59:56.200 cell transplant and we need longer,

NOTE Confidence: 0.843237201304348

00:59:56.200 --> 00:59:58.920 more mature data to guide us on that.

NOTE Confidence: 0.855181127142857

01:00:10.990 --> 01:00:12.607 There is a question of the chat.

NOTE Confidence: 0.855181127142857

01:00:12.610 --> 01:00:14.870 Uh, I think it's uh.

NOTE Confidence: 0.855181127142857

01:00:14.870 --> 01:00:17.090 Uh, to you I'm almaas.

NOTE Confidence: 0.855181127142857

01:00:17.090 --> 01:00:18.536 No, it's it's to Lord us.

NOTE Confidence: 0.857082695

01:00:20.020 --> 01:00:20.910 To the.

NOTE Confidence: 0.687067039

01:00:23.430 --> 01:00:25.538 Mab drug substitute of

NOTE Confidence: 0.687067039

01:00:25.538 --> 01:00:28.700 chemotherapy and a LL or AML.

NOTE Confidence: 0.890131186

01:00:30.230 --> 01:00:32.660 So any, I guess you know any of those drugs,

NOTE Confidence: 0.890131186

01:00:32.660 --> 01:00:37.820 uh, which you know will lead to be 3 like.

NOTE Confidence: 0.496473842

01:00:37.820 --> 01:00:39.770 Going to have actually maps.

NOTE Confidence: 0.686864377333333

01:00:42.250 --> 01:00:46.994 Ohh so so it's a similar question about

NOTE Confidence: 0.686864377333333

01:00:46.994 --> 01:00:50.888 chemotherapy free treatment of ALS and AML.

NOTE Confidence: 0.686864377333333

01:00:50.890 --> 01:00:54.524 And AML, that's an interesting question.

NOTE Confidence: 0.686864377333333

01:00:54.524 --> 01:00:58.070 And I, I took notice of a comment by

NOTE Confidence: 0.686864377333333

01:00:58.163 --> 01:01:01.222 Naval Daver who was saying that there's

NOTE Confidence: 0.686864377333333

01:01:01.222 --> 01:01:04.769 going to be a trial exploring magrou,

NOTE Confidence: 0.686864377333333

01:01:04.770 --> 01:01:06.396 amab and a drug I didn't

NOTE Confidence: 0.686864377333333

01:01:06.396 --> 01:01:08.150 have a chance to touch on,

NOTE Confidence: 0.686864377333333

01:01:08.150 --> 01:01:11.041 which is I think now been given

NOTE Confidence: 0.686864377333333

01:01:11.041 --> 01:01:12.730 the name provoke evoke.

NOTE Confidence: 0.686864377333333

01:01:12.730 --> 01:01:15.052 You could correct me if either

NOTE Confidence: 0.686864377333333

01:01:15.052 --> 01:01:16.618 of you knows how to pronounce

NOTE Confidence: 0.597015555

01:01:16.630 --> 01:01:18.698 that antibody drug conjugate.

NOTE Confidence: 0.8371757

01:01:20.790 --> 01:01:21.309 I don't know,

NOTE Confidence: 0.799112972

01:01:21.650 --> 01:01:26.320 but for CD123 and so that's one

NOTE Confidence: 0.799112972

01:01:26.320 --> 01:01:28.145 that's going to be something

NOTE Confidence: 0.799112972

01:01:28.145 --> 01:01:30.030 that we're going to explore.

NOTE Confidence: 0.799112972

01:01:30.030 --> 01:01:34.570 I think chemotherapy free, you know,

NOTE Confidence: 0.799112972

01:01:34.570 --> 01:01:36.110 there's other possibilities, sorry.

