WEBVTT

NOTE duration:"01:02:36.5230000"

NOTE language:en-us

NOTE Confidence: 0.84039795

00:00:00.000 --> 00:00:02.205 But it's 1202 an Why don't we

NOTE Confidence: 0.84039795

00:00:02.205 --> 00:00:04.140 get started 'cause I want to make

NOTE Confidence: 0.84809178

00:00:04.140 --> 00:00:05.796 sure everyone has time.

NOTE Confidence: 0.84809178

00:00:05.796 --> 00:00:06.916 I welcome everybody.

NOTE Confidence: 0.84809178

00:00:06.916 --> 00:00:09.025 This is actually our last Cancer

NOTE Confidence: 0.84809178

00:00:09.025 --> 00:00:11.140 Center grand rounds of calendar year

NOTE Confidence: 0.84809178

00:00:11.140 --> 00:00:15.419 2020 and what a year it has been. A

NOTE Confidence: 0.8406525

00:00:15.420 --> 00:00:17.710 lot of lot of things

NOTE Confidence: 0.8406525

00:00:17.710 --> 00:00:21.830 have happened, a lot of great work and it

NOTE Confidence: 0.8406525

00:00:21.830 --> 00:00:24.674 seems almost fitting that actually theme

NOTE Confidence: 0.8406525

00:00:24.674 --> 00:00:28.239 for our our last grand rounds is our.

NOTE Confidence: 0.8406525

00:00:28.240 --> 00:00:30.689 Our division of hematology.

NOTE Confidence: 0.8406525

00:00:30.690 --> 00:00:34.380 And which we are extremely proud. And among

NOTE Confidence: 0.86493784

00:00:34.380 --> 00:00:37.140 the highlights of all the many

NOTE Confidence: 0.86493784

00:00:37.140 --> 00:00:38.990 accomplishments in the division

NOTE Confidence: 0.86493784

00:00:38.990 --> 00:00:41.752 was actually the results of our

NOTE Confidence: 0.86493784

00:00:41.752 --> 00:00:44.518 search for our new division chief.

NOTE Confidence: 0.86493784

00:00:44.520 --> 00:00:47.750 As, as you've heard, we had a

NOTE Confidence: 0.86493784

00:00:47.750 --> 00:00:50.050 national search an without question.

NOTE Confidence: 0.86493784

00:00:50.050 --> 00:00:52.360 There was one person that

NOTE Confidence: 0.86493784

00:00:52.360 --> 00:00:54.200 the committee felt very

NOTE Confidence: 0.86493784

00:00:54.200 --> 00:00:56.510 strongly rose to the top,

NOTE Confidence: 0.86493784

00:00:56.510 --> 00:00:59.125 and that is Doctor Stephanie

NOTE Confidence: 0.86493784

00:00:59.125 --> 00:01:00.694 Allyne a recognized.

NOTE Confidence: 0.86493784

00:01:00.700 --> 00:01:01.606 Physician scientists,

NOTE Confidence: 0.86493784

00:01:01.606 --> 00:01:02.966 clinician educator, leader,

NOTE Confidence: 0.86493784

00:01:02.966 --> 00:01:06.146 and which is so pleased to have

NOTE Confidence: 0.86493784

00:01:06.146 --> 00:01:08.873 Stephanie now in that role in

NOTE Confidence: 0.86493784

00:01:08.873 --> 00:01:10.686 the really extraordinary legacy

NOTE Confidence: 0.86493784

00:01:10.686 --> 00:01:12.498 of accomplishment in hematology

NOTE Confidence: 0.8392685

00:01:12.500 --> 00:01:15.680 detail. So I'm going to turn it

NOTE Confidence: 0.8392685

00:01:15.680 --> 00:01:17.952 over to Stephanie to introduce

NOTE Confidence: 0.8392685

00:01:17.952 --> 00:01:19.768 our esteemed 2 speakers.

NOTE Confidence: 0.74015343

00:01:20.910 --> 00:01:23.976 Like Italian, thank you for this honor.

NOTE Confidence: 0.74015343

00:01:23.980 --> 00:01:26.710 So I'm really honored to introduce two

NOTE Confidence: 0.74015343

00:01:26.710 --> 00:01:30.109 over my dear dear colleagues and friends,

NOTE Confidence: 0.74015343

00:01:30.110 --> 00:01:32.826 and our first speaker of the day

NOTE Confidence: 0.74015343

00:01:32.826 --> 00:01:34.930 is Doctor Nikolai productive.

NOTE Confidence: 0.74015343

00:01:34.930 --> 00:01:36.244 He's associate professor,

NOTE Confidence: 0.74015343

00:01:36.244 --> 00:01:38.353 internal medicine, hematology, and Sir.

NOTE Confidence: 0.74015343

00:01:38.353 --> 00:01:40.819 Just as the associate director of

NOTE Confidence: 0.74015343

00:01:40.819 --> 00:01:43.068 Hematology Oncology Fellowship program,

NOTE Confidence: 0.74015343

00:01:43.070 --> 00:01:45.478 he is also the from T for

NOTE Confidence: 0.74015343

00:01:45.478 --> 00:01:47.749 education on the Duffy service.

NOTE Confidence: 0.74015343

00:01:47.750 --> 00:01:50.024 Nicolai received his MD and PhD

NOTE Confidence: 0.74015343

00:01:50.024 --> 00:01:52.040 from Saint Peters Burg State,

NOTE Confidence: 0.74015343

00:01:52.040 --> 00:01:54.152 Pablo Medical University and completed his

NOTE Confidence: 0.74015343

00:01:54.152 --> 00:01:56.719 fellowship at Yale in hematology oncology,

NOTE Confidence: 0.74015343

00:01:56.720 --> 00:01:59.807 after which we get to keep him and Nikolai

NOTE Confidence: 0.74015343

00:01:59.807 --> 00:02:01.939 Nikolai's clinical practice and research

NOTE Confidence: 0.74015343

00:02:01.939 --> 00:02:04.513 are focused on my light neoplasms,

NOTE Confidence: 0.74015343

00:02:04.520 --> 00:02:05.936 including acute minor.

NOTE Confidence: 0.74015343

00:02:05.936 --> 00:02:08.296 Kenya models plastic syndromes and

NOTE Confidence: 0.74015343

00:02:08.296 --> 00:02:10.406 in particular my lucrative neoplasms

NOTE Confidence: 0.74015343

00:02:10.406 --> 00:02:12.961 in which he really is an expert.

NOTE Confidence: 0.74015343

00:02:12.970 --> 00:02:15.525 Nikolai serves as a Pi for a

NOTE Confidence: 0.74015343

00:02:15.525 --> 00:02:17.330 number of clinical studies.

NOTE Confidence: 0.74015343

00:02:17.330 --> 00:02:19.094 Their industry sponsored cooperative

NOTE Confidence: 0.74015343

00:02:19.094 --> 00:02:20.858 group investigator initiated and

NOTE Confidence: 0.74015343

00:02:20.858 --> 00:02:22.870 his clinical care and his trials.

NOTE Confidence: 0.74015343

00:02:22.870 --> 00:02:24.850 He really makes a difference

NOTE Confidence: 0.74015343

00:02:24.850 --> 00:02:26.038 for his patience.

NOTE Confidence: 0.74015343

00:02:26.040 --> 00:02:26.832 So nicholi,

NOTE Confidence: 0.74015343

00:02:26.832 --> 00:02:29.208 we look forward to your time.

NOTE Confidence: 0.77378833

00:02:29.210 --> 00:02:30.395 Thank you Stephanie,

NOTE Confidence: 0.77378833

00:02:30.395 --> 00:02:31.975 for this kind introduction.

NOTE Confidence: 0.77378833

00:02:31.980 --> 00:02:33.560 I'll be talking about

NOTE Confidence: 0.77378833

00:02:33.560 --> 00:02:34.745 polycythemia Vera today.

NOTE Confidence: 0.77378833

00:02:34.750 --> 00:02:37.255 I will talk about Epidemiology, prognosis.

NOTE Confidence: 0.77378833

00:02:37.255 --> 00:02:39.880 And a real world outcomes.

NOTE Confidence: 0.77378833

00:02:39.880 --> 00:02:42.260 Are these are my disclosures?

NOTE Confidence: 0.77378833

00:02:42.260 --> 00:02:43.980 So, first of all,

NOTE Confidence: 0.77378833

00:02:43.980 --> 00:02:45.700 polycythemia Vera belongs to

NOTE Confidence: 0.77378833

00:02:45.700 --> 00:02:48.256 the Group of Milo proliferative

NOTE Confidence: 0.77378833

00:02:48.256 --> 00:02:50.946 neoplasms based on W2 2016

NOTE Confidence: 0.77378833

00:02:50.946 --> 00:02:52.964 classification mpanza divided into

NOTE Confidence: 0.77378833

00:02:52.964 --> 00:02:55.556 pH positive or BCR ABL positive?

NOTE Confidence: 0.77378833

00:02:55.560 --> 00:02:58.416 Or also known as chronic myeloid

NOTE Confidence: 0.77378833

00:02:58.416 --> 00:03:00.780 leukemia as well as BCR,

NOTE Confidence: 0.77378833

00:03:00.780 --> 00:03:03.160 ABL negative Milo proliferative neoplasms,

NOTE Confidence: 0.77378833

00:03:03.160 --> 00:03:05.902 and among them there are classical

NOTE Confidence: 0.77378833

00:03:05.902 --> 00:03:07.273 mpanza including polycythemia

NOTE Confidence: 0.77378833

00:03:07.273 --> 00:03:09.328 Vera we're discussing today.

NOTE Confidence: 0.77378833

00:03:09.330 --> 00:03:11.370 Also essential thrombocythemia.

NOTE Confidence: 0.77378833

00:03:11.370 --> 00:03:14.300 And primary myelofibrosis so the

NOTE Confidence: 0.77378833

00:03:14.300 --> 00:03:16.970 definition is based on WTO 2016

NOTE Confidence: 0.77378833

00:03:16.970 --> 00:03:18.920 criteria represented on the slide.

NOTE Confidence: 0.77378833

00:03:18.920 --> 00:03:22.128 To diagnose the very you have to have

NOTE Confidence: 0.77378833

00:03:22.128 --> 00:03:24.933 three major criteria on the left or

NOTE Confidence: 0.77378833

00:03:24.933 --> 00:03:27.904 two first 2 first major criteria and

NOTE Confidence: 0.77378833

00:03:27.904 --> 00:03:30.790 then minor criterion on the right.

NOTE Confidence: 0.77378833

00:03:30.790 --> 00:03:32.486 The major criteria include

NOTE Confidence: 0.77378833

00:03:32.486 --> 00:03:33.758 elevation of hemoglobin.

NOTE Confidence: 0.77378833

00:03:33.760 --> 00:03:35.875 This is the hallmark feature

NOTE Confidence: 0.77378833

00:03:35.875 --> 00:03:37.144 of this condition,

NOTE Confidence: 0.77378833

00:03:37.150 --> 00:03:39.663 and that's what makes it different from

NOTE Confidence: 0.77378833

00:03:39.663 --> 00:03:42.239 other classical Milo proliferative neoplasms.

NOTE Confidence: 0.77378833

00:03:42.240 --> 00:03:43.593 The bone marrow.

NOTE Confidence: 0.77378833

00:03:43.593 --> 00:03:45.397 Biopsy is necessary and

NOTE Confidence: 0.77378833

00:03:45.397 --> 00:03:47.778 usually shows up on my loses.

NOTE Confidence: 0.77378833

00:03:47.780 --> 00:03:49.800 Excessive presence of red blood

NOTE Confidence: 0.77378833

00:03:49.800 --> 00:03:51.416 cells and myeloid precursors,

NOTE Confidence: 0.77378833

00:03:51.420 --> 00:03:53.838 as well as megakaryocytes and then.

NOTE Confidence: 0.77378833

00:03:53.840 --> 00:03:54.244 Finally,

NOTE Confidence: 0.77378833

00:03:54.244 --> 00:03:57.476 there is one of two Jack two mutations,

NOTE Confidence: 0.77378833

00:03:57.480 --> 00:03:59.500 Jack 2V617F mutation or Jack.

NOTE Confidence: 0.77378833

00:03:59.500 --> 00:04:02.321 Two exon 12 mutation in very rare

NOTE Confidence: 0.77378833

00:04:02.321 --> 00:04:04.346 circumstances, about 2% or less.

NOTE Confidence: 0.77378833

00:04:04.346 --> 00:04:06.770 When this mutations are not present,

NOTE Confidence: 0.77378833

00:04:06.770 --> 00:04:09.752 you need lower throughput and level

NOTE Confidence: 0.77378833

00:04:09.752 --> 00:04:11.740 to diagnose polycythemia Vera.

NOTE Confidence: 0.77378833

00:04:11.740 --> 00:04:14.848 So the history of Mila proliferate

NOTE Confidence: 0.77378833

00:04:14.848 --> 00:04:17.424 diseases is interesting if at

NOTE Confidence: 0.77378833

00:04:17.424 --> 00:04:19.920 first they were described as a

NOTE Confidence: 0.77378833

00:04:19.920 --> 00:04:22.700 group by Doctor William Damashek,

NOTE Confidence: 0.77378833

00:04:22.700 --> 00:04:25.790 he immigrated with his family from

NOTE Confidence: 0.77378833

00:04:25.790 --> 00:04:29.344 Russia to Massachusetts at the age of

NOTE Confidence: 0.77378833

00:04:29.344 --> 00:04:32.158 three and then stayed in Massachusetts,

NOTE Confidence: 0.77378833

00:04:32.160 --> 00:04:35.639 was working in Tufts when he described

NOTE Confidence: 0.77378833

00:04:35.639 --> 00:04:36.633 myeloproliferative diseases.

NOTE Confidence: 0.77378833

00:04:36.640 --> 00:04:39.215 This group of conditions became

NOTE Confidence: 0.77378833

00:04:39.215 --> 00:04:41.790 reportable to seer the lodge.

NOTE Confidence: 0.77378833

00:04:41.790 --> 00:04:45.012 Registry of cancer patients in the

NOTE Confidence: 0.77378833

00:04:45.012 --> 00:04:48.469 United States in 2001 and in 2008

NOTE Confidence: 0.77378833

00:04:48.469 --> 00:04:51.290 W show renamed MP dies to MPs,

NOTE Confidence: 0.77378833

00:04:51.290 --> 00:04:53.670 so from Milo proliferative diseases,

NOTE Confidence: 0.77378833

00:04:53.670 --> 00:04:56.040 they became I'll of proliferative

NOTE Confidence: 0.77378833

00:04:56.040 --> 00:04:59.332 neoplasms in Part B, cause in 2005,

NOTE Confidence: 0.77378833

00:04:59.332 --> 00:05:01.652 Jack 2V617F mutation was identified

NOTE Confidence: 0.77378833

00:05:01.652 --> 00:05:04.908 as a driver mutation in majority of

NOTE Confidence: 0.77378833

00:05:04.908 --> 00:05:08.250 patients with PD ET an Milo fibrosis

NOTE Confidence: 0.77378833

00:05:08.250 --> 00:05:11.799 in 2006 nipple exam 10 mutation another.

NOTE Confidence: 0.77378833

00:05:11.800 --> 00:05:14.158 Driver mutational Jack Stat pathway which

NOTE Confidence: 0.77378833

00:05:14.158 --> 00:05:16.610 is activated in those malignancies,

NOTE Confidence: 0.77378833

00:05:16.610 --> 00:05:19.226 was discovered and then in 2007,

NOTE Confidence: 0.77378833

00:05:19.230 --> 00:05:20.978 another Jack mutation Jack.

NOTE Confidence: 0.77378833

00:05:20.978 --> 00:05:23.600 Two exon 12 mutation was described.

NOTE Confidence: 0.77378833

00:05:23.600 --> 00:05:25.800 Finally in 2013 call reticular

NOTE Confidence: 0.77378833

00:05:25.800 --> 00:05:28.463 mutation was described and if you

NOTE Confidence: 0.77378833

00:05:28.463 --> 00:05:30.791 look at polycythemia Vera which is

NOTE Confidence: 0.77378833

00:05:30.791 --> 00:05:33.650 the subject of my presentation today,

NOTE Confidence: 0.77378833

00:05:33.650 --> 00:05:36.260 most of the patients will have

NOTE Confidence: 0.77378833

00:05:36.260 --> 00:05:38.890 Jack 2V617F mutation 97 percent 1%

NOTE Confidence: 0.77378833

00:05:38.890 --> 00:05:42.746 will have Jack to exam 12 and then.

NOTE Confidence: 0.77378833

00:05:42.750 --> 00:05:46.950 2% of patients will have other drivers.

NOTE Confidence: 0.77378833

00:05:46.950 --> 00:05:49.500 So the polycythemia Vera Epidemiology

NOTE Confidence: 0.77378833

00:05:49.500 --> 00:05:52.650 was recently summarized in our review.

NOTE Confidence: 0.77378833

00:05:52.650 --> 00:05:56.157 As you can see the patients with

NOTE Confidence: 0.77378833

00:05:56.157 --> 00:05:58.350 this diagnosis are older,

NOTE Confidence: 0.77378833

00:05:58.350 --> 00:06:01.969 median age of diagnosis is 65 years.

NOTE Confidence: 0.77378833

00:06:01.970 --> 00:06:05.078 It's not the most common malignancy.

NOTE Confidence: 0.77378833

00:06:05.080 --> 00:06:08.182 The incidence is only .5 to

NOTE Confidence: 0.77378833

00:06:08.182 --> 00:06:09.733 400,000 person years.

NOTE Confidence: 0.77378833

00:06:09.740 --> 00:06:12.150 Estimated prevalence in the USA

NOTE Confidence: 0.77378833

00:06:12.150 --> 00:06:16.309 is 25 to 57 per 100,000 persons.

NOTE Confidence: 0.77378833

00:06:16.310 --> 00:06:18.380 And median overall survival is

NOTE Confidence: 0.77378833

00:06:18.380 --> 00:06:20.036 12 to 14 years,

NOTE Confidence: 0.77378833

00:06:20.040 --> 00:06:21.895 which is less than expected

NOTE Confidence: 0.77378833

00:06:21.895 --> 00:06:23.750 in age and gender matched

NOTE Confidence: 0.8806727

00:06:23.820 --> 00:06:24.590 population.

NOTE Confidence: 0.8806727

00:06:24.590 --> 00:06:28.670 5 year relative survival is 84 to 89%.

NOTE Confidence: 0.8806727

00:06:28.670 --> 00:06:31.614 Uh, so if you look at this graph,

NOTE Confidence: 0.8806727

00:06:31.620 --> 00:06:33.490 you will appreciate that males

NOTE Confidence: 0.8806727

00:06:33.490 --> 00:06:35.360 diagnosed with this condition the

NOTE Confidence: 0.8806727

00:06:35.423 --> 00:06:37.529 little bit more common than females.

NOTE Confidence: 0.8806727

00:06:37.530 --> 00:06:39.738 You can see males and blue.

NOTE Confidence: 0.8806727

00:06:39.740 --> 00:06:42.316 This is divided in different age groups.

NOTE Confidence: 0.8806727

00:06:42.320 --> 00:06:44.462 One other thing you can appreciate here

NOTE Confidence: 0.8806727

00:06:44.462 --> 00:06:46.762 is that this condition is extremely

NOTE Confidence: 0.8806727

00:06:46.762 --> 00:06:48.967 rarely diagnosed in younger patients.

NOTE Confidence: 0.8806727

00:06:48.970 --> 00:06:51.546 Those who look way younger than 40.

NOTE Confidence: 0.8806727

00:06:51.550 --> 00:06:54.421 So this is one of the large cohort studies

NOTE Confidence: 0.8806727

00:06:54.421 --> 00:06:57.076 in one institution and Mayo Clinic,

NOTE Confidence: 0.8806727

00:06:57.080 --> 00:06:59.030 which looked at survival of.

NOTE Confidence: 0.8806727

00:06:59.030 --> 00:07:01.400 Patients with classical Milo proliferative

NOTE Confidence: 0.8806727

00:07:01.400 --> 00:07:04.267 neoplasms and here you can appreciate

NOTE Confidence: 0.8806727

00:07:04.267 --> 00:07:07.200 that 80 survival yellow line is less

NOTE Confidence: 0.8806727

00:07:07.200 --> 00:07:09.628 than survival of general population.

NOTE Confidence: 0.8806727

00:07:09.630 --> 00:07:12.936 The dark blue line and polycythemia

NOTE Confidence: 0.8806727

00:07:12.936 --> 00:07:17.790 Vera in red is worse survival than ET.

NOTE Confidence: 0.8806727

00:07:17.790 --> 00:07:21.978 So the etiology of Milo prolifera.

NOTE Confidence: 0.8806727

00:07:21.980 --> 00:07:23.584 Trackmania plasma goes beyond

NOTE Confidence: 0.8806727

00:07:23.584 --> 00:07:24.386 driver mutations.

NOTE Confidence: 0.8806727

00:07:24.390 --> 00:07:26.390 We know the driver mutations.

NOTE Confidence: 0.8806727

00:07:26.390 --> 00:07:28.796 We also just figured out that

NOTE Confidence: 0.8806727

00:07:28.796 --> 00:07:30.400 they may occur many,

NOTE Confidence: 0.8806727

00:07:30.400 --> 00:07:32.410 many years before MPN diagnosis.

