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 Basically are focused on preliminary data and subsequently some of those results might be modified and they are still not peer reviewed,
00:00:40.270 --> 00:00:45.466 so this is important to keep up in mind as we think about the data that will be presented.

00:00:45.466 --> 00:00:49.962 That there will be a recording of this session and all the sessions.

00:00:49.970 --> 00:00:54.209 This will be available and accessible as in 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.

00:00:54.210 --> 00:00:56.744 For those of you who wants to claim it.

00:00:56.744 --> 00:01:01.710 After you answer a brief evaluation and some feedback about how we can improve the format of the series.

00:01:01.710 --> 00:01:03.552 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 --> 00:01:42.976 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 our 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,

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. 5 year old survival is about 90% and children and still half of that in adults.

NOTE Confidence: 0.88896275
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,
00:04:54.177 --> 00:04:57.166 attacking CD 19 cells on view lymphoblasts.

00:04:57.170 --> 00:04:59.528 This is for patients who are younger than 26 or younger,

00:05:01.860 --> 00:05:04.849 so the mechanism of action is bluna.

00:05:04.850 --> 00:05:07.839 Tumors represent on this slide is bite.

00:05:07.840 --> 00:05:11.224 Through a CD 19 and by means of this attachment increases the.

00:05:11.224 --> 00:05:16.464 A pop ptosis of this tumor cells?

00:05:16.464 --> 00:05:23.831 So the studies which put this on the map and make it available to us are tower phase three study,

00:05:23.831 --> 00:05:26.807 the map and make it available to us are tower phase three study,

00:05:26.807 --> 00:05:31.488 which looked at Glenna to mob
in relapsed refractory disease

and as you can see,

there was a survival difference

which was statistically significant.

Response rate was 44%,

with 76% achieving mean negative,

minimal residual disease.

So this is all control study

Also blinatumomab it’s an.

It’s a phase two study single arm

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 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. So 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

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.
So the primary endpoint of the study was relapse free survival secondary endpoints. You can look at here including overall response rate and MRD negativity rate. So this you are newly diagnosed patients with pH, diagnosed patients with pH, LL patients could receive one cycle induction chemotherapy prior to enrollment. Of course they have to get to MD Anderson from elsewhere where they treated. So 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 on the study. 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,
CD 20 antibody. As well as use of prophylactic chemotherapy sectarian metrics so after finishing this intensive phase, patients would go to blender two more phase where they would receive 4 six 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 one is the secondary points response rates CR after induction was accomplished in 81% of patients and then yes, you know they preceded with Blender two Mob and at the end of 32 patients.
00:10:58.691 --> 00:11:00.806 accomplished a CR and MRD,
00:11:00.810 --> 00:11:02.136 negativity was 71%.
00:11:02.136 --> 00:11:04.762 After induction and 97% at anytime
00:11:04.762 --> 00:11:06.040 during the study,
00:11:06.040 --> 00:11:08.890 early mortality was at 0.
00:11:08.890 --> 00:11:09.310 So.
00:11:09.310 --> 00:11:10.570 I relapse free.
00:11:10.570 --> 00:11:13.697 Survival was not one of the endpoints
00:11:13.697 --> 00:11:17.090 of the study, and as you can see,
00:11:17.090 --> 00:11:20.050 relapse free survival at two years is 71%.
00:11:20.050 --> 00:11:21.196 At one year,
00:11:21.196 --> 00:11:24.490 80% overall survival was at two years of 80%,
00:11:24.490 --> 00:11:26.938 so it’s pretty impressive numbers for
00:11:26.938 --> 00:11:29.298 patients for adults with B cell LL.
00:11:29.300 --> 00:11:32.569 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.

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 BLL 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 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.

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 then MRD was accomplished in 78% of patients with this strategy. 78% of patients with this strategy. So there were some haematological and molecular responses.
As you can see, a total of three and allogeneic stem transplant in remission was provided to three of those patients and one patient went to transplant after relapse so only four patients were transplanted out of this 31. So this is. The primary endpoint is on the right event free survival at one year, so was 87%. So for all the group of patients is actually pretty good and then overall survival at one year was also 87% events were defined, persisting one marrable us after two cycles went into some of relapse or death.
So this is a side effect 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?

