So the abstracts that are selected were chosen by the speakers because they are the most clinically relevant and they are grouped in areas of clinical unmet need. Of course that doesn’t mean that other abstracts that have been presented in the meeting or are as good or important, but you have to choose basically for this type of sessions important to remember. Again, many of the ash presentations. Basically are focused on preliminary data and subsequently some of those results might be modified and they are still not peer reviewed,
so this is important to keep up in mind as we think about the data that will be presented. That there will be a recording of this session and all the sessions. This will be available and accessible as during material in addition to the slides and at the end of the entire series, the six sessions you’ll be able to claim your CME credit. For those of you who wants to claim it. After you answer a brief evaluation and some feedback about how we can improve the format of the series.

So today it’s a pleasure to introduce the speakers.
00:01:20.680 --> 00:01:23.396 Sorry, there’s a typo here is clearly
NOTE Confidence: 0.8310966
00:01:23.396 --> 00:01:26.148 this is not on my Lloyd update.
NOTE Confidence: 0.8310966
00:01:26.150 --> 00:01:28.110 It’s the pediatric leukemia updates.
NOTE Confidence: 0.8310966
00:01:28.110 --> 00:01:31.568 So Doctor but also full start by.
NOTE Confidence: 0.8310966
00:01:31.570 --> 00:01:33.495 Talking to us about major
NOTE Confidence: 0.8310966
00:01:33.495 --> 00:01:35.420 updates from the meeting about
NOTE Confidence: 0.8310966
00:01:35.494 --> 00:01:37.558 Accutane for blastic leukemia.
NOTE Confidence: 0.8310966
00:01:37.560 --> 00:01:39.792 Then Doctor Nina Kadan Lotic will
NOTE Confidence: 0.8310966
00:01:39.792 --> 00:01:42.976 update us and I think some of the
NOTE Confidence: 0.8310966
00:01:42.976 --> 00:01:44.991 most important updates from the
NOTE Confidence: 0.8310966
00:01:44.991 --> 00:01:47.828 ASH meeting on pediatric leukemias,
NOTE Confidence: 0.8310966
00:01:47.830 --> 00:01:49.542 including LL, of course,
NOTE Confidence: 0.8310966
00:01:49.542 --> 00:01:52.110 and then at the end, Dr.
NOTE Confidence: 0.8310966
00:01:52.110 --> 00:01:55.050 Nikita Shah will present to us or
NOTE Confidence: 0.8310966
00:01:55.050 --> 00:01:58.244 will moderate the Q&A session for any
NOTE Confidence: 0.8310966
00:01:58.244 --> 00:02:01.020 questions that will arise about the
talks that will be presented to the.

Abstractly presented, but also about any other additional questions about pediatric hematology, and in general so we look forward to a very exciting discussion, and I would like to start by introducing Doctor Nikolai Bodos. If our associate professor of medicine, here in the hematologist auction, who focuses on Accutane for blastic leukemia. Nicola, you’re on mute. He would go so almost there next. Let me see. Looking for my PowerPoint here ago.
Right, and do you see a single screen?

Yep OK alright. So hold on one second let me just get to the beginning of all this.

Not sure why this happened this way.

So I would like to start from a brief introduction, so this are my disclosures.

And we will be talking about acute lymphoblastic leukemia, which is further abbreviated as a LL.

This is still the disease of the young and I represent adult hematology here, so Nina will be talking to what’s happening in this field in pediatric hematology.

And we certainly learned a lot over the last years from our pediatric colleagues,
so this shows you that about 6000 patients are diagnosed with acute lymphoblastic leukemia per year in the United States, and only about 2000 of them are actually adults. Median age of diagnosis, as you can see, is around 9 years old and about 1500 deaths per year, most of them. So these survival remains very different between pediatric LL patients and adult male patients, and you can see 5 year old survival is about 90% and children and still half of that in adults.
So we’re excited to have approvals for newbs CLL therapies. You can call them immuno therapies. This includes approval of Blinatumomab in 2017 by FDA. It’s a bispecific T cell engager attacking CD 19 positive B cells including the lymphoblasts. Also in 2017 there was an approval notice amalgamation which is antibody drag Queen. You get attacking CD 22 on again B cells and finally approval of. It is a jungle occlusal. The car T cell therapy for younger patients with relapsed refractory disease. Again,
attacking CD 19 cells on view lymphoblasts.

This is for patients who are younger than 26 or younger,

so the mechanism of action is bluna.

Tumors represent on this slide is bite.

Bispecific T cell engager,

which attaches cytotoxic T cells to tumor cells.

Through a CD 19 and by means of this attachment increases the.

A pop ptosis of this tumor cells?

So the studies which put this on the map and make it available to us are tower phase three study,

which looked at Glenna to mob
in relapsed refractory disease
against conventional chemotherapy.
And as you can see,
there was a survival difference
of 7.7 versus four months,
which was statistically significant.
Response rate was 44%,
with 76% achieving mean negative,
minimal residual disease.
So this is all control study
looking at BLT amount for Peach paused,
looking at BLT amount for Peach paused,
available patients and again you can
see that the survival here for this
patients with relapsed refractory pH.
Posted bail is about 7.1 months with a response rate of 36% among those patients. So the drug is approved for both relapse refractory pH positive and pH negative B cell L patients. The next drug is in its mother's advice and its antibody drag Queen you get. Which brings Felicia my son to the B cell positive for CD 22. After internalization, the drug is released inside the cell and code goes to the nucleus to cause DNA damage in a pop ptosis. Some of the drugs you can see can be flexed.
and circulating blood causing the main side effect of this medication in occlusive disease and deliver. So this study we as a Cancer Center participated in and contributed patients to innovate phase three study looked at the data some up again and relapse refractory B cell L patients including Peach posed accomplish negative and showed improved survival when compared to standard therapy group. So the median overall survival was 7.7 versus 6.7 months and response rate was kind of double of what we see in Blender. Two map studies about 80% again with most of the patients 17%.
Accomplishing negative minimal residual disease status. So today I’m going to talk about four studies and basically all of them. Are about adult patients with the introduction of drugs, which I used in relapse refractory setting in the frontline therapy for some of them. We are trying to capitalize on the accomplishment and approval of this drugs and try to move them up front to get our patients to have better responses and ultimately survival. So the studies are grouped based on our approach to management of
these patients and refers to wall.

Look at the patient age and then Peach chromosome status, pH positive and pH. Negative patients are treated quite differently as you will see.

