WEBVTT

NOTE duration:"01:01:44"

NOTE recognizability:0.838

NOTE language:en-us

NOTE Confidence: 0.720982675714286

00:00:00.000 --> 00:00:02.534 What about what come the live audience?

NOTE Confidence: 0.720982675714286

00:00:02.540 --> 00:00:05.092 And I want to welcome everybody who's joining

NOTE Confidence: 0.720982675714286

00:00:05.092 --> 00:00:07.920 us today on zoom for the Sun Special Lecture.

NOTE Confidence: 0.720982675714286

00:00:07.920 --> 00:00:12.176 So I will be introducing Dr Sears

NOTE Confidence: 0.720982675714286

00:00:12.176 --> 00:00:14.320 and today's lecture honoree.

NOTE Confidence: 0.720982675714286

00:00:14.320 --> 00:00:17.732 And and then Doctor Zaiden, who is on zoom

NOTE Confidence: 0.720982675714286

00:00:17.732 --> 00:00:19.400 will be introducing Patrick and Harden.

NOTE Confidence: 0.720982675714286

00:00:19.400 --> 00:00:22.392 So the Blanche Tom and lecture series was

NOTE Confidence: 0.720982675714286

00:00:22.392 --> 00:00:25.380 established in 2012 by Doctor Marvin Sears.

NOTE Confidence: 0.720982675714286

00:00:25.380 --> 00:00:28.188 Dr Sears was a longtime chair and founder

NOTE Confidence: 0.720982675714286

00:00:28.188 --> 00:00:30.589 of Ophthalmology and visual science at Yale.

NOTE Confidence: 0.720982675714286

00:00:30.590 --> 00:00:31.940 And the lecture was established

NOTE Confidence: 0.720982675714286

00:00:31.940 --> 00:00:33.290 in honor of his mother,

NOTE Confidence: 0.720982675714286

00:00:33.290 --> 00:00:35.930 Lange Tolman, who passed away from

NOTE Confidence: 0.720982675714286

00:00:35.930 --> 00:00:37.250 acute myelogenous leukemia.

NOTE Confidence: 0.720982675714286

00:00:37.250 --> 00:00:39.254 This was actually the first lecture

NOTE Confidence: 0.720982675714286

00:00:39.254 --> 00:00:40.970 series dedicated solely to hematologic

NOTE Confidence: 0.720982675714286

00:00:40.970 --> 00:00:42.908 malignancies at Yale and it is

NOTE Confidence: 0.720982675714286

00:00:42.908 --> 00:00:44.904 intended to bring to Yale pioneers

NOTE Confidence: 0.720982675714286

00:00:44.904 --> 00:00:46.519 that have made major contributions

NOTE Confidence: 0.720982675714286

00:00:46.519 --> 00:00:48.810 to under to our understanding of

NOTE Confidence: 0.720982675714286

00:00:48.810 --> 00:00:50.860 the current trends in hematologic

NOTE Confidence: 0.720982675714286

00:00:50.860 --> 00:00:52.909 malignancies and in particular leukemia.

NOTE Confidence: 0.720982675714286

00:00:52.910 --> 00:00:54.029 So doctors Aiden,

NOTE Confidence: 0.720982675714286

00:00:54.029 --> 00:00:56.640 I welcome you to introduce Doctor Kantarjian.

NOTE Confidence: 0.944682032

00:00:58.500 --> 00:01:00.260 Yeah. Thank you so much, Stephanie.

NOTE Confidence: 0.944682032

00:01:00.260 --> 00:01:02.560 It's really a pleasure to

NOTE Confidence: 0.944682032

00:01:02.560 --> 00:01:03.940 introduce Doctor Kantarjian,

NOTE Confidence: 0.944682032

00:01:03.940 --> 00:01:05.494 who I could not think of any,

NOTE Confidence: 0.944682032

00:01:05.500 --> 00:01:07.552 but anyone more suited to give

NOTE Confidence: 0.944682032

00:01:07.552 --> 00:01:09.364 this lecture about new developments

NOTE Confidence: 0.944682032

00:01:09.364 --> 00:01:11.608 on leukemia because he has been

NOTE Confidence: 0.944682032

00:01:11.608 --> 00:01:14.383 a major force in many of the new

NOTE Confidence: 0.944682032

00:01:14.383 --> 00:01:16.375 developments over the last few decades,

NOTE Confidence: 0.944682032

00:01:16.375 --> 00:01:18.280 really in leukemia,

NOTE Confidence: 0.944682032

00:01:18.280 --> 00:01:22.140 both in AML and CLL and CML as well.

NOTE Confidence: 0.944682032

00:01:22.140 --> 00:01:24.170 So Doctor Kantarjian is a professor and

NOTE Confidence: 0.944682032

00:01:24.170 --> 00:01:26.329 chair of the Department of leukemia at

NOTE Confidence: 0.944682032

00:01:26.329 --> 00:01:28.509 the University of Texas and the Anderson.

NOTE Confidence: 0.944682032

00:01:28.510 --> 00:01:29.372 Cancer Center.

NOTE Confidence: 0.944682032

00:01:29.372 --> 00:01:31.527 He's also the Samsung Distinguished

NOTE Confidence: 0.944682032

00:01:31.527 --> 00:01:33.899 Leukemia chair in cancer medicine.

NOTE Confidence: 0.944682032

00:01:33.900 --> 00:01:36.228 His research has focused on translation

NOTE Confidence: 0.944682032

00:01:36.230 --> 00:01:38.375 and clinical development therapeutics in

NOTE Confidence: 0.944682032

00:01:38.375 --> 00:01:40.865 leukemia over the last three decades.

NOTE Confidence: 0.944682032

00:01:40.870 --> 00:01:43.445 He had made significant contributions

NOTE Confidence: 0.944682032

00:01:43.445 --> 00:01:46.020 that improved our understanding of

NOTE Confidence: 0.944682032

00:01:46.095 --> 00:01:48.797 both the prognosis as well as the

NOTE Confidence: 0.944682032

00:01:48.797 --> 00:01:51.381 survival of patients of CMLL as

NOTE Confidence: 0.944682032

00:01:51.381 --> 00:01:53.631 well as discoveries of decitabine

NOTE Confidence: 0.944682032

00:01:53.631 --> 00:01:54.915 in myelodysplastic syndromes

NOTE Confidence: 0.944682032

00:01:54.915 --> 00:01:56.790 and clofarabine in the treatment

NOTE Confidence: 0.944682032

00:01:56.790 --> 00:01:58.700 of leukemias and many other.

NOTE Confidence: 0.944682032

00:01:58.700 --> 00:01:59.072 Medications.

NOTE Confidence: 0.944682032

00:01:59.072 --> 00:01:59.816 In fact,

NOTE Confidence: 0.944682032

00:01:59.816 --> 00:02:02.048 he and his group have contributed

NOTE Confidence: 0.944682032

00:02:02.048 --> 00:02:04.801 to more than 20 develop new drug

NOTE Confidence: 0.944682032

00:02:04.801 --> 00:02:06.870 developments in in this space.

NOTE Confidence: 0.944682032

00:02:06.870 --> 00:02:10.878 He has been an author of more than

NOTE Confidence: 0.944682032

00:02:10.878 --> 00:02:12.846 2000 peer reviewed publications,

NOTE Confidence: 0.944682032

00:02:12.850 --> 00:02:15.562 and he actually has been a major

NOTE Confidence: 0.944682032

00:02:15.562 --> 00:02:17.010 advocate of clinical research.

NOTE Confidence: 0.944682032

00:02:17.010 --> 00:02:19.794 He has mentored hundreds of leukemia

NOTE Confidence: 0.944682032

00:02:19.794 --> 00:02:22.305 doctors and researchers all over the

NOTE Confidence: 0.944682032

00:02:22.305 --> 00:02:25.086 US and the world and has been a big

NOTE Confidence: 0.944682032

00:02:25.086 --> 00:02:27.978 advocate for introduction and use of.

NOTE Confidence: 0.944682032

00:02:27.978 --> 00:02:30.058 Therapy is across the world,

NOTE Confidence: 0.944682032

00:02:30.060 --> 00:02:32.030 especially in low resource countries.

NOTE Confidence: 0.944682032

00:02:32.030 --> 00:02:33.801 So it's really a pleasure to have

NOTE Confidence: 0.944682032

00:02:33.801 --> 00:02:35.233 doctor Kantarjian and who are very

NOTE Confidence: 0.944682032

00:02:35.233 --> 00:02:36.682 grateful to have you speak to us

NOTE Confidence: 0.944682032

00:02:36.733 --> 00:02:38.068 today about acute and plastic

NOTE Confidence: 0.856134666666667

00:02:38.080 --> 00:02:39.268 leukemia. Thank you.

NOTE Confidence: 0.83799161

00:02:40.180 --> 00:02:41.998 Thank you very much, Doctor Zeidan.

NOTE Confidence: 0.83799161

00:02:42.000 --> 00:02:44.765 It's really a great honor and a

NOTE Confidence: 0.83799161

00:02:44.765 --> 00:02:48.801 pleasure to give it the talk at Yale and

NOTE Confidence: 0.83799161

00:02:48.801 --> 00:02:51.140 particularly the special Tallman talk.

NOTE Confidence: 0.83799161

00:02:51.140 --> 00:02:53.692 But I'm going to do is review the

NOTE Confidence: 0.83799161

00:02:53.692 --> 00:02:55.752 progress and research in acute

NOTE Confidence: 0.83799161

00:02:55.752 --> 00:02:58.440 lymphocytic leukemia as it stands today.

NOTE Confidence: 0.83799161

00:02:58.440 --> 00:03:01.088 And a lot of the things I'm going

NOTE Confidence: 0.83799161

00:03:01.088 --> 00:03:04.076 to say may be very different from

NOTE Confidence: 0.83799161

00:03:04.076 --> 00:03:06.900 what you view all treatment today.

NOTE Confidence: 0.83799161

00:03:06.900 --> 00:03:08.500 So bear with me,

NOTE Confidence: 0.83799161

00:03:08.500 --> 00:03:11.490 I'll try to get you through the information.

NOTE Confidence: 0.83799161

00:03:11.490 --> 00:03:14.393 And perhaps convince you that the

NOTE Confidence: 0.83799161

00:03:14.393 --> 00:03:16.608 times are changing very quickly.

NOTE Confidence: 0.83799161

00:03:16.610 --> 00:03:19.286 These are my conflicts of interest.

NOTE Confidence: 0.83799161

00:03:19.290 --> 00:03:21.985 So this is the standard of care

NOTE Confidence: 0.83799161

00:03:21.985 --> 00:03:23.594 in acute lymphocytic leukemia

NOTE Confidence: 0.83799161

00:03:23.594 --> 00:03:25.874 as it stands today we give.

NOTE Confidence: 0.83799161

00:03:25.880 --> 00:03:28.730 A lot of intensive chemotherapy with

NOTE Confidence: 0.83799161

00:03:28.730 --> 00:03:31.075 15 chemotherapy drugs over three

NOTE Confidence: 0.83799161

00:03:31.075 --> 00:03:33.658 years in childhood there L on the

NOTE Confidence: 0.83799161

00:03:33.658 --> 00:03:35.743 left side the investigators have

NOTE Confidence: 0.83799161

00:03:35.743 --> 00:03:38.697 reported your rates of up to 80%.

NOTE Confidence: 0.83799161

00:03:38.700 --> 00:03:40.968 On the right side is the data

NOTE Confidence: 0.83799161

00:03:40.968 --> 00:03:42.969 and adult L MD Anderson.

NOTE Confidence: 0.83799161

00:03:42.970 --> 00:03:45.794 So up till 2010 we were able to

NOTE Confidence: 0.83799161

00:03:45.794 --> 00:03:48.979 claim A5 year survival of maybe 50%.

NOTE Confidence: 0.83799161

00:03:48.980 --> 00:03:51.848 This is regardless of age and

NOTE Confidence: 0.83799161

00:03:51.848 --> 00:03:54.042 it has improved since 2010,

NOTE Confidence: 0.83799161

00:03:54.042 --> 00:03:56.016 but I'm going to show you that.

NOTE Confidence: 0.83799161

00:03:56.020 --> 00:04:00.292 That even the red curve is outdated in 2022.

NOTE Confidence: 0.83799161

00:04:00.292 --> 00:04:02.404 So it's important to just keep

NOTE Confidence: 0.83799161

00:04:02.404 --> 00:04:04.721 an open mind about the things

NOTE Confidence: 0.83799161

00:04:04.721 --> 00:04:06.696 which I'm going to mention,

NOTE Confidence: 0.83799161

00:04:06.700 --> 00:04:09.395 because I truly believe what I will

NOTE Confidence: 0.83799161

00:04:09.395 --> 00:04:12.275 show will be the next standard of

NOTE Confidence: 0.83799161

00:04:12.275 --> 00:04:15.140 care and maybe five years from now.

NOTE Confidence: 0.83799161

00:04:15.140 --> 00:04:19.388 So one of the questions is why is still

NOTE Confidence: 0.83799161

00:04:19.388 --> 00:04:22.548 there 30% difference or 40% difference in

NOTE Confidence: 0.83799161

00:04:22.548 --> 00:04:26.148 the cure rate between childhood and adult L?

NOTE Confidence: 0.83799161

00:04:26.150 --> 00:04:27.635 With intensive chemotherapy,

NOTE Confidence: 0.83799161

00:04:27.635 --> 00:04:32.279 so this is because of four subsets uh which

NOTE Confidence: 0.83799161

00:04:32.279 --> 00:04:35.029 have different incidences and prognosis.

NOTE Confidence: 0.83799161

00:04:35.030 --> 00:04:37.711 So in childhood all the hyper deployed

NOTE Confidence: 0.83799161

00:04:37.711 --> 00:04:40.632 and ETV 6 runx 1 constitute half

NOTE Confidence: 0.83799161

00:04:40.632 --> 00:04:43.595 of childhood all less than 10% of

NOTE Confidence: 0.83799161

00:04:43.595 --> 00:04:46.570 adult all and these have a favorable

NOTE Confidence: 0.83799161

00:04:46.570 --> 00:04:48.930 prognosis with intensive chemotherapy

NOTE Confidence: 0.83799161

00:04:48.930 --> 00:04:51.794 in contrast historically Philadelphia

NOTE Confidence: 0.83799161

00:04:51.794 --> 00:04:55.171 positive and Philadelphia like L

NOTE Confidence: 0.83799161

00:04:55.171 --> 00:04:57.614 which constitute 50% of adult.

NOTE Confidence: 0.83799161

00:04:57.614 --> 00:05:01.865 L and the 15% of childhood L These

NOTE Confidence: 0.83799161

00:05:01.865 --> 00:05:03.893 have had unfavorable outcomes

NOTE Confidence: 0.83799161

00:05:03.893 --> 00:05:06.469 with intensive chemotherapy.

NOTE Confidence: 0.83799161

00:05:06.470 --> 00:05:08.162 I'm going to show you that

NOTE Confidence: 0.83799161

00:05:08.162 --> 00:05:09.850 this does not apply anymore,

NOTE Confidence: 0.83799161

00:05:09.850 --> 00:05:12.070 neither for Philadelphia positive

NOTE Confidence: 0.83799161

00:05:12.070 --> 00:05:15.400 nor for the Philadelphia like it.

NOTE Confidence: 0.83799161

00:05:15.400 --> 00:05:17.296 So if you use the intensive

NOTE Confidence: 0.83799161

00:05:17.296 --> 00:05:18.560 chemotherapy for three years,

NOTE Confidence: 0.83799161

00:05:18.560 --> 00:05:21.344 what is the cost of this

NOTE Confidence: 0.83799161

00:05:21.344 --> 00:05:22.736 traditional intensive chemotherapy?

NOTE Confidence: 0.83799161

00:05:22.740 --> 00:05:24.612 So you're using a lot of

NOTE Confidence: 0.83799161

00:05:24.612 --> 00:05:25.860 chemotherapy over three years.

NOTE Confidence: 0.83799161

00:05:25.860 --> 00:05:27.780 This could be manageable

NOTE Confidence: 0.83799161

00:05:27.780 --> 00:05:29.700 and the ivory towers,

NOTE Confidence: 0.83799161

00:05:29.700 --> 00:05:31.440 leukemia centers of excellence.

NOTE Confidence: 0.83799161

00:05:31.440 --> 00:05:35.279 But if you apply this to the Community

NOTE Confidence: 0.83799161

00:05:35.279 --> 00:05:38.154 practice and emerging nations among

NOTE Confidence: 0.83799161

00:05:38.154 --> 00:05:40.277 poorer and disadvantaged populations,

NOTE Confidence: 0.83799161

00:05:40.277 --> 00:05:42.262 there's a very high dropout

NOTE Confidence: 0.83799161

00:05:42.262 --> 00:05:44.920 rate due to the socioeconomic.

NOTE Confidence: 0.83799161

00:05:44.920 --> 00:05:47.950 Conditions as well as in the

NOTE Confidence: 0.83799161

00:05:47.950 --> 00:05:49.465 infrastructure and support.

NOTE Confidence: 0.83799161

00:05:49.470 --> 00:05:51.420 Even then the frontline therapy

NOTE Confidence: 0.83799161

00:05:51.420 --> 00:05:53.622 will cost half $1,000,000 in the

NOTE Confidence: 0.83799161

00:05:53.622 --> 00:05:55.686 United States and if the patients

NOTE Confidence: 0.83799161

00:05:55.686 --> 00:05:57.004 relapse that's $2,000,000.

NOTE Confidence: 0.83799161

00:05:57.004 --> 00:06:00.952 And moreover there are multiple long term

NOTE Confidence: 0.83799161

00:06:00.952 --> 00:06:03.549 complications including organ dysfunctions,

NOTE Confidence: 0.83799161

00:06:03.550 --> 00:06:04.746 healthcare issues,

NOTE Confidence: 0.83799161

00:06:04.746 --> 00:06:07.138 psychological and social issues.

NOTE Confidence: 0.83799161

00:06:07.140 --> 00:06:09.968 So what is the solution to this?

NOTE Confidence: 0.83799161

00:06:09.970 --> 00:06:12.530 So let me try to show you some

NOTE Confidence: 0.83799161

00:06:12.530 --> 00:06:15.119 data uh from uh other nations.

NOTE Confidence: 0.83799161

00:06:15.120 --> 00:06:18.722 So this is Peru and India and these are

NOTE Confidence: 0.83799161

00:06:18.722 --> 00:06:21.550 recent reports and what they show is

NOTE Confidence: 0.805844978421053

00:06:21.640 --> 00:06:24.216 accurate and childhood L not of 80

NOTE Confidence: 0.805844978421053

00:06:24.216 --> 00:06:27.491 or 90% but in the range of 60 to 70%

NOTE Confidence: 0.805844978421053

00:06:27.491 --> 00:06:30.859 if you go to the older patients see.

NOTE Confidence: 0.805844978421053

00:06:30.860 --> 00:06:32.545 So these are the patients

NOTE Confidence: 0.805844978421053

00:06:32.545 --> 00:06:34.476 that we treat more commonly.

NOTE Confidence: 0.805844978421053

00:06:34.476 --> 00:06:37.682 The cure rate is anywhere from 10

NOTE Confidence: 0.805844978421053

00:06:37.682 --> 00:06:40.876 to 27% and this is simply because.

NOTE Confidence: 0.805844978421053

00:06:40.880 --> 00:06:43.358 The intensive chemotherapy for three years

NOTE Confidence: 0.805844978421053

00:06:43.358 --> 00:06:46.438 is not feasible among many of the patients.

NOTE Confidence: 0.805844978421053

00:06:46.440 --> 00:06:49.203 So the solution in my view is to try

NOTE Confidence: 0.805844978421053

00:06:49.203 --> 00:06:52.012 to develop different regimens which

NOTE Confidence: 0.805844978421053

00:06:52.012 --> 00:06:53.872 incorporate the newer treatments which

NOTE Confidence: 0.805844978421053

00:06:53.872 --> 00:06:56.399 have been discovered in the last 10 years.

NOTE Confidence: 0.805844978421053

00:06:56.400 --> 00:06:58.014 So for example,

NOTE Confidence: 0.805844978421053

00:06:58.014 --> 00:07:01.242 the third generation BCR able kinase

NOTE Confidence: 0.805844978421053

00:07:01.242 --> 00:07:04.315 inhibitors like PONATINIB in Philadelphia

NOTE Confidence: 0.805844978421053

00:07:04.315 --> 00:07:08.291 positive all and also incorporating.

NOTE Confidence: 0.805844978421053

00:07:08.291 --> 00:07:12.399 New antibodies that target CD19CD20

NOTE Confidence: 0.805844978421053

00:07:12.399 --> 00:07:15.033 and CD22 and perhaps consider that

NOTE Confidence: 0.805844978421053

00:07:15.033 --> 00:07:18.086 the best role of the car T cells

NOTE Confidence: 0.805844978421053

00:07:18.086 --> 00:07:20.440 is not an active salvage disease.

NOTE Confidence: 0.805844978421053

00:07:20.440 --> 00:07:23.401 But as a consolidation in remission and

NOTE Confidence: 0.805844978421053

00:07:23.401 --> 00:07:25.768 first second transplant also we need

NOTE Confidence: 0.805844978421053

00:07:25.768 --> 00:07:28.162 to measure the disease in better ways.