NOTE Confidence: 0.8806727

00:07:32.410 --> 00:07:35.210 During this ash meeting a week ago,

NOTE Confidence: 0.8806727

00:07:35.210 --> 00:07:37.968 there was a presentation which showed that

NOTE Confidence: 0.8806727

00:07:37.968 --> 00:07:40.429 these mutations may develop in neutral,

NOTE Confidence: 0.8806727

00:07:40.430 --> 00:07:43.349 but factors leading to the acquisition and

NOTE Confidence: 0.8806727

00:07:43.349 --> 00:07:46.040 development of MPN are much less clear.

NOTE Confidence: 0.8806727

00:07:46.040 --> 00:07:47.369 So in fact,

NOTE Confidence: 0.8806727

00:07:47.369 --> 00:07:49.584 MPM doesn't develop in everyone

NOTE Confidence: 0.8806727

00:07:49.584 --> 00:07:52.209 who has Jack two mutations.

NOTE Confidence: 0.8806727

00:07:52.210 --> 00:07:54.034 The other interesting observation

NOTE Confidence: 0.8806727

00:07:54.034 --> 00:07:57.255 is that there is higher incidence of

NOTE Confidence: 0.8806727

00:07:57.255 --> 00:07:59.300 mpanza in first degree relatives.

NOTE Confidence: 0.8806727

00:07:59.300 --> 00:08:03.368 It's actually 7 times more likely.

NOTE Confidence: 0.8806727

00:08:03.370 --> 00:08:05.794 The patients that first degree relatives

NOTE Confidence: 0.8806727

00:08:05.794 --> 00:08:08.647 are seven times more likely to develop

NOTE Confidence: 0.8806727

00:08:08.647 --> 00:08:10.987 MPs and German driver mutations inject

NOTE Confidence: 0.8806727

00:08:10.987 --> 00:08:13.767 to color it economical genes uncommon.

NOTE Confidence: 0.8806727

00:08:13.770 --> 00:08:16.656 It is felt that congenital predisposition

NOTE Confidence: 0.8806727

00:08:16.656 --> 00:08:19.013 due to certain polymorphisms help

NOTE Confidence: 0.8806727

00:08:19.013 --> 00:08:21.155 to acquire MPM and families overall

NOTE Confidence: 0.8806727

00:08:21.155 --> 00:08:24.454 within 5 to 10% of MPN patients

NOTE Confidence: 0.8806727

00:08:24.454 --> 00:08:26.398 have germline predisposition.

NOTE Confidence: 0.8806727

00:08:26.400 --> 00:08:29.610 So we started the extrinsic factors

NOTE Confidence: 0.8806727

00:08:29.610 --> 00:08:31.750 influencing on the development

NOTE Confidence: 0.8806727

00:08:31.836 --> 00:08:33.540 of polycythemia Vera,

NOTE Confidence: 0.8806727

00:08:33.540 --> 00:08:35.784 among other myeloproliferative neoplasm's,

NOTE Confidence: 0.8806727

00:08:35.784 --> 00:08:39.580 and for that we used in HRP,

NOTE Confidence: 0.8806727

00:08:39.580 --> 00:08:42.874 diet and health study cohort with

NOTE Confidence: 0.8806727

00:08:42.874 --> 00:08:45.070 more than 450,000 participants.

NOTE Confidence: 0.8806727

00:08:45.070 --> 00:08:48.358 Median follow-up was 15 1/2 years.

NOTE Confidence: 0.8806727

00:08:48.360 --> 00:08:51.420 490 ampion cases were discovered

NOTE Confidence: 0.8806727

00:08:51.420 --> 00:08:54.480 among them 190 PV cases.

NOTE Confidence: 0.8806727

00:08:54.480 --> 00:08:57.231 So it is well known that tobacco

NOTE Confidence: 0.8806727

00:08:57.231 --> 00:08:59.570 is a bad carcinogen,

NOTE Confidence: 0.8806727

00:08:59.570 --> 00:09:02.538 and we were able to show that

NOTE Confidence: 0.8806727

00:09:02.538 --> 00:09:05.418 there is increased risk of MPs

NOTE Confidence: 0.8806727

00:09:05.418 --> 00:09:07.438 velopment one smoking women.

NOTE Confidence: 0.8806727

00:09:07.440 --> 00:09:10.056 So the other interesting finding of

NOTE Confidence: 0.8806727

00:09:10.056 --> 00:09:12.352 this study was identification of

NOTE Confidence: 0.8806727

00:09:12.352 --> 00:09:14.767 coffee intake as protective against

NOTE Confidence: 0.8806727

00:09:14.767 --> 00:09:16.699 development of polycythemia Vera.

NOTE Confidence: 0.8806727

00:09:16.700 --> 00:09:19.423 You can see that high versus low

NOTE Confidence: 0.8806727

00:09:19.423 --> 00:09:21.875 coffee intake was associated with

NOTE Confidence: 0.8806727

00:09:21.875 --> 00:09:24.880 decreased incidence of that diagnosis.

NOTE Confidence: 0.8806727

00:09:24.880 --> 00:09:26.696 Consumption of decaffeinated coffee

NOTE Confidence: 0.8806727

00:09:26.696 --> 00:09:28.966 did not have protective effect.

NOTE Confidence: 0.8806727

00:09:28.970 --> 00:09:35.066 We also looked at different micronutrients.

NOTE Confidence: 0.8806727

00:09:35.070 --> 00:09:37.025 And food groups and identified

NOTE Confidence: 0.8806727

00:09:37.025 --> 00:09:39.392 food consumption is one of the

NOTE Confidence: 0.8806727

00:09:39.392 --> 00:09:41.450 risks of the development of PV.

NOTE Confidence: 0.8388302

00:09:45.420 --> 00:09:47.676 He as well as sugar intake,

NOTE Confidence: 0.8388302

00:09:47.680 --> 00:09:49.570 which is also associated navaira.

NOTE Confidence: 0.8388302

00:09:49.570 --> 00:09:51.957 So to conclude, it's good to have

NOTE Confidence: 0.8388302

00:09:51.957 --> 00:09:54.847 a Cup of coffee in the morning,

NOTE Confidence: 0.8388302

00:09:54.850 --> 00:09:57.858 but not with sugar and without a cigarette.

NOTE Confidence: 0.8388302

00:09:57.860 --> 00:10:00.110 So the common clinical features.

NOTE Confidence: 0.8388302

00:10:00.110 --> 00:10:02.850 Of polycythemia Vera include microvascular

NOTE Confidence: 0.8388302

00:10:02.850 --> 00:10:04.494 complications like headache,

NOTE Confidence: 0.8388302

00:10:04.500 --> 00:10:06.144 aerothermal, alja dizziness,

NOTE Confidence: 0.8388302

00:10:06.144 --> 00:10:08.336 paresthesias and blurred vision

NOTE Confidence: 0.8388302

00:10:08.336 --> 00:10:09.432 microvascular complications,

NOTE Confidence: 0.8388302

00:10:09.440 --> 00:10:11.090 including heart attacks,

NOTE Confidence: 0.8388302

00:10:11.090 --> 00:10:13.840 strokes and venous thrombotic events.

NOTE Confidence: 0.8388302

00:10:13.840 --> 00:10:16.580 Patients with PD may suffer

NOTE Confidence: 0.8388302

00:10:16.580 --> 00:10:18.224 from constitutional symptoms,

NOTE Confidence: 0.8388302

00:10:18.230 --> 00:10:20.422 including fatigue, night sweats,

NOTE Confidence: 0.8388302

00:10:20.422 --> 00:10:22.896 weight loss, and teaching.

NOTE Confidence: 0.8388302

00:10:22.896 --> 00:10:24.960 Specifically aquagenic parictis.

NOTE Confidence: 0.8388302

00:10:24.960 --> 00:10:27.140 Splenomegaly occurs in less than

NOTE Confidence: 0.8388302

00:10:27.140 --> 00:10:29.918 half of the patients and patients

NOTE Confidence: 0.8388302

00:10:29.918 --> 00:10:32.483 with PD may have splenomegaly

NOTE Confidence: 0.8388302

00:10:32.483 --> 00:10:34.535 associated symptoms as well.

NOTE Confidence: 0.8388302

00:10:34.540 --> 00:10:37.816 Most of morbidity and mortality in this

NOTE Confidence: 0.8388302

00:10:37.816 --> 00:10:41.190 group of patients comes from thrombo SIS,

NOTE Confidence: 0.8388302

00:10:41.190 --> 00:10:43.582 arterial and venous thrombosis

NOTE Confidence: 0.8388302

00:10:43.582 --> 00:10:45.974 occur in about 20%.

NOTE Confidence: 0.8388302

00:10:45.980 --> 00:10:48.635 Of patience and you can see that this is

NOTE Confidence: 0.8388302

00:10:48.635 --> 00:10:51.496 the data from cohort of more than 1500

NOTE Confidence: 0.8388302

00:10:51.496 --> 00:10:54.379 patients with them in follow up of 6.9 years,

NOTE Confidence: 0.8388302

00:10:54.380 --> 00:10:55.990 but not only promote transposes,

NOTE Confidence: 0.8388302

00:10:55.990 --> 00:10:57.605 the danger that these patients

NOTE Confidence: 0.8388302

00:10:57.605 --> 00:10:59.220 can also develop major hemorrhage,

NOTE Confidence: 0.8388302

00:10:59.220 --> 00:11:01.158 and it is known that polycythemia

NOTE Confidence: 0.8388302

00:11:01.158 --> 00:11:02.127 Vera is strong,

NOTE Confidence: 0.8388302

00:11:02.130 --> 00:11:05.098 but humor odijk disorder.

NOTE Confidence: 0.8388302

00:11:05.100 --> 00:11:07.160 So what is feared most

NOTE Confidence: 0.8388302

00:11:07.160 --> 00:11:08.396 is disease progression,

NOTE Confidence: 0.8388302

00:11:08.400 --> 00:11:10.560 and patients with polycythemia may

NOTE Confidence: 0.8388302

00:11:10.560 --> 00:11:12.720 progress to post PV myelofibrosis

NOTE Confidence: 0.8388302

00:11:12.788 --> 00:11:15.430 about 10% of patients in 10 years.

NOTE Confidence: 0.8388302

00:11:15.430 --> 00:11:17.761 But even more scary with progression to

NOTE Confidence: 0.8388302

00:11:17.761 --> 00:11:20.339 last phase of Milo proliferative neoplasm

NOTE Confidence: 0.8388302

00:11:20.339 --> 00:11:22.854 or secondary acute myeloid leukemia.

NOTE Confidence: 0.8388302

00:11:22.860 --> 00:11:24.508 As you can see,

NOTE Confidence: 0.8388302

00:11:24.508 --> 00:11:26.950 4% of the patients will develop

NOTE Confidence: 0.8388302

00:11:26.950 --> 00:11:29.879 AML after 10 years of follow up.

NOTE Confidence: 0.8388302

00:11:29.880 --> 00:11:33.410 It is a little bit more than 80 but much

NOTE Confidence: 0.8388302

00:11:33.506 --> 00:11:36.686 less than the primary myelofibrosis.

NOTE Confidence: 0.8388302

00:11:36.690 --> 00:11:40.710 So also we sometimes can observe

NOTE Confidence: 0.8388302

00:11:40.710 --> 00:11:43.390 evolution of essential thrombocythemia

NOTE Confidence: 0.8388302

00:11:43.493 --> 00:11:46.955 Jack Two V 617 mutation positive

NOTE Confidence: 0.8388302

00:11:46.955 --> 00:11:48.686 two polycythemia Vera.

NOTE Confidence: 0.8388302

00:11:48.690 --> 00:11:52.506 Can we predict the risk of disease evolution?

NOTE Confidence: 0.8388302

00:11:52.510 --> 00:11:55.204 Can we predict progression to Milo

NOTE Confidence: 0.8388302

00:11:55.204 --> 00:11:57.750 fibrosis or acute myeloid leukemia?

NOTE Confidence: 0.8388302

00:11:57.750 --> 00:12:01.089 So we participated in this multicenter study,

NOTE Confidence: 0.8388302

00:12:01.090 --> 00:12:03.475 which looked at the largest

NOTE Confidence: 0.8388302

00:12:03.475 --> 00:12:05.860 US based PV data set.

NOTE Confidence: 0.8388302

00:12:05.860 --> 00:12:08.275 We contributed 100 patients to

NOTE Confidence: 0.8388302

00:12:08.275 --> 00:12:11.187 this 500 patient cohort and what

NOTE Confidence: 0.8388302

00:12:11.187 --> 00:12:13.635 looked at is Lucas Cytosis over

NOTE Confidence: 0.8388302

00:12:13.635 --> 00:12:16.162 year and its Association with

NOTE Confidence: 0.8388302

00:12:16.162 --> 00:12:19.197 disease evolution and thrombo SIS.

NOTE Confidence: 0.8388302

00:12:19.200 --> 00:12:23.220 It turns out that this.

NOTE Confidence: 0.8388302

00:12:23.220 --> 00:12:25.495 White cell count trajectory did

NOTE Confidence: 0.8388302

00:12:25.495 --> 00:12:27.315 not associate with thrombosis,

NOTE Confidence: 0.8388302

00:12:27.320 --> 00:12:30.554 but was associated with increased risk of

NOTE Confidence: 0.8388302

00:12:30.554 --> 00:12:33.248 transformation to post TV Milo fibrosis,

NOTE Confidence: 0.8388302

00:12:33.250 --> 00:12:35.074 as well as MPs.

NOTE Confidence: 0.8388302

00:12:35.074 --> 00:12:36.898 Unlike my with leukemia,

NOTE Confidence: 0.8388302

00:12:36.900 --> 00:12:39.175 this study used very interesting

NOTE Confidence: 0.8388302

00:12:39.175 --> 00:12:40.085 statistical approach,

NOTE Confidence: 0.8388302

00:12:40.090 --> 00:12:41.914 so-called group based trajectory

NOTE Confidence: 0.8388302

00:12:41.914 --> 00:12:44.650 modeling which is usually used in

NOTE Confidence: 0.8388302

00:12:44.723 --> 00:12:46.631 social and behavioral Sciences

NOTE Confidence: 0.8388302

00:12:46.631 --> 00:12:49.016 and this allowed to capture

NOTE Confidence: 0.8388302

00:12:49.016 --> 00:12:50.883 infrequent or delayed phenomena

NOTE Confidence: 0.8388302

00:12:50.883 --> 00:12:53.083 from the landmark start point.

NOTE Confidence: 0.8388302

00:12:53.090 --> 00:12:55.616 Over the course of the disease,

NOTE Confidence: 0.8388302

00:12:55.620 --> 00:12:58.707 as opposed to other studies which looked

NOTE Confidence: 0.8388302

00:12:58.707 --> 00:13:01.507 at Lucas Cytosis at one time point.

NOTE Confidence: 0.8388302

00:13:01.510 --> 00:13:03.988 So is WBC increases surrogate marker

NOTE Confidence: 0.8388302

00:13:03.988 --> 00:13:06.132 or of disease evolution potential

NOTE Confidence: 0.8388302

00:13:06.132 --> 00:13:08.664 or is a prompt for cytoreduction,

NOTE Confidence: 0.8388302

00:13:08.670 --> 00:13:10.770 allowing us to prevent it?

NOTE Confidence: 0.8388302

00:13:10.770 --> 00:13:13.717 This particular question is not answered yet.

NOTE Confidence: 0.8388302

00:13:13.720 --> 00:13:16.012 I am privileged to represent our

NOTE Confidence: 0.8388302

00:13:16.012 --> 00:13:18.350 Cancer Center 1 NCM guideline,

NOTE Confidence: 0.8388302

00:13:18.350 --> 00:13:20.675 panel developing guidelines for Milo

NOTE Confidence: 0.8388302

00:13:20.675 --> 00:13:23.260 proliferative neoplasm and I'm going to.

NOTE Confidence: 0.8388302

00:13:23.260 --> 00:13:26.164 I show you the section which is related

NOTE Confidence: 0.8388302

00:13:26.164 --> 00:13:28.398 to management of polycythemia Vera.

NOTE Confidence: 0.8388302

00:13:28.400 --> 00:13:30.710 So the goals of management is to

NOTE Confidence: 0.8388302

00:13:30.710 --> 00:13:32.791 reduce the risk of thrombosis

NOTE Confidence: 0.8388302

00:13:32.791 --> 00:13:34.318 and hemorrhage control.

NOTE Confidence: 0.817933

00:13:34.320 --> 00:13:36.690 The symptoms and try to prevent

NOTE Confidence: 0.817933

00:13:36.690 --> 00:13:38.270 and delay disease transformation.

NOTE Confidence: 0.817933

00:13:38.270 --> 00:13:40.580 Everyone with a diagnosis of PV

NOTE Confidence: 0.817933

00:13:40.580 --> 00:13:42.590 should be receiving low dose

NOTE Confidence: 0.817933

00:13:42.590 --> 00:13:44.990 aspirin as well as be phlebotomist.

NOTE Confidence: 0.817933

00:13:44.990 --> 00:13:47.755 Two hematic rate goal of less than

NOTE Confidence: 0.817933

00:13:47.755 --> 00:13:49.586 545% cardiovascular risk factors have

NOTE Confidence: 0.817933

00:13:49.586 --> 00:13:52.767 to be managed as well as this as

NOTE Confidence: 0.817933

00:13:52.767 --> 00:13:54.695 cardiovascular mobility and mortality.

NOTE Confidence: 0.817933

00:13:54.700 --> 00:13:56.920 Is common among these patients,

NOTE Confidence: 0.817933

00:13:56.920 --> 00:13:59.692 so the evidence behind aspirin in

NOTE Confidence: 0.817933

00:13:59.692 --> 00:14:02.010 polycythemia Vera comes from this

NOTE Confidence: 0.817933

00:14:02.010 --> 00:14:04.380 study which was published in 2004

NOTE Confidence: 0.817933

00:14:04.380 --> 00:14:07.130 in New England Journal of medicine.

NOTE Confidence: 0.817933

00:14:07.130 --> 00:14:08.806 Is this so called?

NOTE Confidence: 0.817933

00:14:08.806 --> 00:14:11.320 The CLAP study evaluation of aspirin

NOTE Confidence: 0.817933

00:14:11.404 --> 00:14:14.194 in polycythemia and it looked at

NOTE Confidence: 0.817933

00:14:14.194 --> 00:14:16.899 probability of survival free of marker.

NOTE Confidence: 0.8374873

00:14:19.080 --> 00:14:21.576 Action and stroke and death from

NOTE Confidence: 0.8374873

00:14:21.576 --> 00:14:24.188 cardiovascular causes as well as P and DVT.

NOTE Confidence: 0.8374873

00:14:24.190 --> 00:14:26.362 That was the combined endpoint the

NOTE Confidence: 0.8374873

00:14:26.362 --> 00:14:28.570 aspirin uses as opposed to placebo.

NOTE Confidence: 0.8374873

00:14:28.570 --> 00:14:29.974 Users had 60% risk.

NOTE Confidence: 0.8374873

00:14:29.974 --> 00:14:31.729 Reduction of adverse events and

NOTE Confidence: 0.8374873

00:14:31.729 --> 00:14:33.663 incidents of major bleeding episodes

NOTE Confidence: 0.8374873

00:14:33.663 --> 00:14:35.183 was not significantly different

NOTE Confidence: 0.8374873

00:14:35.183 --> 00:14:37.328 in this low dose aspirin group.

NOTE Confidence: 0.8374873

00:14:37.330 --> 00:14:39.997 So the next recommendation in the guidelines

NOTE Confidence: 0.8374873

00:14:39.997 --> 00:14:42.810 is to keep him at ecrit below 45%.

NOTE Confidence: 0.8374873

00:14:42.810 --> 00:14:45.309 The study which was published in New

NOTE Confidence: 0.8374873

00:14:45.309 --> 00:14:47.550 England Journal of Medicine in 2013,

NOTE Confidence: 0.8374873

00:14:47.550 --> 00:14:49.890 confirmed this goal, which we actually.

NOTE Confidence: 0.8374873

00:14:49.890 --> 00:14:52.070 Using practice for many years,

NOTE Confidence: 0.8374873

00:14:52.070 --> 00:14:54.680 even before this article was published,

NOTE Confidence: 0.8374873

00:14:54.680 --> 00:14:57.662 it turns out that this stricter control

NOTE Confidence: 0.8374873

00:14:57.662 --> 00:14:59.528 of hematocrit using Phlebotomies

NOTE Confidence: 0.8374873

00:14:59.528 --> 00:15:02.093 as well as cytoreductive therapies

NOTE Confidence: 0.8374873

00:15:02.093 --> 00:15:04.711 is associated with four times

NOTE Confidence: 0.8374873

00:15:04.711 --> 00:15:07.176 decreased risk of traumatic events.

NOTE Confidence: 0.8374873

00:15:07.180 --> 00:15:10.402 So in regards to management of

NOTE Confidence: 0.8374873

00:15:10.402 --> 00:15:12.013 cardiovascular risk factors.