So the first study is from MD Anderson Cancer Center and I would like to thank all of the presenting authors who gave me their slides to share with you today. So the first study is about pH, negative B cell L adults who were treated with Hyper Civitan sequential blinatumomab. And again, the speech negative patients. So let’s have a look at the results of this phase two study from MD Anderson.
The primary endpoint of the study was relapse-free survival with secondary endpoints. You can look at overall response rate and MRD negativity rate. This study included newly diagnosed patients with pH-negative B cell, LL patients who received one cycle induction chemotherapy prior to enrollment. Of course, they had to get to MD Anderson from elsewhere where they treated. That's why they kind of broaden the inclusion criteria this way. Interestingly, they included patients age 14 and older.
so this is usually going in the territory where Nina treats patients, so they allowed enrollment of younger patients. Have to be eligible for intensive chemotherapy. Equal Performance status of three or less adequate organ function and no significant CNS involvement. So CNS patients patient was seen as leukemia were excluded, so this is the schema of the study. You can see this is 4 cycles of hyper seaward, part A&B, with addition of Rituxan two patients for CD. 20 positive or over to map another
CD 20 antibody.

As well as use of prophylactic it chemotherapy sectarian metrics 8 so

after finishing this intensive phase,

patients would go to blender two

more phase where they would receive

more phase where they would receive

four cycles of blinatumomab,

four weeks on continuous infusion,

two weeks off and.

go to maintenance phase which

is actually 18 as opposed to 36

months and the blender two map is

incorporated between the cycles of pomp,

chemotherapy and additional

3 cycles of blinatumomab.
As you can see here. So these are the patients who were enrolled in the study, 38 patients. And as you can see the age difference. The H variance was between 17 and 59. The patients about 32% of patients had Adverse karyotype the pH like positive patients were 19% as defined by presence of CRLF 21. Flow cytometry testing, and 27% of patients get TP 53 mutation. So this is one of the secondary points. So this is one of the secondary points. accomplished in 81% of patients and then yes, two Mob and at the end of 32 patients.
accomplished a CR and MRD,

negativity was 71%.

After induction and 97% at anytime during the study,

early mortality was at 0.

So.

Relapse free survival at two years is 71%.

At one year,

80% overall survival was at two years of 80%,

so it’s pretty impressive numbers for patients for adults with B cell LL.

Of course you know this particular group
included younger patients 17 and older.

So this is comparing the results of current study in blue with another study done in the same institution earlier hyper.

See what with over to Mumbai think 60 plus patient 69 patients and you can see that both studies show comparable to overall survival,

but the plateau of no mortality after two years for the current study is very encouraging.

So the side effects specifically adverse events of interest.

Related to Blender two map highlighted in yellow side,
The kind Release syndrome Grade 3 four was only seen in one patient and. It in your logical amounts were seen in 13% of patients. One patient, discontinued blended home up due to toxicity. It was great to encephalopathy and dysphasia, so the conclusion of this presentation is here. Hyper Squad with Sequential Blinatumomab is highly effective. Frontline therapy for pH negative deal adults, MRD rate was 97% year old, survival was 80%. There are no relapses beyond two years.
There was low rate of grade three adverse events related to blinatumomab and at this time protocol is amended and now includes in autism observation. In addition to Blender tomorrow for frontline management of this group of patients. So the 2nd. Study or two studies. I would like to talk about our about older adults and the definition of all the adults in BLD world is different in different places. The first study again from this German leukemia group and you know their definition of older adult was
55 and older and then there will be.

I will present results of meaning high perceived within autism up with or without Minotaur map.

Here the definition is age 60 and older.

So let’s start from the German study.

So this is. Initial one phase two trial which looked at induction treatment with three cycles of inotuzumab instead.

with three cycles of inotuzumab instead of regular chemotherapy induction.

followed by standard to consolidate if approach from Journal Leukemia Group, which as you can see, is reasonably intense. Includes a asparaginase administration.

It looks like 3 times.
Also for CD 20 positive patients

there is rituximab and so on.

So this consolidation requires admission.

And then there is about you know half

of 6 MP methotrexate maintenance.

Uh, so. The results,

which were presented included

mostly 31 patients,

those who received at least one

cycle Organism up induction and

could be assessed for remission.

So the patient characteristics table

shows that patients which were enrolled

were between 56 and 80 years old and

you can see that all of these patients

obviously had CD 22 expression.
Different density of expression is represented here.

So, uh, the secondary point end point of the study was response rates, and you can see that out 31 patients they looked at 100% had response CRCR I. And now this actually, you know, for patients receive three cycles. 84% so some of them have their early relapses and there are no early deaths. 80% of patients with this strategy.

And then MRD was accomplished in 78% of patients with early relapses and there were some haematological responses.
As you can see, a total of three allogeneic stem transplants were provided to three of those patients and one patient went to transplant after relapse, so only four patients were transplanted out of this 31. The primary endpoint is on the right, event free survival at one year, so was 87%. For all the group of patients, overall survival at one year was also 87% events were defined, persisting one marrow usable after two cycles went into some relapse or death.
So this is a side effects are in relation to inductions within a two zone map. As you can see after initial induction that are more cytopenias. But you know this kind of decreases overtime obviously and then the side effect of interest. Here adverse event of interest would be LFT abnormalities because we inclusive disease is one of those things we watch for and then some of treated patients and LFTS elevation were not common and no patients had been occlusive disease. Of course only four.
Patients out of city one went to allogeneic stem cell transplant. The conclusion of the study in this map seems to be highly effective as monotherapy and using haematological remission in all patients with MRD accomplished in more than 70% of patients had acceptable toxicity. No early deaths observed. Novena occlusive disease. Promising survival 80% overall survival benefit survival at one year and finally another man has a great potential to become standard induction option in all the patients with newly diagnosed
So we’re not using this regiment at Yale, and I don’t think it is frequently used in the United States, so we’re kind of more interested in high perceived, which is of course the Backbone Regiment for MD Anderson Cancer Center and many hyper.

See what is something we used in some patients over years? Older patients with?

We sell LL as well as T cell LL.

So I’m going to share with you the results of this mini high perceived study, which added in a tumor band later one blinatumomab for management of all the patients with Vissel.
So here, ages 60 or more before on status up to three. Adequate organ function ejection fraction should be more than 40%. So those reduced so-called meaning hyper see what consists of cyclophosphamide reduced by 50% dexamethasone, reduced by 50%.

There is no under cycling metrics take high dose metrics, a reduced by 75% anhydrous site, urban by 83%.

So the inner tubes mob was added one day, three for the first 4 courses and rituximab was used as usual on D2 and eight with four CD 20 positive patients.
Patients already also received it.