NOTE Confidence: 0.805844978421053

00:07:28.170 --> 00:07:31.537 So there's a way that's called next

NOTE Confidence: 0.805844978421053

00:07:31.537 --> 00:07:33.448 generation sequencing that measures

NOTE Confidence: 0.805844978421053

00:07:33.448 --> 00:07:35.818 the immunoglobulin heavy chain of

NOTE Confidence: 0.805844978421053

00:07:35.818 --> 00:07:38.433 the particular all it can analyze

NOTE Confidence: 0.805844978421053

00:07:38.433 --> 00:07:39.546 up to 3,000,000.

NOTE Confidence: 0.805844978421053

00:07:39.550 --> 00:07:39.865 Yes.

NOTE Confidence: 0.805844978421053

00:07:39.865 --> 00:07:42.700 And this will allow us to decide on changing

NOTE Confidence: 0.805844978421053

00:07:42.772 --> 00:07:45.348 the therapy and the duration of therapy.

NOTE Confidence: 0.805844978421053

00:07:45.350 --> 00:07:48.032 So I'm going to show you at the end

NOTE Confidence: 0.805844978421053

00:07:48.032 --> 00:07:50.695 what we refer to today as the dose

NOTE Confidence: 0.805844978421053

00:07:50.695 --> 00:07:52.768 dance mini CVD in oblina regimen

NOTE Confidence: 0.805844978421053

00:07:52.768 --> 00:07:55.134 with or without the car T cells.

NOTE Confidence: 0.805844978421053

00:07:55.140 --> 00:07:58.108 This is a seven month regiment which

NOTE Confidence: 0.805844978421053

00:07:58.108 --> 00:08:01.499 I'm hoping may become some form of a

NOTE Confidence: 0.805844978421053

00:08:01.499 --> 00:08:04.370 standard of care five years from now.

NOTE Confidence: 0.805844978421053

00:08:04.370 --> 00:08:06.570 This is not fiction.

NOTE Confidence: 0.805844978421053

00:08:06.570 --> 00:08:09.870 We did these studies now and.

NOTE Confidence: 0.805844978421053

00:08:09.870 --> 00:08:12.082 ALS salvage with good results and we

NOTE Confidence: 0.805844978421053

00:08:12.082 --> 00:08:14.490 have moved it to the older patients.

NOTE Confidence: 0.805844978421053

00:08:14.490 --> 00:08:17.829 So this is something that is happening.

NOTE Confidence: 0.805844978421053

00:08:17.830 --> 00:08:20.260 So this is a regimen that

NOTE Confidence: 0.805844978421053

00:08:20.260 --> 00:08:21.707 contains blinatumomab, rituximab,

NOTE Confidence: 0.805844978421053

00:08:21.707 --> 00:08:22.344 inotuzumab,

NOTE Confidence: 0.805844978421053

00:08:22.344 --> 00:08:25.529 the three existing effective antibodies

NOTE Confidence: 0.805844978421053

00:08:25.529 --> 00:08:28.590 and we do a condensed.

NOTE Confidence: 0.805844978421053

00:08:28.590 --> 00:08:30.138 Approach with chemotherapy.

NOTE Confidence: 0.805844978421053

00:08:30.138 --> 00:08:32.718 So rather than sequencing the

NOTE Confidence: 0.805844978421053

00:08:32.718 --> 00:08:34.859 chemotherapy followed by blinatumomab,

NOTE Confidence: 0.805844978421053

00:08:34.860 --> 00:08:37.908 we are doing it as a condensed regiment.

NOTE Confidence: 0.805844978421053

00:08:37.910 --> 00:08:40.304 So this is something that can be

NOTE Confidence: 0.805844978421053

00:08:40.304 --> 00:08:41.330 still improved upon.

NOTE Confidence: 0.805844978421053

00:08:41.330 --> 00:08:44.074 I'll show you some of the results.

NOTE Confidence: 0.805844978421053

00:08:44.080 --> 00:08:46.285 So why do I believe that it is time

NOTE Confidence: 0.805844978421053

00:08:46.285 --> 00:08:48.974 to break with the 40 year old tradition?

NOTE Confidence: 0.805844978421053

00:08:48.980 --> 00:08:51.619 I I believe so because in Philadelphia

NOTE Confidence: 0.805844978421053

00:08:51.619 --> 00:08:54.670 positive L I'll show you that non

NOTE Confidence: 0.805844978421053

00:08:54.670 --> 00:08:56.514 chemotherapy regimens without the

NOTE Confidence: 0.805844978421053

00:08:56.514 --> 00:08:59.399 transplant are giving outstanding results.

NOTE Confidence: 0.805844978421053

00:08:59.400 --> 00:09:02.900 Also in the pre bhal less chemotherapy

NOTE Confidence: 0.805844978421053

00:09:02.900 --> 00:09:05.688 for shorter durations in combination

NOTE Confidence: 0.805844978421053

00:09:05.688 --> 00:09:08.854 with these antibodies are improving

NOTE Confidence: 0.805844978421053

00:09:08.854 --> 00:09:10.900 the outcome significantly.

NOTE Confidence: 0.805844978421053

00:09:10.900 --> 00:09:12.748 I'm not sure about this lol

NOTE Confidence: 0.805844978421053

00:09:12.748 --> 00:09:14.400 because we do not have.

NOTE Confidence: 0.805844978421053

00:09:14.400 --> 00:09:14.893 Antibodies,

NOTE Confidence: 0.805844978421053

00:09:14.893 --> 00:09:16.865 which are broadly available

NOTE Confidence: 0.805844978421053

00:09:16.865 --> 00:09:19.330 to treat T cell L,

NOTE Confidence: 0.805844978421053

00:09:19.330 --> 00:09:21.976 But I'll show you some of the data with

NOTE Confidence: 0.805844978421053

00:09:21.976 --> 00:09:24.211 the incorporation of venetoclax and

NOTE Confidence: 0.805844978421053

00:09:24.211 --> 00:09:27.007 asparagine is nelarabine at the end.

NOTE Confidence: 0.805844978421053

00:09:27.010 --> 00:09:30.616 Now, anytime you break with tradition.

NOTE Confidence: 0.805844978421053

00:09:30.620 --> 00:09:34.575 It it bothers some of the skeptics,

NOTE Confidence: 0.805844978421053

00:09:34.580 --> 00:09:35.554 the traditionalist.

NOTE Confidence: 0.805844978421053

00:09:35.554 --> 00:09:38.476 So I'm showing this slide just

NOTE Confidence: 0.805844978421053

00:09:38.476 --> 00:09:41.300 to show you how times change.

NOTE Confidence: 0.805844978421053

00:09:41.300 --> 00:09:43.395 So this is a slide from 1970.

NOTE Confidence: 0.805844978421053

00:09:43.395 --> 00:09:46.715 This was the time when ARC was discovered

NOTE Confidence: 0.805844978421053

00:09:46.715 --> 00:09:49.789 at three as the treatment for AML.

NOTE Confidence: 0.805844978421053

00:09:49.790 --> 00:09:52.930 And there was a debate then between

NOTE Confidence: 0.805844978421053

00:09:52.930 --> 00:09:55.610 a very eminent hematologist,

NOTE Confidence: 0.805844978421053

00:09:55.610 --> 00:09:58.660 Dr Crosby, and Doctor Friedrich.

NOTE Confidence: 0.816436226666667

00:09:58.660 --> 00:10:00.592 And the question was,

NOTE Confidence: 0.816436226666667

00:10:00.592 --> 00:10:03.007 even though we have arasse,

NOTE Confidence: 0.816436226666667

00:10:03.010 --> 00:10:05.320 should we treat or not treat

NOTE Confidence: 0.816436226666667

00:10:05.320 --> 00:10:06.475 acute myeloid leukemia?

NOTE Confidence: 0.816436226666667

00:10:06.480 --> 00:10:08.740 So the answer is obvious.

NOTE Confidence: 0.816436226666667

00:10:08.740 --> 00:10:11.698 Today we treat almost all leukemias,

NOTE Confidence: 0.816436226666667

00:10:11.700 --> 00:10:14.300 but it was not obvious 50 years ago.

NOTE Confidence: 0.816436226666667

00:10:14.300 --> 00:10:17.540 And this was 15 years after I was born.

NOTE Confidence: 0.816436226666667

00:10:17.540 --> 00:10:20.492 So what? What? What?

NOTE Confidence: 0.816436226666667

00:10:20.492 --> 00:10:22.706 Seems unusual or.

NOTE Confidence: 0.816436226666667

00:10:22.710 --> 00:10:25.014 Out of the norm can become

NOTE Confidence: 0.816436226666667

00:10:25.014 --> 00:10:27.010 very quickly standard of care,

NOTE Confidence: 0.816436226666667

00:10:27.010 --> 00:10:29.850 uh within a lifetime.

NOTE Confidence: 0.816436226666667

00:10:29.850 --> 00:10:31.190 So I think the Anderson,

NOTE Confidence: 0.816436226666667

00:10:31.190 --> 00:10:33.050 we developed the Hyper C

NOTE Confidence: 0.816436226666667

00:10:33.050 --> 00:10:34.607 Weather Regiment in 1992.

NOTE Confidence: 0.816436226666667

00:10:34.607 --> 00:10:37.229 We changed the CNS prophylaxis from

NOTE Confidence: 0.816436226666667

00:10:37.229 --> 00:10:39.049 radiation therapy to intrathecal

NOTE Confidence: 0.816436226666667

00:10:39.049 --> 00:10:41.647 that became a standard of care.

NOTE Confidence: 0.816436226666667

00:10:41.650 --> 00:10:42.388 In 2000.

NOTE Confidence: 0.816436226666667

00:10:42.388 --> 00:10:43.864 We added the rituximab

NOTE Confidence: 0.816436226666667

00:10:43.864 --> 00:10:45.630 to workout and three BL.

NOTE Confidence: 0.816436226666667

00:10:45.630 --> 00:10:47.950 This was confirmed in randomized

NOTE Confidence: 0.816436226666667

00:10:47.950 --> 00:10:49.806 trials which were published

NOTE Confidence: 0.816436226666667

00:10:49.806 --> 00:10:52.574 in 2017 and this has become a

NOTE Confidence: 0.816436226666667

00:10:52.574 --> 00:10:54.618 standard of care in Philadelphia

NOTE Confidence: 0.816436226666667

00:10:54.618 --> 00:10:57.593 positive L it was only in 2000

NOTE Confidence: 0.816436226666667

00:10:57.593 --> 00:11:00.617 that we added IMAGINATE to hyper.

NOTE Confidence: 0.816436226666667

00:11:00.620 --> 00:11:02.684 We replaced it with the Satanic

NOTE Confidence: 0.816436226666667

00:11:02.684 --> 00:11:04.992 in 2006 and with PONATINIB

NOTE Confidence: 0.816436226666667

00:11:04.992 --> 00:11:08.283 in 2010 and the Hyper Cvad.

NOTE Confidence: 0.816436226666667

00:11:08.283 --> 00:11:10.588 The satanic followed by transplant

NOTE Confidence: 0.816436226666667

00:11:10.588 --> 00:11:13.734 is what is currently the standard of

NOTE Confidence: 0.816436226666667

00:11:13.734 --> 00:11:16.496 care in the United States in 2022.

NOTE Confidence: 0.816436226666667

00:11:16.496 --> 00:11:18.752 And I'll show you that it's

NOTE Confidence: 0.816436226666667

00:11:18.752 --> 00:11:19.880 probably old fashioned,

NOTE Confidence: 0.816436226666667

00:11:19.880 --> 00:11:21.700 outdated and perhaps obsolete.

NOTE Confidence: 0.816436226666667

00:11:21.700 --> 00:11:24.430 The big breakthrough came of course

NOTE Confidence: 0.816436226666667

00:11:24.505 --> 00:11:26.863 with the discovery of the new

NOTE Confidence: 0.816436226666667

00:11:26.863 --> 00:11:29.200 antibodies that were highly effective,

NOTE Confidence: 0.816436226666667

00:11:29.200 --> 00:11:30.212 more effective.

NOTE Confidence: 0.816436226666667

00:11:30.212 --> 00:11:32.742 And intensive chemotherapy and which

NOTE Confidence: 0.816436226666667

00:11:32.742 --> 00:11:35.954 targeted 2 of the cluster designation

NOTE Confidence: 0.816436226666667

00:11:35.954 --> 00:11:38.639 so blinatumomab bispecific T cell

NOTE Confidence: 0.816436226666667

00:11:38.639 --> 00:11:40.941 engager that targets CD19 and

NOTE Confidence: 0.816436226666667

00:11:40.941 --> 00:11:43.622 you know to zoom out and antibody

NOTE Confidence: 0.816436226666667

00:11:43.630 --> 00:11:47.236 drug conjugate that targets CD 22.

NOTE Confidence: 0.816436226666667

00:11:47.240 --> 00:11:50.582 So on the left side I show the again

NOTE Confidence: 0.816436226666667

00:11:50.582 --> 00:11:52.688 the data and the younger patients.

NOTE Confidence: 0.816436226666667

00:11:52.690 --> 00:11:56.040 So this is patients up to the age of 60

NOTE Confidence: 0.816436226666667

00:11:56.127 --> 00:11:58.720 and since 2010 there is an improvement.

NOTE Confidence: 0.816436226666667

00:11:58.720 --> 00:12:02.173 So now the five year survival is over 60%.

NOTE Confidence: 0.816436226666667

00:12:02.173 --> 00:12:05.317 On the right side is the data with

NOTE Confidence: 0.816436226666667

00:12:05.317 --> 00:12:07.923 mini CD in Oblina which started

NOTE Confidence: 0.816436226666667

00:12:07.923 --> 00:12:11.432 in 2010 and this is where we had a

NOTE Confidence: 0.816436226666667

00:12:11.432 --> 00:12:13.898 big improvement in the five year

NOTE Confidence: 0.816436226666667

00:12:13.898 --> 00:12:18.018 survival from 20% to about 50%.

NOTE Confidence: 0.816436226666667

00:12:18.020 --> 00:12:20.372 So we still use the Hyper Siva

NOTE Confidence: 0.816436226666667

00:12:20.372 --> 00:12:22.869 that MD Anderson in contrast to

NOTE Confidence: 0.816436226666667

00:12:22.869 --> 00:12:25.229 many other places where pediatric

NOTE Confidence: 0.816436226666667

00:12:25.229 --> 00:12:27.425 inspired regimens are used because

NOTE Confidence: 0.816436226666667

00:12:27.425 --> 00:12:29.783 it's easier to incorporate it into

NOTE Confidence: 0.816436226666667

00:12:29.783 --> 00:12:32.028 the newer targeted therapies and

NOTE Confidence: 0.816436226666667

00:12:32.028 --> 00:12:34.800 because at our institution we found

NOTE Confidence: 0.816436226666667

00:12:34.873 --> 00:12:37.799 that Hyper Cvad which is also a

NOTE Confidence: 0.816436226666667

00:12:37.799 --> 00:12:39.536 pediatric inspired regimen performed

NOTE Confidence: 0.816436226666667

00:12:39.536 --> 00:12:42.392 as well as the asparaginase containing

NOTE Confidence: 0.816436226666667

00:12:42.392 --> 00:12:44.600 regimens during the induction.

NOTE Confidence: 0.816436226666667

00:12:44.600 --> 00:12:47.240 Now for people who use the Hyper Cvad,

NOTE Confidence: 0.816436226666667

00:12:47.240 --> 00:12:48.340 I would like to draw.

NOTE Confidence: 0.816436226666667

00:12:48.340 --> 00:12:50.804 Your attention to a review in cancer

NOTE Confidence: 0.816436226666667

00:12:50.804 --> 00:12:52.589 which gives you some vignettes

NOTE Confidence: 0.816436226666667

00:12:52.589 --> 00:12:55.237 and pearls as to how to reduce the

NOTE Confidence: 0.816436226666667

00:12:55.312 --> 00:12:57.410 myelosuppression complications.

NOTE Confidence: 0.816436226666667

00:12:57.410 --> 00:13:00.650 The key issue is in the event courses

NOTE Confidence: 0.816436226666667

00:13:00.650 --> 00:13:04.056 where reduce the methotrexate by 24 percent,

NOTE Confidence: 0.816436226666667

00:13:04.060 --> 00:13:06.391 25% and the RC from 3 to

NOTE Confidence: 0.816436226666667

00:13:06.391 --> 00:13:08.690 2 grams per meter square.

NOTE Confidence: 0.816436226666667

00:13:08.690 --> 00:13:12.330 But there are other small clues to

NOTE Confidence: 0.816436226666667

00:13:12.330 --> 00:13:15.360 improve the toxicities of this regime.

NOTE Confidence: 0.816436226666667

00:13:15.360 --> 00:13:15.657 Now,

NOTE Confidence: 0.816436226666667

00:13:15.657 --> 00:13:17.439 when I'm going to show you

NOTE Confidence: 0.816436226666667

00:13:17.439 --> 00:13:19.160 the research at MD Anderson,

NOTE Confidence: 0.816436226666667

00:13:19.160 --> 00:13:21.870 you're going to be wondering

NOTE Confidence: 0.816436226666667

00:13:21.870 --> 00:13:24.406 why we're resorting to Bayesian

NOTE Confidence: 0.816436226666667

00:13:24.406 --> 00:13:26.816 designs with signal arm trials.

NOTE Confidence: 0.816436226666667

00:13:26.820 --> 00:13:29.354 And I'll try to explain my position,

NOTE Confidence: 0.816436226666667

00:13:29.360 --> 00:13:31.418 but also why is it that

NOTE Confidence: 0.816436226666667

00:13:31.418 --> 00:13:32.790 different regiments have been

NOTE Confidence: 0.906986124166667

00:13:32.863 --> 00:13:34.289 developed differently?

NOTE Confidence: 0.906986124166667

00:13:34.290 --> 00:13:36.210 And this is essentially because

NOTE Confidence: 0.906986124166667

00:13:36.210 --> 00:13:39.739 a lot of the times it is what we

NOTE Confidence: 0.906986124166667

00:13:39.739 --> 00:13:41.654 propose and the drug companies

NOTE Confidence: 0.906986124166667

00:13:41.654 --> 00:13:44.487 offer us in terms of free drugs, so.

NOTE Confidence: 0.906986124166667

00:13:44.487 --> 00:13:47.423 Uh, the the evolution of a lot of

NOTE Confidence: 0.906986124166667

00:13:47.423 --> 00:13:50.039 the Ind studies at MD Anderson

NOTE Confidence: 0.906986124166667

00:13:50.039 --> 00:13:53.380 where based on if and when the

NOTE Confidence: 0.906986124166667

00:13:53.380 --> 00:13:56.115 antibodies were available and free

NOTE Confidence: 0.906986124166667

00:13:56.115 --> 00:13:59.420 on island studies as well as on

NOTE Confidence: 0.906986124166667

00:13:59.420 --> 00:14:01.495 the maturing Bayesian based data.

NOTE Confidence: 0.906986124166667

00:14:01.500 --> 00:14:06.748 So we started with the mini CVD in 2010,

NOTE Confidence: 0.906986124166667

00:14:06.748 --> 00:14:09.488 we added the BLINATUMOMAB later

NOTE Confidence: 0.906986124166667

00:14:09.488 --> 00:14:12.860 in 2015 and the younger patients,

NOTE Confidence: 0.906986124166667

00:14:12.860 --> 00:14:15.521 the Hyper Cvad started in 2018.

NOTE Confidence: 0.906986124166667

00:14:15.521 --> 00:14:17.326 And I'll show you that.

NOTE Confidence: 0.906986124166667

00:14:17.330 --> 00:14:20.366 And I mentioned that those dense

NOTE Confidence: 0.906986124166667

00:14:20.366 --> 00:14:23.330 mini CVD started only September

NOTE Confidence: 0.906986124166667

00:14:23.330 --> 00:14:25.946 2021 and we opened this study

NOTE Confidence: 0.906986124166667

00:14:25.946 --> 00:14:28.810 for the older AML year later.

NOTE Confidence: 0.906986124166667

00:14:28.810 --> 00:14:31.770 So I'm going to show you some of

NOTE Confidence: 0.906986124166667

00:14:31.770 --> 00:14:33.970 the evolution of these studies.

NOTE Confidence: 0.906986124166667

00:14:33.970 --> 00:14:35.760 So let's start with Philadelphia

NOTE Confidence: 0.906986124166667

00:14:35.760 --> 00:14:37.550 positive and then in 2000,

NOTE Confidence: 0.906986124166667

00:14:37.550 --> 00:14:40.812 this diagnosis was a death sentence unless

NOTE Confidence: 0.906986124166667

00:14:40.812 --> 00:14:43.908 the patient had an allogeneic donor.

NOTE Confidence: 0.906986124166667

00:14:43.910 --> 00:14:46.202 So if the patients did not

NOTE Confidence: 0.906986124166667

00:14:46.202 --> 00:14:48.260 have a donor even zone,

NOTE Confidence: 0.906986124166667

00:14:48.260 --> 00:14:50.661 90% of them went in a complete

NOTE Confidence: 0.906986124166667

00:14:50.661 --> 00:14:52.570 remission with intensive chemotherapy.