NOTE Confidence: 0.8374873

00:15:12.020 --> 00:15:14.799 Our group looked at use of statins

NOTE Confidence: 0.8374873

00:15:14.799 --> 00:15:17.132 and survival among older patients

NOTE Confidence: 0.8374873

00:15:17.132 --> 00:15:19.792 with polycythemia Vera using serum

NOTE Confidence: 0.8374873

00:15:19.792 --> 00:15:22.139 Medicaid and Medicare data set,

NOTE Confidence: 0.8374873

00:15:22.140 --> 00:15:24.440 so we identified them 721

NOTE Confidence: 0.8374873

00:15:24.440 --> 00:15:25.820 polycythemia Vera patients.

NOTE Confidence: 0.8374873

00:15:25.820 --> 00:15:27.200 Little bit more.

NOTE Confidence: 0.8374873

00:15:27.200 --> 00:15:30.420 Half of them use statins after diagnosis.

NOTE Confidence: 0.8374873

00:15:30.420 --> 00:15:33.180 Using univariate analysis on the left,

NOTE Confidence: 0.8374873

00:15:33.180 --> 00:15:35.480 we showed that starting users

NOTE Confidence: 0.8374873

00:15:35.480 --> 00:15:36.860 had improved survival.

NOTE Confidence: 0.8374873

00:15:36.860 --> 00:15:38.381 In multivariate analysis.

NOTE Confidence: 0.8374873

00:15:38.381 --> 00:15:40.916 We also showed that proportion

NOTE Confidence: 0.8374873

00:15:40.916 --> 00:15:42.640 of these covered.

NOTE Confidence: 0.8374873

00:15:42.640 --> 00:15:44.970 By 10 increase of proportion

NOTE Confidence: 0.8374873

00:15:44.970 --> 00:15:47.774 of discovered by 10% led to

NOTE Confidence: 0.8374873

00:15:47.774 --> 00:15:51.043 reduction of risk of death by 18%.

NOTE Confidence: 0.8374873

00:15:51.050 --> 00:15:53.385 So status is certainly beneficial

NOTE Confidence: 0.8374873

00:15:53.385 --> 00:15:55.720 for this group of patients.

NOTE Confidence: 0.8374873

00:15:55.720 --> 00:15:58.516 All the patients with polycythemia Vera,

NOTE Confidence: 0.8374873

00:15:58.520 --> 00:16:01.052 so the center of the algorithm

NOTE Confidence: 0.8374873

00:16:01.052 --> 00:16:03.296 of management of patients with

NOTE Confidence: 0.8374873

00:16:03.296 --> 00:16:05.671 polycythemia is there risk risk

NOTE Confidence: 0.8374873

00:16:05.671 --> 00:16:08.330 stratification based on 11 criteria.

NOTE Confidence: 0.8374873

00:16:08.330 --> 00:16:10.660 So patients are considered high

NOTE Confidence: 0.8374873

00:16:10.660 --> 00:16:12.524 risk for traumatic events,

NOTE Confidence: 0.8374873

00:16:12.530 --> 00:16:13.898 arterial and venous.

NOTE Confidence: 0.8374873

00:16:13.898 --> 00:16:16.634 If they are older than 60,

NOTE Confidence: 0.8374873

00:16:16.640 --> 00:16:18.901 or if they had history of Trumbo

NOTE Confidence: 0.8374873

00:16:18.901 --> 00:16:21.074 SIS so this patients beyond

NOTE Confidence: 0.8374873

00:16:21.074 --> 00:16:23.326 aspirin phlebotomy to America,

NOTE Confidence: 0.8374873

00:16:23.330 --> 00:16:25.435 lesson 45 and modification of

NOTE Confidence: 0.8374873

00:16:25.435 --> 00:16:27.540 cardiovascular risk factors should be

NOTE Confidence: 0.8374873

00:16:27.607 --> 00:16:30.421 on site to re directed therapy and

NOTE Confidence: 0.8374873

00:16:30.421 --> 00:16:32.528 frontline therapy recommended to this

NOTE Confidence: 0.8374873

00:16:32.528 --> 00:16:35.024 patience is either hydroxyurea or interferon.

NOTE Confidence: 0.8374873

00:16:35.030 --> 00:16:38.117 So of course if patients are not high risk

NOTE Confidence: 0.8374873

00:16:38.117 --> 00:16:41.298 and they developed worsening of symptoms,

NOTE Confidence: 0.8374873

00:16:41.300 --> 00:16:43.120 they have new traumatic

NOTE Confidence: 0.8374873

00:16:43.120 --> 00:16:44.940 events or bleeding events.

NOTE Confidence: 0.8374873

00:16:44.940 --> 00:16:47.030 They do not tolerate phlebotomy,

NOTE Confidence: 0.8374873

00:16:47.030 --> 00:16:48.802 which they continuously require,

NOTE Confidence: 0.8374873

00:16:48.802 --> 00:16:51.460 or they have elevated white cell

NOTE Confidence: 0.8374873

00:16:51.536 --> 00:16:53.720 count as well as platelet count.

NOTE Confidence: 0.8374873

00:16:53.720 --> 00:16:56.639 Cytoreductive therapy may be used as well,

NOTE Confidence: 0.8374873

00:16:56.640 --> 00:16:58.530 so there are no randomized

NOTE Confidence: 0.8374873

00:16:58.530 --> 00:17:00.420 studies looking at hydroxyurea in

NOTE Confidence: 0.8374873

00:17:00.484 --> 00:17:02.500 patients with polycythemia Vera.

NOTE Confidence: 0.8374873

00:17:02.500 --> 00:17:05.363 The reason why we're using it is

NOTE Confidence: 0.8374873

00:17:05.363 --> 00:17:07.509 mostly extrapolation from the studies,

NOTE Confidence: 0.8374873

00:17:07.510 --> 00:17:09.600 which were done for essential

NOTE Confidence: 0.8374873

00:17:09.600 --> 00:17:10.436 thrombocythemia patients,

NOTE Confidence: 0.8374873

00:17:10.440 --> 00:17:14.193 so we looked at 820 older patients with TV,

NOTE Confidence: 0.8374873

00:17:14.200 --> 00:17:16.430 once again using CR Medicee.

NOTE Confidence: 0.8374873

00:17:16.430 --> 00:17:19.562 Medicare data set and found out

NOTE Confidence: 0.8374873

00:17:19.562 --> 00:17:22.696 that about 40% of those patients

NOTE Confidence: 0.8374873

00:17:22.696 --> 00:17:26.350 who are high risk under did that,

NOTE Confidence: 0.8374873

00:17:26.350 --> 00:17:29.218 and looking at the treatment with

NOTE Confidence: 0.8374873

00:17:29.218 --> 00:17:32.090 everybody and specifically with hydroxyurea,

NOTE Confidence: 0.8374873

00:17:32.090 --> 00:17:35.776 we found out that every 1010% increase

NOTE Confidence: 0.8374873

00:17:35.776 --> 00:17:39.112 in proportion of days covered by

NOTE Confidence: 0.8374873

00:17:39.112 --> 00:17:41.775 hydroxyurea led to decrease risk

NOTE Confidence: 0.8374873

00:17:41.775 --> 00:17:43.567 of death by 8%.

NOTE Confidence: 0.8374873

00:17:43.570 --> 00:17:47.236 Similarly, increase of PTC by 10%.

NOTE Confidence: 0.8374873

00:17:47.240 --> 00:17:50.360 Lead to decrease of trim bushes by 8%,

NOTE Confidence: 0.8374873

00:17:50.360 --> 00:17:52.460 so this is certainly an effective

NOTE Confidence: 0.8374873

00:17:52.460 --> 00:17:54.722 treatment which are not only helps

NOTE Confidence: 0.8374873

00:17:54.722 --> 00:17:56.717 to prevent traumatic events but

NOTE Confidence: 0.8374873

00:17:56.717 --> 00:17:58.820 also improves survival in older

NOTE Confidence: 0.8374873

00:17:58.820 --> 00:18:00.500 patients with polycythemia Vera.

NOTE Confidence: 0.80290896

00:18:00.500 --> 00:18:03.772 As you can see, the benefit of lobotomy

NOTE Confidence: 0.80290896

00:18:03.772 --> 00:18:06.719 was also confirmed in this study.

NOTE Confidence: 0.80290896

00:18:06.720 --> 00:18:09.919 So why hydroxyurea works for PV patients?

NOTE Confidence: 0.80290896

00:18:09.920 --> 00:18:11.924 It's an oral chemotherapeutic

NOTE Confidence: 0.80290896

00:18:11.924 --> 00:18:13.928 agent that inhibits ribonucleotide

NOTE Confidence: 0.80290896

00:18:13.928 --> 00:18:16.199 reductase and interferes with the

NOTE Confidence: 0.80290896

00:18:16.199 --> 00:18:18.599 process of DNA synthesis and repair.

NOTE Confidence: 0.80290896

00:18:18.600 --> 00:18:22.044 It is cheap and has a reasonably

NOTE Confidence: 0.80290896

00:18:22.044 --> 00:18:24.792 favorable toxicity profile as well as

NOTE Confidence: 0.80290896

00:18:24.792 --> 00:18:27.284 long term safety data, including in

NOTE Confidence: 0.80290896

00:18:27.284 --> 00:18:29.569 children with sickle cell disease.

NOTE Confidence: 0.80290896

00:18:29.570 --> 00:18:33.002 Its mechanism of action in PV is debated

NOTE Confidence: 0.80290896

00:18:33.002 --> 00:18:36.726 but may include impact on blood counts.

NOTE Confidence: 0.80290896

00:18:36.730 --> 00:18:38.970 Ability to reduce neutrophil activity.

NOTE Confidence: 0.80290896

00:18:38.970 --> 00:18:41.465 Decreased expression of the filial

NOTE Confidence: 0.80290896

00:18:41.465 --> 00:18:43.960 adhesion molecules and in use

NOTE Confidence: 0.80290896

00:18:44.043 --> 00:18:46.147 of nitric oxide generation.

NOTE Confidence: 0.80290896

00:18:46.150 --> 00:18:49.086 Side effects occur and the drug is not

NOTE Confidence: 0.80290896

00:18:49.086 --> 00:18:51.272 tolerated by about 20% of patients.

NOTE Confidence: 0.80290896

00:18:51.272 --> 00:18:53.468 The side effects include mild suppression,

NOTE Confidence: 0.80290896

00:18:53.470 --> 00:18:54.202 mucocutaneous ulcers,

NOTE Confidence: 0.80290896

00:18:54.202 --> 00:18:55.666 non Melanoma skin cancers.

NOTE Confidence: 0.80290896

00:18:55.670 --> 00:18:57.774 It is also teratogenic.

NOTE Confidence: 0.80290896

00:18:57.774 --> 00:18:59.878 So the big question,

NOTE Confidence: 0.80290896

00:18:59.880 --> 00:19:02.844 which is still debated during MPM

NOTE Confidence: 0.80290896

00:19:02.844 --> 00:19:06.970 meetings and on the pages of publications,

NOTE Confidence: 0.80290896

00:19:06.970 --> 00:19:08.605 is hydroxyurea relationship

NOTE Confidence: 0.80290896

00:19:08.605 --> 00:19:10.240 with second malignancies,

NOTE Confidence: 0.80290896

00:19:10.240 --> 00:19:11.872 that hydroxyurea increase

NOTE Confidence: 0.80290896

00:19:11.872 --> 00:19:14.048 risk of 2nd malignancies.

NOTE Confidence: 0.80290896

00:19:14.050 --> 00:19:18.145 We again use your Medicare data set to look

NOTE Confidence: 0.80290896

00:19:18.145 --> 00:19:22.769 at second malignancies and one MPN patients.

NOTE Confidence: 0.80290896

00:19:22.770 --> 00:19:26.124 As you can see we started

NOTE Confidence: 0.80290896

00:19:26.124 --> 00:19:28.930 more than 3000 patients and.

NOTE Confidence: 0.80290896

00:19:28.930 --> 00:19:31.667 About 40% of them had polycythemia Vera.

NOTE Confidence: 0.80290896

00:19:31.670 --> 00:19:34.798 This patients were followed up to 10 years.

NOTE Confidence: 0.80290896

00:19:34.800 --> 00:19:37.260 Median follow-up was 2.67 years and

NOTE Confidence: 0.80290896

00:19:37.260 --> 00:19:39.878 median age of diagnosis was 77 years,

NOTE Confidence: 0.80290896

00:19:39.880 --> 00:19:42.624 so it's a little bit older than

NOTE Confidence: 0.80290896

00:19:42.624 --> 00:19:44.866 General PD population because of

NOTE Confidence: 0.80290896

00:19:44.866 --> 00:19:47.346 Medicare requirement for this study.

NOTE Confidence: 0.80290896

00:19:47.350 --> 00:19:50.176 So 65% of patients used hydroxyurea,

NOTE Confidence: 0.80290896

00:19:50.180 --> 00:19:53.484 allowing us to look at two groups,

NOTE Confidence: 0.80290896

00:19:53.490 --> 00:19:55.378 hydroxyurea users and nonusers.

NOTE Confidence: 0.80290896

00:19:55.378 --> 00:19:58.210 It is well known that second

NOTE Confidence: 0.80290896

00:19:58.291 --> 00:20:00.179 malignancy is common in.

NOTE Confidence: 0.80290896

00:20:00.180 --> 00:20:02.430 Patients with mild proliferative neoplasms,

NOTE Confidence: 0.80290896

00:20:02.430 --> 00:20:06.462 it is not really clear exactly why that is,

NOTE Confidence: 0.80290896

00:20:06.470 --> 00:20:09.613 but you can see that in our

NOTE Confidence: 0.80290896

00:20:09.613 --> 00:20:10.960 cohort of patients,

NOTE Confidence: 0.80290896

00:20:10.960 --> 00:20:13.200 about 8.8% developed second malignancy,

NOTE Confidence: 0.80290896

00:20:13.200 --> 00:20:15.900 more than half solid second malignancies,

NOTE Confidence: 0.80290896

00:20:15.900 --> 00:20:17.692 and among patients with

NOTE Confidence: 0.80290896

00:20:17.692 --> 00:20:18.588 hematological malignancies.

NOTE Confidence: 0.80290896

00:20:18.590 --> 00:20:20.905 Majority developed AML and MD

NOTE Confidence: 0.80290896

00:20:20.905 --> 00:20:24.555 S as expected in this group of

NOTE Confidence: 0.80290896

00:20:24.555 --> 00:20:27.035 patients with myeloid neoplasms.

NOTE Confidence: 0.80290896

00:20:27.040 --> 00:20:29.926 So when we compare two groups,

NOTE Confidence: 0.80290896

00:20:29.930 --> 00:20:32.340 hydroxyurea users and non users

NOTE Confidence: 0.80290896

00:20:32.340 --> 00:20:33.786 using univariate analysis,

NOTE Confidence: 0.80290896

00:20:33.790 --> 00:20:36.682 we found no difference in incidence

NOTE Confidence: 0.80290896

00:20:36.682 --> 00:20:38.128 of 2nd malignancies.

NOTE Confidence: 0.80290896

00:20:38.130 --> 00:20:40.365 In the multivariable analysis of

NOTE Confidence: 0.80290896

00:20:40.365 --> 00:20:43.131 hydroxyurea use and type of 2nd

NOTE Confidence: 0.80290896

00:20:43.131 --> 00:20:45.813 malignancies we found no difference in

NOTE Confidence: 0.80290896

00:20:45.813 --> 00:20:48.729 occurrence of all second malignancies,

NOTE Confidence: 0.80290896

00:20:48.730 --> 00:20:51.140 solid second malignancies and he

NOTE Confidence: 0.80290896

00:20:51.140 --> 00:20:53.550 metalogic non myeloid second malignancy's.

NOTE Confidence: 0.80290896

00:20:53.550 --> 00:20:56.550 We also did an analysis specifically.

NOTE Confidence: 0.80290896

00:20:56.550 --> 00:20:58.560 Aimed at my Lloyd second malignancies

NOTE Confidence: 0.80290896

00:20:58.560 --> 00:21:01.398 and there was no difference here either.

NOTE Confidence: 0.80290896

00:21:01.400 --> 00:21:04.100 So moving on this algorithm,

NOTE Confidence: 0.80290896

00:21:04.100 --> 00:21:07.004 if cytoreductive therapy stops

NOTE Confidence: 0.80290896

00:21:07.004 --> 00:21:10.634 working or is not tolerated.

NOTE Confidence: 0.80290896

00:21:10.640 --> 00:21:12.698 Have an option of second line

NOTE Confidence: 0.80290896

00:21:12.698 --> 00:21:14.070 sector reduction with ruxolitinib,

NOTE Confidence: 0.80290896

00:21:14.070 --> 00:21:16.128 which is the only FDA approved

NOTE Confidence: 0.80290896

00:21:16.128 --> 00:21:17.500 drug by the way,

NOTE Confidence: 0.80290896

00:21:17.500 --> 00:21:19.690 in polycythemia Vera neither hydroxyurea

NOTE Confidence: 0.80290896

00:21:19.690 --> 00:21:22.246 nor interferon I approved at this

NOTE Confidence: 0.80290896

00:21:22.246 --> 00:21:24.614 time in the United States by the FDA.

NOTE Confidence: 0.80290896

00:21:24.620 --> 00:21:28.561 So the interferon is used in Milo

NOTE Confidence: 0.80290896

00:21:28.561 --> 00:21:31.360 proliferative neoplasms for many years,

NOTE Confidence: 0.80290896

00:21:31.360 --> 00:21:34.390 and it is associated with decently

NOTE Confidence: 0.80290896

00:21:34.390 --> 00:21:37.156 high rates of haematological response

NOTE Confidence: 0.80290896

00:21:37.156 --> 00:21:39.788 reduction and independence form.

NOTE Confidence: 0.80290896

00:21:39.790 --> 00:21:42.118 Phlebotomies improvement of symptoms,

NOTE Confidence: 0.80290896

00:21:42.118 --> 00:21:45.980 and in some patients up to 30%

NOTE Confidence: 0.80290896

00:21:45.980 --> 00:21:48.224 significant reduction and disappearance

NOTE Confidence: 0.80290896

00:21:48.224 --> 00:21:51.029 of Jack 2V617F positive cells.

NOTE Confidence: 0.80290896

00:21:51.030 --> 00:21:54.876 Side effects include flu like symptoms.

NOTE Confidence: 0.80290896

00:21:54.880 --> 00:21:56.144 Psychiatric conditions and that's

NOTE Confidence: 0.80290896

00:21:56.144 --> 00:21:58.040 why this drug is not given

NOTE Confidence: 0.8312497

00:21:58.097 --> 00:21:59.807 to patients with psychiatric disorders

NOTE Confidence: 0.8312497

00:21:59.807 --> 00:22:02.000 as well as autoimmune side effects.

NOTE Confidence: 0.8312497

00:22:02.000 --> 00:22:03.352 Side effects are better

NOTE Confidence: 0.8312497

00:22:03.352 --> 00:22:04.366 with regulated preparations,

NOTE Confidence: 0.8312497

00:22:04.370 --> 00:22:06.750 which can be given once a week.

NOTE Confidence: 0.8312497

00:22:06.750 --> 00:22:09.116 One other thing which is quite important,

NOTE Confidence: 0.8312497

00:22:09.120 --> 00:22:11.913 this drug is not teratogenic and is

NOTE Confidence: 0.8312497

00:22:11.913 --> 00:22:14.727 preferred for younger patients with P Viera.

NOTE Confidence: 0.8312497

00:22:14.730 --> 00:22:17.390 So it has potential for disease modification

NOTE Confidence: 0.8312497

00:22:17.390 --> 00:22:19.599 by targeting the malignant clone,

NOTE Confidence: 0.8312497

00:22:19.600 --> 00:22:22.235 which is evidenced by disappearance

NOTE Confidence: 0.8312497

00:22:22.235 --> 00:22:24.870 of Jack 2V617F positive cells

NOTE Confidence: 0.8312497

00:22:24.951 --> 00:22:27.136 and some of those patients.

NOTE Confidence: 0.8312497

00:22:27.140 --> 00:22:29.936 This meta analysis of 41 studies,

NOTE Confidence: 0.8312497

00:22:29.940 --> 00:22:31.341 including 12181 patients,

NOTE Confidence: 0.8312497

00:22:31.341 --> 00:22:34.610 more than 500 of them had PV.

NOTE Confidence: 0.8312497

00:22:34.610 --> 00:22:37.990 The overall response rate was 75% with

NOTE Confidence: 0.8312497

00:22:37.990 --> 00:22:40.890 complete haematological response of 50.

NOTE Confidence: 0.8312497

00:22:40.890 --> 00:22:43.386 He presented in meta regression analysis.

NOTE Confidence: 0.8312497

00:22:43.390 --> 00:22:45.886 There was no different from between.

NOTE Confidence: 0.8312497

00:22:45.890 --> 00:22:48.392 No difference between Montag later than

NOTE Confidence: 0.8312497

00:22:48.392 --> 00:22:50.542 pig related interference in regards

NOTE Confidence: 0.8312497

00:22:50.542 --> 00:22:53.008 to response rates and thrombo embolic

NOTE Confidence: 0.8312497

00:22:53.008 --> 00:22:54.718 events and treatment discontinuation

NOTE Confidence: 0.8312497

00:22:54.718 --> 00:22:57.166 due to adverse events were not

NOTE Confidence: 0.8312497

00:22:57.166 --> 00:22:59.654 frequent .5% and 6.5% per year,

NOTE Confidence: 0.8312497

00:22:59.654 --> 00:23:00.070 respectively.