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, again 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 dosing 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 78% and overall in 96% of the patients.

So the reason that why numbers are all different, there’s been.

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 470 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

style studies now amended to

eliminate chemotherapy for patients

for 70 and older 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
00:21:30.908 --> 00:21:33.210 about pH positive DLL patients.

00:21:33.210 --> 00:21:36.963 Again, this is a study from MD Anderson Ann.

00:21:36.970 --> 00:21:39.189 Its interim results of the Phase 1

00:21:39.189 --> 00:21:41.646 two study of the Fanatic Phonetic

00:21:41.646 --> 00:21:43.562 locks and dexamethasone for

00:21:43.562 --> 00:21:46.190 patients with relapsed or refractory

00:21:46.190 --> 00:21:48.438 Philadelphia chromosome positive LL.

00:21:48.440 --> 00:21:49.436 So as you know,

00:21:49.436 --> 00:21:50.930 the never clocks is the drug

00:21:50.990 --> 00:21:53.310 which is currently approved for

00:21:53.310 --> 00:21:55.166 frontline treatment together with

00:21:55.166 --> 00:21:56.869 hyperventilating agents with FI LL

00:21:56.869 --> 00:21:58.633 also approved for treatment of CLL

00:21:58.640 --> 00:22:02.360 and so this is a BCL two inhibitor.

00:22:02.360 --> 00:22:04.649 So what is the logic of trying

36
this drug in patients with DLL Now

NOTE Confidence: 0.83798635

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

NOTE Confidence: 0.83798635

So the PACE trial showed that
the native can induce responses

NOTE Confidence: 0.83798635

and 40% of patients but one year

NOTE Confidence: 0.83798635

progression free survival is only 8%.

NOTE Confidence: 0.83798635

So pH positive LL is highly dependent
on BCL two protein for its survival

NOTE Confidence: 0.83798635

and that’s why potentially there is
a therapeutic role for phonetic lax.

NOTE Confidence: 0.83798635

Preclinical studies also showed
that platinum can cooperate with an
attic locks and be synergistic in
attacking Peach positive LL cells.

NOTE Confidence: 0.83798635

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.

Because Anatomy was known to have cardiovascular toxicity arterial occlusive, occlusive events, 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
that the issue is 26 to 73.

There were no patience with the performance status of three, so half of the patients had T315I mutations. And as you can see it was very heavily pretreated group. 17% order received platinum probably going to my treatment and 56% of patients and prior transplant in 67% of patients. So nine but very heavily pretreated patients with relapsed refractory disease. So we’re not even look like Sundecks didn’t cause any deal tease those limited toxicities. Maximal tolerated dose was not reached.
Three patients were treated or

NOTE Confidence: 0.7313096

magnetic locks 400 milligram those

NOTE Confidence: 0.7313096

level one and six patients receive

NOTE Confidence: 0.7313096

genetic lacks 800 milligrams and

NOTE Confidence: 0.7313096

this was selected to be recommended.

NOTE Confidence: 0.7313096

Phase two dose.

NOTE Confidence: 0.7313096

There are no early mortality so

NOTE Confidence: 0.7313096

the side effects are listed here.

NOTE Confidence: 0.7313096

I think 1 interesting side effect in

NOTE Confidence: 0.7313096

this storm Bolick event which occurred

NOTE Confidence: 0.7313096

in one patient and was graded as Grade 3.

NOTE Confidence: 0.7313096

Patient had DVT MP.

NOTE Confidence: 0.7313096

There are patients who had

NOTE Confidence: 0.7313096

great for Trump aside opinion,

NOTE Confidence: 0.7313096

neutropenia but no febrile neutropenia.

NOTE Confidence: 0.7313096

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 at 400. Those 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
nonresponders they were not relapse patients.

They did not respond to the magnet and Venetic lacks combination.

And as you can see this is six months or less.

3 survival of 100% for five patients is reasonably reassuring.

You once again it’s a small phase one study.