NOTE Confidence: 0.8589319875

01:01:38.580 --> 01:01:42.650 Umm. You know, if if we talk about TI's

NOTE Confidence: 0.8589319875

01:01:42.650 --> 01:01:44.868 and and vanetta clacks, umm, you know,

NOTE Confidence: 0.8589319875

01:01:44.868 --> 01:01:46.584 those are other possibilities as well,

NOTE Confidence: 0.8589319875

01:01:46.590 --> 01:01:48.366 but I think there's a lot of hope

NOTE Confidence: 0.8589319875

01:01:48.366 --> 01:01:50.999 in in the triplets and I don't

NOTE Confidence: 0.8589319875

01:01:50.999 --> 01:01:54.115 know if anyone would comment more.

NOTE Confidence: 0.8589319875

01:01:54.115 --> 01:01:58.290 On terms of, I actually

NOTE Confidence: 0.615838158333333

01:01:58.290 --> 01:02:00.606 actually have a question to Amir.

NOTE Confidence: 0.615838158333333

01:02:00.610 --> 01:02:02.932 So there was nothing mentioned about

NOTE Confidence: 0.615838158333333

01:02:02.932 --> 01:02:05.161 immunotherapy and this malignancy is you

NOTE Confidence: 0.615838158333333

01:02:05.161 --> 01:02:07.027 know so in myeloid malignancies today.

NOTE Confidence: 0.615838158333333

01:02:07.030 --> 01:02:09.118 So what do you think is the role of

NOTE Confidence: 0.615838158333333

01:02:09.118 --> 01:02:10.628 immunotherapy in this group of patients?

NOTE Confidence: 0.811200136

01:02:11.890 --> 01:02:13.708 Yeah, I mean I I talked a little bit

NOTE Confidence: 0.811200136

01:02:13.708 --> 01:02:15.416 about Sabato, Olimov and Margaroli maybe.

NOTE Confidence: 0.811200136

01:02:15.416 --> 01:02:17.908 I mean I I think as immune checkpoint

NOTE Confidence: 0.811200136

01:02:17.908 --> 01:02:20.908 inhibitors I would put them in that category.

NOTE Confidence: 0.811200136

01:02:20.910 --> 01:02:23.822 But I think the other drugs we did

NOTE Confidence: 0.811200136

01:02:23.822 --> 01:02:25.856 not mention or approaches were

NOTE Confidence: 0.811200136

01:02:25.856 --> 01:02:28.548 Karti cells as well as by specific.

NOTE Confidence: 0.811200136

01:02:28.548 --> 01:02:30.851 So the cortices are going to be

NOTE Confidence: 0.811200136

01:02:30.851 --> 01:02:32.606 covered by the cell therapy talk

NOTE Confidence: 0.811200136

01:02:32.606 --> 01:02:35.230 which I think is later in the series.

NOTE Confidence: 0.811200136

01:02:35.230 --> 01:02:36.930 However, in the myeloid space,

NOTE Confidence: 0.811200136

01:02:36.930 --> 01:02:39.380 both of those approaches have been quite.

NOTE Confidence: 0.811200136

01:02:39.380 --> 01:02:42.250 Challenging mostly because of cytokine

NOTE Confidence: 0.811200136

01:02:42.250 --> 01:02:45.120 release syndrome and prolonged cytopenias.

NOTE Confidence: 0.811200136

01:02:45.120 --> 01:02:47.406 B says you can apply it as much as

NOTE Confidence: 0.811200136

01:02:47.406 --> 01:02:50.689 you can without and you can live with

NOTE Confidence: 0.811200136

01:02:50.689 --> 01:02:52.370 no immunoglobulins generally, OK.

NOTE Confidence: 0.811200136

01:02:52.370 --> 01:02:55.240 But in myeloid space it's has been

NOTE Confidence: 0.811200136

01:02:55.240 --> 01:02:58.160 a very difficult development.

NOTE Confidence: 0.811200136

01:02:58.160 --> 01:02:59.525 So it it remains to be seen.

NOTE Confidence: 0.811200136

01:02:59.530 --> 01:03:01.874 There are some phase one trials that are

NOTE Confidence: 0.811200136

01:03:01.874 --> 01:03:04.479 going both with Carti sales and by specifics,

NOTE Confidence: 0.811200136

01:03:04.480 --> 01:03:06.713 but this particular area I think has

NOTE Confidence: 0.811200136

01:03:06.713 --> 01:03:09.518 struggled a lot the antibody drug conjugates.