NOTE Confidence: 0.8312497

00:23:00.070 --> 00:23:00.964 Molecular responses,

NOTE Confidence: 0.8312497

00:23:00.964 --> 00:23:03.199 which is certainly interesting because

NOTE Confidence: 0.8312497

00:23:03.199 --> 00:23:05.909 we hope that this drug is disease.

NOTE Confidence: 0.8312497

00:23:05.910 --> 00:23:07.995 Modifying could not be analyzed

NOTE Confidence: 0.8312497

00:23:07.995 --> 00:23:10.080 in this particular meta analysis.

NOTE Confidence: 0.8312497

00:23:10.080 --> 00:23:11.319 You took heterogeneity.

NOTE Confidence: 0.8312497

00:23:11.319 --> 00:23:13.384 Of definition and outcome assessments.

NOTE Confidence: 0.8312497

00:23:13.390 --> 00:23:14.156 In conclusion,

NOTE Confidence: 0.8312497

00:23:14.156 --> 00:23:16.071 we thought that both regulated

NOTE Confidence: 0.8312497

00:23:16.071 --> 00:23:17.677 interference and non peculated

NOTE Confidence: 0.8312497

00:23:17.677 --> 00:23:20.017 interferon can be effective and safe.

NOTE Confidence: 0.8312497

00:23:20.020 --> 00:23:22.092 One term in P.

NOTE Confidence: 0.8312497

00:23:22.092 --> 00:23:23.128 Vera patients.

NOTE Confidence: 0.8312497

00:23:23.130 --> 00:23:25.140 So this is the response study

NOTE Confidence: 0.8312497

00:23:25.140 --> 00:23:27.752 which led to have the approval of

NOTE Confidence: 0.8312497

00:23:27.752 --> 00:23:30.146 Jack inhibitor rock solid Nip for

NOTE Confidence: 0.8312497

00:23:30.146 --> 00:23:32.447 second line treatment in patients

NOTE Confidence: 0.8312497

00:23:32.447 --> 00:23:34.727 with Vera with primary endpoint

NOTE Confidence: 0.8312497

00:23:34.727 --> 00:23:36.798 being composite reduction of spleen

NOTE Confidence: 0.8312497

00:23:36.798 --> 00:23:38.406 volume and hematocrit control.

NOTE Confidence: 0.8312497

00:23:38.410 --> 00:23:41.217 As you can see it was accomplished

NOTE Confidence: 0.8312497

00:23:41.217 --> 00:23:43.226 in 21% of patients separately.

NOTE Confidence: 0.8312497

00:23:43.226 --> 00:23:45.638 Reduction of spleen volume by 35%

NOTE Confidence: 0.8312497

00:23:45.640 --> 00:23:48.482 was seen in almost 40% of patients

NOTE Confidence: 0.8312497

00:23:48.482 --> 00:23:50.978 and 60% of patients could accomplish

NOTE Confidence: 0.8312497

00:23:50.978 --> 00:23:53.138 schematic control with this treatment.

NOTE Confidence: 0.8312497

00:23:53.140 --> 00:23:54.628 This is important anti-inflammatory

NOTE Confidence: 0.8312497

00:23:54.628 --> 00:23:57.328 medication and one of the side effects

NOTE Confidence: 0.8312497

00:23:57.328 --> 00:23:59.746 may be infections including herpes Auster.

NOTE Confidence: 0.8312497

00:23:59.750 --> 00:24:02.180 So we recommend Shingrix vaccine to

NOTE Confidence: 0.8312497

00:24:02.180 --> 00:24:05.198 all of our patients on rock solid net.

NOTE Confidence: 0.8312497

00:24:05.200 --> 00:24:07.420 Another side effect can be non

NOTE Confidence: 0.8312497

00:24:07.420 --> 00:24:09.326 Melanoma skin cancers which has

NOTE Confidence: 0.8312497

00:24:09.326 --> 00:24:11.111 increased incidence in Brooklyn of

NOTE Confidence: 0.8312497

00:24:11.111 --> 00:24:13.760 users but also in hydroxyurea users.

NOTE Confidence: 0.8312497

00:24:13.760 --> 00:24:17.064 So I refer all my patients for German

NOTE Confidence: 0.8312497

00:24:17.064 --> 00:24:18.760 irregular dermatological evaluations.

NOTE Confidence: 0.8312497

00:24:18.760 --> 00:24:21.868 So we looked at 5 year relative

NOTE Confidence: 0.8312497

00:24:21.868 --> 00:24:24.154 survival probability for PV patients

NOTE Confidence: 0.8312497

00:24:24.154 --> 00:24:25.898 in the United States.

NOTE Confidence: 0.8312497

00:24:25.900 --> 00:24:28.260 Patients who are diagnosed between

NOTE Confidence: 0.8312497

00:24:28.260 --> 00:24:31.470 2001 and 2011 with end of observation

NOTE Confidence: 0.8312497

00:24:31.470 --> 00:24:35.193 in 2016 and as you can see this five

NOTE Confidence: 0.8312497

00:24:35.193 --> 00:24:37.549 year relative survival unfortunately

NOTE Confidence: 0.8312497

00:24:37.549 --> 00:24:39.905 is not getting better,

NOTE Confidence: 0.8312497

00:24:39.910 --> 00:24:43.350 so we need new drugs which may improve

NOTE Confidence: 0.8312497

00:24:43.350 --> 00:24:46.190 survival by modifying the disease.

NOTE Confidence: 0.8312497

00:24:46.190 --> 00:24:49.473 So this study looked at GNU interference

NOTE Confidence: 0.8312497

00:24:49.473 --> 00:24:52.469 formulation so called role peg interferon.

NOTE Confidence: 0.8312497

00:24:52.470 --> 00:24:55.550 This is a European study phase three

NOTE Confidence: 0.8312497

00:24:55.550 --> 00:24:58.010 trial comparing group peginterferon.

NOTE Confidence: 0.8312497

00:24:58.010 --> 00:25:00.275 Against hydroxyurea in high risk

NOTE Confidence: 0.8312497

00:25:00.275 --> 00:25:02.087 TV patient frontline treatment.

NOTE Confidence: 0.8312497

00:25:02.090 --> 00:25:05.359 The goal of the study was to

NOTE Confidence: 0.8312497

00:25:05.359 --> 00:25:07.698 show Noninferiority of Ro peg

NOTE Confidence: 0.8312497

00:25:07.698 --> 00:25:10.236 to hydroxyurea an at one year.

NOTE Confidence: 0.8312497

00:25:10.240 --> 00:25:11.188 Interestingly enough,

NOTE Confidence: 0.8312497

00:25:11.188 --> 00:25:14.032 they did not accomplish that primary

NOTE Confidence: 0.8312497

00:25:14.032 --> 00:25:16.450 endpoint of the hydroxyurea was

NOTE Confidence: 0.8312497

00:25:16.450 --> 00:25:18.785 superior from the standpoint of

NOTE Confidence: 0.8312497

00:25:18.785 --> 00:25:20.188 inducing complete haematological

NOTE Confidence: 0.8312497

00:25:20.188 --> 00:25:23.372 responses as well as you can see here,

NOTE Confidence: 0.8312497

00:25:23.380 --> 00:25:25.670 molecular responses at six months

NOTE Confidence: 0.8312497

00:25:25.670 --> 00:25:27.960 were higher among patients treated

NOTE Confidence: 0.8312497

00:25:28.033 --> 00:25:29.179 with hydroxyurea.

NOTE Confidence: 0.8312497

00:25:29.180 --> 00:25:32.428 So interferon in general takes time to work,

NOTE Confidence: 0.8312497

00:25:32.430 --> 00:25:34.782 and that's what we observed over

NOTE Confidence: 0.8312497

00:25:34.782 --> 00:25:36.350 the course of this

NOTE Confidence: 0.854975

00:25:36.429 --> 00:25:39.501 study. So this is the publication which shows

NOTE Confidence: 0.854975

00:25:39.501 --> 00:25:42.976 data up to three years of follow-up data,

NOTE Confidence: 0.854975

00:25:42.980 --> 00:25:45.890 and you can see that in the second part of

NOTE Confidence: 0.854975

00:25:45.962 --> 00:25:49.308 the study interferon did better from the

NOTE Confidence: 0.854975

00:25:49.308 --> 00:25:51.510 standpoint of haematological responses,

NOTE Confidence: 0.854975

00:25:51.510 --> 00:25:53.274 which were statistically significantly

NOTE Confidence: 0.854975

00:25:53.274 --> 00:25:55.479 better than among patients taking

NOTE Confidence: 0.854975

00:25:55.479 --> 00:25:57.598 hydroxyurea as well as molecular responses,

NOTE Confidence: 0.854975

00:25:57.600 --> 00:26:00.570 and you can see that.

NOTE Confidence: 0.854975

00:26:00.570 --> 00:26:02.830 This is actually improving overtime.

NOTE Confidence: 0.854975

00:26:02.830 --> 00:26:05.662 This ash the follow up of the study

NOTE Confidence: 0.854975

00:26:05.662 --> 00:26:08.712 five year follow up was presented

NOTE Confidence: 0.854975

00:26:08.712 --> 00:26:11.542 showing continues that this translate

NOTE Confidence: 0.854975

00:26:11.542 --> 00:26:14.271 continuing as well as there are

NOTE Confidence: 0.854975

00:26:14.271 --> 00:26:16.351 no significant new side effects.

NOTE Confidence: 0.854975

00:26:16.360 --> 00:26:19.078 So this new formulation of the

NOTE Confidence: 0.854975

00:26:19.078 --> 00:26:21.838 interferon can be given once every

NOTE Confidence: 0.854975

00:26:21.838 --> 00:26:24.834 three to four weeks after the first

NOTE Confidence: 0.854975

00:26:24.834 --> 00:26:28.070 year of treatment and is now approved

NOTE Confidence: 0.854975

00:26:28.070 --> 00:26:30.882 in Europe by European Medicines Agency.

NOTE Confidence: 0.854975

00:26:30.882 --> 00:26:33.362 The company making this medication

NOTE Confidence: 0.854975

00:26:33.362 --> 00:26:36.233 is bringing up to the bringing this

NOTE Confidence: 0.854975

00:26:36.233 --> 00:26:39.152 to the US market and it is likely

NOTE Confidence: 0.854975

00:26:39.152 --> 00:26:41.372 that this medication will become

NOTE Confidence: 0.854975

00:26:41.372 --> 00:26:44.024 available for our patients next year.

NOTE Confidence: 0.854975

00:26:44.024 --> 00:26:46.652 So there are few new treatments

NOTE Confidence: 0.854975

00:26:46.652 --> 00:26:49.561 I wanted to mention before I end

NOTE Confidence: 0.854975

00:26:49.561 --> 00:26:52.393 this talk and few clinical trials

NOTE Confidence: 0.854975

00:26:52.393 --> 00:26:55.288 we're planning to participate in.

NOTE Confidence: 0.854975

00:26:55.290 --> 00:26:57.986 Is giving ability to all patients to enroll

NOTE Confidence: 0.854975

00:26:57.986 --> 00:27:00.919 on this study is offering new treatments,

NOTE Confidence: 0.854975

00:27:00.920 --> 00:27:02.045 some of them?

NOTE Confidence: 0.854975

00:27:02.045 --> 00:27:03.920 Maybe this is modifying so.

NOTE Confidence: 0.854975

00:27:03.920 --> 00:27:06.279 First of all, this is the given

NOTE Confidence: 0.854975

00:27:06.279 --> 00:27:08.789 a staff the age Deccan hitter,

NOTE Confidence: 0.854975

00:27:08.790 --> 00:27:13.254 so leading to a situation of the histone.

NOTE Confidence: 0.854975

00:27:13.260 --> 00:27:15.064 That transcriptions of genes

NOTE Confidence: 0.854975

00:27:15.064 --> 00:27:16.868 responsible for cell growth,

NOTE Confidence: 0.854975

00:27:16.870 --> 00:27:18.271 arrest, differentiation, apoptosis.

NOTE Confidence: 0.854975

00:27:18.271 --> 00:27:22.092 This drug is wanna be started in the

NOTE Confidence: 0.854975

00:27:22.092 --> 00:27:24.462 phase three trial against hydroxyurea

NOTE Confidence: 0.854975

00:27:24.462 --> 00:27:27.181 for the frontline treatment of PV

NOTE Confidence: 0.854975

00:27:27.181 --> 00:27:29.046 patients with high risk disease.

NOTE Confidence: 0.854975

00:27:29.050 --> 00:27:32.326 So the other class of drugs which

NOTE Confidence: 0.854975

00:27:32.326 --> 00:27:34.459 may be interesting is MDM.

NOTE Confidence: 0.854975

00:27:34.460 --> 00:27:35.362 Two inhibitors.

NOTE Confidence: 0.854975

00:27:35.362 --> 00:27:38.970 As you know MDM two inhibits TP53 function,

NOTE Confidence: 0.854975

00:27:38.970 --> 00:27:41.700 and by inhibiting MDM two way

NOTE Confidence: 0.854975

00:27:41.700 --> 00:27:44.400 allowing TP 53 to perform.

NOTE Confidence: 0.854975

00:27:44.400 --> 00:27:45.082 It's wrong,

NOTE Confidence: 0.854975

00:27:45.082 --> 00:27:46.787 not in the malignant cell,

NOTE Confidence: 0.854975

00:27:46.790 --> 00:27:47.681 by the way,

NOTE Confidence: 0.854975

00:27:47.681 --> 00:27:49.463 interfere on one of the mechanisms

NOTE Confidence: 0.854975

00:27:49.463 --> 00:27:51.378 of action of interferon would

NOTE Confidence: 0.854975

00:27:51.378 --> 00:27:52.926 be activations of genes,

NOTE Confidence: 0.854975

00:27:52.930 --> 00:27:54.560 increasing transcription of TP 53

NOTE Confidence: 0.854975

00:27:54.560 --> 00:27:57.304 so the last study I want to mention

NOTE Confidence: 0.854975

00:27:57.304 --> 00:27:59.398 phase two trial of hepcidin analog.

NOTE Confidence: 0.854975

00:27:59.400 --> 00:28:02.039 It's nice to see after discovery of

NOTE Confidence: 0.854975

00:28:02.039 --> 00:28:04.434 hepcidin 20 years ago that we have

NOTE Confidence: 0.854975

00:28:04.434 --> 00:28:06.966 an analog and you know we now have

NOTE Confidence: 0.854975

00:28:06.966 --> 00:28:09.290 a test we can check for hepcidin.

NOTE Confidence: 0.854975

00:28:09.290 --> 00:28:10.136 Very expensive.

NOTE Confidence: 0.854975

00:28:10.136 --> 00:28:13.520 I never was able to do it but

NOTE Confidence: 0.854975

00:28:13.621 --> 00:28:15.877 now we also have a drug.

NOTE Confidence: 0.854975

00:28:15.880 --> 00:28:18.060 Which basically shuts down transport

NOTE Confidence: 0.854975

00:28:18.060 --> 00:28:21.394 of iron and locks it in the cells

NOTE Confidence: 0.854975

00:28:21.394 --> 00:28:23.907 and this drug is used for patients

NOTE Confidence: 0.854975

00:28:23.989 --> 00:28:26.054 with severe who need phlebotomies

NOTE Confidence: 0.854975

00:28:26.054 --> 00:28:28.984 and in an attempt to avoid iron

NOTE Confidence: 0.854975

00:28:28.984 --> 00:28:31.144 deficiency which may have detrimental

NOTE Confidence: 0.854975

00:28:31.144 --> 00:28:33.020 effects on quality of life.

NOTE Confidence: 0.854975

00:28:33.020 --> 00:28:34.241 The preliminary results

NOTE Confidence: 0.854975

00:28:34.241 --> 00:28:35.869 which office to study,

NOTE Confidence: 0.854975

00:28:35.870 --> 00:28:38.726 which were presented at Ash week ago,

NOTE Confidence: 0.854975

00:28:38.730 --> 00:28:39.963 were quite promising.

NOTE Confidence: 0.854975

00:28:39.963 --> 00:28:43.322 No side effects and pretty much everyone on

NOTE Confidence: 0.854975

00:28:43.322 --> 00:28:45.770 this drug does not require phlebotomist.

NOTE Confidence: 0.854975

00:28:45.770 --> 00:28:46.248 Anymore.

NOTE Confidence: 0.854975

00:28:46.248 --> 00:28:49.116 So I'd like to conclude that

NOTE Confidence: 0.854975

00:28:49.116 --> 00:28:51.995 polycythemia Vera is driven by Jack

NOTE Confidence: 0.854975

00:28:51.995 --> 00:28:54.713 2V617F mutation in the majority of

NOTE Confidence: 0.854975

00:28:54.713 --> 00:28:56.830 cases in 97% sugar intake increases

NOTE Confidence: 0.854975

00:28:56.830 --> 00:28:58.990 and coffee intake decreases the risk

NOTE Confidence: 0.854975

00:28:58.990 --> 00:29:01.148 of polycythemia Vera development.

NOTE Confidence: 0.854975

00:29:01.150 --> 00:29:01.982 In fact,

NOTE Confidence: 0.854975

00:29:01.982 --> 00:29:04.062 consumption of coffee moderate amounts

NOTE Confidence: 0.854975

00:29:04.062 --> 00:29:06.978 can be considered part of normal lifestyle.

NOTE Confidence: 0.8039933

00:29:06.980 --> 00:29:09.055 Increased white cell count is

NOTE Confidence: 0.8039933

00:29:09.055 --> 00:29:10.715 associated with PV evolution.

NOTE Confidence: 0.8039933

00:29:10.720 --> 00:29:12.800 To post PD, Mila, fibrosis,

NOTE Confidence: 0.8039933

00:29:12.800 --> 00:29:15.482 MD, SNL user status should be

NOTE Confidence: 0.8039933

00:29:15.482 --> 00:29:17.680 considered in PV patients for.

NOTE Confidence: 0.8039933

00:29:17.680 --> 00:29:19.352 Cardiovascular disease risk reduction,

NOTE Confidence: 0.8039933

00:29:19.352 --> 00:29:21.024 hydroxyurea safe and effective,

NOTE Confidence: 0.8039933

00:29:21.030 --> 00:29:23.970 but interference holds promise to be disease.

NOTE Confidence: 0.8039933

00:29:23.970 --> 00:29:26.065 Modifying and normal treatments to

NOTE Confidence: 0.8039933

00:29:26.065 --> 00:29:28.160 prevent or delay disease transformation.

NOTE Confidence: 0.8039933

00:29:28.160 --> 00:29:28.877 I need it.

NOTE Confidence: 0.8039933

00:29:28.877 --> 00:29:31.151 At the end I would like to acknowledge

NOTE Confidence: 0.8039933

00:29:31.151 --> 00:29:33.801 funding from the Frederick Dilucca

NOTE Confidence: 0.8039933

00:29:33.801 --> 00:29:35.921 Foundation Yellow Corporate Center,

NOTE Confidence: 0.8039933

00:29:35.930 --> 00:29:38.464 allowing us to conduct the studies and

NOTE Confidence: 0.8039933

00:29:38.464 --> 00:29:40.440 my collaborators thank you very much.

NOTE Confidence: 0.73364645

00:29:41.830 --> 00:29:42.709 Nikolai absolute proof.

NOTE Confidence: 0.73364645

00:29:42.709 --> 00:29:44.760 So you can't see my coffee tears.

NOTE Confidence: 0.73364645

00:29:44.760 --> 00:29:47.680 It was coffee right now.

NOTE Confidence: 0.73364645

00:29:47.680 --> 00:29:50.169 Getting my very soon.

NOTE Confidence: 0.73364645

00:29:50.170 --> 00:29:51.838 Yeah, I think we just have.

NOTE Confidence: 0.73364645

00:29:51.840 --> 00:29:53.716 It may be time for just one

NOTE Confidence: 0.73364645

00:29:53.716 --> 00:29:55.148 or two questions because we

NOTE Confidence: 0.73364645

00:29:55.148 --> 00:29:56.840 want to give him his time.

NOTE Confidence: 0.73364645

00:29:56.840 --> 00:29:58.230 So are you thinking right?

NOTE Confidence: 0.73364645

00:29:58.230 --> 00:30:00.246 So for example in the other matters.

NOTE Confidence: 0.73364645

00:30:00.250 --> 00:30:02.030 Order in chronic malaria leukemia.

NOTE Confidence: 0.73364645

00:30:02.030 --> 00:30:03.962 We're thinking about Q or we

NOTE Confidence: 0.73364645

00:30:03.962 --> 00:30:06.126 want to get people off these

NOTE Confidence: 0.73364645

00:30:06.126 --> 00:30:07.726 long years of medication?

NOTE Confidence: 0.73364645

00:30:07.730 --> 00:30:09.505 Do you for see something

NOTE Confidence: 0.73364645

00:30:09.505 --> 00:30:10.925 like that for polycythemia

NOTE Confidence: 0.78337675

00:30:10.930 --> 00:30:13.149 Vera? You know you would hope that

NOTE Confidence: 0.78337675

00:30:13.149 --> 00:30:15.355 there is known driver and inhibiting

NOTE Confidence: 0.78337675

00:30:15.355 --> 00:30:17.335 it will cure this patience.