NOTE Confidence: 0.906986124166667

00:14:52.570 --> 00:14:54.766 They almost all relapsed and died.

NOTE Confidence: 0.906986124166667

00:14:54.770 --> 00:14:55.950 If they had the donor,

NOTE Confidence: 0.906986124166667

00:14:55.950 --> 00:14:57.795 we gave them the transplant

NOTE Confidence: 0.906986124166667

00:14:57.795 --> 00:14:59.640 and their mission and the

NOTE Confidence: 0.906986124166667

00:14:59.711 --> 00:15:01.797 cure rate was about 30 to 40%.

NOTE Confidence: 0.906986124166667

00:15:01.800 --> 00:15:03.042 At MD Anderson,

NOTE Confidence: 0.906986124166667

00:15:03.042 --> 00:15:06.679 we added the imatinib to Hyper Cvad in 2000.

NOTE Confidence: 0.906986124166667

00:15:06.680 --> 00:15:09.150 Allogeneic transplant was almost always

NOTE Confidence: 0.906986124166667

00:15:09.150 --> 00:15:11.620 done in first complete remission.

NOTE Confidence: 0.906986124166667

00:15:11.620 --> 00:15:12.384 In 2006,

NOTE Confidence: 0.906986124166667

00:15:12.384 --> 00:15:14.676 we replaced that with the SAT

NOTE Confidence: 0.906986124166667

00:15:14.676 --> 00:15:17.760 in it and we started doing the

NOTE Confidence: 0.906986124166667

00:15:17.760 --> 00:15:20.080 transplant only if the patients

NOTE Confidence: 0.906986124166667

00:15:20.165 --> 00:15:22.817 were still PCR positive in 2010,

NOTE Confidence: 0.906986124166667

00:15:22.817 --> 00:15:25.302 because 20% of the relapses

NOTE Confidence: 0.906986124166667

00:15:25.302 --> 00:15:27.644 were with the T315I clone.

NOTE Confidence: 0.906986124166667

00:15:27.644 --> 00:15:30.176 We replace the satanic with ponatinib,

NOTE Confidence: 0.906986124166667

00:15:30.180 --> 00:15:32.358 the patients who are living longer.

NOTE Confidence: 0.906986124166667

00:15:32.360 --> 00:15:34.508 10 to 15% were developing CNS

NOTE Confidence: 0.906986124166667

00:15:34.508 --> 00:15:37.120 leukemia with the 8 intraceuticals.

NOTE Confidence: 0.906986124166667

00:15:37.120 --> 00:15:40.011 So we increased this to 12 intraceuticals

NOTE Confidence: 0.906986124166667

00:15:40.011 --> 00:15:42.923 and we did the transplant less and

NOTE Confidence: 0.906986124166667

00:15:42.923 --> 00:15:45.946 only if there was no major molecular

NOTE Confidence: 0.906986124166667

00:15:45.946 --> 00:15:48.476 response in 2017 we switched.

NOTE Confidence: 0.906986124166667

00:15:48.476 --> 00:15:51.308 So this was the drastic change

NOTE Confidence: 0.906986124166667

00:15:51.308 --> 00:15:52.934 eliminating chemotherapy and

NOTE Confidence: 0.906986124166667

00:15:52.934 --> 00:15:55.609 transplant and using two targeted

NOTE Confidence: 0.906986124166667

00:15:55.609 --> 00:15:58.399 therapies for net and Lina tuna.

NOTE Confidence: 0.906986124166667

00:15:58.400 --> 00:16:00.570 So I'm going to show you the

NOTE Confidence: 0.906986124166667

00:16:00.570 --> 00:16:02.420 sequence of the studies but.

NOTE Confidence: 0.906986124166667

00:16:02.420 --> 00:16:04.796 I'd like to draw your attention that none

NOTE Confidence: 0.906986124166667

00:16:04.796 --> 00:16:07.239 of these studies were randomized trial.

NOTE Confidence: 0.906986124166667

00:16:07.240 --> 00:16:09.711 And I'm gonna come back to this

NOTE Confidence: 0.906986124166667

00:16:09.711 --> 00:16:12.305 for the sake of the younger

NOTE Confidence: 0.906986124166667

00:16:12.305 --> 00:16:14.715 students and others because they,

NOTE Confidence: 0.906986124166667

00:16:14.720 --> 00:16:16.994 we and they have been indoctrinated

NOTE Confidence: 0.906986124166667

00:16:16.994 --> 00:16:19.310 that the only way to advance

NOTE Confidence: 0.906986124166667

00:16:19.310 --> 00:16:21.494 research in medicine and in cancer

NOTE Confidence: 0.906986124166667

00:16:21.494 --> 00:16:24.158 is in through randomized trials.

NOTE Confidence: 0.906986124166667

00:16:24.160 --> 00:16:27.604 And I'm going to probably state

NOTE Confidence: 0.906986124166667

00:16:27.604 --> 00:16:31.448 that that depends on where we are.

NOTE Confidence: 0.906986124166667

00:16:31.450 --> 00:16:33.934 So this is the progress in

NOTE Confidence: 0.906986124166667

00:16:33.934 --> 00:16:36.030 Philadelphia positive L before 2000,

NOTE Confidence: 0.906986124166667

00:16:36.030 --> 00:16:40.230 the patients died since 2002,

NOTE Confidence: 0.906986124166667

00:16:40.230 --> 00:16:42.830 2010 these cure rate or

NOTE Confidence: 0.906986124166667

00:16:42.830 --> 00:16:44.910 survival improved to 40%.

NOTE Confidence: 0.906986124166667

00:16:44.910 --> 00:16:47.586 Since 2010 it went to A5

NOTE Confidence: 0.906986124166667

00:16:47.586 --> 00:16:49.359 year survival of 70%.

NOTE Confidence: 0.906986124166667

00:16:49.359 --> 00:16:51.933 Now the hyper Cvad Desatino was

NOTE Confidence: 0.906986124166667

00:16:51.933 --> 00:16:54.890 taken by the SW Oncology group.

NOTE Confidence: 0.906986124166667

00:16:54.890 --> 00:16:57.144 It was tested in a single arm

NOTE Confidence: 0.906986124166667

00:16:57.144 --> 00:16:59.415 trial and they found that they

NOTE Confidence: 0.906986124166667

00:16:59.415 --> 00:17:01.875 could reproduce the data from the

NOTE Confidence: 0.906986124166667

00:17:01.875 --> 00:17:04.643 single institution CR rate of 88%

NOTE Confidence: 0.906986124166667

00:17:04.643 --> 00:17:08.375 and a three-year survival of 70%.

NOTE Confidence: 0.906986124166667

00:17:08.375 --> 00:17:10.565 And they showed at that time

NOTE Confidence: 0.906986124166667

00:17:10.565 --> 00:17:11.660 that doing allogeneic

NOTE Confidence: 0.800246754941176

00:17:11.726 --> 00:17:13.658 transplant in first remission

NOTE Confidence: 0.800246754941176

00:17:13.658 --> 00:17:15.107 improved the outcome.

NOTE Confidence: 0.800246754941176

00:17:15.110 --> 00:17:17.630 So this became and is still the

NOTE Confidence: 0.800246754941176

00:17:17.630 --> 00:17:20.357 standard of care in the United States.

NOTE Confidence: 0.800246754941176

00:17:20.360 --> 00:17:22.630 I perceive that this afternoon

NOTE Confidence: 0.800246754941176

00:17:22.630 --> 00:17:24.446 followed by allogeneic transplant

NOTE Confidence: 0.800246754941176

00:17:24.446 --> 00:17:26.669 in first complete remission.

NOTE Confidence: 0.800246754941176

00:17:26.670 --> 00:17:29.310 Now people question whether the satanic

NOTE Confidence: 0.800246754941176

00:17:29.310 --> 00:17:31.965 was superior to imatinib and they

NOTE Confidence: 0.800246754941176

00:17:31.965 --> 00:17:34.025 waited for the randomized trials.

NOTE Confidence: 0.800246754941176

00:17:34.030 --> 00:17:35.590 So this randomized trial did

NOTE Confidence: 0.800246754941176

00:17:35.590 --> 00:17:37.630 not come from the United States,

NOTE Confidence: 0.800246754941176

00:17:37.630 --> 00:17:40.564 it came actually from China where

NOTE Confidence: 0.800246754941176

00:17:40.564 --> 00:17:42.620 children with Philadelphia positive

NOTE Confidence: 0.800246754941176

00:17:42.620 --> 00:17:45.190 L were randomized to chemotherapy

NOTE Confidence: 0.800246754941176

00:17:45.263 --> 00:17:47.388 with these satanic or imatinib.

NOTE Confidence: 0.800246754941176

00:17:47.390 --> 00:17:50.442 And that study showed clearly that the

NOTE Confidence: 0.800246754941176

00:17:50.442 --> 00:17:53.210 four year survival was superior with

NOTE Confidence: 0.800246754941176

00:17:53.210 --> 00:17:57.000 desatnik 88 versus 69% but notice on either.

NOTE Confidence: 0.800246754941176

00:17:57.000 --> 00:18:00.087 From the results are better than in adult L,

NOTE Confidence: 0.800246754941176

00:18:00.090 --> 00:18:02.028 so this is a common scene.

NOTE Confidence: 0.800246754941176

00:18:02.030 --> 00:18:05.486 Children with L do better than adults with L,

NOTE Confidence: 0.800246754941176

00:18:05.490 --> 00:18:07.850 whether they receive intensive chemotherapy,

NOTE Confidence: 0.800246754941176

00:18:07.850 --> 00:18:09.010 allogeneic transplant,

NOTE Confidence: 0.800246754941176

00:18:09.010 --> 00:18:11.590 car T cells, antibodies,

NOTE Confidence: 0.800246754941176

00:18:11.590 --> 00:18:16.630 or any other modalities so far.

NOTE Confidence: 0.800246754941176

00:18:16.630 --> 00:18:19.354 Now the hyper Cvad, Ponatinib started

NOTE Confidence: 0.800246754941176

00:18:19.354 --> 00:18:22.560 in 2010 because Ponatinib was toxic.

NOTE Confidence: 0.800246754941176

00:18:22.560 --> 00:18:25.437 We reduced the dose very quickly to

NOTE Confidence: 0.800246754941176

00:18:25.437 --> 00:18:28.557 30 milligrams in CR to 15 milligrams

NOTE Confidence: 0.800246754941176

00:18:28.557 --> 00:18:30.812 in complete molecular response and

NOTE Confidence: 0.800246754941176

00:18:30.812 --> 00:18:33.851 we published the data on the 86

NOTE Confidence: 0.800246754941176

00:18:33.851 --> 00:18:36.574 patients treated with this regimen.

NOTE Confidence: 0.800246754941176

00:18:36.574 --> 00:18:39.512 CR 800%, PCR negativity 84%,

NOTE Confidence: 0.800246754941176

00:18:39.512 --> 00:18:43.670 five year survival shown on the left

NOTE Confidence: 0.800246754941176

00:18:43.785 --> 00:18:47.506 side 75% and now we have a longer follow-up,

NOTE Confidence: 0.800246754941176

00:18:47.510 --> 00:18:48.214 so we.

NOTE Confidence: 0.800246754941176

00:18:48.214 --> 00:18:49.974 This is very solid data,

NOTE Confidence: 0.800246754941176

00:18:49.980 --> 00:18:52.196 but for the first time on the right

NOTE Confidence: 0.800246754941176

00:18:52.196 --> 00:18:54.944 side of the slide we showed that

NOTE Confidence: 0.800246754941176

00:18:54.944 --> 00:18:56.219 perhaps allogeneic transplantation

NOTE Confidence: 0.800246754941176

00:18:56.219 --> 00:18:58.818 is not necessary in all patients.

NOTE Confidence: 0.800246754941176

00:18:58.820 --> 00:19:01.361 So the blue curve is actually the

NOTE Confidence: 0.800246754941176

00:19:01.361 --> 00:19:03.589 patients who did undergo transplantation

NOTE Confidence: 0.800246754941176

00:19:03.589 --> 00:19:07.313 either by physician or by patients choice.

NOTE Confidence: 0.800246754941176

00:19:07.320 --> 00:19:10.442 So this was 1/4 of the patients

NOTE Confidence: 0.800246754941176

00:19:10.442 --> 00:19:12.500 and they did worse.

NOTE Confidence: 0.800246754941176

00:19:12.500 --> 00:19:14.988 The 12 intraceuticals abrogated

NOTE Confidence: 0.800246754941176

00:19:14.988 --> 00:19:18.098 or eliminated the CNS leukemia.

NOTE Confidence: 0.800246754941176

00:19:18.100 --> 00:19:20.500 So now we're sticking with 12

NOTE Confidence: 0.800246754941176

00:19:20.500 --> 00:19:23.045 intraceuticals and this is the best

NOTE Confidence: 0.800246754941176

00:19:23.045 --> 00:19:26.270 we could do to convince people who

NOTE Confidence: 0.800246754941176

00:19:26.270 --> 00:19:28.260 wish for the randomized trials.

NOTE Confidence: 0.800246754941176

00:19:28.260 --> 00:19:31.380 We did the propensity score analysis

NOTE Confidence: 0.800246754941176

00:19:31.380 --> 00:19:34.657 that showed that ponatinib was superior

NOTE Confidence: 0.800246754941176

00:19:34.657 --> 00:19:37.999 to desatnik in our institutional studies.

NOTE Confidence: 0.800246754941176

00:19:38.000 --> 00:19:40.160 Now in the meantime,

NOTE Confidence: 0.800246754941176

00:19:40.160 --> 00:19:43.700 Lena and Inotuzumab were undergoing uh,

NOTE Confidence: 0.800246754941176

00:19:43.700 --> 00:19:45.800 the single and randomized trials.

NOTE Confidence: 0.800246754941176

00:19:45.800 --> 00:19:47.745 And the randomized trials showed

NOTE Confidence: 0.800246754941176

00:19:47.745 --> 00:19:50.942 that in the subset of patients with

NOTE Confidence: 0.800246754941176

00:19:50.942 --> 00:19:53.290 Philadelphia positive L refractory

NOTE Confidence: 0.800246754941176

00:19:53.290 --> 00:19:55.638 relapsed blinatumomab and INOTUZUMAB

NOTE Confidence: 0.800246754941176

00:19:55.638 --> 00:19:58.568 were superior to intensive chemotherapy

NOTE Confidence: 0.800246754941176

00:19:58.568 --> 00:20:02.396 in terms of improving the CRA and

NOTE Confidence: 0.800246754941176

00:20:02.396 --> 00:20:04.452 perhaps improving survival modesty.

NOTE Confidence: 0.800246754941176

00:20:04.460 --> 00:20:05.808 So because of this,

NOTE Confidence: 0.800246754941176

00:20:05.808 --> 00:20:08.618 we went to a regiment in 2017.

NOTE Confidence: 0.800246754941176

00:20:08.618 --> 00:20:11.413 That skipped the intensive chemotherapy

NOTE Confidence: 0.800246754941176

00:20:11.413 --> 00:20:14.140 and skipped the transplant.

NOTE Confidence: 0.800246754941176

00:20:14.140 --> 00:20:16.990 And we use Ponatinib and blinatumomab

NOTE Confidence: 0.800246754941176

00:20:16.990 --> 00:20:19.493 during the induction and then

NOTE Confidence: 0.800246754941176

00:20:19.493 --> 00:20:21.577 blinatumomab for five cycles.

NOTE Confidence: 0.800246754941176

00:20:21.580 --> 00:20:24.576 The Ponatinib is as of today indefinitely,

NOTE Confidence: 0.800246754941176

00:20:24.580 --> 00:20:28.596 but but based on the NGH smurd studies,

NOTE Confidence: 0.800246754941176

00:20:28.600 --> 00:20:31.342 we're thinking to follow a strategy

NOTE Confidence: 0.800246754941176

00:20:31.342 --> 00:20:35.219 similar to CML where if the patients are NGS,

NOTE Confidence: 0.800246754941176

00:20:35.220 --> 00:20:37.500 MRD negative for five years,

NOTE Confidence: 0.800246754941176

00:20:37.500 --> 00:20:39.460 maybe we'll stop the treatment,

NOTE Confidence: 0.800246754941176

00:20:39.460 --> 00:20:41.360 but we're not there yet.

NOTE Confidence: 0.800246754941176

00:20:41.360 --> 00:20:43.760 But let me show you the data which

NOTE Confidence: 0.800246754941176

00:20:43.760 --> 00:20:46.352 is going to be published in Lancet

NOTE Confidence: 0.800246754941176

00:20:46.352 --> 00:20:49.040 hematology in the next couple of months.

NOTE Confidence: 0.800246754941176

00:20:49.040 --> 00:20:51.660 So we treated 63 patients,

NOTE Confidence: 0.800246754941176

00:20:51.660 --> 00:20:53.765 43 where newly diagnosed Philadelphia

NOTE Confidence: 0.800246754941176

00:20:53.765 --> 00:20:57.083 positive L so if you look at those

NOTE Confidence: 0.800246754941176

00:20:57.083 --> 00:20:59.357 43 patients in the middle column,

NOTE Confidence: 0.800246754941176

00:20:59.360 --> 00:21:02.200 the CR rate is universal

NOTE Confidence: 0.878950760434783

00:21:02.200 --> 00:21:03.772 complete molecular response rate

NOTE Confidence: 0.878950760434783

00:21:03.772 --> 00:21:06.510 also in most of the patients and

NOTE Confidence: 0.878950760434783

00:21:06.510 --> 00:21:08.364 for the first time they estimated

NOTE Confidence: 0.878950760434783

00:21:08.364 --> 00:21:10.868 2 to three years survival is 95%.

NOTE Confidence: 0.878950760434783

00:21:10.868 --> 00:21:13.316 So this is better than anything

NOTE Confidence: 0.878950760434783

00:21:13.316 --> 00:21:16.660 we've ever had and only one of the

NOTE Confidence: 0.878950760434783

00:21:16.660 --> 00:21:18.700 43 patients went to transplant.

NOTE Confidence: 0.878950760434783

00:21:18.700 --> 00:21:21.810 Now for patients with refractory

NOTE Confidence: 0.878950760434783

00:21:21.810 --> 00:21:24.195 relapsed Philadelphia positive AML

NOTE Confidence: 0.878950760434783

00:21:24.195 --> 00:21:27.285 or CML chronic phase that evolved

NOTE Confidence: 0.878950760434783

00:21:27.285 --> 00:21:30.240 into the lymphoid blastic phase,

NOTE Confidence: 0.878950760434783

00:21:30.240 --> 00:21:31.700 the outcome is still bad.

NOTE Confidence: 0.878950760434783

00:21:31.700 --> 00:21:34.705 So we still use the hyper Cvad, ponatinib,

NOTE Confidence: 0.878950760434783

00:21:34.705 --> 00:21:38.330 blinatumomab in those two subsets.

NOTE Confidence: 0.878950760434783

00:21:38.330 --> 00:21:40.906 And this is to show you how quickly

NOTE Confidence: 0.878950760434783

00:21:40.906 --> 00:21:43.169 the patients achieve PCR negativity.

NOTE Confidence: 0.878950760434783

00:21:43.170 --> 00:21:46.964 So if you treat Philadelphia positive CLL,

NOTE Confidence: 0.878950760434783

00:21:46.970 --> 00:21:49.346 you are used to the fact that the

NOTE Confidence: 0.878950760434783

00:21:49.346 --> 00:21:51.461 PCR does not become negative till

NOTE Confidence: 0.878950760434783

00:21:51.461 --> 00:21:54.410 three to six months into a remission.

NOTE Confidence: 0.878950760434783

00:21:54.410 --> 00:21:57.659 Here I show and we did this the PCR

NOTE Confidence: 0.878950760434783

00:21:57.659 --> 00:22:00.737 weekly simply to see whether we're going

NOTE Confidence: 0.878950760434783

00:22:00.737 --> 00:22:04.506 to see some major signal and we were

NOTE Confidence: 0.878950760434783

00:22:04.506 --> 00:22:08.518 surprised to notice that within the four.

NOTE Confidence: 0.878950760434783

00:22:08.520 --> 00:22:10.388 Weeks of induction therapy,

NOTE Confidence: 0.878950760434783

00:22:10.388 --> 00:22:13.190 2/3 of the patients became PCR

NOTE Confidence: 0.878950760434783

00:22:13.271 --> 00:22:16.169 negative and before the next course,

NOTE Confidence: 0.878950760434783

00:22:16.170 --> 00:22:19.354 3/4 of the patients had become PCR negative.

NOTE Confidence: 0.878950760434783

00:22:19.360 --> 00:22:22.054 So very quick achievement of PCR

NOTE Confidence: 0.878950760434783

00:22:22.054 --> 00:22:24.840 negativity and NGS MRD negativity.

NOTE Confidence: 0.878950760434783

00:22:24.840 --> 00:22:27.368 And now I show the survival in the

NOTE Confidence: 0.878950760434783

00:22:27.368 --> 00:22:29.655 red with the ponatinib blinatumomab

NOTE Confidence: 0.878950760434783

00:22:29.655 --> 00:22:32.799 compared to the hyper cvad ponatinib.

NOTE Confidence: 0.878950760434783

00:22:32.800 --> 00:22:36.112 So the question is will you do a

NOTE Confidence: 0.878950760434783

00:22:36.112 --> 00:22:38.970 randomized study today comparing poneto?