Chemotherapy prophylaxis.

So this is the schema of the study.

You can see that there are the eight cycles with it chemotherapy administered during the first 4 as well as in ministered.

As I specified overtime, the dozing off into some other Wolf first six patients higher dose than those was like lower dose than hide.

Those was escalated, and then finally at the end they settled on a dose of 1.3 on cycle one and one.

On Cycle 2,
So the study was further modified after enrollment of 49 patients, and here you can see that four out of eight cycles, we only have 4 cycles of chemotherapy. Now Inotuzumab is given twice per cycle, and the dosing is here and blender to map. 4 cycles of blinatumomab I added in consolidation phase and maintenance was reduced from 36 months to 18 months and now also includes four cycles of blinatumomab. So once again, this is starting from patient 50. An further total number of patients enrolled in this phase.
Two trial with 70 patients. So 20 patients receive treatment this way. So this is characteristics of the patients. And as you can see that you know these are all the patients 6281 and there are 41% of them are 70 or older. The complex karyotype as well as other cytogenetic abnormalities which I usually associate with worse outcomes. I seen in at least a third of those patients. As well as quite a few patients had that Peach like disease and TP53 mutated disease, so the overall response rate was 98%. This includes CR,
CR P&CRI and there were no early deaths.

MRD response on the 21 I was observed in

So the reason that why numbers

Five patients were enrolled in

CR on this

study. This is the patients who received

one cycle before they were enrolled

because they have to make it to MD

Anderson to start their treatment.

So these are grade three adverse

events and I just highlighted here

being occlusive disease, which was

seen only in nine percent of patients.

So this is the complete remission duration,
which at three years was 79%.

That’s the top blue line.

The Red line is overall survival line 56% at three years.

Once again these are all the patients and there’s a pretty good results for this population of patients.

So this slide highlights worse outcomes in patients who are 70 and older.

This is the blue line.

As you can see,

three azerate three year survival rate

was 65 for patients who are 60 to 69 and.

Only 43 for patients 70 and older.

So I think you can see that.
Conclusions are based on this results.

Overall response rate was 98%.

There were no early deaths.

3 SCR duration was 79.

Overall survival of 56%.

Best outcomes of course.

In patients who are 60 to 69 and 70 and older.

A longer follow-up is of course needed to determine if a low dose fractionated into some oven blender to warm up will improve outcomes.

So finally the last study is
NOTE Confidence: 0.83798635
00:21:30.908 --> 00:21:33.210 about pH positive DLL patients.
NOTE Confidence: 0.83798635
00:21:33.210 --> 00:21:36.963 Again, this is a study from MD Anderson Ann.
NOTE Confidence: 0.83798635
00:21:36.970 --> 00:21:39.189 Its interim results of the Phase 1
NOTE Confidence: 0.83798635
00:21:39.189 --> 00:21:41.646 two study of the Fanatic Phonetic
NOTE Confidence: 0.83798635
00:21:41.646 --> 00:21:43.562 locks and dexamethasone for
NOTE Confidence: 0.83798635
00:21:43.562 --> 00:21:46.190 patients with relapsed or refractory
NOTE Confidence: 0.83798635
00:21:46.190 --> 00:21:48.438 Philadelphia chromosome positive LL.
NOTE Confidence: 0.83798635
00:21:48.440 --> 00:21:49.436 So as you know,
NOTE Confidence: 0.83798635
00:21:49.436 --> 00:21:50.930 the never clocks is the drug
NOTE Confidence: 0.83798635
00:21:50.990 --> 00:21:53.310 which is currently approved for
NOTE Confidence: 0.83798635
00:21:53.310 --> 00:21:55.166 frontline treatment together with
NOTE Confidence: 0.83798635
00:21:55.166 --> 00:21:56.869 hyperventilating agents with FI LL
NOTE Confidence: 0.83798635
00:21:56.869 --> 00:21:58.633 also approved for treatment of CLL
NOTE Confidence: 0.83798635
00:21:58.640 --> 00:22:02.360 and so this is a BCL two inhibitor.
NOTE Confidence: 0.83798635
00:22:02.360 --> 00:22:04.649 So what is the logic of trying
NOTE Confidence: 0.83798635
this drug in patients with DLL Now

the outcomes of relapse refractory disease in Peach posted below poor.

So the PACE trial showed that the native can induce responses and 40% of patients but one year progression free survival is only 8%.

So pH positive LL is highly dependent on BCL two protein for its survival and that’s why potentially there is a therapeutic role for phonetic lax. Preclinical studies also showed that platinum can cooperate with an attic locks and be synergistic in attacking Peach positive LL cells. So there is synergistic inhibition of growth.
An induction of Opelousas, and perhaps the reason for it is inhibition of Lynn tires in Chinese by platinum and it increases beam and. Which prevents MCL one upregulation MCL. One is another anti up anti optic protein and usually in escape route when BCL two anti apoptosis is inhibited. So the results which were presented at ASH 2020 were results of the phase one of the study. Only nine patients. But you know, they are quite interesting and that’s why I selected this for the discussion today.
course to identify maximal tolerated dose of another class in combination with platinum and dexamethasone.

There are secondary endpoint including CMR 8 Relapse free survival, overall survival and of course, safety.

The patients who were included on the study where patients with relapsed refractory Peach positive LL with CML in lymphoid space and they have to be treated by at least one desireable TTI prior to the study.