NOTE Confidence: 0.78337675

00:30:17.340 --> 00:30:18.764 But unfortunately, like now,

NOTE Confidence: 0.78337675

00:30:18.764 --> 00:30:20.188 with rooks Lid NAP,

NOTE Confidence: 0.78337675

00:30:20.190 --> 00:30:23.030 which is in an incubator of Jack two,

NOTE Confidence: 0.78337675

00:30:23.030 --> 00:30:24.810 we don't really see that.

NOTE Confidence: 0.78337675

00:30:24.810 --> 00:30:27.967 In fact it is not disease modifying

NOTE Confidence: 0.78337675

00:30:27.967 --> 00:30:31.379 if you ask me that you know so.

NOTE Confidence: 0.78337675

00:30:31.380 --> 00:30:31.807 Unfortunately,

NOTE Confidence: 0.78337675

00:30:31.807 --> 00:30:34.796 the successes we've had in CML did

NOTE Confidence: 0.78337675

00:30:34.796 --> 00:30:37.009 not translate to pH negative MPs,

NOTE Confidence: 0.78337675

00:30:37.010 --> 00:30:38.213 but you know,

NOTE Confidence: 0.78337675

00:30:38.213 --> 00:30:40.218 we have promising future medications.

NOTE Confidence: 0.78337675

00:30:40.220 --> 00:30:42.458 Or perhaps we'll have something which

NOTE Confidence: 0.78337675

00:30:42.458 --> 00:30:44.900 is going to decrease or eliminate

NOTE Confidence: 0.78337675

00:30:44.900 --> 00:30:46.660 that difference in survival.

NOTE Confidence: 0.78337675

00:30:46.660 --> 00:30:48.665 Our PV patients have when

NOTE Confidence: 0.78337675

00:30:48.665 --> 00:30:50.269 compared to regular population.

NOTE Confidence: 0.8129642

00:30:51.460 --> 00:30:54.178 OK, I see we have a comment from armor,

NOTE Confidence: 0.8129642

00:30:54.180 --> 00:30:55.884 great talk and many new exciting

NOTE Confidence: 0.8129642

00:30:55.884 --> 00:30:57.500 options available for these patients.

NOTE Confidence: 0.8129642

00:30:57.500 --> 00:30:59.314 So that was thank you Emerson.

NOTE Confidence: 0.8129642

00:30:59.314 --> 00:31:00.522 I share you enthusiasm.

NOTE Confidence: 0.8129642

00:31:00.522 --> 00:31:02.027 It is actually very challenging

NOTE Confidence: 0.8129642

00:31:02.030 --> 00:31:03.962 to do study for those patients because

NOTE Confidence: 0.8129642

00:31:03.962 --> 00:31:05.820 they have such a good prognosis

NOTE Confidence: 0.8129642

00:31:05.820 --> 00:31:07.764 comparing to all other cancer patients.

NOTE Confidence: 0.8129642

00:31:07.770 --> 00:31:10.173 So really have to have drugs which are not

NOTE Confidence: 0.8129642

00:31:10.173 --> 00:31:12.598 only working well but also well tolerated.

NOTE Confidence: 0.7842143

00:31:13.460 --> 00:31:14.114 Yeah, excellent.

NOTE Confidence: 0.7842143

00:31:14.114 --> 00:31:16.076 Well hematology is going to be

NOTE Confidence: 0.7842143

00:31:16.076 --> 00:31:17.970 around for many many more years.

NOTE Confidence: 0.7842143

00:31:17.970 --> 00:31:19.214 So thank you, Nicola.

NOTE Confidence: 0.7842143

00:31:19.214 --> 00:31:22.148 I think we should move on with Tama talk,

NOTE Confidence: 0.7842143

00:31:22.150 --> 00:31:24.404 so let me introduce Doctor to Microbee.

NOTE Confidence: 0.7842143

00:31:24.410 --> 00:31:26.050 He's associate Professor of Medicine

NOTE Confidence: 0.7842143

00:31:26.050 --> 00:31:27.690 and the medical director informed

NOTE Confidence: 0.7842143

00:31:27.739 --> 00:31:29.239 Chief of Operations and Quality.

NOTE Confidence: 0.7842143

00:31:29.240 --> 00:31:31.208 And I think everybody knows that

NOTE Confidence: 0.7842143

00:31:31.208 --> 00:31:32.929 tomorrow with the entire Smilow

NOTE Confidence: 0.7842143

00:31:32.929 --> 00:31:34.999 team has gotten the he malignancy

NOTE Confidence: 0.7842143

00:31:34.999 --> 00:31:36.926 service through the 1st surge of

NOTE Confidence: 0.7842143

00:31:36.926 --> 00:31:38.576 Covid an now the second surge.

NOTE Confidence: 0.7842143

00:31:38.580 --> 00:31:40.708 So thank you so much for that

NOTE Confidence: 0.7842143

00:31:40.708 --> 00:31:42.738 tomorrow also serves as the disease

NOTE Confidence: 0.7842143

00:31:42.738 --> 00:31:44.498 aligned research team or direct

NOTE Confidence: 0.7842143

00:31:44.498 --> 00:31:46.610 leader from my light malignancies.

NOTE Confidence: 0.7842143

00:31:46.610 --> 00:31:48.500 And tomorrow completed his doctorate

NOTE Confidence: 0.7842143

00:31:48.500 --> 00:31:50.390 in hematology oncology in Lyon,

NOTE Confidence: 0.7842143

00:31:50.390 --> 00:31:52.484 France, and then joined the Institute

NOTE Confidence: 0.7842143

00:31:52.484 --> 00:31:54.550 Power Lee comment in Marseille,

NOTE Confidence: 0.7842143

00:31:54.550 --> 00:31:55.252 in France,

NOTE Confidence: 0.7842143

00:31:55.252 --> 00:31:57.709 and he completed a fellowship at Johns

NOTE Confidence: 0.7842143

00:31:57.709 --> 00:32:00.220 Hopkins University as a Fulbright alumnus,

NOTE Confidence: 0.7842143

00:32:00.220 --> 00:32:02.536 and I think that's how eventually

NOTE Confidence: 0.7842143

00:32:02.536 --> 00:32:05.129 we got tomorrow to join us here.

NOTE Confidence: 0.7842143

00:32:05.130 --> 00:32:07.392 So Demott is focused on again

NOTE Confidence: 0.7842143

00:32:07.392 --> 00:32:08.523 pilot malignancy's leukemia,

NOTE Confidence: 0.7842143

00:32:08.530 --> 00:32:11.698 and I think his top will speak for his

NOTE Confidence: 0.7842143

00:32:11.698 --> 00:32:14.114 amazing expertise in treating these

NOTE Confidence: 0.7842143

00:32:14.114 --> 00:32:17.096 diseases and taking care of patients.

NOTE Confidence: 0.7842143

00:32:17.100 --> 00:32:19.898 So. To my valuers.

NOTE Confidence: 0.8486074

00:32:25.650 --> 00:32:30.040 Hope that everybody is seeing my screen now.

NOTE Confidence: 0.80601865

00:32:30.040 --> 00:32:34.675 OK so for today I want to focus my

NOTE Confidence: 0.80601865

00:32:34.675 --> 00:32:38.723 presentation and one on the topic of

NOTE Confidence: 0.80601865

00:32:38.723 --> 00:32:41.937 Milo dysplastic syndrome and more

NOTE Confidence: 0.80601865

00:32:41.937 --> 00:32:44.972 precisely, on the patient exposed,

NOTE Confidence: 0.80601865

00:32:44.972 --> 00:32:47.737 hyperventilating agent and we experience

NOTE Confidence: 0.80601865

00:32:47.737 --> 00:32:50.269 hyper mediating agent failure.

NOTE Confidence: 0.30600467

00:32:52.640 --> 00:32:57.230 Anne. So here are my disclosures.

NOTE Confidence: 0.7758981

00:33:00.920 --> 00:33:03.237 An ad to start wanted just to

NOTE Confidence: 0.7758981

00:33:03.237 --> 00:33:06.102 to do a really quick reminder

NOTE Confidence: 0.7758981

00:33:06.102 --> 00:33:09.067 on my love dysplastic syndrome.

NOTE Confidence: 0.7758981

00:33:09.070 --> 00:33:12.647 Stressing that we have with this disease,

NOTE Confidence: 0.7758981

00:33:12.650 --> 00:33:14.698 Arelia turgeon's group of

NOTE Confidence: 0.7758981

00:33:14.698 --> 00:33:16.746 clonal bone marrow neoplasms,

NOTE Confidence: 0.7758981

00:33:16.750 --> 00:33:20.292 we have the cytopenias due to the

NOTE Confidence: 0.7758981

00:33:20.292 --> 00:33:22.822 ineffective in multiple years is

NOTE Confidence: 0.7758981

00:33:22.822 --> 00:33:25.588 we have abnormal blood and bone

NOTE Confidence: 0.7758981

00:33:25.588 --> 00:33:28.805 marrow cell morphology and the risk

NOTE Confidence: 0.7758981

00:33:28.805 --> 00:33:31.555 of clonal evolution and progression

NOTE Confidence: 0.7758981

00:33:31.555 --> 00:33:33.649 to acute myeloid leukemia.

NOTE Confidence: 0.73165816

00:33:36.610 --> 00:33:39.122 From a molecular standpoint,

NOTE Confidence: 0.73165816

00:33:39.122 --> 00:33:42.890 these diseases are extremely generous with

NOTE Confidence: 0.73165816

00:33:42.985 --> 00:33:46.350 some main driver spliceosome mutation,

NOTE Confidence: 0.73165816

00:33:46.350 --> 00:33:50.826 such as the three one mutation

NOTE Confidence: 0.73165816

00:33:50.826 --> 00:33:54.397 epigenetic targeted mutation such as

NOTE Confidence: 0.73165816

00:33:54.397 --> 00:34:00.830 at Ted 2 for example, and EMT 3A and.

NOTE Confidence: 0.73165816

00:34:00.830 --> 00:34:02.730 This eternity is also something

NOTE Confidence: 0.73165816

00:34:02.730 --> 00:34:04.630 we see in the prognosis.

NOTE Confidence: 0.73165816

00:34:04.630 --> 00:34:06.569 I'm not going to go in the

NOTE Confidence: 0.73165816

00:34:06.569 --> 00:34:08.547 details of the risk stratification

NOTE Confidence: 0.73165816

00:34:08.547 --> 00:34:10.707 of Milo dysplastic syndrome,

NOTE Confidence: 0.73165816

00:34:10.710 --> 00:34:13.486 but I just want you to focus your

NOTE Confidence: 0.73165816

00:34:13.486 --> 00:34:15.674 attention on the right side of

NOTE Confidence: 0.73165816

00:34:15.674 --> 00:34:18.304 the panel where you would see that

NOTE Confidence: 0.73165816

00:34:18.304 --> 00:34:21.258 when we see a patient with mild

NOTE Confidence: 0.73165816

00:34:21.258 --> 00:34:22.776 dysplastic syndrome in clinic,

NOTE Confidence: 0.73165816

00:34:22.776 --> 00:34:25.440 we can see someone who has a median

NOTE Confidence: 0.73165816

00:34:25.521 --> 00:34:28.566 overall survival of more than eight years,

NOTE Confidence: 0.73165816

00:34:28.570 --> 00:34:30.830 as well as people that.

NOTE Confidence: 0.73165816

00:34:30.830 --> 00:34:33.530 In the worst case scenario,

NOTE Confidence: 0.73165816

00:34:33.530 --> 00:34:36.230 can progress to leukemia and

NOTE Confidence: 0.73165816

00:34:36.230 --> 00:34:38.390 die within a year,

NOTE Confidence: 0.73165816

00:34:38.390 --> 00:34:41.090 and so addressing this eternity

NOTE Confidence: 0.73165816

00:34:41.090 --> 00:34:44.870 is something that is on your mind.

NOTE Confidence: 0.73165816

00:34:44.870 --> 00:34:47.570 Each time we're seeing patient

NOTE Confidence: 0.73165816

00:34:47.570 --> 00:34:49.730 from the treatment standpoint,

NOTE Confidence: 0.73165816

00:34:49.730 --> 00:34:53.160 we can go from a pure observation

NOTE Confidence: 0.73165816

00:34:53.160 --> 00:34:55.973 for patients without any symptoms

NOTE Confidence: 0.73165816

00:34:55.973 --> 00:34:59.103 or significant cytopenia to some

NOTE Confidence: 0.73165816

00:34:59.103 --> 00:35:01.800 low intensity treatment such as.

NOTE Confidence: 0.73165816

00:35:01.800 --> 00:35:02.943 Activating stimulating agent

NOTE Confidence: 0.73165816

00:35:02.943 --> 00:35:04.467 for patients with anemia,

NOTE Confidence: 0.73165816

00:35:04.470 --> 00:35:06.762 but in the context of the

NOTE Confidence: 0.73165816

00:35:06.762 --> 00:35:07.908 higher risk disease,

NOTE Confidence: 0.73165816

00:35:07.910 --> 00:35:10.154 the mainstay of treatment as being

NOTE Confidence: 0.73165816

00:35:10.154 --> 00:35:12.110 to use iPod mitigating agent,

NOTE Confidence: 0.73165816

00:35:12.110 --> 00:35:16.340 namely as cited in or decide to be in.

NOTE Confidence: 0.73165816

00:35:16.340 --> 00:35:19.332 Over the last few years and for the

NOTE Confidence: 0.73165816

00:35:19.332 --> 00:35:21.979 few patient eligible allogeneic stem

NOTE Confidence: 0.73165816

00:35:21.979 --> 00:35:24.399 cell transplantation is obviously

NOTE Confidence: 0.73165816

00:35:24.399 --> 00:35:28.290 something that we would consider frontline.

NOTE Confidence: 0.73165816

00:35:28.290 --> 00:35:32.578 That's a pretty classic for all NDS talk.

NOTE Confidence: 0.73165816

00:35:32.580 --> 00:35:34.712 That's basically the registration

NOTE Confidence: 0.73165816

00:35:34.712 --> 00:35:38.470 study of as a sighted in MD's,

NOTE Confidence: 0.73165816

00:35:38.470 --> 00:35:41.970 showing that with Asia we are able

NOTE Confidence: 0.73165816

00:35:41.970 --> 00:35:44.801 to prolong the median overall

NOTE Confidence: 0.73165816

00:35:44.801 --> 00:35:48.473 survival of probably nine months in

NOTE Confidence: 0.73165816

00:35:48.473 --> 00:35:52.360 median as compared to conventional.

NOTE Confidence: 0.73165816

00:35:52.360 --> 00:35:54.530 Care we definitely have evidences

NOTE Confidence: 0.73165816

00:35:54.530 --> 00:35:57.615 that the 24 months of median overall

NOTE Confidence: 0.73165816

00:35:57.615 --> 00:36:00.541 survival that we see in this study

NOTE Confidence: 0.73165816

00:36:00.541 --> 00:36:03.210 are probably a bit overestimated as

NOTE Confidence: 0.73165816

00:36:03.210 --> 00:36:06.682 compared to what we see in real life.

NOTE Confidence: 0.73165816

00:36:06.682 --> 00:36:08.418 Probably around 18 months.

NOTE Confidence: 0.73165816

00:36:08.420 --> 00:36:11.168 And that's many works from basically

NOTE Confidence: 0.73165816

00:36:11.168 --> 00:36:14.188 the registry studies such as the group

NOTE Confidence: 0.73165816

00:36:14.188 --> 00:36:16.148 Uncle Phone, Digital Displays E,

NOTE Confidence: 0.73165816

00:36:16.148 --> 00:36:18.990 but also some really nice work of

NOTE Confidence: 0.73165816

00:36:19.067 --> 00:36:23.660 Stephen Armor. For example on CS.

NOTE Confidence: 0.73165816

00:36:23.660 --> 00:36:25.052 Data. So.

NOTE Confidence: 0.73165816

00:36:25.052 --> 00:36:28.636 What do we call activating agent failure?

NOTE Confidence: 0.73165816

00:36:28.640 --> 00:36:32.048 Because we know that at the end 90

NOTE Confidence: 0.73165816

00:36:32.048 --> 00:36:35.174 to 95% of the patient that we start

NOTE Confidence: 0.73165816

00:36:35.174 --> 00:36:37.246 treating with this iPod mediating

NOTE Confidence: 0.73165816

00:36:37.246 --> 00:36:40.564 agent will experience on the real failure.

NOTE Confidence: 0.73165816

00:36:40.570 --> 00:36:42.964 We classically defined that as a

NOTE Confidence: 0.73165816

00:36:42.964 --> 00:36:45.040 lack of response or progression

NOTE Confidence: 0.73165816

00:36:45.040 --> 00:36:47.833 after at least four to six cycle

NOTE Confidence: 0.73165816

00:36:47.833 --> 00:36:49.939 of iPod mediating agent,

NOTE Confidence: 0.73165816

00:36:49.940 --> 00:36:52.929 there's no difference between as cited in

NOTE Confidence: 0.73165816

00:36:52.929 --> 00:36:56.229 or decided in from this standpoint and.

NOTE Confidence: 0.73165816

00:36:56.230 --> 00:36:59.002 One of the main features that

NOTE Confidence: 0.73165816

00:36:59.002 --> 00:37:00.850 we see is really,

NOTE Confidence: 0.73165816

00:37:00.850 --> 00:37:02.890 really limited overall survival

NOTE Confidence: 0.73165816

00:37:02.890 --> 00:37:04.930 for patients experiencing failure

NOTE Confidence: 0.73165816

00:37:04.930 --> 00:37:06.785 treatment within average four

NOTE Confidence: 0.73165816

00:37:06.785 --> 00:37:08.695 to six months median survival,

NOTE Confidence: 0.73165816

00:37:08.700 --> 00:37:10.840 and that's something that,

NOTE Confidence: 0.73165816

00:37:10.840 --> 00:37:14.050 as that we initially described almost

NOTE Confidence: 0.73165816

00:37:14.143 --> 00:37:17.487 10 years ago and that has been since

NOTE Confidence: 0.73165816

00:37:17.487 --> 00:37:20.340 reproduced in many different studies.

NOTE Confidence: 0.73165816

00:37:20.340 --> 00:37:21.122 So Interestingly,

NOTE Confidence: 0.73165816

00:37:21.122 --> 00:37:23.859 we have many reason why this hyper

NOTE Confidence: 0.73165816

00:37:23.859 --> 00:37:26.180 mitigating agent resistant can developed,

NOTE Confidence: 0.73165816

00:37:26.180 --> 00:37:29.114 but so far we can say that we have

NOTE Confidence: 0.73165816

00:37:29.114 --> 00:37:32.705 a home run we don't consider that we

NOTE Confidence: 0.73165816

00:37:32.705 --> 00:37:35.516 have a unifying theory to explain

NOTE Confidence: 0.73165816

00:37:35.516 --> 00:37:38.687 why we have this failure of this

NOTE Confidence: 0.7949301

00:37:38.690 --> 00:37:39.474 iPod engagement.

NOTE Confidence: 0.7949301

00:37:39.474 --> 00:37:41.434 We see phenomenon of clonal

NOTE Confidence: 0.7949301

00:37:41.434 --> 00:37:43.280 selection and clonal evolution,

NOTE Confidence: 0.7949301

00:37:43.280 --> 00:37:45.410 maybe potentially with some difference

NOTE Confidence: 0.7949301

00:37:45.410 --> 00:37:47.994 of profiling between the patient that

NOTE Confidence: 0.7949301

00:37:47.994 --> 00:37:50.358 are completely refractory to the disease.

NOTE Confidence: 0.7949301

00:37:50.360 --> 00:37:52.184 In the patient that.

NOTE Confidence: 0.7949301

00:37:52.184 --> 00:37:54.920 Response and then progress after treatment.

NOTE Confidence: 0.7949301

00:37:54.920 --> 00:37:56.925 But many other mechanisms have

NOTE Confidence: 0.7949301

00:37:56.925 --> 00:37:59.353 been potentially put on the table

NOTE Confidence: 0.7949301

00:37:59.353 --> 00:38:01.775 as explaining what we see or to

NOTE Confidence: 0.7949301

00:38:01.775 --> 00:38:04.284 fatty affect change in nucleotide

NOTE Confidence: 0.7949301

00:38:04.284 --> 00:38:06.608 analogue transporter expression of

NOTE Confidence: 0.7949301

00:38:06.608 --> 00:38:08.774 immune checkpoint inhibitors and

NOTE Confidence: 0.7949301

00:38:08.774 --> 00:38:11.258 regulators and we will circle back

NOTE Confidence: 0.7949301

00:38:11.258 --> 00:38:14.178 on that later in the presentation.

NOTE Confidence: 0.7949301

00:38:14.180 --> 00:38:16.714 So for the moment there's still a

NOTE Confidence: 0.7949301

00:38:16.714 --> 00:38:19.923 lot of open questions on explaining

NOTE Confidence: 0.7949301

00:38:19.923 --> 00:38:22.639 this hypomethylating agent failure.