NOTE Confidence: 0.878950760434783

00:22:38.970 --> 00:22:40.270 Lena to map to hyper.

NOTE Confidence: 0.878950760434783

00:22:40.270 --> 00:22:43.698 See that? Um, imagine it.

NOTE Confidence: 0.878950760434783

00:22:43.698 --> 00:22:46.610 So this is an important question and

NOTE Confidence: 0.878950760434783

00:22:46.690 --> 00:22:49.858 I have to tell you that this is a

NOTE Confidence: 0.878950760434783

00:22:49.858 --> 00:22:52.770 randomized study that's ongoing in Europe.

NOTE Confidence: 0.878950760434783

00:22:52.770 --> 00:22:56.106 So you have to decide is this randomized

NOTE Confidence: 0.878950760434783

00:22:56.106 --> 00:22:58.549 trial which provides equipoise,

NOTE Confidence: 0.878950760434783

00:22:58.550 --> 00:23:01.510 which is the basis of a randomized trial,

NOTE Confidence: 0.878950760434783

00:23:01.510 --> 00:23:04.546 meaning that the investigator does not

NOTE Confidence: 0.878950760434783

00:23:04.546 --> 00:23:08.238 know whether one or the other arms

NOTE Confidence: 0.878950760434783

00:23:08.238 --> 00:23:10.858 of the randomization is superior.

NOTE Confidence: 0.878950760434783

00:23:10.860 --> 00:23:12.556 So as I mentioned,

NOTE Confidence: 0.878950760434783

00:23:12.556 --> 00:23:14.676 we still use intensive chemotherapy

NOTE Confidence: 0.878950760434783

00:23:14.676 --> 00:23:17.648 with ponatinib blinatumomab in CML

NOTE Confidence: 0.878950760434783

00:23:17.648 --> 00:23:19.868 chronic phase that evolves into

NOTE Confidence: 0.878950760434783

00:23:19.868 --> 00:23:22.324 a blastic phase and refractory

NOTE Confidence: 0.878950760434783

00:23:22.324 --> 00:23:24.396 relapsed Philadelphia positive L

NOTE Confidence: 0.878950760434783

00:23:24.396 --> 00:23:28.119 and then in two other rare subsets.

NOTE Confidence: 0.878950760434783

00:23:28.120 --> 00:23:29.752 So patients with Philadelphia

NOTE Confidence: 0.878950760434783

00:23:29.752 --> 00:23:32.684 positive L but where the fish is

NOTE Confidence: 0.878950760434783

00:23:32.684 --> 00:23:35.120 positive on the mature granular sites,

NOTE Confidence: 0.878950760434783

00:23:35.120 --> 00:23:38.780 these are patients mostly with P210,

NOTE Confidence: 0.878950760434783

00:23:38.780 --> 00:23:41.660 Philadelphia positive L and another rare.

NOTE Confidence: 0.878950760434783

00:23:41.660 --> 00:23:45.090 Upset, which we did not think existed,

NOTE Confidence: 0.878950760434783

00:23:45.090 --> 00:23:47.960 but we had now 7 cases of

NOTE Confidence: 0.878950760434783

00:23:47.960 --> 00:23:50.369 Philadelphia positive L and CRLF two.

NOTE Confidence: 0.878950760434783

00:23:50.370 --> 00:23:53.460 These do badly and they need

NOTE Confidence: 0.878950760434783

00:23:53.460 --> 00:23:55.005 the intensive chemotherapy.

NOTE Confidence: 0.878950760434783

00:23:55.010 --> 00:23:58.394 Now next I'm going to move to Philadelphia

NOTE Confidence: 0.878950760434783

00:23:58.394 --> 00:24:02.129 like so for the students and the fellows.

NOTE Confidence: 0.878950760434783

00:24:02.130 --> 00:24:05.588 Philadelphia Lucky L is an L entity

NOTE Confidence: 0.878950760434783

00:24:05.588 --> 00:24:09.134 where the cytogenetics do not show the

NOTE Confidence: 0.878950760434783

00:24:09.134 --> 00:24:11.218 translocation 922 and the molecular

NOTE Confidence: 0.878950760434783

00:24:11.218 --> 00:24:14.418 studies do not show the BCR able

NOTE Confidence: 0.878950760434783

00:24:14.418 --> 00:24:16.608 translocation molecular events,

NOTE Confidence: 0.878950760434783

00:24:16.610 --> 00:24:19.058 but they have a genomic profile

NOTE Confidence: 0.878950760434783

00:24:19.058 --> 00:24:21.274 which is identical to Philadelphia

NOTE Confidence: 0.878950760434783

00:24:21.274 --> 00:24:23.779 positive all and different from

NOTE Confidence: 0.878950760434783

00:24:23.779 --> 00:24:26.170 the other subsets of all.

NOTE Confidence: 0.878950760434783

00:24:26.170 --> 00:24:28.366 So what we've learned is Philadelphia,

NOTE Confidence: 0.878950760434783

00:24:28.370 --> 00:24:31.034 like L has a bad prognosis

NOTE Confidence: 0.878950760434783

00:24:31.034 --> 00:24:32.366 with intensive chemotherapy.

NOTE Confidence: 0.878950760434783

00:24:32.370 --> 00:24:34.870 On the left side is the data from Saint Jude,

NOTE Confidence: 0.878950760434783

00:24:34.870 --> 00:24:37.054 on the right side is the data

NOTE Confidence: 0.878950760434783

00:24:37.054 --> 00:24:37.990 from MD Anderson.

NOTE Confidence: 0.878950760434783

00:24:37.990 --> 00:24:40.654 And what you notice is historically

NOTE Confidence: 0.878950760434783

00:24:40.654 --> 00:24:41.986 with intensive chemotherapy,

NOTE Confidence: 0.878950760434783

00:24:41.990 --> 00:24:45.169 the cure rate in children was 25%.

NOTE Confidence: 0.878950760434783

00:24:45.169 --> 00:24:49.930 The cure rate and adult also was below 20%.

NOTE Confidence: 0.88114062631579

00:24:49.930 --> 00:24:53.282 We now know that this is more common

NOTE Confidence: 0.88114062631579

00:24:53.282 --> 00:24:56.030 in Hispanics because they have got

NOTE Confidence: 0.88114062631579

00:24:56.030 --> 00:24:58.988 a 3 variant that increases CRF2,

NOTE Confidence: 0.88114062631579

00:24:58.988 --> 00:25:04.412 so they have a lot of Philadelphia like.

NOTE Confidence: 0.88114062631579

00:25:04.420 --> 00:25:06.510 So Philadelphia like LL is

NOTE Confidence: 0.88114062631579

00:25:06.510 --> 00:25:08.182 divided into 2 entities.

NOTE Confidence: 0.88114062631579

00:25:08.190 --> 00:25:12.900 So this is just 1/4 of pre BL,

NOTE Confidence: 0.88114062631579

00:25:12.900 --> 00:25:17.000 but 50% of Hispanics pre B all,

NOTE Confidence: 0.88114062631579

00:25:17.000 --> 00:25:19.968 most of them 80% have CRLF two

NOTE Confidence: 0.88114062631579

00:25:19.968 --> 00:25:22.177 over expression and half of

NOTE Confidence: 0.88114062631579

00:25:22.177 --> 00:25:24.297 these have a Jack mutation.

NOTE Confidence: 0.88114062631579

00:25:24.300 --> 00:25:28.040 So if you take 100 patients with L25,

NOTE Confidence: 0.88114062631579

00:25:28.040 --> 00:25:30.140 we'll have Philadelphia like Disease,

NOTE Confidence: 0.88114062631579

00:25:30.140 --> 00:25:31.996 20 will be CRLF,

NOTE Confidence: 0.88114062631579

00:25:31.996 --> 00:25:34.780 2 overexpressed and 10 of them.

NOTE Confidence: 0.88114062631579

00:25:34.780 --> 00:25:37.660 Will be Jack 2 mutated and these are bad.

NOTE Confidence: 0.88114062631579

00:25:37.660 --> 00:25:41.128 These patients may still need

NOTE Confidence: 0.88114062631579

00:25:41.128 --> 00:25:42.436 the allogeneic transplantation,

NOTE Confidence: 0.88114062631579

00:25:42.440 --> 00:25:44.290 but otherwise the other Philadelphia

NOTE Confidence: 0.88114062631579

00:25:44.290 --> 00:25:46.950 like I'll show you do well with

NOTE Confidence: 0.88114062631579

00:25:46.950 --> 00:25:48.815 the addition of the antibodies.

NOTE Confidence: 0.88114062631579

00:25:48.820 --> 00:25:50.860 Then there's an uncommon subset,

NOTE Confidence: 0.88114062631579

00:25:50.860 --> 00:25:53.805 so five of the 100 or 20% of

NOTE Confidence: 0.88114062631579

00:25:53.805 --> 00:25:56.430 the Philadelphia like that have

NOTE Confidence: 0.88114062631579

00:25:56.430 --> 00:25:57.480 able translocations.

NOTE Confidence: 0.88114062631579

00:25:57.480 --> 00:25:59.678 So this is not the BCR able,

NOTE Confidence: 0.88114062631579

00:25:59.680 --> 00:26:02.180 but they are able translocations

NOTE Confidence: 0.88114062631579

00:26:02.180 --> 00:26:05.184 to other genes and these patients.

NOTE Confidence: 0.88114062631579

00:26:05.184 --> 00:26:08.190 Respond to BCR able kinase inhibitors.

NOTE Confidence: 0.88114062631579

00:26:08.190 --> 00:26:11.046 So here I show it more schematically.

NOTE Confidence: 0.88114062631579

00:26:11.050 --> 00:26:16.994 In blue are the translocations of able one.

NOTE Confidence: 0.88114062631579

00:26:17.000 --> 00:26:20.732 To other genes that produce enable

NOTE Confidence: 0.88114062631579

00:26:20.732 --> 00:26:24.376 translocation that responds to the BCR

NOTE Confidence: 0.88114062631579

00:26:24.376 --> 00:26:27.532 able kinase inhibitors also the same

NOTE Confidence: 0.88114062631579

00:26:27.532 --> 00:26:31.179 applies to PDGFR beta translocations.

NOTE Confidence: 0.88114062631579

00:26:31.180 --> 00:26:33.790 So these patients with Abel

NOTE Confidence: 0.88114062631579

00:26:33.790 --> 00:26:35.878 or PD GFR fusions,

NOTE Confidence: 0.88114062631579

00:26:35.880 --> 00:26:38.190 we treat them on the

NOTE Confidence: 0.88114062631579

00:26:38.190 --> 00:26:39.576 Philadelphia positive protocols.

NOTE Confidence: 0.88114062631579

00:26:39.580 --> 00:26:41.908 There is another subset with not

NOTE Confidence: 0.88114062631579

00:26:41.908 --> 00:26:44.835 Jack 2 mutations but with Jack to

NOTE Confidence: 0.88114062631579

00:26:44.835 --> 00:26:46.990 translocations and it is possible.

NOTE Confidence: 0.88114062631579

00:26:46.990 --> 00:26:48.700 That these may respond to resolution

NOTE Confidence: 0.88114062631579

00:26:48.700 --> 00:26:51.208 and we do not know and they are rare,

NOTE Confidence: 0.88114062631579

00:26:51.210 --> 00:26:53.982 so we haven't been able to

NOTE Confidence: 0.88114062631579

00:26:53.982 --> 00:26:56.780 treat them on our studies.

NOTE Confidence: 0.88114062631579

00:26:56.780 --> 00:27:01.190 This is a study from France where

NOTE Confidence: 0.88114062631579

00:27:01.190 --> 00:27:03.122 24 patients with essentially

NOTE Confidence: 0.88114062631579

00:27:03.122 --> 00:27:05.054 able translocations were treated

NOTE Confidence: 0.88114062631579

00:27:05.054 --> 00:27:07.820 with BCR able kinase inhibitors

NOTE Confidence: 0.88114062631579

00:27:07.820 --> 00:27:09.545 and intensive chemotherapy.

NOTE Confidence: 0.88114062631579

00:27:09.550 --> 00:27:12.707 And they showed in this study that

NOTE Confidence: 0.88114062631579

00:27:12.707 --> 00:27:15.054 like Philadelphia positive all these

NOTE Confidence: 0.88114062631579

00:27:15.054 --> 00:27:16.886 patients who receive chemotherapy

NOTE Confidence: 0.88114062631579

00:27:16.886 --> 00:27:19.662 and BCR ABL kinase inhibitor have

NOTE Confidence: 0.88114062631579

00:27:19.662 --> 00:27:22.656 a high response rate close to 90%

NOTE Confidence: 0.88114062631579

00:27:22.656 --> 00:27:25.610 and the four year survival of 60%.

NOTE Confidence: 0.88114062631579

00:27:25.610 --> 00:27:27.176 So these able.

NOTE Confidence: 0.88114062631579

00:27:27.176 --> 00:27:28.220 Mislocated lol.

NOTE Confidence: 0.88114062631579

00:27:28.220 --> 00:27:30.810 We treat the same way as Philadelphia

NOTE Confidence: 0.88114062631579

00:27:30.810 --> 00:27:31.550 positive L.

NOTE Confidence: 0.88114062631579

00:27:31.550 --> 00:27:32.807 So to summarize,

NOTE Confidence: 0.88114062631579

00:27:32.807 --> 00:27:35.740 Philadelphia like L has the same genomic

NOTE Confidence: 0.88114062631579

00:27:35.822 --> 00:27:38.397 profile as Philadelphia positive L,

NOTE Confidence: 0.88114062631579

00:27:38.400 --> 00:27:42.040 but not the 922 translocation and

NOTE Confidence: 0.88114062631579

00:27:42.040 --> 00:27:45.160 not the BCR able molecular events.

NOTE Confidence: 0.88114062631579

00:27:45.160 --> 00:27:48.190 It constitutes 25% of the adults.

NOTE Confidence: 0.88114062631579

00:27:48.190 --> 00:27:50.236 Historically it has a poor prognosis,

NOTE Confidence: 0.88114062631579

00:27:50.240 --> 00:27:51.719 but not anymore.

NOTE Confidence: 0.88114062631579

00:27:51.719 --> 00:27:54.677 It is more common among Hispanics

NOTE Confidence: 0.88114062631579

00:27:54.677 --> 00:27:57.640 and it is 2 distinct entities.

NOTE Confidence: 0.88114062631579

00:27:57.640 --> 00:28:00.088 The CRF2 overexpressed and

NOTE Confidence: 0.88114062631579

00:28:00.088 --> 00:28:01.924 they're able translocated.

NOTE Confidence: 0.88114062631579

00:28:01.930 --> 00:28:04.456 Which we treat like Philadelphia positively.

NOTE Confidence: 0.88114062631579

00:28:04.460 --> 00:28:07.148 And so the newer approaches are

NOTE Confidence: 0.88114062631579

00:28:07.148 --> 00:28:08.940 actually improving the outcome

NOTE Confidence: 0.88114062631579

00:28:09.019 --> 00:28:10.899 in both of these entities.

NOTE Confidence: 0.88114062631579

00:28:10.900 --> 00:28:14.008 And I'll show you that for the

NOTE Confidence: 0.88114062631579

00:28:14.008 --> 00:28:17.710 particular subset of CRF2 overexpression.

NOTE Confidence: 0.88114062631579

00:28:17.710 --> 00:28:20.251 Next I'm going to talk about the

NOTE Confidence: 0.88114062631579

00:28:20.251 --> 00:28:21.633 therapeutic revolution in the

NOTE Confidence: 0.88114062631579

00:28:21.633 --> 00:28:23.465 L and I show it on the slide.

NOTE Confidence: 0.88114062631579

00:28:23.470 --> 00:28:25.330 It comes from 2 subsets.

NOTE Confidence: 0.88114062631579

00:28:25.330 --> 00:28:29.032 The first one are the newer

NOTE Confidence: 0.88114062631579

00:28:29.032 --> 00:28:30.836 antibodies including antibody

NOTE Confidence: 0.88114062631579

00:28:30.836 --> 00:28:34.394 drug conjugates and by specific T

NOTE Confidence: 0.88114062631579

00:28:34.394 --> 00:28:37.289 cell engagers that are targeting

NOTE Confidence: 0.88114062631579

00:28:37.290 --> 00:28:40.727 CD19CD20 and CD2CD22 and CD20.

NOTE Confidence: 0.88114062631579

00:28:40.727 --> 00:28:44.344 So you may be aware of the CD 20 bytes

NOTE Confidence: 0.88114062631579

00:28:44.344 --> 00:28:47.046 which have shown very high efficacy in

NOTE Confidence: 0.876509035714286

00:28:47.125 --> 00:28:49.670 lymphoma. So we'd like to use

NOTE Confidence: 0.876509035714286

00:28:49.670 --> 00:28:51.150 them to replace rituximab.

NOTE Confidence: 0.876509035714286

00:28:51.150 --> 00:28:53.341 And that way we have 3 antibodies

NOTE Confidence: 0.876509035714286

00:28:53.341 --> 00:28:54.970 which are highly effective.

NOTE Confidence: 0.876509035714286

00:28:54.970 --> 00:28:57.210 On the right side are the cartel cells,

NOTE Confidence: 0.876509035714286

00:28:57.210 --> 00:28:59.475 which are a revolution in

NOTE Confidence: 0.876509035714286

00:28:59.475 --> 00:29:01.287 both lymphoma and myeloma.

NOTE Confidence: 0.876509035714286

00:29:01.290 --> 00:29:03.270 But I think for them to

NOTE Confidence: 0.876509035714286

00:29:03.270 --> 00:29:04.830 be important in the L,

NOTE Confidence: 0.876509035714286

00:29:04.830 --> 00:29:07.670 they have to be used in the setting

NOTE Confidence: 0.876509035714286

00:29:07.670 --> 00:29:09.779 of minimal residual disease.

NOTE Confidence: 0.876509035714286

00:29:09.780 --> 00:29:14.296 So in 2009 at MD Anderson,

NOTE Confidence: 0.876509035714286

00:29:14.296 --> 00:29:17.530 we were aware of the INOTUZUMAB

NOTE Confidence: 0.876509035714286

00:29:17.634 --> 00:29:19.190 studies and lymphoma.

NOTE Confidence: 0.876509035714286

00:29:19.190 --> 00:29:22.095 And so we convinced the company to

NOTE Confidence: 0.876509035714286

00:29:22.095 --> 00:29:25.179 give us an investigator in this study,

NOTE Confidence: 0.876509035714286

00:29:25.180 --> 00:29:27.550 which we did initially with

NOTE Confidence: 0.876509035714286

00:29:27.550 --> 00:29:31.055 single dose per course and then in

NOTE Confidence: 0.876509035714286

00:29:31.055 --> 00:29:33.610 fractionated doses and that study

NOTE Confidence: 0.876509035714286

00:29:33.707 --> 00:29:36.941 matured into 90 patients that showed

NOTE Confidence: 0.876509035714286

00:29:36.941 --> 00:29:40.010 that a single antibody produced.

NOTE Confidence: 0.876509035714286

00:29:40.010 --> 00:29:42.140 Mario CR rate of 58%.

NOTE Confidence: 0.876509035714286

00:29:42.140 --> 00:29:43.427 In the meantime,

NOTE Confidence: 0.876509035714286

00:29:43.427 --> 00:29:45.143 the randomized trials and

NOTE Confidence: 0.876509035714286

00:29:45.143 --> 00:29:46.950 lymphoma with INOTUZUMAB failed.

NOTE Confidence: 0.876509035714286

00:29:46.950 --> 00:29:50.338 So the company went ahead with the

NOTE Confidence: 0.876509035714286

00:29:50.338 --> 00:29:52.940 randomized trial and I show here the

NOTE Confidence: 0.876509035714286

00:29:52.940 --> 00:29:55.070 the data in the randomized trial.

NOTE Confidence: 0.876509035714286

00:29:55.070 --> 00:29:58.280 So there were two studies.

NOTE Confidence: 0.876509035714286

00:29:58.280 --> 00:30:02.180 Two parallel trials with Blinatumomab

NOTE Confidence: 0.876509035714286

00:30:02.180 --> 00:30:04.712 and these were both randomized

NOTE Confidence: 0.876509035714286

00:30:04.712 --> 00:30:07.318 trials that compared the antibodies

NOTE Confidence: 0.876509035714286

00:30:07.318 --> 00:30:10.028 to intensive chemotherapy and both

NOTE Confidence: 0.876509035714286

00:30:10.028 --> 00:30:13.093 trials showed that blinatumomab and

NOTE Confidence: 0.876509035714286

00:30:13.093 --> 00:30:16.148 inotuzumab were superior to intensive

NOTE Confidence: 0.876509035714286

00:30:16.148 --> 00:30:18.550 chemotherapy in refractory relaxed.

NOTE Confidence: 0.876509035714286

00:30:18.550 --> 00:30:21.098 I want you all to also notice

NOTE Confidence: 0.876509035714286

00:30:21.098 --> 00:30:23.095 that even though we reported

NOTE Confidence: 0.876509035714286

00:30:23.095 --> 00:30:25.972 Amaro CR rate in the MD Anderson

NOTE Confidence: 0.876509035714286

00:30:25.972 --> 00:30:28.158 studies of 59% because of the.