Age was 18 and older. Oclock performance status
like in previous study.
Adequate organ function nor uncontrolled active cardiovascular disease.
Becausw Anatomy was known to have cardiovascular toxicity arterial occlusive, and no prior use of genetic lacks.
So this is the schema of the study.
Initially, patients were open at 9:45 for seven days, then the network locks ramp up together with dexamethasone for four days at 40 milligrams, so the phase one included ramping up to 400 milligrams, or 800 milligrams.
So this were two. Those are some phonetic lacks which were accomplished in this study, so not new, but those was further reduced with. Haematological response to 30 milligrams and for patients with accomplished complete molecular response to. To avoid arterial occlusive events and other side effects so as you can see, patients also received CNS prophylaxis and Rituxan if they were CD 20 positive. So this is the characteristic of this. Nine patients enrolled on this phase. One of the study you can see
NOTE Confidence: 0.7313096
00:25:02.821 --> 00:25:05.249 that the issue is 26 to 73.
NOTE Confidence: 0.7313096
00:25:05.250 --> 00:25:07.452 There were no patience with the
NOTE Confidence: 0.7313096
00:25:07.452 --> 00:25:09.370 with performance status of three,
NOTE Confidence: 0.7313096
00:25:09.370 --> 00:25:12.370 so half of the patients had T315I mutations.
NOTE Confidence: 0.7313096
00:25:12.370 --> 00:25:15.258 And as you can see it was very
NOTE Confidence: 0.7313096
00:25:15.258 --> 00:25:16.500 heavily pretreated group.
NOTE Confidence: 0.7313096
00:25:16.500 --> 00:25:18.435 17% order received platinum probably
NOTE Confidence: 0.7313096
00:25:18.435 --> 00:25:21.370 going to my treatment and 56% of patients
NOTE Confidence: 0.7313096
00:25:21.370 --> 00:25:23.988 and prior transplant in 67% of patients.
NOTE Confidence: 0.7313096
00:25:23.988 --> 00:25:26.202 So nine but very heavily pretreated
NOTE Confidence: 0.7313096
NOTE Confidence: 0.7313096
00:25:28.670 --> 00:25:30.650 So we’re not even look like
NOTE Confidence: 0.7313096
00:25:30.650 --> 00:25:32.484 Sundecks didn’t cause any deal
NOTE Confidence: 0.7313096
00:25:32.484 --> 00:25:34.276 tease those limited toxicities.
NOTE Confidence: 0.7313096
00:25:34.280 --> 00:25:36.518 Maximal tolerated dose was not reached.
NOTE Confidence: 0.7313096
Three patients were treated or magnetic locks 400 milligram those level one and six patients receive genetic lacks 800 milligrams and this was selected to be recommended. Phase two dose. There are no early mortality so the side effects are listed here. I think 1 interesting side effect in this storm Bolick event which occurred in one patient and was graded as Grade 3. Patient had DVT MP. There are patients who had great for Trump aside opinion, neutropenia but no febrile neutropenia. Not great four.
So reasonably acceptable.

Side effect profile for this heavily pretreated group of relapse refractory patients.

So the response rate was 56%.

Of course, it’s five out of nine patients, 44% of four now had CR and one had CR.

I complete.

Molecular response was accomplished.

I’m on 4 out of nine patients and complete molecular response after first cycle was in three patients.

One patient actually responded by decreasing blossom mirror from
94 to 6% had neutrophil recovery in place with recovery, but was not counted as responded because Blacks were still about 5% in the marrow. So this is to highlight that phonetic likes those 800 milligram patients are the only patients who responded. None of the three patients who received an attic LAX responded, but five out of 6. Our patients in those two with 800 milligrams of another class had response, so this is of course 9 patients. Only two patients died and those were
NOTE Confidence: 0.8183674
00:27:16.236 --> 00:27:18.598 nonresponders they were not relapse patients.
NOTE Confidence: 0.8183674
00:27:18.600 --> 00:27:20.924 They did not respond to the magnet
NOTE Confidence: 0.8183674
00:27:20.924 --> 00:27:22.750 and Venetic lacks combination.
NOTE Confidence: 0.8183674
00:27:22.750 --> 00:27:24.916 And as you can see this
NOTE Confidence: 0.8183674
00:27:24.916 --> 00:27:26.910 is six months or less.
NOTE Confidence: 0.8183674
00:27:26.910 --> 00:27:30.690 3 survival of 100% for five
NOTE Confidence: 0.8183674
00:27:30.690 --> 00:27:34.623 patients is reasonably reassuring.
NOTE Confidence: 0.8183674
00:27:34.630 --> 00:27:35.659 You once again it’s a small phase one study.
NOTE Confidence: 0.8183674
00:27:35.659 --> 00:27:39.570 effective in heavily pretreated,
NOTE Confidence: 0.8183674
00:27:39.570 --> 00:27:41.850 and this looks like safe and
NOTE Confidence: 0.8183674
00:27:41.850 --> 00:27:43.370 effective in heavily pretreated,
NOTE Confidence: 0.8183674
00:27:43.370 --> 00:27:44.510 post available patients.
NOTE Confidence: 0.8183674
00:27:44.510 --> 00:27:45.650 Peach
NOTE Confidence: 0.8183674
Maximal tolerated dose was not reached, and those selected for phase two of this study is 800 MG CR rate was 56 on CMR rate was 44% responses were observed across subgroups, but may be high in Veneta clocks. 800 milligram daily Group estimated one year old survival 63% no relapses today. Correlative studies ongoing to better understand mechanism of response and resistance. So what do we do with yell to introduce this new drugs? Our two frontline management of our patients so we are opening this alliance study phase two trial
NOTE Confidence: 0.8183674
00:28:22.074 --> 00:28:23.990 overnight as a mob induction,
NOTE Confidence: 0.8183674
00:28:23.990 --> 00:28:25.958 followed by Glenna to map consolidation
NOTE Confidence: 0.8183674
00:28:25.958 --> 00:28:27.690 for patients with newly diagnosed
NOTE Confidence: 0.8183674
00:28:27.690 --> 00:28:29.146 or relapse refractory CD.
NOTE Confidence: 0.8183674
00:28:29.150 --> 00:28:30.430 22 points of DLL.
NOTE Confidence: 0.8183674
00:28:30.430 --> 00:28:33.876 I have to say that CD 19 and CD 22
NOTE Confidence: 0.8183674
00:28:33.876 --> 00:28:36.042 positivity is seen in more than
NOTE Confidence: 0.8183674
00:28:36.124 --> 00:28:37.854 90% of patients with SLE,
NOTE Confidence: 0.8183674
00:28:37.854 --> 00:28:40.080 so this cohort one includes patients
NOTE Confidence: 0.8183674
00:28:40.148 --> 00:28:42.500 older than 60 and older and we will
NOTE Confidence: 0.8183674
00:28:42.500 --> 00:28:44.629 be looking at event free survival,
NOTE Confidence: 0.8183674
00:28:44.630 --> 00:28:46.206 one event free survival.
NOTE Confidence: 0.8183674
00:28:46.206 --> 00:28:48.176 For this transplant in eligible
NOTE Confidence: 0.8183674
00:28:48.176 --> 00:28:50.489 patient group with newly diagnosed LL,
NOTE Confidence: 0.8183674
00:28:50.490 --> 00:28:52.524 the cohort two is for younger
NOTE Confidence: 0.8183674
patients who have relapsed refractory disease and you know, of course this patients potentially can go to transplant if they have response. So this combination makes sense because of the existing vanity. Zoom up within occlusive disease post transplant and even without transplant. And that's why we would like to separate transplant by giving other treatments to this patients in between. Another modern transplant itself. So I would like to wrap it up at this point and next speaker doctor, Nina, Kate and Logic will be talking.
about pediatric AOL studies.