So in conclusion, this is oral regimen of banana phonetic likes and dexamethasone, and this looks like safe and effective in heavily pretreated, relapsed refractory Peach post available patients.
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
00:28:22.074 --> 00:28:23.990 overnight as a mob induction,
00:28:23.990 --> 00:28:25.958 followed by Glenna to map consolidation
00:28:25.958 --> 00:28:27.690 for patients with newly diagnosed
00:28:27.690 --> 00:28:29.146 or relapse refractory CD.
00:28:29.150 --> 00:28:30.430 22 points of DLL.
00:28:30.430 --> 00:28:33.876 I have to say that CD 19 and CD 22
00:28:33.876 --> 00:28:36.042 positivity is seen in more than
00:28:36.124 --> 00:28:37.854 90% of patients with SLE,
00:28:37.854 --> 00:28:40.080 so this cohort one includes patients
00:28:40.148 --> 00:28:42.500 older than 60 and older and we will
00:28:42.500 --> 00:28:44.629 be looking at event free survival,
00:28:44.630 --> 00:28:46.206 one event free survival.
00:28:46.206 --> 00:28:48.176 For this transplant in eligible
00:28:48.176 --> 00:28:50.489 patient group with newly diagnosed LL,
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.

So 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 Pertuzumab
was studied and which cranial radiation was illuminated for 90% of patients.

Next, I’m going to discuss results of using Blue Netuma map versus intensive chemo in children in high risk.

First, relapse of B cell LL. Anne, and then I’m going to discuss some results regarding the prior use of Luna to map. As associated with karty outcomes.

And then I’m going to shift and talk a bit about toxicity related to asparagine ease and maybe some of the factors associated with that toxicity.

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. 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, intermediate 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, 90% of patients do not get
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 not and was. Found to be. Very much an advantage to having allara been with event free survival. 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. Oh, that's what I did.

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 first thing that was examined was in those who got a little over 3, which would be known allara being an induction, 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. So while the?
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, we had this opportunity to look in 043, four. 90% of patients had cranial radiation. While in the current 1231, only 10% did and can see that the. 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 to mmap 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. 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
00:41:14.885 --> 00:41:17.610 survival in the blue netuma Bab arm.

00:41:20.030 --> 00:41:23.060 There was superior MRD remission that

00:41:23.060 --> 00:41:26.365 was assessed by PCR in the billing

00:41:26.365 --> 00:41:29.701 to mmap arm overall and it was more

00:41:29.701 --> 00:41:32.865 remarkable or in those that had a

00:41:32.865 --> 00:41:35.495 higher tumor burden load initially,

00:41:35.495 --> 00:41:39.520 so it was most remarkable in those

00:41:39.630 --> 00:41:42.558 who had more MRD at baseline.

00:41:42.560 --> 00:41:45.435 There was very notably much

00:41:45.435 --> 00:41:46.585 decreased toxicity,

00:41:46.590 --> 00:41:50.040 so while overall toxicity was similar,

00:41:50.040 --> 00:41:54.135 there was a much lower rate of

00:41:54.135 --> 00:41:57.510 serious toxicity of 24% versus 43%,

00:41:57.510 --> 00:42:01.535 and those are greater than Grade 3,

00:42:01.540 --> 00:42:04.399 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,
NOTE Confidence: 0.78015244
00:42:47.550 --> 00:42:50.742 so the third study that also relates
NOTE Confidence: 0.78015244
00:42:50.742 --> 00:42:54.162 to blend into my map has to do
NOTE Confidence: 0.78015244
00:42:54.162 --> 00:42:56.580 with whether Blend into my map.
NOTE Confidence: 0.78015244
00:42:56.580 --> 00:43:01.690 Treatment prior to car affects car outcomes.
NOTE Confidence: 0.78015244
00:43:01.690 --> 00:43:04.630 And this is a multi site study.
NOTE Confidence: 0.78015244
00:43:04.630 --> 00:43:07.150 I'm so just there will be
NOTE Confidence: 0.78015244
00:43:07.150 --> 00:43:08.830 a separate car session,
NOTE Confidence: 0.78015244
00:43:08.830 --> 00:43:11.693 but this slide is here if people
NOTE Confidence: 0.78015244
00:43:11.693 --> 00:43:14.288 want to look at this later.
NOTE Confidence: 0.78015244
00:43:14.290 --> 00:43:17.332 But basically a patients T cells
NOTE Confidence: 0.78015244
00:43:17.332 --> 00:43:19.926 are harvested and then they
NOTE Confidence: 0.78015244
00:43:19.926 --> 00:43:22.770 are expanded and then they are.
NOTE Confidence: 0.78015244
00:43:22.770 --> 00:43:28.446 They. Are transfected to T cells
NOTE Confidence: 0.78015244
00:43:28.446 --> 00:43:32.230 via viral vector 2.
NOTE Confidence: 0.78015244
00:43:32.230 --> 00:43:36.365 Have T cell receptor gamma and
NOTE Confidence: 0.78015244
then often something else.