NOTE Confidence: 0.876509035714286

00:30:28.158 --> 00:30:30.450 Better selection in the randomized trials.

NOTE Confidence: 0.876509035714286

00:30:30.450 --> 00:30:33.438 Actually the randomized trial showed higher

NOTE Confidence: 0.876509035714286

00:30:33.438 --> 00:30:37.150 mercy RA than our institutional study.

NOTE Confidence: 0.876509035714286

00:30:37.150 --> 00:30:41.525 So both these agents became FDA approved

NOTE Confidence: 0.876509035714286

00:30:41.525 --> 00:30:46.382 in 2014 and in 2017 as single agents for

NOTE Confidence: 0.876509035714286

00:30:46.382 --> 00:30:50.250 the treatment of refractory relapse AML.

NOTE Confidence: 0.876509035714286

00:30:50.250 --> 00:30:52.302 But what you see is the

NOTE Confidence: 0.876509035714286

00:30:52.302 --> 00:30:53.670 benefit is very modest.

NOTE Confidence: 0.876509035714286

00:30:53.670 --> 00:30:56.316 So very quickly we decided this is

NOTE Confidence: 0.876509035714286

00:30:56.316 --> 00:30:59.690 not how we are going to use them

NOTE Confidence: 0.876509035714286

00:30:59.690 --> 00:31:02.150 and we incorporated them rapidly

NOTE Confidence: 0.876509035714286

00:31:02.150 --> 00:31:05.110 into the standard chemotherapy.

NOTE Confidence: 0.876509035714286

00:31:05.110 --> 00:31:08.170 So I'm going to show you next the data

NOTE Confidence: 0.876509035714286

00:31:08.170 --> 00:31:11.369 with Hyper Cvad blinatumomab in pre Bal.

NOTE Confidence: 0.876509035714286

00:31:11.370 --> 00:31:13.590 So the design of the original

NOTE Confidence: 0.876509035714286

00:31:13.590 --> 00:31:16.123 study was four cycles of intensive

NOTE Confidence: 0.876509035714286

00:31:16.123 --> 00:31:18.558 chemotherapy and because the prevailing

NOTE Confidence: 0.876509035714286

00:31:18.558 --> 00:31:21.400 notion was you cannot dose dense.

NOTE Confidence: 0.876509035714286

00:31:21.400 --> 00:31:22.636 With the chemotherapy,

NOTE Confidence: 0.876509035714286

00:31:22.636 --> 00:31:24.284 because the chemotherapy kills

NOTE Confidence: 0.876509035714286

00:31:24.284 --> 00:31:25.970 the these T cells,

NOTE Confidence: 0.876509035714286

00:31:25.970 --> 00:31:27.950 so theoretically blinatumomab

NOTE Confidence: 0.876509035714286

00:31:27.950 --> 00:31:30.590 would be less effective.

NOTE Confidence: 0.876509035714286

00:31:30.590 --> 00:31:32.963 The company allowed us only to use

NOTE Confidence: 0.876509035714286

00:31:32.963 --> 00:31:35.599 it in sequence and then we shorten

NOTE Confidence: 0.876509035714286

00:31:35.599 --> 00:31:37.534 the duration of the maintenance

NOTE Confidence: 0.876509035714286

00:31:37.534 --> 00:31:39.517 from two years to one year.

NOTE Confidence: 0.876509035714286

00:31:39.520 --> 00:31:42.138 And later on the other company uh

NOTE Confidence: 0.876509035714286

00:31:42.138 --> 00:31:44.779 allowed us to add inotuzumab um.

NOTE Confidence: 0.876509035714286

00:31:44.780 --> 00:31:47.740 So we had two of the antibodies as

NOTE Confidence: 0.876509035714286

00:31:47.740 --> 00:31:51.056 three drugs that we incorporated into

NOTE Confidence: 0.876509035714286

00:31:51.056 --> 00:31:54.276 the high perceived blinatumomab inotuzumab.

NOTE Confidence: 0.876509035714286

00:31:54.280 --> 00:31:56.842 So we are going to publish the

NOTE Confidence: 0.876509035714286

00:31:56.842 --> 00:31:59.750 data in the 1st 63% again unless it

NOTE Confidence: 0.876509035714286

00:31:59.750 --> 00:32:02.320 hematology in the next couple of months.

NOTE Confidence: 0.876509035714286

00:32:02.320 --> 00:32:04.772 The CR8 was 100%,

NOTE Confidence: 0.876509035714286

00:32:04.772 --> 00:32:07.744 MRD negativity 95% and for the

NOTE Confidence: 0.876509035714286

00:32:07.744 --> 00:32:11.721 first time in pre BLA in adult pre

NOTE Confidence: 0.876509035714286

00:32:11.721 --> 00:32:15.250 BL the three-year survival was 85%.

NOTE Confidence: 0.876509035714286

00:32:15.250 --> 00:32:18.530 On the right side I showed the the

NOTE Confidence: 0.876509035714286

00:32:18.530 --> 00:32:21.840 data since we added the inotuzumab,

NOTE Confidence: 0.876509035714286

00:32:21.840 --> 00:32:23.912 so by adding inotuzumab.

NOTE Confidence: 0.876509035714286

00:32:23.912 --> 00:32:26.502 To the high perceived blinatumomab

NOTE Confidence: 0.876509035714286

00:32:26.502 --> 00:32:28.870 we improved the outcome,

NOTE Confidence: 0.876509035714286

00:32:28.870 --> 00:32:31.504 perhaps because we so far have

NOTE Confidence: 0.876509035714286

00:32:31.504 --> 00:32:33.260 not seen any relapses.

NOTE Confidence: 0.876509035714286

00:32:33.260 --> 00:32:35.710 So that's why I think that this

NOTE Confidence: 0.876509035714286

00:32:35.710 --> 00:32:37.769 is perhaps a potential standard

NOTE Confidence: 0.876509035714286

00:32:37.769 --> 00:32:40.094 of care in the future.

NOTE Confidence: 0.823395777692308

00:32:40.100 --> 00:32:43.016 Now let's look at the data compared to the

NOTE Confidence: 0.823395777692308

00:32:43.016 --> 00:32:45.912 previous high perceived ofatumumab, a 20%

NOTE Confidence: 0.823395777692308

00:32:45.912 --> 00:32:48.894 difference in the survival at three years.

NOTE Confidence: 0.823395777692308

00:32:48.900 --> 00:32:52.986 And this shows the subset in blue of patients

NOTE Confidence: 0.823395777692308

00:32:52.986 --> 00:32:56.516 with Philadelphia like disease where the

NOTE Confidence: 0.823395777692308

00:32:56.516 --> 00:33:00.220 survival is not anymore 20% as I showed you,

NOTE Confidence: 0.823395777692308

00:33:00.220 --> 00:33:04.210 but it has gone up to 70% and this shows the.

NOTE Confidence: 0.823395777692308

00:33:04.210 --> 00:33:06.616 Survival with or without the transplant,

NOTE Confidence: 0.823395777692308

00:33:06.620 --> 00:33:09.524 again suggesting that the role of

NOTE Confidence: 0.823395777692308

00:33:09.524 --> 00:33:12.028 transplant is not that important

NOTE Confidence: 0.823395777692308

00:33:12.028 --> 00:33:15.360 and not for all patients with ALS.

NOTE Confidence: 0.823395777692308

00:33:15.360 --> 00:33:17.576 So I showed you the top two slides,

NOTE Confidence: 0.823395777692308

00:33:17.580 --> 00:33:20.828 the top two studies from MD Anderson and

NOTE Confidence: 0.823395777692308

00:33:20.828 --> 00:33:24.539 what you see is this is a common trend now.

NOTE Confidence: 0.823395777692308

00:33:24.540 --> 00:33:27.908 So even though randomized trials has been or

NOTE Confidence: 0.823395777692308

00:33:27.908 --> 00:33:31.818 is the standard of care in Cancer Research,

NOTE Confidence: 0.823395777692308

00:33:31.820 --> 00:33:33.692 what you see is many of

NOTE Confidence: 0.823395777692308

00:33:33.692 --> 00:33:34.940 the studies from Germany,

NOTE Confidence: 0.823395777692308

00:33:34.940 --> 00:33:36.796 France and other places,

NOTE Confidence: 0.823395777692308

00:33:36.796 --> 00:33:40.115 they are using single arm trials in

NOTE Confidence: 0.823395777692308

00:33:40.115 --> 00:33:42.803 order to optimize the regimens before

NOTE Confidence: 0.823395777692308

00:33:42.803 --> 00:33:45.779 taking them to a final randomized.

NOTE Confidence: 0.823395777692308

00:33:45.780 --> 00:33:48.620 One and they are showing similar data with

NOTE Confidence: 0.823395777692308

00:33:48.620 --> 00:33:51.537 high CR rates and high survival rates.

NOTE Confidence: 0.823395777692308

00:33:51.540 --> 00:33:54.978 Now, I mentioned randomized trial and

NOTE Confidence: 0.823395777692308

00:33:54.978 --> 00:33:57.786 Bayesian designs for several times

NOTE Confidence: 0.823395777692308

00:33:57.786 --> 00:34:00.863 and I want to explain myself perhaps

NOTE Confidence: 0.823395777692308

00:34:00.863 --> 00:34:04.230 not to the senior physicians who.

NOTE Confidence: 0.89252306

00:34:07.050 --> 00:34:08.930 May be skeptical about this,

NOTE Confidence: 0.89252306

00:34:08.930 --> 00:34:12.136 but perhaps for the fellows and students

NOTE Confidence: 0.89252306

00:34:12.136 --> 00:34:15.105 who have been educated to appreciate

NOTE Confidence: 0.89252306

00:34:15.105 --> 00:34:18.612 randomized trials as the only way to

NOTE Confidence: 0.89252306

00:34:18.698 --> 00:34:22.345 advance research in medicine and in cancer.

NOTE Confidence: 0.89252306

00:34:22.350 --> 00:34:25.514 So we started the studies with INOTUZUMAB

NOTE Confidence: 0.89252306

00:34:25.514 --> 00:34:29.010 in 2010, with BLINATUMOMAB in 2012.

NOTE Confidence: 0.89252306

00:34:29.010 --> 00:34:31.686 These drugs were FDA approved in

NOTE Confidence: 0.89252306

00:34:31.690 --> 00:34:37.318 2014 and 17 in 2022 a decade later.

NOTE Confidence: 0.89252306

00:34:37.318 --> 00:34:40.810 We still use Blinatumomab and inotuzumab

NOTE Confidence: 0.89252306

00:34:40.913 --> 00:34:43.967 as single agents in ASL solvers.

NOTE Confidence: 0.89252306

00:34:43.970 --> 00:34:46.706 We have not yet established the

NOTE Confidence: 0.89252306

00:34:46.706 --> 00:34:49.239 combinations as a standard of care.

NOTE Confidence: 0.89252306

00:34:49.240 --> 00:34:50.018 Now what?

NOTE Confidence: 0.89252306

00:34:50.018 --> 00:34:52.352 Let's go back to the history

NOTE Confidence: 0.89252306

00:34:52.352 --> 00:34:53.730 of randomized trials.

NOTE Confidence: 0.89252306

00:34:53.730 --> 00:34:57.517 What people may not know is the

NOTE Confidence: 0.89252306

00:34:57.517 --> 00:35:00.288 randomized trial started only in 1955.

NOTE Confidence: 0.89252306

00:35:00.288 --> 00:35:02.128 The first randomized trial in

NOTE Confidence: 0.89252306

00:35:02.128 --> 00:35:04.829 cancer was done by Doctor Friedrich.

NOTE Confidence: 0.89252306

00:35:04.830 --> 00:35:07.827 This was a time when he was at the

NOTE Confidence: 0.89252306

00:35:07.827 --> 00:35:11.021 NIH and he showed a correlation

NOTE Confidence: 0.89252306

00:35:11.021 --> 00:35:13.786 between low platelets and bleeding.

NOTE Confidence: 0.89252306

00:35:13.790 --> 00:35:16.614 So people ask him to do a randomized

NOTE Confidence: 0.89252306

00:35:16.614 --> 00:35:19.389 trial where he and he gave fresh blood

NOTE Confidence: 0.89252306

00:35:19.389 --> 00:35:22.489 and he showed that the bleeding decreased.

NOTE Confidence: 0.89252306

00:35:22.490 --> 00:35:23.402 In those days,

NOTE Confidence: 0.89252306

00:35:23.402 --> 00:35:25.530 we did not have to resist machines,

NOTE Confidence: 0.89252306

00:35:25.530 --> 00:35:28.563 so he was asked to do a randomized trial

NOTE Confidence: 0.89252306

00:35:28.563 --> 00:35:31.496 of fresh blood versus stored blood.

NOTE Confidence: 0.89252306

00:35:31.500 --> 00:35:33.768 To show that fresh blood would

NOTE Confidence: 0.89252306

00:35:33.768 --> 00:35:35.675 reduce the bleeding in children

NOTE Confidence: 0.89252306

00:35:35.675 --> 00:35:38.564 with a L and he showed that and when

NOTE Confidence: 0.89252306

00:35:38.636 --> 00:35:40.916 the trial turned to be positive,

NOTE Confidence: 0.89252306

00:35:40.920 --> 00:35:43.895 they accused him of falsifying the data.

NOTE Confidence: 0.89252306

00:35:43.900 --> 00:35:47.748 So this shows you a trend that perhaps a

NOTE Confidence: 0.89252306

00:35:47.748 --> 00:35:51.018 randomized trials are established today,

NOTE Confidence: 0.89252306

00:35:51.020 --> 00:35:53.138 but maybe we can question them.

NOTE Confidence: 0.89252306

00:35:53.140 --> 00:35:55.556 So let me tell you why we should

NOTE Confidence: 0.89252306

00:35:55.556 --> 00:35:56.160 question them.

NOTE Confidence: 0.89252306

00:35:56.160 --> 00:35:59.388 So today in Europe there is

NOTE Confidence: 0.89252306

00:35:59.388 --> 00:36:02.229 a phase three study of 1.

NOTE Confidence: 0.89252306

00:36:02.230 --> 00:36:03.950 Versus intensive chemotherapy, imagine.

NOTE Confidence: 0.89252306

00:36:03.950 --> 00:36:07.589 I do not believe there is real equipoise,

NOTE Confidence: 0.89252306

00:36:07.590 --> 00:36:11.370 so the basis of all randomized trials.

NOTE Confidence: 0.89252306

00:36:11.370 --> 00:36:13.350 Is that they assume there's

NOTE Confidence: 0.89252306

00:36:13.350 --> 00:36:14.538 the knowledge equipoise.

NOTE Confidence: 0.89252306

00:36:14.540 --> 00:36:16.238 So you're sitting in the room

NOTE Confidence: 0.89252306

00:36:16.238 --> 00:36:17.879 with the patient and you say,

NOTE Confidence: 0.89252306

00:36:17.880 --> 00:36:20.575 I'm going to randomize you to this

NOTE Confidence: 0.89252306

00:36:20.575 --> 00:36:23.573 protocol and I truly and honestly do

NOTE Confidence: 0.89252306

00:36:23.573 --> 00:36:26.213 not believe that the new treatment

NOTE Confidence: 0.89252306

00:36:26.296 --> 00:36:28.420 is better than the old one.

NOTE Confidence: 0.89252306

00:36:28.420 --> 00:36:30.268 Now randomized trials are OK if

NOTE Confidence: 0.89252306

00:36:30.268 --> 00:36:32.699 you are in a research desert.

NOTE Confidence: 0.89252306

00:36:32.700 --> 00:36:36.708 So if you were in 1965 or 1970 or

NOTE Confidence: 0.89252306

00:36:36.708 --> 00:36:39.240 1980 where there was very little

NOTE Confidence: 0.89252306

00:36:39.337 --> 00:36:41.537 to offer to the patients,

NOTE Confidence: 0.89252306

00:36:41.540 --> 00:36:43.983 you could do a randomized trial with

NOTE Confidence: 0.89252306

00:36:43.983 --> 00:36:47.406 the new drug X or if you have a highly

NOTE Confidence: 0.89252306

00:36:47.406 --> 00:36:48.980 curable disease like ALS today,

NOTE Confidence: 0.89252306

00:36:48.980 --> 00:36:51.380 we are in the land of research plenty.

NOTE Confidence: 0.89252306

00:36:51.380 --> 00:36:53.725 There are multiple targeted therapies

NOTE Confidence: 0.89252306

00:36:53.725 --> 00:36:57.787 in ASL and if you do a randomized

NOTE Confidence: 0.89252306

00:36:57.787 --> 00:36:59.410 trial that randomizes.

NOTE Confidence: 0.89252306

00:36:59.410 --> 00:37:01.720 The patients to the standard of

NOTE Confidence: 0.89252306

00:37:01.720 --> 00:37:04.089 care versus standard of care versus

NOTE Confidence: 0.89252306

00:37:04.089 --> 00:37:06.735 drug X that the results of that

NOTE Confidence: 0.89252306

00:37:06.735 --> 00:37:08.643 randomized trial will be outdated

NOTE Confidence: 0.89252306

00:37:08.643 --> 00:37:10.827 by the time the data matures.

NOTE Confidence: 0.89252306

00:37:10.830 --> 00:37:12.420 And if you think about it,

NOTE Confidence: 0.89252306

00:37:12.420 --> 00:37:14.982 our whole life experience is actually

NOTE Confidence: 0.89252306

00:37:14.982 --> 00:37:16.560 not randomized. It's Bayesian.

NOTE Confidence: 0.89252306

00:37:16.560 --> 00:37:18.720 The way we raise our children,

NOTE Confidence: 0.89252306

00:37:18.720 --> 00:37:21.499 the the schools we choose for them,

NOTE Confidence: 0.89252306

00:37:21.500 --> 00:37:22.780 the restaurants we choose,

NOTE Confidence: 0.89252306

00:37:22.780 --> 00:37:24.324 the careers, the partners.

NOTE Confidence: 0.89252306

00:37:24.324 --> 00:37:27.940 You do not go out 50 times with

NOTE Confidence: 0.89252306

00:37:27.940 --> 00:37:30.348 a new person and 50 times with

NOTE Confidence: 0.89252306

00:37:30.348 --> 00:37:32.572 another new person and then look

NOTE Confidence: 0.89252306

00:37:32.572 --> 00:37:34.804 at your experience and decide which

NOTE Confidence: 0.89252306

00:37:34.804 --> 00:37:36.797 one you're going to marry.

NOTE Confidence: 0.799205624285714

00:37:36.800 --> 00:37:41.079 You actually switch from person A to B&C.

NOTE Confidence: 0.799205624285714

00:37:41.079 --> 00:37:45.132 Very quickly and gain a cumulative experience

NOTE Confidence: 0.799205624285714

00:37:45.132 --> 00:37:49.010 that allows you to decide on what to do.

NOTE Confidence: 0.799205624285714

00:37:49.010 --> 00:37:53.518 Now in in the editorials you you

NOTE Confidence: 0.799205624285714

00:37:53.518 --> 00:37:56.566 may have read those two examples,

NOTE Confidence: 0.799205624285714

00:37:56.570 --> 00:37:58.210 which are obvious examples.

NOTE Confidence: 0.799205624285714

00:37:58.210 --> 00:37:59.850 So parachutes were not

NOTE Confidence: 0.799205624285714

00:37:59.850 --> 00:38:01.989 based on randomized trials.

NOTE Confidence: 0.799205624285714

00:38:01.990 --> 00:38:04.874 We did not throw 50 people without

NOTE Confidence: 0.799205624285714

00:38:04.874 --> 00:38:07.638 a parachute and 50 people with

NOTE Confidence: 0.799205624285714

00:38:07.638 --> 00:38:09.931 a parachute from airplanes to

NOTE Confidence: 0.799205624285714

00:38:09.931 --> 00:38:11.736 decide that parachutes save lives.

NOTE Confidence: 0.799205624285714

00:38:11.740 --> 00:38:15.286 And the same applied to seatbelts and so on.

NOTE Confidence: 0.799205624285714

00:38:15.290 --> 00:38:17.530 Now for the young people,

NOTE Confidence: 0.799205624285714

00:38:17.530 --> 00:38:19.792 they search Google all the time

NOTE Confidence: 0.799205624285714

00:38:19.792 --> 00:38:20.923 for the truth.

NOTE Confidence: 0.799205624285714

00:38:20.930 --> 00:38:23.688 So there are Google algorithm that we

NOTE Confidence: 0.799205624285714

00:38:23.688 --> 00:38:26.960 use in our daily practice to decide

NOTE Confidence: 0.799205624285714

00:38:26.960 --> 00:38:29.510 what's good and what's not good.

NOTE Confidence: 0.799205624285714

00:38:29.510 --> 00:38:32.310 So I'm going to propose that perhaps

NOTE Confidence: 0.799205624285714

00:38:32.310 --> 00:38:35.674 what we have to do in Cancer Research

NOTE Confidence: 0.799205624285714

00:38:35.674 --> 00:38:38.433 and in medical research is develop

NOTE Confidence: 0.799205624285714

00:38:38.433 --> 00:38:40.972 apps that incorporate the research.