You know, now you have to share your slides. I just unshared. Thank you.

I'm going to now shift the focus.

Two childhood adolescent and young adult ELL and I'm including young adult because often the eligibility for our studies extend well into the 20s and sometimes older.

So I'm going to focus most of my time on the 1st three abstracts. The first is our Presented the results of our recently closed T cell lymphoblastic leukemia.

Lymphoma study AALL 1231 in which Per-tuzumab
00:30:37.948 --> 00:30:41.044 was studied and which cranial radiation
00:30:41.044 --> 00:30:44.144 was illuminated for 90% of patients.
00:30:44.144 --> 00:30:47.553 Next, I'm going to discuss results of
00:30:47.553 --> 00:30:50.660 using Blue Netuna map versus intensive
00:30:50.660 --> 00:30:53.710 chemo in children in high risk.
00:30:53.710 --> 00:30:57.406 First, relapse of B cell LL.
00:30:57.410 --> 00:31:00.518 Anne, and then I'm going to
00:31:00.518 --> 00:31:02.590 discuss some results regarding
00:31:02.687 --> 00:31:05.368 the prior use of Luna to mmap.
00:31:05.370 --> 00:31:11.090 As associated with karty outcomes.
00:31:11.090 --> 00:31:13.866 And then I'm going to shift and talk
00:31:13.866 --> 00:31:16.594 a bit about toxicity related to
00:31:16.594 --> 00:31:20.185 asparagine ease and maybe some of the
00:31:20.185 --> 00:31:23.075 factors associated with that toxicity.
00:31:27.970 --> 00:31:31.394 The first study is by the study chair,
Doctor Teachey and I would like to also thank all the authors, investigators who slides I will present. And this is a ALL 1231. The reason that there is a T allow study even though. Three year event free survival approaches 90% is that T cell patients can’t really be salvage. They have really. Abysmal outcomes. If they relapse, so the goal is to try to treat them up front as much as possible. So part is Amab is a proteasome inhibitor. It inhibits Dave teaching would call it the garbage can of the cell it inhibits. And is supposed to be pretty old.
Zones are supposed to take care of waste from the cell. Inhibitors inhibit a number of the regulatory proteins, including NF KB, which is very important in T cell LL pathogenesis. It’s been shown in relapse studies to be well tolerated and effective. So therefore it was the basis of this study and the Burtis amab is an upfront randomization that starts an induction and those randomized get a total of eight doses of autism. The induction backbone changed for
TLL compared to past studies in a nonrandomized way based on British data in which all patients get dexamethasone and two doses of peg. Asparagine, Ace, and then randomization. Is based on end of consolidation MRD. So one is classified as standard risk or very high risk. Based on that and the backbone very slightly in terms of the intensive therapy based on risk status. The only group that gets radiation are the very high risk patients. For those who are seen as positive at diagnosis,
radiation and this was decided.

And that was one of the decisions for using dexamethasone induction because of the CNS penetration.

There was a great goal in our group because of the high cure rates in the long term.

Late effects to try to eliminate this radiation.

The T lymphoblastic lymphoma patients were also eligible for this study and their end of consolidation.

MRD was based on Image Ng and I do want to emphasize patients 1 to 30 years were eligible and we
do have patients throughout that range so the majority are under 18. This time is expected to accrue 1400 patients over 4.4 years, most powered for a 5% difference in four year EFS. However, it only enrolled 847 patients because went at that point to the results of the precursor study was available in that precursor study. AALL 0434 randomized to know Larabee and was. Found to be. Advantage of about 5% and also at lower CNS recurrence rate. So that’s the study was
amended and closed early and.

This is what was presented is the patients that were enrolled at 800 approximately 800 patients and for TI.

Don’t know why this keeps moving for TLL, there was no difference.

Arm A was the standard arm in ARM, B was upper to some arm.

There was no difference in three year EFS or in three year.

Overall survival by arm.

But when one looked at it by risk group, those who were standard risk or who had the lowest MRD at the end of consolidation had a clear advantage.
00:36:08.607 --> 00:36:11.520 of 92% versus 85% in three year FS.
NOTE Confidence: 0.7045952
00:36:11.520 --> 00:36:13.956 And there was a similar advantage
NOTE Confidence: 0.7045952
00:36:13.956 --> 00:36:15.580 in their intermediate risk.
NOTE Confidence: 0.7045952
00:36:15.580 --> 00:36:18.415 There was no advantage for purchase map,
NOTE Confidence: 0.7045952
00:36:18.420 --> 00:36:21.849 but in fact those who got burnt to the
NOTE Confidence: 0.7045952
00:36:21.849 --> 00:36:25.326 map did worse for very high risk TLL.
NOTE Confidence: 0.7045952
00:36:25.330 --> 00:36:27.646 Those who had high.
NOTE Confidence: 0.7045952
00:36:27.646 --> 00:36:31.770 End of consolidation burden or who were?
NOTE Confidence: 0.7045952
00:36:31.770 --> 00:36:34.595 Early relapse patients and this
NOTE Confidence: 0.7045952
00:36:34.595 --> 00:36:36.290 was statistically significant
NOTE Confidence: 0.7045952
00:36:36.290 --> 00:36:38.120 for unclear reasons,
NOTE Confidence: 0.7045952
00:36:38.120 --> 00:36:41.956 though it was speculated by the authors
NOTE Confidence: 0.7045952
00:36:41.956 --> 00:36:46.198 that this could relate to early toxicity.
NOTE Confidence: 0.7045952
00:36:46.200 --> 00:36:49.080 So in terms of the
NOTE Confidence: 0.7045952
00:36:49.080 --> 00:36:50.808 lymphoblastic lymphoma outcomes,
NOTE Confidence: 0.7045952
00:36:50.810 --> 00:36:53.106 there was an advantage.
A statistically clear advantage of Virtusa ma'am, both for event free survival and overall survival. Up about 7 to 8%. We wanted to compare outcomes on 12th. Ok, so the differences in induction therapy were remarkable in that there was a higher. So actually, going back with this and with this study truncated and with the recent AALLO 434 results, there were some opportunities to compare some strategies because
the Miller Bing was not included in this current study because those results were not known and. Therefore, the. The.

First thing that was examined was in those who got a little over 3, which would be known allara being an induction, but could get in conduct consolidation and then now I’m sorry this is end of induction, MRD.