NOTE Confidence: 0.811200136

01:03:09.520 --> 01:03:11.020 And you could debate whether

NOTE Confidence: 0.811200136

01:03:11.020 --> 01:03:12.520 this is immunotherapy or not.

NOTE Confidence: 0.811200136

01:03:12.520 --> 01:03:15.794 I tend to think of them more as targeted

NOTE Confidence: 0.811200136

01:03:15.794 --> 01:03:18.998 delivery of agents rather than immunotherapy.

NOTE Confidence: 0.811200136

01:03:19.000 --> 01:03:20.338 I think there is more progress.

NOTE Confidence: 0.811200136

01:03:20.340 --> 01:03:22.400 We clearly have gemtuzumab ozogamicin

NOTE Confidence: 0.811200136

01:03:22.400 --> 01:03:25.220 already approved and then the CD 123

NOTE Confidence: 0.811200136

01:03:25.220 --> 01:03:27.179 agent that took tremendous mentioned

NOTE Confidence: 0.811200136

01:03:27.179 --> 01:03:29.813 and in the transplant session which

NOTE Confidence: 0.811200136

01:03:29.813 --> 01:03:31.860 I encourage everybody to attend,

NOTE Confidence: 0.811200136

01:03:31.860 --> 01:03:34.980 there is this I map drug.

NOTE Confidence: 0.811200136

01:03:34.980 --> 01:03:36.604 There was a just a couple of

NOTE Confidence: 0.811200136

01:03:36.604 --> 01:03:38.084 days presentation in the tandem

NOTE Confidence: 0.811200136

01:03:38.084 --> 01:03:38.818 transplant meetings.

NOTE Confidence: 0.811200136

01:03:38.820 --> 01:03:39.954 This is a.

NOTE Confidence: 0.811200136

01:03:39.954 --> 01:03:41.088 Radio immuno conjugate,

NOTE Confidence: 0.811200136

01:03:41.090 --> 01:03:43.590 so it's radioactive iodine conjugated

NOTE Confidence: 0.811200136

01:03:43.590 --> 01:03:46.316 to CD45 and there was an improvement

NOTE Confidence: 0.811200136

01:03:46.316 --> 01:03:49.022 in overall survival when it's given as

NOTE Confidence: 0.811200136

01:03:49.022 --> 01:03:51.326 part of the conditioning for transplant.

NOTE Confidence: 0.811200136

01:03:51.330 --> 01:03:53.090 So there is some movement with the ADC,

NOTE Confidence: 0.811200136

01:03:53.090 --> 01:03:56.842 but bytes and drug cartels for myeloid

NOTE Confidence: 0.811200136

01:03:56.842 --> 01:04:00.388 malignancies have been a bit of a challenge.

NOTE Confidence: 0.846804899230769

01:04:02.010 --> 01:04:03.250 Yep. Thank you, Amir.

NOTE Confidence: 0.846804899230769

01:04:03.250 --> 01:04:05.909 So I think we're going to wrap it up.

NOTE Confidence: 0.846804899230769

01:04:05.910 --> 01:04:08.326 Uh, uh, hematology tumor board is coming up.

NOTE Confidence: 0.846804899230769

01:04:08.330 --> 01:04:10.258 So I have to say goodbye to everyone.

NOTE Confidence: 0.846804899230769

01:04:10.260 --> 01:04:12.087 And if you guys have any questions,

NOTE Confidence: 0.846804899230769

01:04:12.090 --> 01:04:14.442 you can certainly e-mail us and

NOTE Confidence: 0.846804899230769

01:04:14.442 --> 01:04:16.680 contact us after this meeting.

NOTE Confidence: 0.877488686666667

01:04:19.080 --> 01:04:19.779 Thank you, thank

NOTE Confidence: 0.749152685

01:04:19.790 --> 01:04:20.638 you. Thank you everyone.