NOTE Confidence: 0.799205624285714

00:38:40.972 --> 00:38:43.639 In cancer for example and then we

NOTE Confidence: 0.799205624285714

00:38:43.639 --> 00:38:46.517 ask the app based on the preclinical

NOTE Confidence: 0.799205624285714

00:38:46.517 --> 00:38:49.260 data and the clinical trials so far,

NOTE Confidence: 0.799205624285714

00:38:49.260 --> 00:38:51.804 what would be the best design

NOTE Confidence: 0.799205624285714

00:38:51.804 --> 00:38:54.903 to investigate a new drug in in

NOTE Confidence: 0.799205624285714

00:38:54.903 --> 00:38:56.217 the Cancer Research.

NOTE Confidence: 0.799205624285714

00:38:56.220 --> 00:38:59.870 So think about it and see if if if it's

NOTE Confidence: 0.799205624285714

00:38:59.967 --> 00:39:03.424 something that could that could maybe

NOTE Confidence: 0.799205624285714

00:39:03.424 --> 00:39:06.064 challenge the concept of randomized

NOTE Confidence: 0.799205624285714

00:39:06.064 --> 00:39:08.358 trials and this is not new knowledge.

NOTE Confidence: 0.799205624285714

00:39:08.360 --> 00:39:10.202 So what you notice is that

NOTE Confidence: 0.799205624285714

00:39:10.202 --> 00:39:12.260 the A today is approving.

NOTE Confidence: 0.799205624285714

00:39:12.260 --> 00:39:14.689 Several drugs not based on randomized trials,

NOTE Confidence: 0.799205624285714

00:39:14.690 --> 00:39:17.903 but based on the results of even

NOTE Confidence: 0.799205624285714

00:39:17.903 --> 00:39:20.914 phase one studies and we were

NOTE Confidence: 0.799205624285714

00:39:20.914 --> 00:39:23.484 told historically that phase one

NOTE Confidence: 0.799205624285714

00:39:23.484 --> 00:39:25.950 studies are purely to identify

NOTE Confidence: 0.799205624285714

00:39:25.950 --> 00:39:29.070 toxicities and the phase two dose.

NOTE Confidence: 0.799205624285714

00:39:29.070 --> 00:39:32.101 Now we know that there are several

NOTE Confidence: 0.799205624285714

00:39:32.101 --> 00:39:34.646 drugs like crizotinib and non small

NOTE Confidence: 0.799205624285714

00:39:34.646 --> 00:39:36.968 cell lung cancer and then roughly

NOTE Confidence: 0.799205624285714

00:39:36.968 --> 00:39:39.640 in Melanoma that were approved based

NOTE Confidence: 0.799205624285714

00:39:39.640 --> 00:39:43.850 on the results of Phase 1/2 trials.

NOTE Confidence: 0.799205624285714

00:39:43.850 --> 00:39:46.114 So I'm going to propose at least for

NOTE Confidence: 0.799205624285714

00:39:46.114 --> 00:39:49.040 a L which is a land of the resource

NOTE Confidence: 0.799205624285714

00:39:49.040 --> 00:39:51.409 plenty that we hold the randomized

NOTE Confidence: 0.799205624285714

00:39:51.409 --> 00:39:54.043 styles because they will slow the

NOTE Confidence: 0.799205624285714

00:39:54.043 --> 00:39:56.382 progress and the discoveries and

NOTE Confidence: 0.799205624285714

00:39:56.382 --> 00:39:58.747 replace them with Bayesian trials.

NOTE Confidence: 0.799205624285714

00:39:58.750 --> 00:40:00.590 Actually randomized trials which are

NOTE Confidence: 0.799205624285714

00:40:00.590 --> 00:40:03.170 poorly designed can give you false leads.

NOTE Confidence: 0.799205624285714

00:40:03.170 --> 00:40:05.826 So there was in fact an all study

NOTE Confidence: 0.799205624285714

00:40:05.826 --> 00:40:08.760 using a pediatric inspired regimen.

NOTE Confidence: 0.799205624285714

00:40:08.760 --> 00:40:11.508 It was a cooperative trial in

NOTE Confidence: 0.799205624285714

00:40:11.508 --> 00:40:13.790 the United States that had.

NOTE Confidence: 0.799205624285714

00:40:13.790 --> 00:40:16.885 Randomized patients to using a

NOTE Confidence: 0.799205624285714

00:40:16.885 --> 00:40:19.361 regimen with ASPARAGINASE and

NOTE Confidence: 0.799205624285714

00:40:19.361 --> 00:40:21.240 randomization to inotuzumab.

NOTE Confidence: 0.799205624285714

00:40:21.240 --> 00:40:23.580 I objected vehemently to that study

NOTE Confidence: 0.799205624285714

00:40:23.580 --> 00:40:25.754 because I said that Asparaginase

NOTE Confidence: 0.799205624285714

00:40:25.754 --> 00:40:28.449 and Inotuzumab will cause vino

NOTE Confidence: 0.799205624285714

00:40:28.449 --> 00:40:30.605 occlusive disease and mortality.

NOTE Confidence: 0.799205624285714

00:40:30.610 --> 00:40:33.130 This was not believed and the study

NOTE Confidence: 0.799205624285714

00:40:33.130 --> 00:40:36.066 was stopped two months ago after 400

NOTE Confidence: 0.799205624285714

00:40:36.066 --> 00:40:38.736 patients were entered because as expected,

NOTE Confidence: 0.799205624285714

00:40:38.740 --> 00:40:41.446 there was a higher mortality in

NOTE Confidence: 0.799205624285714

00:40:41.446 --> 00:40:43.250 the investigational arm because

NOTE Confidence: 0.799205624285714

00:40:43.328 --> 00:40:44.690 of the anticipated.

NOTE Confidence: 0.799205624285714

00:40:44.690 --> 00:40:46.858 A synergistic toxicity of

NOTE Confidence: 0.799205624285714

00:40:46.858 --> 00:40:48.484 asparaginase and inotuzumab.

NOTE Confidence: 0.799205624285714

00:40:48.490 --> 00:40:50.785 So I think at least in ASL we have

NOTE Confidence: 0.799205624285714

00:40:50.785 --> 00:40:53.468 to revert to single arm trials until

NOTE Confidence: 0.799205624285714

00:40:53.468 --> 00:40:55.829 we optimize the regimen that could

NOTE Confidence: 0.799205624285714

00:40:55.829 --> 00:40:58.349 be compared to the standard of care.

NOTE Confidence: 0.799205624285714

00:40:58.350 --> 00:41:00.726 Now next I'm going to discuss

NOTE Confidence: 0.799205624285714

00:41:00.726 --> 00:41:01.914 minimal residual disease.

NOTE Confidence: 0.799205624285714

00:41:01.920 --> 00:41:04.452 I'm going to draw your attention

NOTE Confidence: 0.799205624285714

00:41:04.452 --> 00:41:06.542 to figure the this is,

NOTE Confidence: 0.799205624285714

00:41:06.542 --> 00:41:09.830 this is patients with adult AL who are

NOTE Confidence: 0.799205624285714

00:41:09.923 --> 00:41:13.248 in remission and who are MRD positive.

NOTE Confidence: 0.799205624285714

00:41:13.250 --> 00:41:16.330 So what you see is their cure rate is at

NOTE Confidence: 0.8738667475

00:41:16.413 --> 00:41:18.794 best 10% compared to over 50%

NOTE Confidence: 0.8738667475

00:41:18.794 --> 00:41:21.440 for the patients who become MRD

NOTE Confidence: 0.8738667475

00:41:21.532 --> 00:41:23.908 negative by any methodology.

NOTE Confidence: 0.8738667475

00:41:23.910 --> 00:41:27.550 But this was mostly by flow cytometry.

NOTE Confidence: 0.8738667475

00:41:27.550 --> 00:41:30.896 So this is. Where we started using

NOTE Confidence: 0.8738667475

00:41:30.896 --> 00:41:33.670 BLINATUMOMAB for five courses in the

NOTE Confidence: 0.8738667475

00:41:33.670 --> 00:41:37.172 setting of MRD positive L in first or

NOTE Confidence: 0.8738667475

00:41:37.172 --> 00:41:40.094 second remission we observed that 80%

NOTE Confidence: 0.8738667475

00:41:40.100 --> 00:41:42.902 of the patients became MRD negative

NOTE Confidence: 0.8738667475

00:41:42.902 --> 00:41:46.718 and the four year survival was not 10%,

NOTE Confidence: 0.8738667475

00:41:46.720 --> 00:41:48.860 it went up to 60%.

NOTE Confidence: 0.8738667475

00:41:48.860 --> 00:41:51.852 And on the right side I showed that

NOTE Confidence: 0.8738667475

00:41:51.852 --> 00:41:54.800 the effect of transplant was minimal.

NOTE Confidence: 0.8738667475

00:41:54.800 --> 00:41:56.977 So perhaps this is where we can

NOTE Confidence: 0.8738667475

00:41:56.977 --> 00:41:58.400 do the cartel cells.

NOTE Confidence: 0.8738667475

00:41:58.400 --> 00:41:59.579 Instead of transplant,

NOTE Confidence: 0.8738667475

00:41:59.579 --> 00:42:01.544 because if you avoid the

NOTE Confidence: 0.8738667475

00:42:01.544 --> 00:42:02.990 transplant related mortality,

NOTE Confidence: 0.8738667475

00:42:02.990 --> 00:42:06.006 maybe the cure rate will be even higher.

NOTE Confidence: 0.8738667475

00:42:06.010 --> 00:42:08.578 So This is why it's important

NOTE Confidence: 0.8738667475

00:42:08.578 --> 00:42:11.428 to Measure Mart not by flow

NOTE Confidence: 0.8738667475

00:42:11.428 --> 00:42:14.048 cytometry looking at 10,000 cells,

NOTE Confidence: 0.8738667475

00:42:14.050 --> 00:42:16.864 but by the next generation sequencing

NOTE Confidence: 0.8738667475

00:42:16.864 --> 00:42:19.599 for the immunoglobulin heavy chain that

NOTE Confidence: 0.8738667475

00:42:19.599 --> 00:42:22.727 looks at the million to three million cells.

NOTE Confidence: 0.8738667475

00:42:22.730 --> 00:42:25.502 So this is a study in the older AL,

NOTE Confidence: 0.8738667475

00:42:25.510 --> 00:42:27.958 so I'm going to show you an update

NOTE Confidence: 0.8738667475

00:42:27.958 --> 00:42:30.429 for just for information purposes.

NOTE Confidence: 0.8738667475

00:42:30.430 --> 00:42:33.647 So this is the study that we did and

NOTE Confidence: 0.8738667475

00:42:33.647 --> 00:42:36.500 we took from the L salvage where we did

NOTE Confidence: 0.8738667475

00:42:36.579 --> 00:42:38.735 minimal chemotherapy with inotuzumab

NOTE Confidence: 0.8738667475

00:42:38.735 --> 00:42:41.969 and added the BLINATUMOMAB later on.

NOTE Confidence: 0.8738667475

00:42:41.970 --> 00:42:45.498 And we showed that by matched analysis

NOTE Confidence: 0.8738667475

00:42:45.498 --> 00:42:48.591 that the new study was superior

NOTE Confidence: 0.8738667475

00:42:48.591 --> 00:42:52.049 to the old study of Hyper Siva.

NOTE Confidence: 0.8738667475

00:42:52.050 --> 00:42:52.770 The question?

NOTE Confidence: 0.8738667475

00:42:52.770 --> 00:42:56.086 Is can we do a randomized trial and what

NOTE Confidence: 0.8738667475

00:42:56.086 --> 00:42:58.966 it would be the control arm now that

NOTE Confidence: 0.8738667475

00:42:58.966 --> 00:43:01.397 there's a significant difference in

NOTE Confidence: 0.8738667475

00:43:01.397 --> 00:43:04.391 the outcome compared to historical data?

NOTE Confidence: 0.8738667475

00:43:04.400 --> 00:43:06.955 And this is the same happening elsewhere.

NOTE Confidence: 0.8738667475

00:43:06.960 --> 00:43:09.608 So in the United States there was a

NOTE Confidence: 0.8738667475

00:43:09.608 --> 00:43:12.142 single arm swork trial of chemotherapy

NOTE Confidence: 0.8738667475

00:43:12.142 --> 00:43:14.647 with blinatumomab and similar studies

NOTE Confidence: 0.8738667475

00:43:14.647 --> 00:43:17.325 were conducted again in Germany and

NOTE Confidence: 0.8738667475

00:43:17.325 --> 00:43:19.533 Australia and by the French group.

NOTE Confidence: 0.8738667475

00:43:19.540 --> 00:43:23.145 All of them are single arm trials

NOTE Confidence: 0.8738667475

00:43:23.145 --> 00:43:25.672 combining chemotherapy with one of

NOTE Confidence: 0.8738667475

00:43:25.672 --> 00:43:27.907 the two antibodies producing high

NOTE Confidence: 0.8738667475

00:43:27.907 --> 00:43:31.029 CR rates and good early outcomes.

NOTE Confidence: 0.8738667475

00:43:31.030 --> 00:43:33.844 Now in this LL, as I mentioned,

NOTE Confidence: 0.8738667475

00:43:33.850 --> 00:43:36.010 we do not have an antibody.

NOTE Confidence: 0.8738667475

00:43:36.010 --> 00:43:38.356 But what we have is something

NOTE Confidence: 0.8738667475

00:43:38.356 --> 00:43:39.529 that might work,

NOTE Confidence: 0.8738667475

00:43:39.530 --> 00:43:42.434 so intensive chemotherapy with a lot

NOTE Confidence: 0.8738667475

00:43:42.434 --> 00:43:44.893 of methotrexate and asparaginase and

NOTE Confidence: 0.8738667475

00:43:44.893 --> 00:43:48.031 recently we have seen that nelarabine

NOTE Confidence: 0.8738667475

00:43:48.031 --> 00:43:51.708 works there and venetoclax might work.

NOTE Confidence: 0.8738667475

00:43:51.710 --> 00:43:54.788 So we have started combining these

NOTE Confidence: 0.8738667475

00:43:54.788 --> 00:43:59.159 drugs in a trial and error formulation.

NOTE Confidence: 0.8738667475

00:43:59.160 --> 00:44:02.490 And the other thing that is

NOTE Confidence: 0.8738667475

00:44:02.490 --> 00:44:06.408 important is the fact that T cell L,

NOTE Confidence: 0.8738667475

00:44:06.410 --> 00:44:10.388 there's a subset of T cell AL shown here

NOTE Confidence: 0.8738667475

00:44:10.388 --> 00:44:14.466 that has a genomic profile more like AML.

NOTE Confidence: 0.8738667475

00:44:14.470 --> 00:44:17.246 I think this is the precursor T cell

NOTE Confidence: 0.8738667475

00:44:17.246 --> 00:44:20.703 all where we need to start considering

NOTE Confidence: 0.8738667475

00:44:20.703 --> 00:44:23.383 treatments that incorporate AML therapies.

NOTE Confidence: 0.8738667475

00:44:23.390 --> 00:44:26.225 So this is the subset of the

NOTE Confidence: 0.8738667475

00:44:26.225 --> 00:44:29.580 cell L with methylation profile.

NOTE Confidence: 0.8738667475

00:44:29.580 --> 00:44:31.725 Identical to acute myeloid leukemia

NOTE Confidence: 0.8738667475

00:44:31.725 --> 00:44:34.327 and perhaps these are the patients

NOTE Confidence: 0.8738667475

00:44:34.327 --> 00:44:37.147 that should be treated like M so

NOTE Confidence: 0.8738667475

00:44:37.147 --> 00:44:39.782 this is the multiple reiterations

NOTE Confidence: 0.8738667475

00:44:39.782 --> 00:44:43.260 of the hyper cvad asparaginase,

NOTE Confidence: 0.8738667475

00:44:43.260 --> 00:44:46.125 nelarabine regimen and not yet

NOTE Confidence: 0.8738667475

00:44:46.125 --> 00:44:48.417 ready for prime time,

NOTE Confidence: 0.8738667475

00:44:48.420 --> 00:44:52.128 but in the past two studies where we added

NOTE Confidence: 0.8738667475

00:44:52.128 --> 00:44:54.799 venetoclax and nelarabine asparaginase,

NOTE Confidence: 0.8738667475

00:44:54.800 --> 00:44:57.878 we're getting survivals not of 60%,

NOTE Confidence: 0.8738667475

00:44:57.880 --> 00:44:59.413 but over 70%.

NOTE Confidence: 0.8738667475

00:44:59.413 --> 00:45:00.946 And we are,

NOTE Confidence: 0.8738667475

00:45:00.950 --> 00:45:03.362 we hope that this will continue

NOTE Confidence: 0.8738667475

00:45:03.362 --> 00:45:04.568 with the updates.

NOTE Confidence: 0.838236597333333

00:45:04.570 --> 00:45:07.500 Now one of the questions is then when do we

NOTE Confidence: 0.838236597333333

00:45:07.570 --> 00:45:10.570 use allogeneic transplantation in remission.

NOTE Confidence: 0.838236597333333

00:45:10.570 --> 00:45:14.602 So we still use it in the patients with

NOTE Confidence: 0.838236597333333

00:45:14.602 --> 00:45:16.913 translocation 11Q23IN precursor TLL

NOTE Confidence: 0.838236597333333

00:45:16.913 --> 00:45:20.018 and patients with complex karyotypes,

NOTE Confidence: 0.838236597333333

00:45:20.020 --> 00:45:23.248 so abnormalities more than five and

NOTE Confidence: 0.838236597333333

00:45:23.248 --> 00:45:26.936 in the Philadelphia like L with CRLF

NOTE Confidence: 0.838236597333333

00:45:26.936 --> 00:45:29.810 two with Jack 2 mutations otherwise.

NOTE Confidence: 0.838236597333333

00:45:29.810 --> 00:45:31.394 So this constitutes.

NOTE Confidence: 0.838236597333333

00:45:31.394 --> 00:45:35.052 About maybe 15 to 20% of adult

NOTE Confidence: 0.838236597333333

00:45:35.052 --> 00:45:38.088 AML where we still use allogeneic

NOTE Confidence: 0.838236597333333

00:45:38.088 --> 00:45:40.533 transplant today and where we may

NOTE Confidence: 0.838236597333333

00:45:40.533 --> 00:45:43.230 use car T cells in the future.

NOTE Confidence: 0.838236597333333

00:45:43.230 --> 00:45:46.326 So this is an update in the AL solver.

NOTE Confidence: 0.838236597333333

00:45:46.330 --> 00:45:48.227 So this is where it all started.

NOTE Confidence: 0.838236597333333

00:45:48.230 --> 00:45:50.414 So even though I'm showing it at

NOTE Confidence: 0.838236597333333

00:45:50.414 --> 00:45:52.390 the end because it's L salvage,

NOTE Confidence: 0.838236597333333

00:45:52.390 --> 00:45:54.364 this is where all the research

NOTE Confidence: 0.838236597333333

00:45:54.364 --> 00:45:55.680 started with the MACD,

NOTE Confidence: 0.838236597333333

00:45:55.680 --> 00:45:58.687 you know to Zuma blinatumomab and

NOTE Confidence: 0.838236597333333

00:45:58.687 --> 00:46:01.170 I showed the update in the 112

NOTE Confidence: 0.838236597333333

00:46:01.170 --> 00:46:03.010 patients treated so far,

NOTE Confidence: 0.838236597333333

00:46:03.010 --> 00:46:05.386 marrow CR 883%,

NOTE Confidence: 0.838236597333333

00:46:05.386 --> 00:46:06.970 MRD negativity,

NOTE Confidence: 0.838236597333333

00:46:06.970 --> 00:46:10.410 83% define occlusive disease after

NOTE Confidence: 0.838236597333333

00:46:10.410 --> 00:46:13.162 we fractionated the inotuzumab.

NOTE Confidence: 0.838236597333333

00:46:13.170 --> 00:46:17.520 And kept the doors has gone from 9% to 1%.

NOTE Confidence: 0.838236597333333

00:46:17.520 --> 00:46:21.440 AML relapse used to be again death

NOTE Confidence: 0.838236597333333

00:46:21.440 --> 00:46:24.664 sentence and the overall 112 patients.

NOTE Confidence: 0.838236597333333

00:46:24.664 --> 00:46:27.256 The five year survival is 30%.

NOTE Confidence: 0.838236597333333

00:46:27.260 --> 00:46:29.260 Since we added the blinatumomab

NOTE Confidence: 0.838236597333333

00:46:29.260 --> 00:46:32.106 we have shown like in the younger

NOTE Confidence: 0.838236597333333

00:46:32.106 --> 00:46:34.801 patients when we added in auto blina

NOTE Confidence: 0.838236597333333

00:46:34.801 --> 00:46:37.447 we showed an improvement in the

NOTE Confidence: 0.838236597333333

00:46:37.447 --> 00:46:40.450 survival and the salvage when we added

NOTE Confidence: 0.838236597333333

00:46:40.450 --> 00:46:43.285 BLINATUMOMAB to the mini CD you know.

NOTE Confidence: 0.838236597333333

00:46:43.290 --> 00:46:46.038 We have shown an improvement in

NOTE Confidence: 0.838236597333333

00:46:46.038 --> 00:46:48.270 the three-year survival to 50%.