Those who got no LL Bean versus all comers for 1231. There was actually much higher MRD negativity in those in the later study. The 1231 that looked at Partism.
Which is interesting because MRD says we typically think of as predictive of long-term outcomes, but not. It's not the only predictor in that kind of emphasizes that. The other thing that was really remarkable was that there was a lot more high grade toxicity in the PARTISM study compared to the previous Miller being study, and this is not clear why it’s speculated to be due to the dexamethasone and the extra peg asparagine ease.
Total number of events or toxic events were higher in the precursor study that 0434. There was a much higher rate of higher grade ones and they were due to infections predominantly and particularly fungal infections. The next thing that was examined was the cranial radiation, 'cause again, 90% of patients had cranial radiation. While in the current 1231, only 10% did and can see that the CNS relapse rate was higher in the 1231 study. But not overall relapse,
and that’s what we call Pete sometimes. The Pillsbury Doughboy effect where you shift relapses to bone marrow relapses, but there was no diff. And overall relapses, so this was felt as justification that cranial radiation could be illuminated. So next I’d like to go to an abstract that looks at Linda's mmm versus intensive chemo for first relapse, standard of care in first relapse therapy is to give three blocks of intensive chemotherapy. This is from a European study and they call those blocks HC 1 HC 2.
and HD three in this study after the first 2 blocks patients were randomized to blend into mmap or two. Third block and then they went to stem cell transplant if they could. And this study also ended early. It was supposed to enroll 202 patients and only 100 patients or so were enrolled because there was a clear result that there was an advantage of blended to mmap both in. Event free survival and in time from diagnosis to relapse. There is also an advantage. A significant advantage in overall
survival in the blue netuma Bab arm.

There was superior MRD remission that was assessed by PCR in the billing to mmap arm overall and it was more remarkable or in those that had a higher tumor burden load initially, so it was most remarkable in those who had more MRD at baseline.

There was very notably much decreased toxicity, so while overall toxicity was similar, there was a much lower rate of serious toxicity of 24% versus 43%, and those are greater than Grade 3, so this changes.
The construct, because previously the standard, was to get three blocks of chemotherapy. Before transplant in first relapse and this also mirrors a similar see OG study that also found some results that were reported last year. What there is always concerned about neurological toxicity with cytokine release syndrome with netuma. But while there were more neurological events, there were no Grade 3 or higher events in CR S and there weren’t. There was really not an increase in severe events or moderate or severe events,
00:42:47.550 --> 00:42:50.742 so the third study that also relates

00:42:50.742 --> 00:42:54.162 to blend into my map has to do

00:42:54.162 --> 00:42:56.580 with whether Blend into my map.

00:42:56.580 --> 00:43:01.690 Treatment prior to car affects car outcomes.

00:43:01.690 --> 00:43:04.630 And this is a multi site study.

00:43:04.630 --> 00:43:07.150 I’m so just there will be

00:43:07.150 --> 00:43:08.830 a separate car session,

00:43:08.830 --> 00:43:11.693 but this slide is here if people

00:43:11.693 --> 00:43:14.288 want to look at this later.

00:43:14.290 --> 00:43:17.332 But basically a patients T cells

00:43:17.332 --> 00:43:19.926 are harvested and then they

00:43:19.926 --> 00:43:22.770 are expanded and then they are.

00:43:22.770 --> 00:43:28.446 They are transfected to T cells

00:43:28.446 --> 00:43:32.230 via viral vector 2.

00:43:32.230 --> 00:43:36.365 Have T cell receptor gamma and

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244

NOTE Confidence: 0.78015244
then often something else.

In this case it was for one BB, but it can be different things and it's reinfused and then it can.

Go after the particular marker on the tumor.

So sitting 19 modulation represents a mechanism of resistance to CD 19 targeting.

It's both blue 2:00 AM AB and CD19 car T cells are associated lineages.

Switch CD 19. Law son CD.

19 antigen downregulation becoming dim, and there's just limited impact on the how they impact each other.

This was a multicenter study.
There were three different car T cell constructs, and it was a seven site study. Their median post infusion followed was 2.3 years and this occurred over seven years. 75 of the 420 patients had had previous blenner, of which 57.3% achieved CR and the median time from last minute to the current Fusion in these patients was 129 days. So there was no difference in those who had had Blender and prior blenna and those who did not in terms of MRD status.
whether they had an empty or M3 marrow
NOTE Confidence: 0.78015244
CNS status, extramedullary disease,
NOTE Confidence: 0.78015244
or circulating glass.
NOTE Confidence: 0.78015244
There was a higher rate in those who had
NOTE Confidence: 0.78015244
prior brunette with the KM T2A R mutation,
NOTE Confidence: 0.78015244
maybe indicating that there were more younger
NOTE Confidence: 0.78015244
patients 'cause that occurs more in infants.
NOTE Confidence: 0.78015244
And the overall response to the
car was great in these 120 patients,
NOTE Confidence: 0.78015244
91% achieved CR,
NOTE Confidence: 0.78015244
88% were MRD negative and the
relapse rate was 39.8%,
NOTE Confidence: 0.78015244
33.023 88% were MRD negative and the
reap rate was 39.8%,
NOTE Confidence: 0.78015244
however.
NOTE Confidence: 0.78015244
Blender patients are the ones
who had previously know were more
NOTE Confidence: 0.78015244
likely to have residual disease.
Post CD 19 car, so it was 18% if one had prior blina and only 7% if there was previous blender. This also corresponded to worse relapse free survival both at six months. Anna, 12 months and the median relapse. Free survival was twenty months. If one had had previous planner and 45 months. If there had been no blender. So we’re not is associated. Also was also associated with a higher incidence of CD 19 modulation pre car. So the incidents of CD 19, negative, dim or partial expression prior to the car was.
Was higher in prior blender patients, 13% versus 6% and in patients in which there was a pre and post Lena CD 19 dim expression. Going to change gears now and talk a little bit about toxicities because young adults were found to have inferior outcomes compared to children and do better when they are treated with PD type. Regiments we can talk about this a little bit more, but there's some trade-offs. And so especially in the early 20s, there is an advantage with pediatric regiments rather than this C vad.
00:47:16.100 --> 00:47:19.364 this has to be reassessed in the era of cellular therapy.
00:47:19.364 --> 00:47:22.570 So the goal of this study was to look at bone toxicities and it was found that this is a retrospective study of Dana Farber consortia patients who were up to 50 years and initially they were true with the coli based ones and had 30 weeks of asparagine depletion and then later, this changed to PEG. And steroid Dennis Progenies associates Austin across is glucose corduroy, corticoids, disrupt osteoblasts and cause ischaemia.
It’s not really clear how asparagine ease results in Aston across is, but it is highly associated, maybe due to hypercoagulability in altered lipid metabolism and previous ranges and kids was incidents of osteonecrosis of 69% much higher in adolescence as high in the high teens or 20s. And a good proportion needs surgery and joint replacement as as 20 year olds. So the goal is to understand this incidence and risk factors. This has this study had 367 patients from 25 institutions. And it was found that 17% of them developed osteonecrosis and a
median time to event was 1.6 years and 12% developed a fracture with median time to event of 1.4 years. When one looked at risk factors, those under 30 years had a 21% risk, so this is really a condition of adolescents and young adults. With only 8% in those over 30 years and there was a much higher risk in those who had peg based therapy. Rather than E. Coli based therapy, almost a fivefold increased risk. So the potential mechanisms are not known in the later eras,
00:49:23.570 --> 00:49:25.550 along with Pegasus Virginis
NOTE Confidence: 0.84853727
00:49:25.550 --> 00:49:26.540 more dexamethasone.
NOTE Confidence: 0.84853727
00:49:26.540 --> 00:49:28.845 Dexamethasone is uniformly used and
NOTE Confidence: 0.84853727
00:49:28.845 --> 00:49:31.150 it was proposed that asparagine
NOTE Confidence: 0.84853727
00:49:31.219 --> 00:49:33.487 ease could cause hypoalbuminemia,
NOTE Confidence: 0.84853727
00:49:33.490 --> 00:49:35.786 which decreases dex clearance,
NOTE Confidence: 0.84853727
00:49:35.786 --> 00:49:39.230 and dexamethasone is a steroid more
NOTE Confidence: 0.84853727
00:49:39.325 --> 00:49:42.457 than Prednisone that is a much
NOTE Confidence: 0.84853727
00:49:42.457 --> 00:49:44.545 higher risk of osteonecrosis.
NOTE Confidence: 0.84853727
00:49:44.550 --> 00:49:46.325 And Asperges clearance is higher
NOTE Confidence: 0.84853727
00:49:46.325 --> 00:49:48.448 free collide that Nino Peg Lated
NOTE Confidence: 0.84853727
00:49:48.448 --> 00:49:50.450 is meant to be there along time,
NOTE Confidence: 0.84853727
00:49:50.450 --> 00:49:51.630 and maybe that’s it.
NOTE Confidence: 0.84853727
00:49:51.630 --> 00:49:53.400 The investigators plan to look at
NOTE Confidence: 0.84853727
00:49:53.457 --> 00:49:56.026 asparagine ace levels more closely, and this.
NOTE Confidence: 0.84853727
00:49:56.026 --> 00:49:57.338 I’ll just summarize this.