In this case it was for one BB,

but it can be different things and

Go after the particular marker

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.

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. Um, 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

NOTE Confidence: 0.78015244

car was great in these 120 patients,

NOTE Confidence: 0.78015244

91% achieved CR,

NOTE Confidence: 0.78015244

were MRD negative and the

NOTE Confidence: 0.78015244

relapse rate was 39.8%,

NOTE Confidence: 0.78015244

however.

NOTE Confidence: 0.78015244

Blender patients are the ones

NOTE Confidence: 0.78015244

who had previously know were more

NOTE Confidence: 0.78015244

likely to have residual disease.
00:45:43.610 --> 00:45:45.378 Post CD 19 car,
00:45:45.378 --> 00:45:49.365 so it was 18% if one had prior blina
00:45:49.365 --> 00:45:52.910 and only 7% if there was previous blender.
00:45:52.910 --> 00:45:55.574 This also corresponded to worse relapse
00:45:55.574 --> 00:45:58.230 free survival both at six months.
00:45:58.230 --> 00:46:01.324 Anna, 12 months and the median relapse.
00:46:01.330 --> 00:46:03.540 Free survival was twenty months.
00:46:03.540 --> 00:46:07.236 If one had had previous planner and 45
00:46:07.236 --> 00:46:08.930 months. If there had been no blender.
00:46:11.940 --> 00:46:13.760 So we’re not is associated.
00:46:13.760 --> 00:46:16.259 Also was also associated with a higher
00:46:16.259 --> 00:46:18.859 incidence of CD 19 modulation pre car.
00:46:18.860 --> 00:46:21.038 So the incidents of CD 19,
00:46:21.040 --> 00:46:22.768 negative, dim or partial
00:46:22.768 --> 00:46:25.360 expression prior to the car was.
Was higher in prior blender patients,:

NOTE Confidence: 0.8373493

13% versus 6% and in patients in which:

NOTE Confidence: 0.8373493

there was a pre and post Lena CD 19

NOTE Confidence: 0.8373493

expression 11% had evolution to CD.

NOTE Confidence: 0.8373493

19 dim expression.

NOTE Confidence: 0.84853727

Going to change gears now and talk a

NOTE Confidence: 0.84853727

little bit about toxicities because

NOTE Confidence: 0.84853727

and listen to young adults were

NOTE Confidence: 0.84853727

found to have inferior outcomes

NOTE Confidence: 0.84853727

compared to children and do better

NOTE Confidence: 0.84853727

when they are treated with PD type.

NOTE Confidence: 0.84853727

Regimens we can talk about this a little

NOTE Confidence: 0.84853727

bit more, but there’s some trade offs.

NOTE Confidence: 0.84853727

And so especially in the early 20s,

NOTE Confidence: 0.84853727

there is an advantage with pediatric

NOTE Confidence: 0.84853727

regimens rather than this C vad,
this has to be reassessed in the era of cellular therapy. 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 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 across is glucose corduroy, 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,
along with Pegasus Virginis

Dexamethasone is uniformly used and it was proposed that asparagine ease could cause hypoalbuminemia, which decreases dex clearance, and dexamethasone is a steroid more than Prednisone that is a much higher risk of osteonecrosis. And Asperges clearance is higher free collide that Nino Peg Lated is meant to be there along time, and maybe that’s it. The investigators plan to look at asparagine ace levels more closely, and this. I’ll just summarize this.
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 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. 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. That's any age. And finally, we have a study where bout to open a blender to mmab 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 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.