NOTE Confidence: 0.838236597333333

00:46:48.270 --> 00:46:49.581 In salvage one,

NOTE Confidence: 0.838236597333333

00:46:49.581 --> 00:46:52.640 the potential five year survival is now

NOTE Confidence: 0.838236597333333

00:46:52.722 --> 00:46:55.448 40% and we do not see a difference with

NOTE Confidence: 0.838236597333333

00:46:55.448 --> 00:46:57.569 or without alot transplant because I

NOTE Confidence: 0.838236597333333

00:46:57.569 --> 00:47:00.342 think we're losing a lot of patience

NOTE Confidence: 0.838236597333333

00:47:00.342 --> 00:47:02.558 to the transplant complications.

NOTE Confidence: 0.838236597333333

00:47:02.560 --> 00:47:05.440 So if we do the car T cells maybe we'll

NOTE Confidence: 0.838236597333333

00:47:05.519 --> 00:47:09.720 improve the survival further than 40%.

NOTE Confidence: 0.838236597333333

00:47:09.720 --> 00:47:11.020 Now people may say, well,

NOTE Confidence: 0.838236597333333

00:47:11.020 --> 00:47:12.280 we have the cartee cells,

NOTE Confidence: 0.838236597333333

00:47:12.280 --> 00:47:14.320 why have you ignored them?

NOTE Confidence: 0.838236597333333

00:47:14.320 --> 00:47:15.680 So on the left side,

NOTE Confidence: 0.838236597333333

00:47:15.680 --> 00:47:17.828 I showed you data with inotuzumab.

NOTE Confidence: 0.838236597333333

00:47:17.830 --> 00:47:19.558 We're not curing too many patients,

NOTE Confidence: 0.838236597333333

00:47:19.560 --> 00:47:20.616 maybe 20%.

NOTE Confidence: 0.838236597333333

00:47:20.616 --> 00:47:24.098 And we need the transplant here in

NOTE Confidence: 0.838236597333333

00:47:24.098 --> 00:47:26.562 the middle or the newer car T cells,

NOTE Confidence: 0.838236597333333

00:47:26.570 --> 00:47:29.895 the approved car T cells for the

NOTE Confidence: 0.838236597333333

00:47:29.895 --> 00:47:32.815 older patients and what you see is the

NOTE Confidence: 0.838236597333333

00:47:32.815 --> 00:47:35.646 two year survival is probably 20%.

NOTE Confidence: 0.838236597333333

00:47:35.650 --> 00:47:39.810 And now I show you the the UM in blue,

NOTE Confidence: 0.838236597333333

00:47:39.810 --> 00:47:42.145 the post amendment where the

NOTE Confidence: 0.838236597333333

00:47:42.145 --> 00:47:44.013 three-year survival is 50%.

NOTE Confidence: 0.838236597333333

00:47:44.020 --> 00:47:46.540 So I think in L salvage if I

NOTE Confidence: 0.838236597333333

00:47:46.540 --> 00:47:49.518 have a patient who has relapsed,

NOTE Confidence: 0.838236597333333

00:47:49.520 --> 00:47:51.784 I would use the mini CVD in oblina

NOTE Confidence: 0.838236597333333

00:47:51.784 --> 00:47:54.519 and then I would do the Carticel to

NOTE Confidence: 0.838236597333333

00:47:54.519 --> 00:47:56.320 improve the potential cure rate.

NOTE Confidence: 0.838236597333333

00:47:56.320 --> 00:47:58.846 Now why have I insisted several

NOTE Confidence: 0.838236597333333

00:47:58.846 --> 00:48:02.139 times on the CART sales to be

NOTE Confidence: 0.838236597333333

00:48:02.139 --> 00:48:04.664 tested in minimal residual disease?

NOTE Confidence: 0.838236597333333

00:48:04.670 --> 00:48:06.364 I think the car T cells today

NOTE Confidence: 0.838236597333333

00:48:06.364 --> 00:48:07.870 are being used the same way.

NOTE Confidence: 0.838236597333333

00:48:07.870 --> 00:48:09.374 We use allogeneic transplant

NOTE Confidence: 0.838236597333333

00:48:09.374 --> 00:48:12.034 in the 1970s in active disease

NOTE Confidence: 0.838236597333333

00:48:12.034 --> 00:48:14.890 and we're curing 20 to 30%.

NOTE Confidence: 0.838236597333333

00:48:14.890 --> 00:48:17.473 If we start using the car T cells and

NOTE Confidence: 0.838236597333333

00:48:17.473 --> 00:48:19.801 minimal residual disease the same way

NOTE Confidence: 0.838236597333333

00:48:19.801 --> 00:48:22.230 as allogeneic transplant is used today,

NOTE Confidence: 0.838236597333333

00:48:22.230 --> 00:48:24.258 then perhaps we we will cure

NOTE Confidence: 0.838236597333333

00:48:24.258 --> 00:48:25.610 many more of them.

NOTE Confidence: 0.838236597333333

00:48:25.610 --> 00:48:28.214 Now people will object to this saying,

NOTE Confidence: 0.838236597333333

00:48:28.220 --> 00:48:29.284 well no,

NOTE Confidence: 0.838236597333333

00:48:29.284 --> 00:48:31.944 you need active disease to

NOTE Confidence: 0.838236597333333

00:48:31.950 --> 00:48:34.788 to expand the car T cells.

NOTE Confidence: 0.858727813

00:48:34.790 --> 00:48:36.578 But the real world data shows

NOTE Confidence: 0.858727813

00:48:36.578 --> 00:48:39.450 that in fact when you do the car T

NOTE Confidence: 0.858727813

00:48:39.450 --> 00:48:41.065 cells in minimal residual disease,

NOTE Confidence: 0.858727813

00:48:41.070 --> 00:48:43.350 which are the red and the blue curve,

NOTE Confidence: 0.858727813

00:48:43.350 --> 00:48:45.490 you potentially cure more patients

NOTE Confidence: 0.858727813

00:48:45.490 --> 00:48:49.235 than if you do it in the setting

NOTE Confidence: 0.858727813

00:48:49.235 --> 00:48:51.259 of minimal residual disease.

NOTE Confidence: 0.858727813

00:48:51.260 --> 00:48:52.550 So in summary,

NOTE Confidence: 0.858727813

00:48:52.550 --> 00:48:54.700 I think in Philadelphia positive

NOTE Confidence: 0.858727813

00:48:54.700 --> 00:48:56.793 L Ponatinib BLINATUMOMAB will be

NOTE Confidence: 0.858727813

00:48:56.793 --> 00:48:59.495 the future form of therapy and I

NOTE Confidence: 0.858727813

00:48:59.572 --> 00:49:01.812 think the future of pre BL will

NOTE Confidence: 0.858727813

00:49:01.812 --> 00:49:04.022 be with much less chemotherapy

NOTE Confidence: 0.858727813

00:49:04.022 --> 00:49:07.127 for shorter duration combined with

NOTE Confidence: 0.858727813

00:49:07.127 --> 00:49:10.357 the antibodies using the car T

NOTE Confidence: 0.858727813

00:49:10.357 --> 00:49:12.907 cells in the setting of minimal

NOTE Confidence: 0.858727813

00:49:12.907 --> 00:49:15.181 residual disease and monitoring

NOTE Confidence: 0.858727813

00:49:15.181 --> 00:49:18.106 patients by next generation MRD.

NOTE Confidence: 0.858727813

00:49:18.110 --> 00:49:20.476 Now can we do better than this?

NOTE Confidence: 0.858727813

00:49:20.480 --> 00:49:22.824 So this is what I showed you with

NOTE Confidence: 0.858727813

00:49:22.824 --> 00:49:25.645 what I call the break or the dose

NOTE Confidence: 0.858727813

00:49:25.645 --> 00:49:28.278 dense mini CBD regimen and this is

NOTE Confidence: 0.858727813

00:49:28.278 --> 00:49:31.050 what we are testing today in older

NOTE Confidence: 0.858727813

00:49:31.138 --> 00:49:34.405 all and we may move it to younger all.

NOTE Confidence: 0.858727813

00:49:34.410 --> 00:49:36.076 So this is very similar to what

NOTE Confidence: 0.858727813

00:49:36.076 --> 00:49:37.380 you do in lymphoma,

NOTE Confidence: 0.858727813

00:49:37.380 --> 00:49:40.313 just six courses of therapy and perhaps

NOTE Confidence: 0.858727813

00:49:40.313 --> 00:49:43.707 the need of car T cell consolidation,

NOTE Confidence: 0.858727813

00:49:43.710 --> 00:49:45.348 but can we do better than this.

NOTE Confidence: 0.858727813

00:49:45.350 --> 00:49:48.458 So you may be aware that.

NOTE Confidence: 0.858727813

00:49:48.460 --> 00:49:52.240 There are T cell engagers which

NOTE Confidence: 0.858727813

00:49:52.240 --> 00:49:55.150 target more than CD19 or CD20.

NOTE Confidence: 0.858727813

00:49:55.150 --> 00:49:57.530 This is what we call the Tetra

NOTE Confidence: 0.858727813

00:49:57.614 --> 00:49:59.550 specific T cell engagers.

NOTE Confidence: 0.858727813

00:49:59.550 --> 00:50:01.630 This is not science fiction.

NOTE Confidence: 0.858727813

00:50:01.630 --> 00:50:04.024 These will be developed and there

NOTE Confidence: 0.858727813

00:50:04.024 --> 00:50:06.521 are also cartee cells which target

NOTE Confidence: 0.858727813

00:50:06.521 --> 00:50:08.165 more than one target,

NOTE Confidence: 0.858727813

00:50:08.170 --> 00:50:11.404 so dulci 19 and 20 cart set.

NOTE Confidence: 0.858727813

00:50:11.410 --> 00:50:13.690 So it is possible that in the future

NOTE Confidence: 0.858727813

00:50:13.690 --> 00:50:16.011 we will use very little chemotherapy

NOTE Confidence: 0.858727813

00:50:16.011 --> 00:50:18.537 to induce the patients in remission.

NOTE Confidence: 0.858727813

00:50:18.540 --> 00:50:20.785 Consolidate them with the Tetra

NOTE Confidence: 0.858727813

00:50:20.785 --> 00:50:23.606 specific T cell engagers and then

NOTE Confidence: 0.858727813

00:50:23.606 --> 00:50:25.590 we'll further consolidate them

NOTE Confidence: 0.858727813

00:50:25.590 --> 00:50:27.078 with Karti cells.

NOTE Confidence: 0.858727813

00:50:27.080 --> 00:50:28.916 So in total duration of therapy

NOTE Confidence: 0.858727813

00:50:28.916 --> 00:50:30.660 of three to four months,

NOTE Confidence: 0.858727813

00:50:30.660 --> 00:50:33.404 which will not be toxic and which

NOTE Confidence: 0.858727813

00:50:33.404 --> 00:50:36.007 will be highly effective and

NOTE Confidence: 0.858727813

00:50:36.007 --> 00:50:38.017 potentially highly curable.

NOTE Confidence: 0.858727813

00:50:38.020 --> 00:50:39.946 Thank you for your attention and

NOTE Confidence: 0.858727813

00:50:39.946 --> 00:50:42.159 I'm happy to answer any questions.

NOTE Confidence: 0.49338372

00:50:52.040 --> 00:50:56.340 Did I thank you for this absolutely fantastic

NOTE Confidence: 0.816172336666667

00:50:56.340 --> 00:50:58.902 lecture? And we actually have hematology

NOTE Confidence: 0.816172336666667

00:50:58.902 --> 00:51:01.279 faculty and trainees in the room.

NOTE Confidence: 0.816172336666667

00:51:01.280 --> 00:51:03.055 So I encourage everybody to

NOTE Confidence: 0.816172336666667

00:51:03.055 --> 00:51:04.475 ask questions in person.

NOTE Confidence: 0.816172336666667

00:51:04.480 --> 00:51:06.587 You're welcome to come up to the

NOTE Confidence: 0.816172336666667

00:51:06.587 --> 00:51:08.770 podium or I'm happy to repeat

NOTE Confidence: 0.816172336666667

00:51:08.770 --> 00:51:10.780 your questions from the audience.

NOTE Confidence: 0.816172336666667

00:51:10.780 --> 00:51:13.335 And then are you seeing

NOTE Confidence: 0.816172336666667

00:51:13.335 --> 00:51:15.379 questions from in soon?

NOTE Confidence: 0.841299015714286

00:51:20.980 --> 00:51:22.340 So I don't see questions

NOTE Confidence: 0.841299015714286

00:51:22.340 --> 00:51:25.280 in either that. Question.

NOTE Confidence: 0.820887385714286

00:51:27.180 --> 00:51:29.715 OK. Thank you for that

NOTE Confidence: 0.820887385714286

00:51:29.715 --> 00:51:30.729 excellent presentation.

NOTE Confidence: 0.820887385714286

00:51:30.730 --> 00:51:33.362 I think the pH positive word is largely

NOTE Confidence: 0.820887385714286

00:51:33.362 --> 00:51:35.980 driven by what happens at MD Anderson.

NOTE Confidence: 0.820887385714286

00:51:35.980 --> 00:51:37.515 And it's interesting to see

NOTE Confidence: 0.820887385714286

00:51:37.515 --> 00:51:39.393 it's negative disease and ALS is

NOTE Confidence: 0.820887385714286

00:51:39.393 --> 00:51:40.828 going that direction as well.

NOTE Confidence: 0.820887385714286

00:51:40.830 --> 00:51:44.316 Thank you for those excellent slides.

NOTE Confidence: 0.820887385714286

00:51:44.320 --> 00:51:46.518 You show a couple of interesting but

NOTE Confidence: 0.820887385714286

00:51:46.518 --> 00:51:49.500 equally provocative slides, right?

NOTE Confidence: 0.820887385714286

00:51:49.500 --> 00:51:51.008 Innovate and leaner trials,

NOTE Confidence: 0.820887385714286

00:51:51.008 --> 00:51:52.139 when published historically

NOTE Confidence: 0.820887385714286

00:51:52.139 --> 00:51:53.859 compared them against standard of

NOTE Confidence: 0.820887385714286

00:51:53.860 --> 00:51:56.708 chemo while the Cartesian trials.

NOTE Confidence: 0.820887385714286

00:51:56.708 --> 00:51:59.759 At INA and Lena failure in my mind,

NOTE Confidence: 0.820887385714286

00:51:59.760 --> 00:52:02.598 those were probably more refractory diseases.

NOTE Confidence: 0.820887385714286

00:52:02.600 --> 00:52:04.912 Based on the CR and the MRD rate

NOTE Confidence: 0.820887385714286

00:52:04.912 --> 00:52:07.201 that are reported across Kartes as

NOTE Confidence: 0.820887385714286

00:52:07.201 --> 00:52:09.655 is approved with the FDA agents.

NOTE Confidence: 0.820887385714286

00:52:09.660 --> 00:52:11.670 What's the hesitation of you

NOTE Confidence: 0.820887385714286

00:52:11.670 --> 00:52:12.876 trying them first?

NOTE Confidence: 0.820887385714286

00:52:12.880 --> 00:52:15.048 And why are we still pursuing with Inar

NOTE Confidence: 0.820887385714286

00:52:15.048 --> 00:52:16.520 Deena approaches with chemotherapy?

NOTE Confidence: 0.820887385714286

00:52:16.520 --> 00:52:17.600 I think the answer to that

NOTE Confidence: 0.820887385714286

00:52:17.600 --> 00:52:18.970 will lead to my next question.

NOTE Confidence: 0.793569498333333

00:52:19.700 --> 00:52:21.656 So that's a very important question.

NOTE Confidence: 0.793569498333333

00:52:21.660 --> 00:52:24.140 And the answer to this is I do

NOTE Confidence: 0.793569498333333

00:52:24.140 --> 00:52:26.245 not compare the single agent

NOTE Confidence: 0.793569498333333

00:52:26.245 --> 00:52:28.595 antibodies to the cartica results,

NOTE Confidence: 0.793569498333333

00:52:28.600 --> 00:52:31.840 but you have to do is compare the hyper

NOTE Confidence: 0.793569498333333

00:52:31.840 --> 00:52:35.200 cvad in oblina and salvage to the Carticel.

NOTE Confidence: 0.793569498333333

00:52:35.200 --> 00:52:36.380 So with the cart cells,

NOTE Confidence: 0.793569498333333

00:52:36.380 --> 00:52:37.900 if you take 100 patients,

NOTE Confidence: 0.793569498333333

00:52:37.900 --> 00:52:40.686 you're infusing probably only 2/3 of them

NOTE Confidence: 0.793569498333333

00:52:40.686 --> 00:52:43.400 because you lose some of the patients.

NOTE Confidence: 0.793569498333333

00:52:43.400 --> 00:52:46.368 In the process with the mini CD and

NOTE Confidence: 0.793569498333333

00:52:46.368 --> 00:52:48.876 Oblina you are treating 100% of

NOTE Confidence: 0.793569498333333

00:52:48.876 --> 00:52:51.024 the patients and you're getting a

NOTE Confidence: 0.793569498333333

00:52:51.024 --> 00:52:53.910 mirror CR rate of 85% and that does

NOTE Confidence: 0.793569498333333

00:52:53.910 --> 00:52:56.310 not negate the need and potential

NOTE Confidence: 0.793569498333333

00:52:56.388 --> 00:52:58.503 use of either allogeneic transplant

NOTE Confidence: 0.793569498333333

00:52:58.503 --> 00:53:01.800 or Cathy cell as a consolidation.

NOTE Confidence: 0.793569498333333

00:53:01.800 --> 00:53:05.283 So I do not see the antibodies and Carty

NOTE Confidence: 0.793569498333333

00:53:05.283 --> 00:53:09.039 cells as either or or competitive modalities,

NOTE Confidence: 0.793569498333333

00:53:09.040 --> 00:53:12.010 I see them as in fact

NOTE Confidence: 0.793569498333333

00:53:12.010 --> 00:53:13.495 synergistic modalities that.

NOTE Confidence: 0.793569498333333

00:53:13.500 --> 00:53:15.420 Have to be used in the proper sequence.

NOTE Confidence: 0.795680875

00:53:16.270 --> 00:53:18.490 I think that begs the question,

NOTE Confidence: 0.795680875

00:53:18.490 --> 00:53:20.300 since we're competing for the

NOTE Confidence: 0.795680875

00:53:20.300 --> 00:53:22.570 CD19 targets with Lena and Carti,

NOTE Confidence: 0.795680875

00:53:22.570 --> 00:53:24.691 why not just stick to your mini

NOTE Confidence: 0.795680875

00:53:24.691 --> 00:53:26.562 hyper Cvad prasina to Zoom app and

NOTE Confidence: 0.795680875

00:53:26.562 --> 00:53:27.812 then a different target, right?

NOTE Confidence: 0.795680875

00:53:27.812 --> 00:53:31.160 Because it's 19 or 22 expressions.

NOTE Confidence: 0.795680875

00:53:31.160 --> 00:53:32.412 Because the bigger question

NOTE Confidence: 0.795680875

00:53:32.412 --> 00:53:33.977 of how to sequence this,

NOTE Confidence: 0.795680875

00:53:33.980 --> 00:53:36.676 should blina be avoided,

NOTE Confidence: 0.795680875

00:53:36.676 --> 00:53:38.698 especially in car?

NOTE Confidence: 0.795680875

00:53:38.700 --> 00:53:39.771 Likely coordinating patients

NOTE Confidence: 0.795680875

00:53:39.771 --> 00:53:41.556 or however you design it,

NOTE Confidence: 0.795680875

00:53:41.560 --> 00:53:42.826 because there are some issues of

NOTE Confidence: 0.795680875

00:53:42.826 --> 00:53:44.409 competing for the same antigenic targets.

NOTE Confidence: 0.820880795714286

00:53:45.730 --> 00:53:47.395 So that's an important question

NOTE Confidence: 0.820880795714286

00:53:47.395 --> 00:53:49.060 and the Carticel experts have

NOTE Confidence: 0.820880795714286

00:53:49.122 --> 00:53:50.490 always brought the issue.

NOTE Confidence: 0.820880795714286

00:53:50.490 --> 00:53:53.248 If you treat the patients with blinatumomab,

NOTE Confidence: 0.820880795714286

00:53:53.250 --> 00:53:54.630 you may lose the target.

NOTE Confidence: 0.820880795714286

00:53:54.630 --> 00:53:56.562 And there were data that showed

NOTE Confidence: 0.820880795714286

00:53:56.562 --> 00:53:58.469 that the outcome may be worse.

NOTE Confidence: 0.820880795714286

00:53:58.470 --> 00:54:00.878 But there is this real world data

NOTE Confidence: 0.820880795714286

00:54:00.878 --> 00:54:03.504 which I've shown you have updated the

NOTE Confidence: 0.820880795714286

00:54:03.504 --> 00:54:05.778 results and they've shown that the

NOTE Confidence: 0.820880795714286

00:54:05.852 --> 00:54:07.952 results were worse with blinatumomab

NOTE Confidence: 0.820880795714286

00:54:07.952 --> 00:54:10.505 only in the patients who failed

NOTE Confidence: 0.820880795714286

00:54:10.505 --> 00:54:13.175 blinatumomab and the patients who respond

NOTE Confidence: 0.820880795714286

00:54:13.175 --> 00:54:15.420 to blinatumomab when they relapse.