76
This abstract would seem to be made for this. In which this group looked at asperges levels and toxicity and found that high levels of this urge nice was not associated with an increased risk of any of the known toxicities, including pancreatitis, thromboembolism, or osteonecrosis. So the answer it may be not as simple as that and may have to be looked at a little more closely. We have several studies open here at Yale that build on this. We have a study of Tessa Jean Luc’s Loosle Carty 19.
Made by Novartis in first line, high risk patients who are MRD positive and end up consolidation that goes up to 25 years of age were investigating blinatumomab in standard risk patients, again with a similar goal of trying to limit chemotherapy eventually and then we're staying in a choose the map in high risk PML patients. To 25 years and we have a study of Pseudomonas derived asparagine ease for those who had hypersensitive reaction to E. Coli drive, despair genese. That's any age. And finally, we have a study where bout to open a blender to mmap with Nivo.
And first relapse for patients up to 31 years. So with that, I think you and I hand the floor over to moderate are Doctor Shaw. Thank you very much Doctor Nikolai and talk to Nina for summarizing on the newer data, which were presented at ASH last year. Regarding both pediatric, any Delta LL. So now session is open for questions and when we are waiting for so I think there are some questions there in the chat. Yeah I saw that. Some of them are just comments, but you know. So one of them is addressed to me.
Yeah, would you use Hyper C Vad

plus blinatumomab approach in your practice today to avoid transplant?

So I do have to mention that in that study which I think enrolled about 39 patients, 12 patients went to transplant and you know 10 of them actually went before relapse. So even folks in MD Anderson who are using this approach, they still using transplant as a modality for this patient after they accomplished CR with without minimal residual disease. So I think the transplant is reserved for high risk patients as defined by their karyotype of maletis pH like status. Anti P53 expression.
I have TP 53 mutations so I don’t think it is too soon to say that this particular approach will eliminate the transplant but certainly gives hope to patients who cannot have transplant for whatever reason. An at least maybe a choice for some of those patients who have disease with less risky features. So I and I would say that that is a point of convergence in our literature. So a patient in their 20s, if they came in through a pediatric treatment center, would not accept for certain molecular findings.
Would not automatically get transplanted first remission because we have it.

We don’t use the high perceived backbone, we use the BFM backbone.

And use a lot more asparagine ease and methotrexate.

But the and and antimetabolites, but the we have we have survival event free survival in the in the 80s in that group, but what I think.

Even in patients in their 20s who
we call the older patients rather, they have higher rates of infection. They have higher rates of AVN. They have had higher rates of pancreatitis and, and it’s not clear how to balance those two things, balance those two things, but they would be treated very differently and they would have good disease free outcomes. So we just want comment. We do use pediatric protocols. Pediatric like protocols become backbone protocols and we’re participating in Lion study which
uses inotuzumab randomization.

So phase three study after initial induction, randomizing patients to two cycles in a tourism up or regular consolidation.

This is between H20 and 39, so you know how I perceive what is usually something you would consider for patients who are older than that.

And we tried to use again DFM. Backbone augmented BFM backbone protocols for younger patients,

so there is a question in the chat. I think both Amarillo Heath and the doctors 8 and that was it was our introduction which reduced us and Doctor Gowda who is one of our
adult transplanters asking about. Blender two map consolidation instead of usage of tag asparaginase which is certainly much more difficult for all the patients to tolerate and one of the reasons why you know a lot of people who all the cannot go on pediatric protocols. Can this eliminate usable in a tomb? Up eliminate need for US Virgin eyes? And how do we explain so good outcomes with high perceived cannot be cause younger patients were enrolled well so they tried to enroll patients 14 and older. I think the youngest patients was 17.
On that study and the oldest patient was 59, so certainly some of the outcomes can be explained by patient selection, but decent number of these patients have the you know, karyotype abnormalities, Peach like disease and very high number had TP 53 mutations, so it’s challenging to say and again comparing head to head tag you know comparing head to head tag asparaginase containing BFM type protocols with MD Anderson Hyper. See what will not be possible but you know. This is ongoing argument. Which one is better for adult patients? And I think there is one more
discussion question to both of you with all this novel Agents of Lena Nine. It is a man.