NOTE Confidence: 0.7949301

00:38:22.640 --> 00:38:24.876 There's obviously also something

NOTE Confidence: 0.7949301

00:38:24.876 --> 00:38:28.230 that is pretty clear which is

NOTE Confidence: 0.7949301

00:38:28.324 --> 00:38:30.670 the role of the stem cell.

NOTE Confidence: 0.7949301

00:38:30.670 --> 00:38:33.676 Quiescence and resistance MD's are stamps,

NOTE Confidence: 0.7949301

00:38:33.680 --> 00:38:35.186 stem cell diseases,

NOTE Confidence: 0.7949301

00:38:35.186 --> 00:38:37.696 and even in responding patients.

NOTE Confidence: 0.7949301

00:38:37.700 --> 00:38:38.638 For example,

NOTE Confidence: 0.7949301

00:38:38.638 --> 00:38:41.452 correct there IMO globin and that

NOTE Confidence: 0.7949301

00:38:41.452 --> 00:38:45.229 have a decrease in their blast counts,

NOTE Confidence: 0.7949301

00:38:45.230 --> 00:38:49.246 like here in there in the blue line,

NOTE Confidence: 0.7949301

00:38:49.250 --> 00:38:51.302 we can still detect

NOTE Confidence: 0.7949301

00:38:51.302 --> 00:38:52.328 cytogenetics abnormalities.

NOTE Confidence: 0.7949301

00:38:52.330 --> 00:38:53.416 And more Interestingly,

NOTE Confidence: 0.7949301

00:38:53.416 --> 00:38:55.588 we can still detect stem cells

NOTE Confidence: 0.7949301

00:38:55.588 --> 00:38:57.299 like LTC IC's for example,

NOTE Confidence: 0.7949301

00:38:57.300 --> 00:38:59.075 that harbors marker of the

NOTE Confidence: 0.7949301

00:38:59.075 --> 00:39:00.140 minor dysplastic syndrome,

NOTE Confidence: 0.7949301

00:39:00.140 --> 00:39:02.108 and so that's something that is

NOTE Confidence: 0.7949301

00:39:02.108 --> 00:39:04.264 important when it comes to the

NOTE Confidence: 0.7949301

00:39:04.264 --> 00:39:05.816 way we're considering treatment,

NOTE Confidence: 0.7949301

00:39:05.820 --> 00:39:07.244 not only for relapse,

NOTE Confidence: 0.7949301

00:39:07.244 --> 00:39:09.752 but on a more general basis from

NOTE Confidence: 0.7949301

00:39:09.752 --> 00:39:12.080 the from the from the get go on

NOTE Confidence: 0.7949301

00:39:12.080 --> 00:39:14.339 the diagnosis of this patient.

NOTE Confidence: 0.835378

00:39:17.010 --> 00:39:19.938 Let's talk about the treatment now.

NOTE Confidence: 0.835378

00:39:19.940 --> 00:39:22.868 We reviewed a few years ago.

NOTE Confidence: 0.835378

00:39:22.870 --> 00:39:26.027 What were the option for this patient

NOTE Confidence: 0.835378

00:39:26.027 --> 00:39:28.720 with some health care treatment?

NOTE Confidence: 0.835378

00:39:28.720 --> 00:39:31.688 And let's say that nothing is really

NOTE Confidence: 0.835378

00:39:31.688 --> 00:39:34.947 satisfying with the exception of the few

NOTE Confidence: 0.835378

00:39:34.947 --> 00:39:37.809 patient that can potentially transition to

NOTE Confidence: 0.835378

00:39:37.889 --> 00:39:40.919 an allogeneic stem cell transplantation,

NOTE Confidence: 0.835378

00:39:40.920 --> 00:39:43.360 either directly after relapse, or,

NOTE Confidence: 0.835378

00:39:43.360 --> 00:39:46.070 for example, after intensive cytoreduction.

NOTE Confidence: 0.835378

00:39:46.070 --> 00:39:46.896 With chemotherapy,

NOTE Confidence: 0.835378

00:39:46.896 --> 00:39:49.787 so there's been a lot of basically

NOTE Confidence: 0.835378

00:39:49.787 --> 00:39:51.742 investigation around what we can do

NOTE Confidence: 0.835378

00:39:51.742 --> 00:39:53.900 when it comes to intensive treatment.

NOTE Confidence: 0.835378

00:39:53.900 --> 00:39:56.138 Brute force approaches for HMA failure.

NOTE Confidence: 0.835378

00:39:56.140 --> 00:40:00.320 We try to dig deeper, a bit on the data that.

NOTE Confidence: 0.835378

00:40:00.320 --> 00:40:02.180 We initially generated.

NOTE Confidence: 0.835378

00:40:02.180 --> 00:40:05.772 On induction, as we may have a lot

NOTE Confidence: 0.835378

00:40:05.772 --> 00:40:08.400 of different type of induction,

NOTE Confidence: 0.835378

00:40:08.400 --> 00:40:11.564 we can potentially use in this context.

NOTE Confidence: 0.835378

00:40:11.570 --> 00:40:14.754 Conventional 7 + 3 regimen like we would

NOTE Confidence: 0.835378

00:40:14.754 --> 00:40:17.989 be doing in newly diagnosed AML Internet

NOTE Confidence: 0.835378

00:40:17.989 --> 00:40:21.080 to hide those site arabien regimen.

NOTE Confidence: 0.835378

00:40:21.080 --> 00:40:23.350 And that's something we're doing,

NOTE Confidence: 0.835378

00:40:23.350 --> 00:40:26.325 mostly on the European side as well

NOTE Confidence: 0.835378

00:40:26.325 --> 00:40:29.142 as pure in analog based regimen

NOTE Confidence: 0.835378

00:40:29.142 --> 00:40:32.509 such as flag or flag idea that.

NOTE Confidence: 0.835378

00:40:32.510 --> 00:40:37.140 We see on both side of the of the Atlantic,

NOTE Confidence: 0.835378

00:40:37.140 --> 00:40:40.938 and so we gather basically group

NOTE Confidence: 0.835378

00:40:40.938 --> 00:40:42.837 of 15 different.

NOTE Confidence: 0.835378

00:40:42.840 --> 00:40:47.358 Investigator you ran in the US and put

NOTE Confidence: 0.835378

00:40:47.358 --> 00:40:50.408 together basically a data set of 307

NOTE Confidence: 0.835378

00:40:50.408 --> 00:40:52.793 patient with maladies plastic syndrome

NOTE Confidence: 0.835378

00:40:52.793 --> 00:40:55.510 treated with induction chemotherapy.

NOTE Confidence: 0.835378

00:40:55.510 --> 00:40:58.750 We found that roughly.

NOTE Confidence: 0.835378

00:40:58.750 --> 00:41:01.666 41% of the patient will achieve

NOTE Confidence: 0.835378

00:41:01.666 --> 00:41:04.641 a complete remission with only a

NOTE Confidence: 0.835378

00:41:04.641 --> 00:41:07.455 median overall survival of 11 months.

NOTE Confidence: 0.835378

00:41:07.460 --> 00:41:10.820 The two take home message from this

NOTE Confidence: 0.835378

00:41:10.820 --> 00:41:14.327 work that we developed at here with

NOTE Confidence: 0.835378

00:41:14.327 --> 00:41:18.294 Brian Bowl a few years ago was one

NOTE Confidence: 0.835378

00:41:18.294 --> 00:41:21.974 that we do not so any real significant

NOTE Confidence: 0.835378

00:41:21.980 --> 00:41:24.665 difference between the conventional 7

NOTE Confidence: 0.835378

00:41:24.665 --> 00:41:28.759 + 3 the intensive hydac regimen or the.

NOTE Confidence: 0.835378

00:41:28.760 --> 00:41:29.240 Genopro,

NOTE Confidence: 0.835378

00:41:29.240 --> 00:41:32.600 Fabian based regimen and I think also

NOTE Confidence: 0.835378

00:41:32.600 --> 00:41:34.652 pretty importantly that all patient

NOTE Confidence: 0.835378

00:41:34.652 --> 00:41:37.962 that did not have a chance to bridge to

NOTE Confidence: 0.835378

00:41:37.962 --> 00:41:40.102 analogy in transplantation died within

NOTE Confidence: 0.835378

00:41:40.102 --> 00:41:43.098 a year of the initiation of treatment.

NOTE Confidence: 0.835378

00:41:43.098 --> 00:41:45.660 So that's pretty telling on the

NOTE Confidence: 0.835378

00:41:45.735 --> 00:41:48.081 fact that we definitely need to

NOTE Confidence: 0.835378

00:41:48.081 --> 00:41:50.650 develop more option for this patient,

NOTE Confidence: 0.835378

00:41:50.650 --> 00:41:53.176 including from the initiation of response,

NOTE Confidence: 0.835378

00:41:53.180 --> 00:41:56.008 but also on the transplant to make

NOTE Confidence: 0.835378

00:41:56.008 --> 00:41:59.028 sure that we can maximize access.

NOTE Confidence: 0.835378

00:41:59.030 --> 00:42:05.078 Uh, to transplant for all of these patients.

NOTE Confidence: 0.835378

00:42:05.080 --> 00:42:08.440 One of the extension and one of the.

NOTE Confidence: 0.835378

00:42:08.440 --> 00:42:10.184 Development following this initial

NOTE Confidence: 0.835378

00:42:10.184 --> 00:42:13.738 study was to maybe try to use a

NOTE Confidence: 0.835378

00:42:13.738 --> 00:42:15.883 better drug for induction chemo

NOTE Confidence: 0.835378

00:42:15.883 --> 00:42:17.830 chemotherapy for this patient,

NOTE Confidence: 0.835378

00:42:17.830 --> 00:42:20.452 and we had CP351D liposomal formulation

NOTE Confidence: 0.835378

00:42:20.452 --> 00:42:23.517 of Donna Mycin and Sitara been that

NOTE Confidence: 0.835378

00:42:23.517 --> 00:42:26.415 was approved two years ago three years

NOTE Confidence: 0.835378

00:42:26.494 --> 00:42:29.338 ago now for acute myeloid leukemia

NOTE Confidence: 0.835378

00:42:29.338 --> 00:42:31.763 arising from Milo dysplastic syndrome.

NOTE Confidence: 0.835378

00:42:31.763 --> 00:42:34.901 And so we're thinking about this

NOTE Confidence: 0.835378

00:42:34.901 --> 00:42:38.124 internally approaches that was kind of a

NOTE Confidence: 0.835378

00:42:38.124 --> 00:42:40.870 natural conclusion to basically try to use.

NOTE Confidence: 0.835378

00:42:40.870 --> 00:42:44.398 Pretty similar drug to achieve response in

NOTE Confidence: 0.835378

00:42:44.398 --> 00:42:47.960 HMA resistant BI lo dysplastic syndrome.

NOTE Confidence: 0.835378

00:42:47.960 --> 00:42:51.915 That's a phase two study that we

NOTE Confidence: 0.835378

00:42:51.915 --> 00:42:54.720 developed with Prajwal Bodo at

NOTE Confidence: 0.835378

00:42:54.720 --> 00:42:57.215 Yale as a multicenter IIT,

NOTE Confidence: 0.835378

00:42:57.220 --> 00:43:01.116 and the plan is basically to give two

NOTE Confidence: 0.835378

00:43:01.116 --> 00:43:04.567 cycles of induction with two days

NOTE Confidence: 0.835378

00:43:04.567 --> 00:43:08.113 of CPX in acute myeloid leukemia.

NOTE Confidence: 0.835378

00:43:08.120 --> 00:43:12.316 We usually use three days of CPX, 4.

NOTE Confidence: 0.835378

00:43:12.316 --> 00:43:12.692 Induction,

NOTE Confidence: 0.835378

00:43:12.692 --> 00:43:15.700 but there's some data showing that from a

NOTE Confidence: 0.826597555

00:43:15.777 --> 00:43:17.009 safety standpoint,

NOTE Confidence: 0.826597555

00:43:17.010 --> 00:43:19.338 especially in elderly patient two days,

NOTE Confidence: 0.826597555

00:43:19.340 --> 00:43:20.896 maybe probably more appropriate,

NOTE Confidence: 0.826597555

00:43:20.896 --> 00:43:23.230 and the patient that are responding,

NOTE Confidence: 0.826597555

00:43:23.230 --> 00:43:25.652 we can continue for six cycle of

NOTE Confidence: 0.826597555

00:43:25.652 --> 00:43:28.474 maintenance with one day of civics or

NOTE Confidence: 0.826597555

00:43:28.474 --> 00:43:30.614 transition to bone marrow transplantation.

NOTE Confidence: 0.826597555

00:43:30.620 --> 00:43:33.973 The study is open to accrual after

NOTE Confidence: 0.826597555

00:43:33.973 --> 00:43:36.958 the Covid adventures that we had over

NOTE Confidence: 0.826597555

00:43:36.958 --> 00:43:39.940 the last year and we open running.

NOTE Confidence: 0.826597555

00:43:39.940 --> 00:43:42.646 So all these non selected approach,

NOTE Confidence: 0.826597555

00:43:42.650 --> 00:43:44.510 induction chemotherapy but also

NOTE Confidence: 0.826597555

00:43:44.510 --> 00:43:46.835 basically non targeted agent that

NOTE Confidence: 0.826597555

00:43:46.835 --> 00:43:49.430 we have developed over the years.

NOTE Confidence: 0.826597555

00:43:49.430 --> 00:43:50.729 For the moment,

NOTE Confidence: 0.826597555

00:43:50.729 --> 00:43:53.760 let's say that we have not found

NOTE Confidence: 0.826597555

00:43:53.859 --> 00:43:56.024 any real good candidate to

NOTE Confidence: 0.826597555

00:43:56.024 --> 00:43:58.920 be a standard of care option,

NOTE Confidence: 0.826597555

00:43:58.920 --> 00:44:01.180 especially for patients that are

NOTE Confidence: 0.826597555

00:44:01.180 --> 00:44:03.440 not eligible for aggressive chemo.

NOTE Confidence: 0.826597555

00:44:03.440 --> 00:44:06.961 I've just listed here a few of

NOTE Confidence: 0.826597555

00:44:06.961 --> 00:44:10.220 the studies but as you can see.

NOTE Confidence: 0.826597555

00:44:10.220 --> 00:44:13.142 In lots of these general studies

NOTE Confidence: 0.826597555

00:44:13.142 --> 00:44:15.090 without any real targeting,

NOTE Confidence: 0.826597555

00:44:15.090 --> 00:44:17.265 when situation where the response

NOTE Confidence: 0.826597555

00:44:17.265 --> 00:44:20.450 rates are low and more importantly,

NOTE Confidence: 0.826597555

00:44:20.450 --> 00:44:22.885 the overall survival seems still

NOTE Confidence: 0.826597555

00:44:22.885 --> 00:44:25.320 stuck below below one year,

NOTE Confidence: 0.826597555

00:44:25.320 --> 00:44:30.108 so we definitely need to do better.

NOTE Confidence: 0.826597555

00:44:30.110 --> 00:44:32.910 And that goes back to the way we

NOTE Confidence: 0.826597555

00:44:32.910 --> 00:44:34.268 considering the pathophysiology

NOTE Confidence: 0.826597555

00:44:34.268 --> 00:44:36.017 of this disease,

NOTE Confidence: 0.826597555

00:44:36.020 --> 00:44:39.388 and acknowledge that this HMA failure or not,

NOTE Confidence: 0.826597555

00:44:39.390 --> 00:44:40.656 and imaginas situation,

NOTE Confidence: 0.826597555

00:44:40.656 --> 00:44:42.766 just to give an example.

NOTE Confidence: 0.826597555

00:44:42.770 --> 00:44:45.423 We see that from just a clinical

NOTE Confidence: 0.826597555

00:44:45.423 --> 00:44:47.636 standpoint we see different outcome

NOTE Confidence: 0.826597555

00:44:47.636 --> 00:44:50.636 in patients at our primary refractory

NOTE Confidence: 0.826597555

00:44:50.636 --> 00:44:53.199 and really do not respond at

NOTE Confidence: 0.826597555

00:44:53.199 --> 00:44:55.425 all to hyper mediating agent in

NOTE Confidence: 0.826597555

00:44:55.430 --> 00:44:57.114 patients with relapsing disease.

NOTE Confidence: 0.826597555

00:44:57.114 --> 00:44:59.219 That basically seems to have

NOTE Confidence: 0.826597555

00:44:59.219 --> 00:45:00.979 a bit more favorable.

NOTE Confidence: 0.826597555

00:45:00.980 --> 00:45:02.960 Outcome in this context so

NOTE Confidence: 0.826597555

00:45:02.960 --> 00:45:06.952 still a lot of work to do on the

NOTE Confidence: 0.826597555

00:45:06.952 --> 00:45:09.347 translational and basic science side.

NOTE Confidence: 0.826597555

00:45:09.350 --> 00:45:12.661 One way we've tried to tackle this

NOTE Confidence: 0.826597555

00:45:12.661 --> 00:45:15.463 difference of outcome based on this

NOTE Confidence: 0.826597555

00:45:15.463 --> 00:45:18.049 clinical finding was to deal with

NOTE Confidence: 0.826597555

00:45:18.049 --> 00:45:21.187 the stable disease with a slightly

NOTE Confidence: 0.826597555

00:45:21.187 --> 00:45:23.807 different term than just using.

NOTE Confidence: 0.826597555

00:45:23.810 --> 00:45:26.285 Regular treatment by adding on

NOTE Confidence: 0.826597555

00:45:26.285 --> 00:45:28.265 on the hyperventilating agent,

NOTE Confidence: 0.826597555

00:45:28.270 --> 00:45:30.945 potentially drug that may be

NOTE Confidence: 0.826597555

00:45:30.945 --> 00:45:34.152 synergistic based on their mode of

NOTE Confidence: 0.826597555

00:45:34.152 --> 00:45:37.197 action or based on in vitro studies.

NOTE Confidence: 0.826597555

00:45:37.200 --> 00:45:40.176 We had several attempts at this

NOTE Confidence: 0.826597555

00:45:40.176 --> 00:45:42.160 over the last years.

NOTE Confidence: 0.826597555

00:45:42.160 --> 00:45:44.600 An easy combination and logical

NOTE Confidence: 0.826597555

00:45:44.600 --> 00:45:47.705 combination was to add on the

NOTE Confidence: 0.826597555

00:45:47.705 --> 00:45:50.560 almighty engage in the second

NOTE Confidence: 0.826597555

00:45:50.560 --> 00:45:52.273 epigenetic targeted agent.

NOTE Confidence: 0.826597555

00:45:52.280 --> 00:45:54.224 As such, as H.

NOTE Confidence: 0.826597555

00:45:54.224 --> 00:45:55.196 Dark inhibitor,

NOTE Confidence: 0.826597555

00:45:55.200 --> 00:45:58.595 then we treated 19 patient with vorinostat,

NOTE Confidence: 0.826597555

00:45:58.600 --> 00:46:02.023 which is one of the first in

NOTE Confidence: 0.826597555

00:46:02.023 --> 00:46:04.429 Class Age document or with,

NOTE Confidence: 0.826597555

00:46:04.430 --> 00:46:04.937 unfortunately,

NOTE Confidence: 0.826597555

00:46:04.937 --> 00:46:06.965 pretty limited outcome really

NOTE Confidence: 0.826597555

00:46:06.965 --> 00:46:10.259 knows how that rate of only 10%,

NOTE Confidence: 0.826597555

00:46:10.260 --> 00:46:13.932 but the median survival of 12 months in

NOTE Confidence: 0.826597555

00:46:13.932 --> 00:46:17.280 potentially a pretty selected population.

NOTE Confidence: 0.826597555

00:46:17.280 --> 00:46:20.304 We also tried to use a bit more recently,

NOTE Confidence: 0.826597555

00:46:20.310 --> 00:46:23.006 and that's not a fully public published yet.

NOTE Confidence: 0.826597555

00:46:23.010 --> 00:46:24.906 The addition of a smooth and

NOTE Confidence: 0.826597555

00:46:24.906 --> 00:46:26.951 inhibitor to try to use really

NOTE Confidence: 0.826597555

00:46:26.951 --> 00:46:29.075 work on the stem cell component.

NOTE Confidence: 0.826597555

00:46:29.080 --> 00:46:31.720 There's some individual data showing that

NOTE Confidence: 0.826597555

00:46:31.720 --> 00:46:34.670 this moves on emitter can potentially.

NOTE Confidence: 0.826597555

00:46:34.670 --> 00:46:35.978 Abrogates the resistance

NOTE Confidence: 0.826597555

00:46:35.978 --> 00:46:37.286 to hypomethylating agent,

NOTE Confidence: 0.826597555

00:46:37.290 --> 00:46:39.912 but so far the results were

NOTE Confidence: 0.826597555

00:46:39.912 --> 00:46:41.223 pretty disappointing too.

NOTE Confidence: 0.826597555

00:46:41.230 --> 00:46:43.846 Well not to be completely gloom.

NOTE Confidence: 0.826597555

00:46:43.850 --> 00:46:46.895 There's end at the at the probably

NOTE Confidence: 0.826597555

00:46:46.895 --> 00:46:49.969 light at the end of the tunnel.

NOTE Confidence: 0.826597555

00:46:49.970 --> 00:46:52.150 I need to highlight the

NOTE Confidence: 0.826597555

00:46:52.150 --> 00:46:53.894 work presented by armor.