NOTE Confidence: 0.820880795714286

00:54:15.420 --> 00:54:17.065 And they get the car T cells,

NOTE Confidence: 0.820880795714286

00:54:17.070 --> 00:54:19.146 the results are still as good.

NOTE Confidence: 0.820880795714286

00:54:19.150 --> 00:54:22.970 So it was a selection of the patients

NOTE Confidence: 0.820880795714286

00:54:22.970 --> 00:54:25.370 who are refractory to blinatumomab who

NOTE Confidence: 0.820880795714286

00:54:25.370 --> 00:54:28.087 were also refractory to the cartesius.

NOTE Confidence: 0.820880795714286

00:54:28.090 --> 00:54:31.780 So I have no hesitation and no issues with

NOTE Confidence: 0.820880795714286

00:54:31.780 --> 00:54:35.347 using blinatumomab before the car T cells,

NOTE Confidence: 0.820880795714286

00:54:35.350 --> 00:54:39.410 because loss of the target is minimal,

NOTE Confidence: 0.820880795714286

00:54:39.410 --> 00:54:41.438 if at all,

NOTE Confidence: 0.820880795714286

00:54:41.438 --> 00:54:45.494 and also because the updated data.

NOTE Confidence: 0.820880795714286

00:54:45.500 --> 00:54:48.125 Does not show that exposure to blinatumomab

NOTE Confidence: 0.820880795714286

00:54:48.125 --> 00:54:50.447 worsens the outcome of the car T cells.

NOTE Confidence: 0.820880795714286

00:54:50.450 --> 00:54:53.186 It was an epiphenomenon of the

NOTE Confidence: 0.820880795714286

00:54:53.186 --> 00:54:55.010 patients who are refractory,

NOTE Confidence: 0.820880795714286

00:54:55.010 --> 00:54:57.452 truly refractory to blina that also

NOTE Confidence: 0.820880795714286

00:54:57.452 --> 00:54:59.800 are refractory to the cortices.

NOTE Confidence: 0.752436460666667

00:55:00.760 --> 00:55:02.335 OK. Thank you. And last comment was

NOTE Confidence: 0.752436460666667

00:55:02.335 --> 00:55:04.225 going to make was now I'll let others

NOTE Confidence: 0.752436460666667

00:55:04.225 --> 00:55:06.157 take the question because a couple of my

NOTE Confidence: 0.752436460666667

00:55:06.157 --> 00:55:07.823 other colleagues have to go for Nicola.

NOTE Confidence: 0.724480298

00:55:10.280 --> 00:55:10.934 It's a nickel.

NOTE Confidence: 0.724480298

00:55:10.934 --> 00:55:12.460 I guess you have just one question.

NOTE Confidence: 0.724480298

00:55:12.460 --> 00:55:14.260 Have you noticed that you know

NOTE Confidence: 0.724480298

00:55:14.260 --> 00:55:15.944 by maybe not running phase

NOTE Confidence: 0.724480298

00:55:15.944 --> 00:55:17.636 three trial randomized trials,

NOTE Confidence: 0.724480298

00:55:17.640 --> 00:55:20.314 but these early phase trials that you

NOTE Confidence: 0.724480298

00:55:20.314 --> 00:55:22.309 have better inclusion of you know,

NOTE Confidence: 0.724480298

00:55:22.310 --> 00:55:23.845 people who may be more

NOTE Confidence: 0.724480298

00:55:23.845 --> 00:55:25.380 hesitant to enroll in trials,

NOTE Confidence: 0.724480298

00:55:25.380 --> 00:55:27.978 so underrepresented population.

NOTE Confidence: 0.837536906

00:55:28.640 --> 00:55:30.410 Well that's one issue because

NOTE Confidence: 0.837536906

00:55:30.410 --> 00:55:32.695 as I mentioned today with all

NOTE Confidence: 0.837536906

00:55:32.695 --> 00:55:34.915 the targeted therapies with the

NOTE Confidence: 0.837536906

00:55:34.915 --> 00:55:36.691 multitudes of targeted therapies,

NOTE Confidence: 0.837536906

00:55:36.700 --> 00:55:39.436 it's very difficult for an investigator.

NOTE Confidence: 0.837536906

00:55:39.440 --> 00:55:42.312 We truly and transparently

NOTE Confidence: 0.837536906

00:55:42.312 --> 00:55:44.598 states a situation of equipoise,

NOTE Confidence: 0.837536906

00:55:44.598 --> 00:55:46.950 meaning that you tell the patient,

NOTE Confidence: 0.837536906

00:55:46.950 --> 00:55:51.540 look, I have hyper cvad. Um.

NOTE Confidence: 0.618526289555556

00:55:55.430 --> 00:55:57.830 Imagine versus ponatinib, blinatumomab

NOTE Confidence: 0.618526289555556

00:55:57.830 --> 00:56:02.302 and I truly believe that I do not know

NOTE Confidence: 0.618526289555556

00:56:02.302 --> 00:56:05.365 the answer to to that, to that strategy.

NOTE Confidence: 0.618526289555556

00:56:05.365 --> 00:56:09.030 So I think if you tell the patient,

NOTE Confidence: 0.618526289555556

00:56:09.030 --> 00:56:11.389 look, we have gathered all our knowledge

NOTE Confidence: 0.618526289555556

00:56:11.389 --> 00:56:13.684 and to the best of my knowledge

NOTE Confidence: 0.618526289555556

00:56:13.684 --> 00:56:16.169 this is a trial that will help you.

NOTE Confidence: 0.618526289555556

00:56:16.170 --> 00:56:20.614 First, it would reduce the restrictive

NOTE Confidence: 0.618526289555556

00:56:20.614 --> 00:56:24.070 eligibility criteria, which was.

NOTE Confidence: 0.618526289555556

00:56:24.070 --> 00:56:26.982 You can. You can negotiate better within

NOTE Confidence: 0.618526289555556

00:56:26.982 --> 00:56:30.109 your own Ind studies and in single

NOTE Confidence: 0.618526289555556

00:56:30.109 --> 00:56:32.797 ARM trials to reduce the obstacles.

NOTE Confidence: 0.618526289555556

00:56:32.800 --> 00:56:34.710 And second, you probably can

NOTE Confidence: 0.618526289555556

00:56:34.710 --> 00:56:36.620 convince the patients better that

NOTE Confidence: 0.618526289555556

00:56:36.685 --> 00:56:38.683 what you're offering them is truly

NOTE Confidence: 0.618526289555556

00:56:38.683 --> 00:56:40.938 what you believe is best for them.

NOTE Confidence: 0.774941991666667

00:56:41.670 --> 00:56:43.410 Thank you so much Doctor Baldev,

NOTE Confidence: 0.774941991666667

00:56:43.410 --> 00:56:44.420 come on to the podium.

NOTE Confidence: 0.652388093333333

00:56:47.590 --> 00:56:49.005 Doctor Contagion, thank you very

NOTE Confidence: 0.652388093333333

00:56:49.005 --> 00:56:50.137 much for excellent presentation.

NOTE Confidence: 0.652388093333333

00:56:50.140 --> 00:56:53.094 My question is about use of Ponatinib

NOTE Confidence: 0.652388093333333

00:56:53.094 --> 00:56:55.074 and BLINATUMOMAB and pH positive

NOTE Confidence: 0.652388093333333

00:56:55.074 --> 00:56:57.016 L so you know this is applicable

NOTE Confidence: 0.652388093333333

00:56:57.016 --> 00:56:58.735 to younger and older patients and

NOTE Confidence: 0.652388093333333

00:56:58.735 --> 00:57:00.744 obviously there is a lot of concern

NOTE Confidence: 0.652388093333333

00:57:00.744 --> 00:57:02.527 about the natib related toxicity.

NOTE Confidence: 0.652388093333333

00:57:02.530 --> 00:57:03.955 Would you see any contraindications

NOTE Confidence: 0.652388093333333

00:57:03.955 --> 00:57:06.034 and what do you think about long

NOTE Confidence: 0.652388093333333

00:57:06.034 --> 00:57:07.534 term use of management after

NOTE Confidence: 0.652388093333333

00:57:07.534 --> 00:57:08.990 you finished initial treatment,

NOTE Confidence: 0.652388093333333

00:57:08.990 --> 00:57:10.230 how long should we continue?

NOTE Confidence: 0.793629846666667

00:57:11.240 --> 00:57:13.825 So you're absolutely correct that

NOTE Confidence: 0.793629846666667

00:57:13.825 --> 00:57:15.893 Ponatinib has significant toxicities.

NOTE Confidence: 0.793629846666667

00:57:15.900 --> 00:57:18.643 That's why we reduce it from 45.

NOTE Confidence: 0.793629846666667

00:57:18.643 --> 00:57:20.958 Actually in the ponatinib Lina,

NOTE Confidence: 0.793629846666667

00:57:20.960 --> 00:57:23.340 we start with 30 milligrams and we

NOTE Confidence: 0.793629846666667

00:57:23.340 --> 00:57:25.591 reduce it to 15 milligrams usually

NOTE Confidence: 0.793629846666667

00:57:25.591 --> 00:57:28.279 within a month as I showed you.

NOTE Confidence: 0.793629846666667

00:57:28.280 --> 00:57:30.518 But your question is very legitimate.

NOTE Confidence: 0.793629846666667

00:57:30.520 --> 00:57:33.310 What do we do with all the patients who

NOTE Confidence: 0.793629846666667

00:57:33.310 --> 00:57:36.098 have already existing arterial occlusive

NOTE Confidence: 0.793629846666667

00:57:36.098 --> 00:57:38.498 events or cardiovascular events.

NOTE Confidence: 0.793629846666667

00:57:38.500 --> 00:57:41.190 So in those situations there's.

NOTE Confidence: 0.793629846666667

00:57:41.190 --> 00:57:44.920 One could design a trial

NOTE Confidence: 0.793629846666667

00:57:44.920 --> 00:57:47.158 with Bosutinib Blinatumomab.

NOTE Confidence: 0.793629846666667

00:57:47.160 --> 00:57:50.530 Or with the satanic Blinatumomab,

NOTE Confidence: 0.793629846666667

00:57:50.530 --> 00:57:53.370 but you're going to encounter

NOTE Confidence: 0.793629846666667

00:57:53.370 --> 00:57:56.254 perhaps relapse rate of maybe

NOTE Confidence: 0.793629846666667

00:57:56.254 --> 00:57:59.492 10 to 20% with 315I clones.

NOTE Confidence: 0.793629846666667

00:57:59.492 --> 00:58:01.547 You hope that the Blinatumomab

NOTE Confidence: 0.793629846666667

00:58:01.547 --> 00:58:03.310 will suppress these clones,

NOTE Confidence: 0.793629846666667

00:58:03.310 --> 00:58:06.230 and if you try to design A regimen like this,

NOTE Confidence: 0.793629846666667

00:58:06.230 --> 00:58:09.023 I would encourage to use the blinatumomab

NOTE Confidence: 0.793629846666667

00:58:09.023 --> 00:58:11.448 starting day one with the induction

NOTE Confidence: 0.793629846666667

00:58:11.448 --> 00:58:14.143 rather than as the Italians did where

NOTE Confidence: 0.793629846666667

00:58:14.219 --> 00:58:17.179 they used it three months into a remission.

NOTE Confidence: 0.793629846666667

00:58:17.180 --> 00:58:20.956 So today if I have a patient with

NOTE Confidence: 0.793629846666667

00:58:20.956 --> 00:58:22.140 cardiovascular contraindications,

NOTE Confidence: 0.793629846666667

00:58:22.140 --> 00:58:24.270 arterial occlusive events.

NOTE Confidence: 0.793629846666667

00:58:24.270 --> 00:58:29.368 Then by all means I I could start

NOTE Confidence: 0.793629846666667

00:58:29.368 --> 00:58:32.047 them with with desatino blinatumomab,

NOTE Confidence: 0.793629846666667

00:58:32.047 --> 00:58:35.890 but then you have to somehow carve

NOTE Confidence: 0.793629846666667

00:58:35.980 --> 00:58:39.018 out a time space where you give

NOTE Confidence: 0.793629846666667

00:58:39.018 --> 00:58:41.912 them ponatinib to try to eliminate

NOTE Confidence: 0.793629846666667

00:58:41.912 --> 00:58:44.380 those perhaps 10% of the patients

NOTE Confidence: 0.793629846666667

00:58:44.380 --> 00:58:46.872 who can relapse with the T315 icron.

NOTE Confidence: 0.793629846666667

00:58:46.872 --> 00:58:49.102 Alternatively you can see what

NOTE Confidence: 0.793629846666667

00:58:49.102 --> 00:58:51.660 the residual disease is left with

NOTE Confidence: 0.793629846666667

00:58:51.660 --> 00:58:53.570 next generation sequencing and if

NOTE Confidence: 0.793629846666667

00:58:53.570 --> 00:58:55.966 you see it there then you can.

NOTE Confidence: 0.793629846666667

00:58:55.970 --> 00:58:57.060 Change 2.18.

NOTE Confidence: 0.734378402083333

00:58:58.220 --> 00:58:59.936 So following with Jim, next Gen

NOTE Confidence: 0.734378402083333

00:58:59.936 --> 00:59:01.593 sequencing rather than with PCR is

NOTE Confidence: 0.734378402083333

00:59:01.593 --> 00:59:02.961 what you suggest because you know

NOTE Confidence: 0.734378402083333

00:59:02.961 --> 00:59:04.878 PCR is reasonably sensitive as well.

NOTE Confidence: 0.811219101666667

00:59:05.510 --> 00:59:08.786 So the PCR detects 100,000 cells.

NOTE Confidence: 0.811219101666667

00:59:08.790 --> 00:59:12.150 The NGS when successful can

NOTE Confidence: 0.811219101666667

00:59:12.150 --> 00:59:14.166 measure 3,000,000 cents.

NOTE Confidence: 0.811219101666667

00:59:14.170 --> 00:59:16.220 We're doing both of them.

NOTE Confidence: 0.811219101666667

00:59:16.220 --> 00:59:17.888 Another interesting finding which

NOTE Confidence: 0.811219101666667

00:59:17.888 --> 00:59:20.390 I didn't mention is we have

NOTE Confidence: 0.811219101666667

00:59:20.459 --> 00:59:22.509 patients who are NCGS negative

NOTE Confidence: 0.811219101666667

00:59:22.510 --> 00:59:24.568 and PCR positive at low levels.

NOTE Confidence: 0.811219101666667

00:59:24.570 --> 00:59:26.910 So you could say, well is this a fluke,

NOTE Confidence: 0.811219101666667

00:59:26.910 --> 00:59:28.446 how can that be?

NOTE Confidence: 0.811219101666667

00:59:28.446 --> 00:59:30.750 And we think that the eggs,

NOTE Confidence: 0.811219101666667

00:59:30.750 --> 00:59:33.222 because it measures the immunoglobulin heavy

NOTE Confidence: 0.811219101666667

00:59:33.222 --> 00:59:36.119 chain is looking only at the lymphoblast.

NOTE Confidence: 0.811219101666667

00:59:36.120 --> 00:59:40.544 But there could be some BCR able

NOTE Confidence: 0.811219101666667

00:59:40.550 --> 00:59:44.387 signals in the myeloid cells which

NOTE Confidence: 0.811219101666667

00:59:44.387 --> 00:59:47.249 will not cause an ACL relapse.

NOTE Confidence: 0.811219101666667

00:59:47.250 --> 00:59:49.923 And in fact this is what we are noticing.

NOTE Confidence: 0.811219101666667

00:59:49.930 --> 00:59:52.030 There's a subset of patients

NOTE Confidence: 0.811219101666667

00:59:52.030 --> 00:59:54.130 who are NGS MRD negative,

NOTE Confidence: 0.811219101666667

00:59:54.130 --> 00:59:58.368 PCR positive at low level 0.01 or 0.1%.

NOTE Confidence: 0.811219101666667

00:59:58.368 --> 01:00:00.804 And these patients are not relapsing,

NOTE Confidence: 0.811219101666667

01:00:00.810 --> 01:00:03.491 so we're not sending them to transplant

NOTE Confidence: 0.811219101666667

01:00:03.491 --> 01:00:05.999 if they are NGS MRD negative.

NOTE Confidence: 0.811219101666667

01:00:06.000 --> 01:00:07.578 But we haven't published on this.

NOTE Confidence: 0.811219101666667

01:00:07.580 --> 01:00:08.528 It's A twist.

NOTE Confidence: 0.8402872825

01:00:10.560 --> 01:00:14.340 To some patients so more specialized

NOTE Confidence: 0.8402872825

01:00:14.340 --> 01:00:16.710 than what? What one needs to know.

NOTE Confidence: 0.654074203384615

01:00:17.590 --> 01:00:19.280 And duration of Inactive and

NOTE Confidence: 0.654074203384615

01:00:19.280 --> 01:00:20.632 younger patients receive treatment

NOTE Confidence: 0.654074203384615

01:00:20.632 --> 01:00:22.418 with minor ponatinib combination.

NOTE Confidence: 0.827764602

01:00:22.690 --> 01:00:24.010 So we do not know,

NOTE Confidence: 0.827764602

01:00:24.010 --> 01:00:25.886 but here's what we're going to do.

NOTE Confidence: 0.827764602

01:00:25.890 --> 01:00:28.946 We're going to adopt strategy similar to CML.

NOTE Confidence: 0.827764602

01:00:28.950 --> 01:00:31.098 We're going to say if the

NOTE Confidence: 0.827764602

01:00:31.098 --> 01:00:32.530 patient is NCGS negative,

NOTE Confidence: 0.827764602

01:00:32.530 --> 01:00:34.950 MRD negative for five years,

NOTE Confidence: 0.827764602

01:00:34.950 --> 01:00:37.498 we are going to either stop the

NOTE Confidence: 0.827764602

01:00:37.498 --> 01:00:39.405 treatment for toxicities or accidentally

NOTE Confidence: 0.827764602

01:00:39.405 --> 01:00:42.002 if the patient doesn't want it or

NOTE Confidence: 0.827764602

01:00:42.002 --> 01:00:44.066 perhaps in the future on purpose,

NOTE Confidence: 0.827764602

01:00:44.070 --> 01:00:46.482 we're going to tell them you have been NGS,

NOTE Confidence: 0.827764602

01:00:46.490 --> 01:00:48.170 MRD negative for five years.

NOTE Confidence: 0.827764602

01:00:48.170 --> 01:00:50.898 They think the disease is not going to

NOTE Confidence: 0.827764602

01:00:50.898 --> 01:00:53.614 relapse and perhaps ponatinib will will

NOTE Confidence: 0.827764602

01:00:53.614 --> 01:00:56.338 buy you more problems than benefits.

NOTE Confidence: 0.827764602

01:00:56.340 --> 01:00:58.532 So we're going to stop and see what

NOTE Confidence: 0.827764602

01:00:58.532 --> 01:01:00.887 happens the same way as we do in

NOTE Confidence: 0.827764602

01:01:00.887 --> 01:01:02.505 chronic myeloid leukemia with the

NOTE Confidence: 0.827764602

01:01:02.505 --> 01:01:04.450 concept of treatment free remission.

NOTE Confidence: 0.827764602

01:01:04.450 --> 01:01:05.600 But we're not there yet.

NOTE Confidence: 0.827764602

01:01:05.600 --> 01:01:08.000 We need to get to a population of

NOTE Confidence: 0.827764602

01:01:08.000 --> 01:01:09.901 patients who are NGS MRD negative

NOTE Confidence: 0.827764602

01:01:09.901 --> 01:01:12.137 for five years or at least three

NOTE Confidence: 0.827764602

01:01:12.137 --> 01:01:14.093 years to offer them that kind

NOTE Confidence: 0.827764602

01:01:14.093 --> 01:01:16.160 of a treatment option if they

NOTE Confidence: 0.827764602

01:01:16.160 --> 01:01:17.960 have toxicities or side effects.

NOTE Confidence: 0.827764602

01:01:18.950 --> 01:01:19.480 Thank you.

NOTE Confidence: 0.801806937692308

01:01:20.960 --> 01:01:22.010 Right. I think we're at the top

NOTE Confidence: 0.801806937692308

01:01:22.010 --> 01:01:23.229 of the hour at Doctor Kantarjian.

NOTE Confidence: 0.801806937692308

01:01:23.230 --> 01:01:25.138 Thank you so much for this

NOTE Confidence: 0.801806937692308

01:01:25.138 --> 01:01:26.092 absolutely spectacular lecture.

NOTE Confidence: 0.801806937692308

01:01:26.100 --> 01:01:28.872 And Dr Sears, thank you for

NOTE Confidence: 0.801806937692308

01:01:28.872 --> 01:01:30.720 bringing these amazing advances

NOTE Confidence: 0.801806937692308

01:01:30.802 --> 01:01:32.837 to our lecture hall today.

NOTE Confidence: 0.801806937692308

01:01:32.840 --> 01:01:33.944 So thank you so much and thank you,

NOTE Confidence: 0.801806937692308

01:01:33.950 --> 01:01:35.550 Amar, for the wonderful introduction.

NOTE Confidence: 0.865950278571429

01:01:36.020 --> 01:01:38.092 Thank you very much for the honor of

NOTE Confidence: 0.865950278571429

01:01:38.092 --> 01:01:39.967 inviting me to this special lecture.