Can you see the use of car T still in the relapse refractory patients?

Yeah, you know. So I think there’s certainly enroll for car T cells, and we recently had a discussion about young adult who I’m taking care of.

And she’s actually going for car T cells after she didn’t respond to Blender to map.

And you know, for some of these patients, it can be a curative treatment. Depending on the construct.
So I still hope that some of those patients who fail or who are failed by transplant can be rescued and some well known cases. Nationally where this happened and people survive for many years afterwards. So certainly car T cells is a nice addition to the armamentarium we have for management of these patients. Unfortunately, right now is only for patients or twenty 1625 in. Is only approved for this group of patients and I didn’t touch on those studies because I hope some of them will be addressed by the session for two weeks so,
but we’re hoping that this treatment will become safer and may be used for patients who are all that is definitely something we would like to see for our old LL patients. Yeah, but I’m an maybe at that time we need to just keep in mind that data. Mirali presented with Nina, included in her today is that the prior Lena exposure. May have effect on the Carty outcome, so I think there should be some selection of the patients where we need to right away. Start cleaner if you are really thinking of them offering Cardi,
we need to double check whether we need to give those glena front option or not. So I think there should be some selection of the patients who one of the mechanisms of resistance is of course loss of CD 19 expression right so and then you know you lose the target. Fortunately it doesn’t happen too frequently. So, but nevertheless, the point in world is well taken. Yes no, I agree, and I think one of the things that the investigation that study discussed in this session afterwards with the questions. Is that they would like to understand what was their response to the
blender and weather because it may be that even with the karty. I'm sorry even with the CD 19 expression, there's something different about those individuals that needs to be recognized and then the other. Thing is that I think just pairing it with that other study that I presented where the outcomes are better if one receives blina prior to transplant. So one can think about I definitely agree about having car. T in the arm and it arium. But whether one should think about transplant versus party as the next step,
00:59:32.110 --> 00:59:34.413 and then I think those are those
NOTE Confidence: 0.8002771
00:59:34.413 --> 00:59:36.167 are the complicated equations and
NOTE Confidence: 0.8002771
00:59:36.167 --> 00:59:38.624 we almost have too many choices now.
NOTE Confidence: 0.8002771
00:59:38.630 --> 00:59:39.656 Well, you know,
NOTE Confidence: 0.8002771
00:59:39.656 --> 00:59:41.708 it’s nice to have more choices
NOTE Confidence: 0.81426054
00:59:41.710 --> 00:59:43.822 and I wish we have more
NOTE Confidence: 0.81426054
00:59:43.822 --> 00:59:45.490 choices for T cell L.
NOTE Confidence: 0.81426054
00:59:45.490 --> 00:59:47.807 As you know, adults with this disease
NOTE Confidence: 0.81426054
00:59:47.807 --> 00:59:50.290 do not do as well as children.
NOTE Confidence: 0.81426054
00:59:50.290 --> 00:59:51.316 Certainly Laura being.
NOTE Confidence: 0.81426054
00:59:51.316 --> 00:59:52.684 Is that reasonable option,
NOTE Confidence: 0.81426054
00:59:52.690 --> 00:59:56.180 but there are no studies in adults on T cell.
NOTE Confidence: 0.81426054
00:59:56.180 --> 00:59:57.254 Disease of course.
NOTE Confidence: 0.81426054
00:59:57.254 --> 01:00:00.416 Most of the patients have diesel L 85% only.
NOTE Confidence: 0.81426054
01:00:00.416 --> 01:00:02.346 15% have T cell disease,
NOTE Confidence: 0.81426054
01:00:02.350 --> 01:00:03.910 but this is certainly unmet
need as not a lot of studies

addressing this patients right

now, especially adults, and one of

the questions which Lloyd is just

asking with regard to this discussion

of car T versus other newer regions.

Can these new region across the CNS?

Yeah, you know.

It’s challenging questions,

so you know we know.

That you know we’re not counting

on Blender to my boy Natuzzi map to

address CNS disease in these patients

were excluded from those studies,

so we don’t really have those
questions answered by the studies which led to the approval of these drugs in regards to car T cells.

Again, you know this patients with CNS disease are usually excluded, so we don’t know. But we presume that this has to be addressed separately from systemic therapies and there is some data from CHOP actually for car, T for CNS positivity and maybe Doctor shopping go into. To that a little more, but there’s it’s small numbers, but it seems to be covering CNS disease,
not necessarily testicular disease. But yes, that is the same as penetration with the Carty, and we have seen the success rate particularly, and again, it’s need to be now as parties commercially available. We need to review those data also down the rain so you know, for us, it’s a move to, you know, to zoom out Blender to map, you know, without the systemic administration of site error. Why does it say Terminatrix 8? So you know this is certainly
a very pertinent issue, which puts a lot of pressure on giving out chemotherapy in adequate numbers to those patients. As we don’t know really, you know about the effects of the tool.

My last question to Doctor Nikolai and I'm pediatric transplant are so, but looking at this good day to our financials, demandment cleaner to ma’am. Would you consider this in this? You’re more than 60 year old older adult, so how you see in changing your algorithm for those group of LL
01:02:11.582 --> 01:02:13.730 patient highly scalable patients

01:02:13.730 --> 01:02:16.466 so you know I think 4.

01:02:16.470 --> 01:02:22.130 Older patients, the question about

01:02:22.216 --> 01:02:24.766 you know the outcomes are worse.

01:02:24.770 --> 01:02:29.356 give hope that some of these patients

01:02:29.356 --> 01:02:31.096 may be cured without transplant.

01:02:31.100 --> 01:02:33.764 Having said that, I don’t think we know

01:02:33.764 --> 01:02:36.419 yet how many of them will be cured,

01:02:36.420 --> 01:02:38.418 so that’s why I cannot clearly

01:02:38.418 --> 01:02:39.417 answer that question.

01:02:39.420 --> 01:02:40.398 And I apologize.

01:02:40.398 --> 01:02:42.354 I have to leave because I’m

01:02:42.354 --> 01:02:43.748 running that your board,
which starts at 1:00 o’clock.

When on that note, thank you so much.

Tower speakers at Doctor Baddour said doctor catalytic and overloaded and moderate are Doctor Nikita Shad excellent talks.

And if you have any additional questions.

Feel free to follow up directly with the speakers and we look forward to our next session next Friday about benign hematology and have a great weekend.

Everyone take care.

Bye bye.