NOTE Confidence: 0.826597555

00:46:53.900 --> 00:46:56.516 If you have a year ago.

NOTE Confidence: 0.826597555

00:46:56.520 --> 00:46:58.245 Basically at the ash meeting

NOTE Confidence: 0.826597555

00:46:58.245 --> 00:47:01.205 on the add on of venetoclax in

NOTE Confidence: 0.826597555

00:47:01.205 --> 00:47:03.509 maybe less selected population.

NOTE Confidence: 0.775830976

00:47:03.510 --> 00:47:06.288 24 patient is. Resistance with this

NOTE Confidence: 0.775830976

00:47:06.288 --> 00:47:10.488 edition of the BCL, two inhibitor or some

NOTE Confidence: 0.775830976

00:47:10.488 --> 00:47:14.010 real complete remission and some marrow.

NOTE Confidence: 0.775830976

00:47:14.010 --> 00:47:17.626 Chimia Free State with a six months program.

NOTE Confidence: 0.775830976

00:47:17.630 --> 00:47:20.535 French fries survival 76% that from our

NOTE Confidence: 0.775830976

00:47:20.535 --> 00:47:23.069 standard is pretty pretty promising.

NOTE Confidence: 0.775830976

00:47:23.070 --> 00:47:26.686 So statue and we will have more information,

NOTE Confidence: 0.775830976

00:47:26.690 --> 00:47:29.903 but that's one of the Avenue that

NOTE Confidence: 0.775830976

00:47:29.903 --> 00:47:32.660 we are currently investigating.

NOTE Confidence: 0.775830976

00:47:32.660 --> 00:47:35.152 Stop. That's. Pretty good,

NOTE Confidence: 0.775830976

00:47:35.152 --> 00:47:38.267 that's basically based on a

NOTE Confidence: 0.775830976

00:47:38.267 --> 00:47:40.690 combination of mode of action.

NOTE Confidence: 0.775830976

00:47:40.690 --> 00:47:43.534 That's still not something that really

NOTE Confidence: 0.775830976

00:47:43.534 --> 00:47:46.388 address the specificity of the clone

NOTE Confidence: 0.775830976

00:47:46.388 --> 00:47:48.578 of the Milo dysplastic syndrome,

NOTE Confidence: 0.775830976

00:47:48.580 --> 00:47:51.172 and maybe instead of using brute

NOTE Confidence: 0.775830976

00:47:51.172 --> 00:47:54.610 force to try to induce a response,

NOTE Confidence: 0.775830976

00:47:54.610 --> 00:47:57.501 we can maybe try to outsmart the

NOTE Confidence: 0.775830976

00:47:57.501 --> 00:48:00.255 disease rather than just using those

NOTE Confidence: 0.775830976

00:48:00.255 --> 00:48:02.640 intensity or non selected approaches

NOTE Confidence: 0.775830976

00:48:02.640 --> 00:48:05.817 in the context of Milo dysplastic.

NOTE Confidence: 0.775830976

00:48:05.820 --> 00:48:06.159 Syndrome,

NOTE Confidence: 0.775830976

00:48:06.159 --> 00:48:08.193 where a bit less fortunate that

NOTE Confidence: 0.775830976

00:48:08.193 --> 00:48:10.468 in the acute model in the world,

NOTE Confidence: 0.775830976

00:48:10.470 --> 00:48:13.368 as we don't have so many targeted agent that

NOTE Confidence: 0.775830976

00:48:13.368 --> 00:48:16.436 we can use at the majority of the patient,

NOTE Confidence: 0.775830976

00:48:16.440 --> 00:48:18.645 will have as a freebie wanted two

NOTE Confidence: 0.775830976

00:48:18.645 --> 00:48:21.031 SS two mutation that are for the

NOTE Confidence: 0.775830976

00:48:21.031 --> 00:48:22.746 moment at least non targetable,

NOTE Confidence: 0.775830976

00:48:22.750 --> 00:48:24.875 even if there's some basically

NOTE Confidence: 0.775830976

00:48:24.875 --> 00:48:27.783 development on the side and I'm going

NOTE Confidence: 0.775830976

00:48:27.783 --> 00:48:30.247 to take the example of some product

NOTE Confidence: 0.775830976

00:48:30.247 --> 00:48:33.163 we have done in the in the IDH world.

NOTE Confidence: 0.775830976

00:48:33.170 --> 00:48:35.600 And that can potentially be avenues

NOTE Confidence: 0.775830976

00:48:35.600 --> 00:48:38.326 that we going to explore in the

NOTE Confidence: 0.775830976

00:48:38.326 --> 00:48:40.720 future to try to get a better

NOTE Confidence: 0.775830976

00:48:40.806 --> 00:48:42.910 outcome for these patients.

NOTE Confidence: 0.775830976

00:48:42.910 --> 00:48:45.454 So we have this idea inhibit

NOTE Confidence: 0.775830976

00:48:45.454 --> 00:48:47.150 or letter basically allosteric

NOTE Confidence: 0.775830976

00:48:47.229 --> 00:48:49.819 inhibitors from IDH two and IDH one.

NOTE Confidence: 0.775830976

00:48:49.820 --> 00:48:51.035 I did too.

NOTE Confidence: 0.775830976

00:48:51.035 --> 00:48:54.278 That's in a Sydney IDs, one that's evil.

NOTE Confidence: 0.775830976

00:48:54.278 --> 00:48:57.120 Setting it in both of the phase.

NOTE Confidence: 0.775830976

00:48:57.120 --> 00:48:59.556 One study of this compounds model,

NOTE Confidence: 0.775830976

00:48:59.560 --> 00:49:02.050 spastic syndrome patient were allowed

NOTE Confidence: 0.775830976

00:49:02.050 --> 00:49:05.689 after at least one line of treatment.

NOTE Confidence: 0.775830976

00:49:05.690 --> 00:49:09.900 76% of the patient seems to be able to to

NOTE Confidence: 0.775830976

00:49:10.005 --> 00:49:14.518 respond with the IDH two sorry 559% of the

NOTE Confidence: 0.775830976

00:49:14.518 --> 00:49:18.710 patient seems to be able to respond to IDH,

NOTE Confidence: 0.775830976

00:49:18.710 --> 00:49:22.805 two inhibitor and maybe a bit more in the

NOTE Confidence: 0.775830976

00:49:22.805 --> 00:49:26.620 IDH one subclone with a 71% response rate.

NOTE Confidence: 0.775830976

00:49:26.620 --> 00:49:28.480 As you can see,

NOTE Confidence: 0.775830976

00:49:28.480 --> 00:49:31.270 that's pretty small samples of patient.

NOTE Confidence: 0.775830976

00:49:31.270 --> 00:49:32.662 There's ongoing investigation

NOTE Confidence: 0.775830976

00:49:32.662 --> 00:49:34.518 with this IDH inhibitor,

NOTE Confidence: 0.775830976

00:49:34.520 --> 00:49:36.064 single agent or combination.

NOTE Confidence: 0.775830976

00:49:36.064 --> 00:49:39.060 The one thing that is pretty striking,

NOTE Confidence: 0.775830976

00:49:39.060 --> 00:49:41.286 the fact that we're probably in a

NOTE Confidence: 0.775830976

00:49:41.286 --> 00:49:43.077 situation where the duration of

NOTE Confidence: 0.775830976

00:49:43.077 --> 00:49:45.007 response is still pretty limited,

NOTE Confidence: 0.775830976

00:49:45.010 --> 00:49:45.435 so.

NOTE Confidence: 0.775830976

00:49:45.435 --> 00:49:47.560 Potentially we can try to

NOTE Confidence: 0.775830976

00:49:47.560 --> 00:49:49.811 find some alternatives to IDH

NOTE Confidence: 0.775830976

00:49:49.811 --> 00:49:51.667 inhibitor on this context,

NOTE Confidence: 0.775830976

00:49:51.670 --> 00:49:54.070 and that's potentially when I was

NOTE Confidence: 0.775830976

00:49:54.070 --> 00:49:55.670 mentioning outsmarting the disease.

NOTE Confidence: 0.775830976

00:49:55.670 --> 00:49:57.670 I'm not that smart guy,

NOTE Confidence: 0.775830976

00:49:57.670 --> 00:50:00.014 but I had the chance and that will

NOTE Confidence: 0.775830976

00:50:00.014 --> 00:50:02.296 work with really intelligent people

NOTE Confidence: 0.775830976

00:50:02.296 --> 00:50:04.464 branded Bindra Stephanie Allen,

NOTE Confidence: 0.775830976

00:50:04.470 --> 00:50:05.202 for example,

NOTE Confidence: 0.775830976

00:50:05.202 --> 00:50:07.764 and you may know the story that

NOTE Confidence: 0.775830976

00:50:07.764 --> 00:50:10.275 was developed by Ranjit over the

NOTE Confidence: 0.775830976

00:50:10.275 --> 00:50:12.824 last years about the fact that

NOTE Confidence: 0.775830976

00:50:12.824 --> 00:50:15.254 when you have an IDH mutation

NOTE Confidence: 0.775830976

00:50:15.254 --> 00:50:17.142 that was initially basically.

NOTE Confidence: 0.775830976

00:50:17.142 --> 00:50:21.174 Developed and found in gliomas the

NOTE Confidence: 0.775830976

00:50:21.174 --> 00:50:25.490 fact of having these two hydroxy

NOTE Confidence: 0.775830976

00:50:25.490 --> 00:50:29.130 glutarate will basically impair the

NOTE Confidence: 0.775830976

00:50:29.130 --> 00:50:33.276 activity of the X Rays in the cell,

NOTE Confidence: 0.775830976

00:50:33.280 --> 00:50:35.581 decrease malicious recommendation,

NOTE Confidence: 0.775830976

00:50:35.581 --> 00:50:40.183 repair and create a braknis phenotype.

NOTE Confidence: 0.775830976

00:50:40.190 --> 00:50:43.178 That obviously is interesting as a

NOTE Confidence: 0.775830976

00:50:43.178 --> 00:50:45.170 potentially chemo radio sensitizer,

NOTE Confidence: 0.775830976

00:50:45.170 --> 00:50:47.655 but from all standpoints were

NOTE Confidence: 0.775830976

00:50:47.655 --> 00:50:49.643 especially interested in our.

NOTE Confidence: 0.7622402

00:50:49.650 --> 00:50:52.740 Potentially, we can use pop emitters

NOTE Confidence: 0.7622402

00:50:52.740 --> 00:50:55.297 to create synthetic lethality with

NOTE Confidence: 0.7622402

00:50:55.297 --> 00:50:57.898 this agent, and when we tested,

NOTE Confidence: 0.7622402

00:50:57.898 --> 00:51:01.209 basically when we move from gliomas to

NOTE Confidence: 0.7622402

00:51:01.209 --> 00:51:04.089 leukemias and Milo dysplastic syndromes,

NOTE Confidence: 0.7622402

00:51:04.090 --> 00:51:07.036 indeed, that's what we found that

NOTE Confidence: 0.7622402

00:51:07.036 --> 00:51:10.310 we were able to potentially.

NOTE Confidence: 0.7622402

00:51:10.310 --> 00:51:13.226 Induce apoptosis in samples of patient

NOTE Confidence: 0.7622402

00:51:13.226 --> 00:51:16.490 that were exposed to hyperventilate.

NOTE Confidence: 0.7622402

00:51:16.490 --> 00:51:19.814 Engagement that were exposed to IDH

NOTE Confidence: 0.7622402

00:51:19.814 --> 00:51:23.680 inhibitor an that I came to development

NOTE Confidence: 0.7622402

00:51:23.680 --> 00:51:28.290 with NCI study right now of the olaparib.

NOTE Confidence: 0.7622402

00:51:28.290 --> 00:51:32.210 The 1st in Class I DH pop inhibitor

NOTE Confidence: 0.7622402

00:51:32.210 --> 00:51:35.598 for patient offering IDH mutation.

NOTE Confidence: 0.7622402

00:51:35.600 --> 00:51:40.184 So that's patient that as a diagnosis of.

NOTE Confidence: 0.7622402

00:51:40.190 --> 00:51:42.620 Acute myeloid leukemia or marriages.

NOTE Confidence: 0.7622402

00:51:42.620 --> 00:51:45.512 Plastic syndrome with an IDH one

NOTE Confidence: 0.7622402

00:51:45.512 --> 00:51:48.970 or IDH two mutation and at least

NOTE Confidence: 0.7622402

00:51:48.970 --> 00:51:51.350 one prior line of treatment,

NOTE Confidence: 0.7622402

00:51:51.350 --> 00:51:54.260 including in lot of this patient

NOTE Confidence: 0.7622402

00:51:54.260 --> 00:51:55.230 I permitting.

NOTE Confidence: 0.7622402

00:51:55.230 --> 00:51:57.650 Agent there are four cohorts

NOTE Confidence: 0.7622402

00:51:57.650 --> 00:51:59.586 that are currently investigated.

NOTE Confidence: 0.7622402

00:51:59.590 --> 00:52:02.990 One for patients with IDH, one IDH,

NOTE Confidence: 0.7622402

00:52:02.990 --> 00:52:05.415 two mutant email without prior

NOTE Confidence: 0.7622402

00:52:05.415 --> 00:52:06.870 exposure to IDH.

NOTE Confidence: 0.7622402

00:52:06.870 --> 00:52:10.307 And if it or one with my

NOTE Confidence: 0.7622402

00:52:10.307 --> 00:52:11.780 dysplastic syndrome without.

NOTE Confidence: 0.7622402

00:52:11.780 --> 00:52:12.824 Exposure to ideas,

NOTE Confidence: 0.7622402

00:52:12.824 --> 00:52:13.172 debit,

NOTE Confidence: 0.7622402

00:52:13.172 --> 00:52:16.681 or an arm two and four are for patient

NOTE Confidence: 0.7622402

00:52:16.681 --> 00:52:19.375 in acute myeloid leukemia and maladies

NOTE Confidence: 0.7622402

00:52:19.375 --> 00:52:21.583 plastic syndrome that were already

NOTE Confidence: 0.7622402

00:52:21.583 --> 00:52:24.103 exposed to IDH inhibitor in the

NOTE Confidence: 0.7622402

00:52:24.110 --> 00:52:26.987 patient that are naive of IDH inhibitor.

NOTE Confidence: 0.7622402

00:52:26.990 --> 00:52:29.606 We have an early response assessments

NOTE Confidence: 0.7622402

00:52:29.606 --> 00:52:32.927 after one cycle and if we do not

NOTE Confidence: 0.7622402

00:52:32.927 --> 00:52:34.797 see any clear clinical benefit,

NOTE Confidence: 0.7622402

00:52:34.800 --> 00:52:36.850 this patient are usually discontinued.

NOTE Confidence: 0.7622402

00:52:36.850 --> 00:52:38.562 An transition classical IDH

NOTE Confidence: 0.7622402

00:52:38.562 --> 00:52:41.130 inhibitor for the patient that are

NOTE Confidence: 0.7622402

00:52:41.209 --> 00:52:44.197 responding to the patient that were

NOTE Confidence: 0.7622402

00:52:44.197 --> 00:52:46.189 previously exposed to accommodating.

NOTE Confidence: 0.7622402

00:52:46.190 --> 00:52:47.986 Agent and IDH numitor.

NOTE Confidence: 0.7622402

00:52:47.986 --> 00:52:50.680 We are reassessing response after three,

NOTE Confidence: 0.7622402

00:52:50.680 --> 00:52:52.472 69 and 12 cycles,

NOTE Confidence: 0.7622402

00:52:52.472 --> 00:52:54.712 continuing the treatment until progression.

NOTE Confidence: 0.7622402

00:52:54.720 --> 00:52:57.522 The study has been activated this

NOTE Confidence: 0.7622402

00:52:57.522 --> 00:53:00.311 year and we're pretty happy to

NOTE Confidence: 0.7622402

00:53:00.311 --> 00:53:02.795 have over the last few months.

NOTE Confidence: 0.7622402

00:53:02.800 --> 00:53:06.574 Three patient included an in treatment

NOTE Confidence: 0.7622402

00:53:06.574 --> 00:53:10.130 an three patienten screening right now.

NOTE Confidence: 0.7622402

00:53:10.130 --> 00:53:13.014 One of the big interest of this

NOTE Confidence: 0.7622402

00:53:13.014 --> 00:53:16.695 work is also to see the pretty

NOTE Confidence: 0.7622402

00:53:16.695 --> 00:53:19.039 extensive collaboration we have.

NOTE Confidence: 0.7622402

00:53:19.040 --> 00:53:21.164 From a translational standpoint,

NOTE Confidence: 0.7622402

00:53:21.164 --> 00:53:23.288 that's collaboration with the

NOTE Confidence: 0.7622402

00:53:23.288 --> 00:53:26.189 NCI through more calf or what

NOTE Confidence: 0.7622402

00:53:26.189 --> 00:53:27.949 exam sequencing and sequencing.

NOTE Confidence: 0.7622402

00:53:27.950 --> 00:53:31.286 That's a lot of study done in hours

NOTE Confidence: 0.7622402

00:53:31.286 --> 00:53:34.469 at Yale with Ranjit and Stephanie

NOTE Confidence: 0.7622402

00:53:34.469 --> 00:53:37.841 to explore from ex vivo samples.

NOTE Confidence: 0.7622402

00:53:37.850 --> 00:53:38.852 DNA damage.

NOTE Confidence: 0.7622402

00:53:38.852 --> 00:53:39.353 Response,

NOTE Confidence: 0.7622402

00:53:39.353 --> 00:53:42.359 but also all these cells will

NOTE Confidence: 0.7622402

00:53:42.359 --> 00:53:45.859 behave put in the Mr Jimmys model

NOTE Confidence: 0.7622402

00:53:45.859 --> 00:53:47.795 that Stephanie is developing.

NOTE Confidence: 0.7622402

00:53:47.800 --> 00:53:50.140 We have collaboration with Domino's

NOTE Confidence: 0.7622402

00:53:50.140 --> 00:53:53.025 thanks to Pat Larusso and that

NOTE Confidence: 0.7622402

00:53:53.025 --> 00:53:55.833 collaboration with Jiggly to assess the

NOTE Confidence: 0.7622402

00:53:55.833 --> 00:53:58.925 evolution of the two hydroxy glutarate

NOTE Confidence: 0.7622402

00:53:58.925 --> 00:54:01.610 and some metabolomics marker Anne.

NOTE Confidence: 0.7622402

00:54:01.610 --> 00:54:05.730 Right now we are starting starting to work

NOTE Confidence: 0.7622402

00:54:05.730 --> 00:54:09.297 with winning Wong from the West Campus.

NOTE Confidence: 0.7622402

00:54:09.300 --> 00:54:14.646 On single cell sequencing for this.

NOTE Confidence: 0.7622402

00:54:14.650 --> 00:54:16.170 Specific samples an studies,

NOTE Confidence: 0.7622402

00:54:16.170 --> 00:54:18.450 as we definitely think that we

NOTE Confidence: 0.7622402

00:54:18.520 --> 00:54:20.722 will have some clonal selection as

NOTE Confidence: 0.7622402

00:54:20.722 --> 00:54:22.690 potentially one of the mechanism

NOTE Confidence: 0.7622402

00:54:22.690 --> 00:54:24.840 of resistance in this context.

NOTE Confidence: 0.7622402

00:54:24.840 --> 00:54:25.881 So stay tuned.

NOTE Confidence: 0.7622402

00:54:25.881 --> 00:54:28.310 That's a bit early to make any

NOTE Confidence: 0.7622402

00:54:28.392 --> 00:54:29.550 any conclusion.

NOTE Confidence: 0.7622402

00:54:29.550 --> 00:54:31.674 We just have a few patients

NOTE Confidence: 0.7622402

00:54:31.674 --> 00:54:34.250 in a few months on treatment,

NOTE Confidence: 0.7622402

00:54:34.250 --> 00:54:37.730 but that's a developing story.

NOTE Confidence: 0.7622402

00:54:37.730 --> 00:54:39.440 As I was saying earlier,

NOTE Confidence: 0.7622402

00:54:39.440 --> 00:54:41.904 one of the things that has also been

NOTE Confidence: 0.7622402

00:54:41.904 --> 00:54:44.227 mentioned as a mechanism of resistance,

NOTE Confidence: 0.7622402

00:54:44.230 --> 00:54:47.598 and I try to go fast on that.

NOTE Confidence: 0.7622402

00:54:47.600 --> 00:54:48.452 Is uh,

NOTE Confidence: 0.7622402

00:54:48.452 --> 00:54:51.434 even though logic escape of the matter.

NOTE Confidence: 0.72344524

00:54:51.440 --> 00:54:52.294 Dysplastic syndrome.

NOTE Confidence: 0.72344524

00:54:52.294 --> 00:54:55.283 We have an over expression of PD,

NOTE Confidence: 0.72344524

00:54:55.290 --> 00:54:59.364 One PD L1 and C A4 in.

NOTE Confidence: 0.72344524

00:54:59.370 --> 00:55:01.222 Patient with hypomethylating agent

NOTE Confidence: 0.72344524

00:55:01.222 --> 00:55:04.000 failure and that's led to several

NOTE Confidence: 0.72344524

00:55:04.075 --> 00:55:06.530 several studies I'm mentioning here.

NOTE Confidence: 0.72344524

00:55:06.530 --> 00:55:08.434 Studies with basically ipis,

NOTE Confidence: 0.72344524

00:55:08.434 --> 00:55:10.338 nivo or Pam bro.

NOTE Confidence: 0.72344524

00:55:10.340 --> 00:55:12.951 I also need obviously to to mention

NOTE Confidence: 0.72344524

00:55:12.951 --> 00:55:16.122 that the study led by armor with

NOTE Confidence: 0.72344524

00:55:16.122 --> 00:55:18.094 basically edge darkening bitters

NOTE Confidence: 0.72344524

00:55:18.094 --> 00:55:20.348 plus checkpoint blockade inhibitors

NOTE Confidence: 0.72344524

00:55:20.348 --> 00:55:22.736 that was recently published.

NOTE Confidence: 0.72344524

00:55:22.740 --> 00:55:24.222 For the moment,

NOTE Confidence: 0.72344524

00:55:24.222 --> 00:55:29.598 let's say that we are not at the point where.

NOTE Confidence: 0.72344524

00:55:29.600 --> 00:55:30.888 It's a game changer.

NOTE Confidence: 0.72344524

00:55:30.888 --> 00:55:33.520 There may be some kind of response,

NOTE Confidence: 0.72344524

00:55:33.520 --> 00:55:34.940 but for the moment,

NOTE Confidence: 0.72344524

00:55:34.940 --> 00:55:36.715 nothing that is really perfect.

NOTE Confidence: 0.72344524

00:55:36.720 --> 00:55:39.568 So still a lot of work to do.

NOTE Confidence: 0.72344524

00:55:39.570 --> 00:55:42.958 One way we thought about that is

NOTE Confidence: 0.72344524

00:55:42.958 --> 00:55:45.839 potentially to try to bring this.

NOTE Confidence: 0.72344524

00:55:45.840 --> 00:55:47.664 Potentially checkpoint inhibitor

NOTE Confidence: 0.72344524

00:55:47.664 --> 00:55:50.096 earlier in the development,

NOTE Confidence: 0.72344524

00:55:50.100 --> 00:55:52.038 and for instance,

NOTE Confidence: 0.72344524

00:55:52.038 --> 00:55:55.914 we're currently developing a study in

NOTE Confidence: 0.72344524

00:55:55.914 --> 00:56:00.593 an MD S an email of idea 2012 plus

NOTE Confidence: 0.72344524

00:56:00.593 --> 00:56:05.026 nivolumab in Phase one pilot study for

NOTE Confidence: 0.72344524

00:56:05.026 --> 00:56:08.366 patients that were already exposed

NOTE Confidence: 0.72344524

00:56:08.370 --> 00:56:13.800 to chemotherapy or iPod mediating agent.

NOTE Confidence: 0.72344524

00:56:13.800 --> 00:56:16.656 Another study has been on all and has

NOTE Confidence: 0.72344524

00:56:16.656 --> 00:56:19.959 to be restructured because of covid,

NOTE Confidence: 0.72344524

00:56:19.960 --> 00:56:22.160 but we're back in business

NOTE Confidence: 0.72344524

00:56:22.160 --> 00:56:24.360 and open to accrual oor.

NOTE Confidence: 0.72344524

00:56:24.360 --> 00:56:26.560 Since basically lost last week.

NOTE Confidence: 0.72344524

00:56:26.560 --> 00:56:28.890 Once again translation and collective

NOTE Confidence: 0.72344524

00:56:28.890 --> 00:56:31.220 studies are really important and

NOTE Confidence: 0.72344524

00:56:31.293 --> 00:56:33.323 we have some ongoing collaboration

NOTE Confidence: 0.72344524

00:56:33.323 --> 00:56:36.960 with Stephanie and will in one so.

NOTE Confidence: 0.72344524

00:56:36.960 --> 00:56:39.669 If I need to to summarize a bit where

NOTE Confidence: 0.72344524

00:56:39.669 --> 00:56:42.524 we are really quickly for the moment

NOTE Confidence: 0.72344524

00:56:42.524 --> 00:56:44.847 for this patient with permitting

NOTE Confidence: 0.72344524

00:56:44.847 --> 00:56:47.782 agent failure with Steven situation

NOTE Confidence: 0.72344524

00:56:47.782 --> 00:56:50.130 where aggressive management for

NOTE Confidence: 0.72344524

00:56:50.130 --> 00:56:51.513 transplant allogeneic transplant

NOTE Confidence: 0.72344524

00:56:51.513 --> 00:56:54.279 candidate makes sense as we don't

NOTE Confidence: 0.72344524

00:56:54.279 --> 00:56:56.572 have any really reliable other

NOTE Confidence: 0.72344524

00:56:56.572 --> 00:56:58.777 option besides maybe some targeted

NOTE Confidence: 0.72344524

00:56:58.777 --> 00:57:01.106 therapy on small number of patients,

NOTE Confidence: 0.72344524

00:57:01.110 --> 00:57:04.454 we do not have a reliable standard of

NOTE Confidence: 0.72344524

00:57:04.454 --> 00:57:08.208 care for patients and fit for treatment.

NOTE Confidence: 0.72344524

00:57:08.210 --> 00:57:09.342 Maybe even eight o'clock,

NOTE Confidence: 0.72344524

00:57:09.342 --> 00:57:11.040 maybe some other drug will come

NOTE Confidence: 0.72344524

00:57:11.097 --> 00:57:12.687 and will be confirmed as option,

NOTE Confidence: 0.72344524

00:57:12.690 --> 00:57:14.370 but for the moment that's still

NOTE Confidence: 0.72344524

00:57:14.370 --> 00:57:14.930 pretty struggling.

NOTE Confidence: 0.83678097

00:57:17.220 --> 00:57:19.971 The way the field is moving is

NOTE Confidence: 0.83678097

00:57:19.971 --> 00:57:22.033 interesting and we are learning

NOTE Confidence: 0.83678097

00:57:22.033 --> 00:57:24.439 a lot from the email world.

NOTE Confidence: 0.83678097

00:57:24.440 --> 00:57:27.032 At the same time, we probably

NOTE Confidence: 0.83678097

00:57:27.032 --> 00:57:28.760 cannot really completely extrapolate

NOTE Confidence: 0.83678097

00:57:28.834 --> 00:57:31.256 everything we do from the email side,

NOTE Confidence: 0.83678097

00:57:31.260 --> 00:57:33.260 we know that the microenvironment,

NOTE Confidence: 0.83678097

00:57:33.260 --> 00:57:35.265 for example in Milo dysplastic

NOTE Confidence: 0.83678097

00:57:35.265 --> 00:57:36.869 syndrome is definitely different.

NOTE Confidence: 0.83678097

00:57:36.870 --> 00:57:39.600 We know that the ability of this

NOTE Confidence: 0.83678097

00:57:39.600 --> 00:57:41.766 patient to sustain any aggressive

NOTE Confidence: 0.83678097

00:57:41.766 --> 00:57:44.520 treatment is definitely less than what

NOTE Confidence: 0.83678097

00:57:44.520 --> 00:57:47.807 we see in AML on other malignancy so.

NOTE Confidence: 0.83678097

00:57:47.810 --> 00:57:49.755 That's something that we need

NOTE Confidence: 0.83678097

00:57:49.755 --> 00:57:51.700 to work on and so.

NOTE Confidence: 0.83678097

00:57:51.700 --> 00:57:54.598 The best way we have to deal with this

NOTE Confidence: 0.83678097

00:57:54.598 --> 00:57:57.700 HTML file is ready to try to avoid it

NOTE Confidence: 0.83678097

00:57:57.700 --> 00:58:00.258 and optimize the frontline treatment.

NOTE Confidence: 0.83678097

00:58:00.260 --> 00:58:02.330 We have lots of currently really

NOTE Confidence: 0.83678097

00:58:02.330 --> 00:58:04.350 exciting drugs in the pipeline.

NOTE Confidence: 0.83678097

00:58:04.350 --> 00:58:07.275 Lots of data that we presented at the Ash

NOTE Confidence: 0.83678097

00:58:07.275 --> 00:58:10.295 this year on Venetoclax Magnolia Map team.

NOTE Confidence: 0.83678097

00:58:10.300 --> 00:58:10.998 Three BitTorrent.

NOTE Confidence: 0.83678097

00:58:10.998 --> 00:58:14.390 Amar has been part of some of these studies,

NOTE Confidence: 0.83678097

00:58:14.390 --> 00:58:17.610 so statue MBS Field is really moving

NOTE Confidence: 0.83678097

00:58:17.610 --> 00:58:20.908 and we hope to see the type of.

NOTE Confidence: 0.83678097

00:58:20.910 --> 00:58:23.502 Change in landscape that we have seen over

NOTE Confidence: 0.83678097

00:58:23.502 --> 00:58:26.606 at the last year in acute myeloid leukemia.

NOTE Confidence: 0.83678097

00:58:26.610 --> 00:58:27.594 So in conclusion,

NOTE Confidence: 0.83678097

00:58:27.594 --> 00:58:29.562 this this situation of hyper mediating

NOTE Confidence: 0.83678097

00:58:29.562 --> 00:58:31.388 agent failure really represent some

NOTE Confidence: 0.83678097

00:58:31.388 --> 00:58:33.548 academic challenges we need to improve

NOTE Confidence: 0.83678097

00:58:33.603 --> 00:58:35.508 our understanding of the Physiology.

NOTE Confidence: 0.83678097

00:58:35.510 --> 00:58:37.270 Pathophysiology of this situation to

NOTE Confidence: 0.83678097

00:58:37.270 --> 00:58:40.158 be able to help us to better define

NOTE Confidence: 0.83678097

00:58:40.158 --> 00:58:42.622 the standard of care for this patient,

NOTE Confidence: 0.83678097

00:58:42.630 --> 00:58:45.825 we need to build resources we need to build,

NOTE Confidence: 0.83678097

00:58:45.830 --> 00:58:47.306 represent repository and logical.

NOTE Confidence: 0.83678097

00:58:47.306 --> 00:58:49.520 Follow up for this patient which

NOTE Confidence: 0.83678097

00:58:49.581 --> 00:58:50.979 is sometimes challenging.

NOTE Confidence: 0.83678097

00:58:50.980 --> 00:58:52.750 I.

NOTE Confidence: 0.83678097

00:58:52.750 --> 00:58:55.294 In the context of a disease that is

NOTE Confidence: 0.83678097

00:58:55.294 --> 00:58:57.867 treated in both small and big centers,

NOTE Confidence: 0.83678097

00:58:57.870 --> 00:58:59.655 we need to collaborate around

NOTE Confidence: 0.83678097

00:58:59.655 --> 00:59:02.262 academics to be able to really have

NOTE Confidence: 0.83678097

00:59:02.262 --> 00:59:04.524 significant number of patients to be

NOTE Confidence: 0.83678097

00:59:04.524 --> 00:59:07.100 able to answer the right question.

NOTE Confidence: 0.83678097

00:59:07.100 --> 00:59:08.786 I also think that it's important

NOTE Confidence: 0.83678097

00:59:08.786 --> 00:59:11.377 to keep in mind that there are some

NOTE Confidence: 0.83678097

00:59:11.377 --> 00:59:13.132 clinical care challenges for that.

NOTE Confidence: 0.83678097

00:59:13.140 --> 00:59:15.042 The access to innovation to Center

NOTE Confidence: 0.83678097

00:59:15.042 --> 00:59:16.955 of excellence is not something that

NOTE Confidence: 0.83678097

00:59:16.955 --> 00:59:18.978 is a modulus in the country or

NOTE Confidence: 0.83678097

00:59:18.978 --> 00:59:20.769 just a modulus in Connecticut.

NOTE Confidence: 0.83678097

00:59:20.770 --> 00:59:22.996 And that's definitely one of the mission.

NOTE Confidence: 0.83678097

00:59:23.000 --> 00:59:25.574 I think we have at scale to be able

NOTE Confidence: 0.83678097

00:59:25.574 --> 00:59:28.128 to promote the access to innovation

NOTE Confidence: 0.83678097

00:59:28.128 --> 00:59:31.205 and promote the access to the Center

NOTE Confidence: 0.83678097

00:59:31.205 --> 00:59:33.635 of excellence that that we have.

NOTE Confidence: 0.83678097

00:59:33.640 --> 00:59:36.016 We know that patients in Connecticut

NOTE Confidence: 0.83678097

00:59:36.016 --> 00:59:37.600 without without snowstorm like

NOTE Confidence: 0.83678097

00:59:37.666 --> 00:59:39.676 tomorrow will have potentially some

NOTE Confidence: 0.83678097

00:59:39.676 --> 00:59:42.090 some issues limiting the ability to

NOTE Confidence: 0.83678097

00:59:42.090 --> 00:59:44.118 to basically get to academic centers,

NOTE Confidence: 0.83678097

00:59:44.120 --> 00:59:45.516 get to clinical trial,

NOTE Confidence: 0.83678097

00:59:45.516 --> 00:59:48.421 and so I think that one of the

NOTE Confidence: 0.83678097

00:59:48.421 --> 00:59:50.605 mission that we have as academics

NOTE Confidence: 0.83678097

00:59:50.605 --> 00:59:54.051 is also to make sure that we can

NOTE Confidence: 0.83678097

00:59:54.051 --> 00:59:55.368 potentially bring research.

NOTE Confidence: 0.83678097

00:59:55.370 --> 00:59:58.040 Bring basically knew therapy and exciting

NOTE Confidence: 0.83678097

00:59:58.040 --> 01:00:00.655 therapy to the different sites where

NOTE Confidence: 0.83678097

01:00:00.655 --> 01:00:03.727 the patients are treated close to their home.

NOTE Confidence: 0.83678097

01:00:03.730 --> 01:00:07.874 With that I would like to thanks everyone.

NOTE Confidence: 0.83678097

01:00:07.880 --> 01:00:08.384 Right?

NOTE Confidence: 0.83678097

01:00:08.384 --> 01:00:11.408 Participate to this effort for sure.

NOTE Confidence: 0.83678097

01:00:11.410 --> 01:00:13.050 The Yellow Cancer Center

NOTE Confidence: 0.83678097

01:00:13.050 --> 01:00:13.870 group alphabetically.

NOTE Confidence: 0.83678097

01:00:13.870 --> 01:00:14.686 Steve Gore.

NOTE Confidence: 0.83678097

01:00:14.686 --> 01:00:17.542 My mentor Stephanie for lot of collaboration.

NOTE Confidence: 0.83678097

01:00:17.550 --> 01:00:17.965 Nicolai,

NOTE Confidence: 0.83678097

01:00:17.965 --> 01:00:20.455 Rory and armor for being such

NOTE Confidence: 0.83678097

01:00:20.455 --> 01:00:23.353 trooper an such a great group to

NOTE Confidence: 0.83678097

01:00:23.353 --> 01:00:25.318 work with my dear colleagues,

NOTE Confidence: 0.83678097

01:00:25.320 --> 01:00:27.370 colleagues from the group Francophone,

NOTE Confidence: 0.83678097

01:00:27.370 --> 01:00:29.006 the Mirror Displays E,

NOTE Confidence: 0.83678097

01:00:29.006 --> 01:00:31.460 as well as collaborators in US,

NOTE Confidence: 0.76293355

01:00:31.460 --> 01:00:33.908 Europe. And now I should say,

NOTE Confidence: 0.76293355

01:00:33.910 --> 01:00:35.950 knew K should probably split.

NOTE Confidence: 0.76293355

01:00:35.950 --> 01:00:38.967 You can Europe now two weeks anyway.

NOTE Confidence: 0.76293355

01:00:38.970 --> 01:00:40.728 On that I'll take any questions

NOTE Confidence: 0.76293355

01:00:40.728 --> 01:00:43.045 I would like to thank you for

NOTE Confidence: 0.76293355

01:00:43.045 --> 01:00:44.730 your attention. Thanks so much.

NOTE Confidence: 0.7688253

01:00:45.920 --> 01:00:48.880 Sounds fantastic to my thank you so much.

NOTE Confidence: 0.7688253

01:00:48.880 --> 01:00:53.029 Really true for some, and MD's and AML and.

NOTE Confidence: 0.7688253

01:00:53.030 --> 01:00:54.788 You know, as we are presenting,

NOTE Confidence: 0.7688253

01:00:54.790 --> 01:00:55.672 you've actually answered

NOTE Confidence: 0.7688253

01:00:55.672 --> 01:00:56.848 like my burning questions.

NOTE Confidence: 0.7688253

01:00:56.850 --> 01:00:59.964 We just get rid of a society in, you know,

NOTE Confidence: 0.7688253

01:00:59.964 --> 01:01:03.020 and use it for salvage after everything else.

NOTE Confidence: 0.7688253

01:01:03.020 --> 01:01:05.018 And that is certainly very exciting

NOTE Confidence: 0.7688253

01:01:05.018 --> 01:01:07.882 to see how you and the whole team are

NOTE Confidence: 0.7688253

01:01:07.882 --> 01:01:10.480 going to come up with exciting trials.

NOTE Confidence: 0.7688253

01:01:10.480 --> 01:01:13.522 I think we're a little bit after the hour,

NOTE Confidence: 0.7688253

01:01:13.530 --> 01:01:16.673 but maybe. Say something sad,

NOTE Confidence: 0.7688253

01:01:16.673 --> 01:01:18.378 or Nickelodeon request and then

NOTE Confidence: 0.7688253

01:01:18.378 --> 01:01:20.745 we have to let people go for two

NOTE Confidence: 0.7688253

01:01:20.745 --> 01:01:22.598 or getting kicked out of the room.

NOTE Confidence: 0.7688253

01:01:22.600 --> 01:01:23.368 Which is correct?

NOTE Confidence: 0.79769796

01:01:25.720 --> 01:01:27.630 No, I think that's definitely

NOTE Confidence: 0.79769796

01:01:27.630 --> 01:01:30.279 the HMA is a sign of care,

NOTE Confidence: 0.79769796

01:01:30.280 --> 01:01:32.560 but that's not a perfect one.

NOTE Confidence: 0.79769796

01:01:32.560 --> 01:01:34.460 So developing new agents or

NOTE Confidence: 0.79769796

01:01:34.460 --> 01:01:35.862 new formulation, for example,

NOTE Confidence: 0.79769796

01:01:35.862 --> 01:01:38.109 we have now access to oral formulation

NOTE Confidence: 0.79769796

01:01:38.109 --> 01:01:40.158 of these hypomethylating agent.

NOTE Confidence: 0.79769796

01:01:40.160 --> 01:01:42.345 That's definitely something that we

NOTE Confidence: 0.79769796

01:01:42.345 --> 01:01:45.233 want to continue to develop with the

NOTE Confidence: 0.79769796

01:01:45.233 --> 01:01:47.729 idea that even if it may not improve

NOTE Confidence: 0.79769796

01:01:47.806 --> 01:01:50.056 the response rate or the overall

NOTE Confidence: 0.79769796

01:01:50.056 --> 01:01:52.434 survival and that may be something

NOTE Confidence: 0.79769796

01:01:52.434 --> 01:01:55.930 we can discuss as the way we can.

NOTE Confidence: 0.79769796

01:01:55.930 --> 01:01:58.667 I use this medication is a bit

NOTE Confidence: 0.79769796

01:01:58.667 --> 01:01:59.840 different than conventional

NOTE Confidence: 0.79769796

01:01:59.916 --> 01:02:01.771 accommodating age and we can

NOTE Confidence: 0.79769796

01:02:01.771 --> 01:02:03.970 improve quality of life of the.

NOTE Confidence: 0.79769796

01:02:03.970 --> 01:02:05.294 And access to care,

NOTE Confidence: 0.79769796

01:02:05.294 --> 01:02:06.618 so that's definitely something

NOTE Confidence: 0.79769796

01:02:06.618 --> 01:02:08.890 that is that is important for sure.

NOTE Confidence: 0.7976982

01:02:10.000 --> 01:02:11.416 Yeah, fantastic so Charlie,

NOTE Confidence: 0.7976982

01:02:11.416 --> 01:02:13.540 do you want to tell me?

NOTE Confidence: 0.7976982

01:02:13.540 --> 01:02:15.312 We probably have to break.

NOTE Confidence: 0.7976982

01:02:15.312 --> 01:02:17.080 No thank you tomorrow and

NOTE Confidence: 0.7976982

01:02:17.080 --> 01:02:18.849 Nikolai for two superb talks

NOTE Confidence: 0.7976982

01:02:18.850 --> 01:02:21.326 really as two to four's on two

NOTE Confidence: 0.7976982

01:02:21.326 --> 01:02:23.099 important areas of human logic.

NOTE Confidence: 0.7976982

01:02:23.100 --> 01:02:25.419 Malignancy's, thank you.

NOTE Confidence: 0.7976982

01:02:25.420 --> 01:02:26.311 Thank you alright.

NOTE Confidence: 0.7976982

01:02:26.311 --> 01:02:28.844 Well thank you so much and look forward

NOTE Confidence: 0.7976982

01:02:28.844 --> 01:02:30.779 to tackling these problems over

NOTE Confidence: 0.81829655

01:02:30.780 --> 01:02:32.120 the years. Thank you.

NOTE Confidence: 0.81829655

01:02:32.120 --> 01:02:33.460 Thanks everyone. Alright bye.