I 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 would say that that is a point of convergence in our literature. 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

But I think the challenges and what 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
NOTE Confidence: 0.7732424
00:55:19.376 --> 00:55:22.320 adult transplanters asking about.
NOTE Confidence: 0.7732424
00:55:22.320 --> 00:55:24.190 Blender two map consolidation instead
NOTE Confidence: 0.7732424
00:55:24.190 --> 00:55:26.455 of usage of tag asparaginase which
NOTE Confidence: 0.7732424
00:55:26.455 --> 00:55:28.125 is certainly much more difficult
NOTE Confidence: 0.7732424
00:55:28.125 --> 00:55:30.056 for all the patients to tolerate
NOTE Confidence: 0.7732424
00:55:30.056 --> 00:55:31.918 and one of the reasons why you
NOTE Confidence: 0.7732424
00:55:31.918 --> 00:55:34.003 know a lot of people who all the
NOTE Confidence: 0.7732424
00:55:34.003 --> 00:55:36.139 cannot go on pediatric protocols.
NOTE Confidence: 0.7732424
00:55:36.140 --> 00:55:38.436 Can this eliminate usable in a tomb?
NOTE Confidence: 0.7732424
00:55:38.440 --> 00:55:40.736 Up eliminate need for US Virgin eyes?
NOTE Confidence: 0.7732424
00:55:40.740 --> 00:55:42.988 And how do we explain so good outcomes
NOTE Confidence: 0.7732424
00:55:42.988 --> 00:55:45.118 with high perceived cannot be cause
NOTE Confidence: 0.7732424
00:55:45.118 --> 00:55:47.368 younger patients were enrolled well so
NOTE Confidence: 0.7732424
00:55:47.435 --> 00:55:49.955 they tried to enroll patients 14 and older.
NOTE Confidence: 0.7732424
00:55:49.960 --> 00:55:52.529 I think the youngest patients was 17.
NOTE Confidence: 0.7732424
On that study and the oldest patient was 59, so certainly some of the outcomes can be explained by patient selection, but a decent number of these patients have karyotype abnormalities, Pea-like disease and very high number had TP 53 mutations, so it’s challenging to say and again 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
NOTE Confidence: 0.82373655
00:56:31.767 --> 00:56:33.612 discussion question to both of
NOTE Confidence: 0.82373655
00:56:33.612 --> 00:56:35.580 you with all this novel Agents
NOTE Confidence: 0.82373655
00:56:35.580 --> 00:56:37.750 of Lena Nine. It is a man.
NOTE Confidence: 0.82373655
00:56:37.750 --> 00:56:40.817 Can you see the use of car T still
NOTE Confidence: 0.82373655
00:56:40.817 --> 00:56:43.087 in the relapse refractory patients?
NOTE Confidence: 0.82373655
00:56:43.090 --> 00:56:44.518 Yeah, you know. So
NOTE Confidence: 0.82373655
00:56:44.520 --> 00:56:45.944 I think there’s certainly
NOTE Confidence: 0.82373655
00:56:45.944 --> 00:56:47.724 enroll for car T cells,
NOTE Confidence: 0.82373655
00:56:47.730 --> 00:56:50.278 and we recently had a discussion about
NOTE Confidence: 0.82373655
00:56:50.278 --> 00:56:52.730 young adult who I’m taking care of.
NOTE Confidence: 0.82373655
00:56:52.730 --> 00:56:55.978 And she’s actually going for car T cells
NOTE Confidence: 0.82373655
00:56:55.978 --> 00:56:59.547 after she didn’t respond to Blender to map.
NOTE Confidence: 0.82373655
00:56:59.550 --> 00:57:02.638 And you know, for some of these patients,
NOTE Confidence: 0.82373655
00:57:02.640 --> 00:57:04.950 it can be a curative treatment.
NOTE Confidence: 0.82373655
00:57:04.950 --> 00:57:06.678 Depending on the construct.
NOTE Confidence: 0.82373655

87
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
for car T cells so should link.
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.
and then I think those are those complicated equations and we almost have too many choices now. Well, you know, it’s nice to have more choices and I wish we have more choices for T cell L.

As you know, adults with this disease do not do as well as children. Certainly Laura being. Is that reasonable option, but there are no studies in adults on T cell.

Most of the patients have diesel L 85% only. 15% have T cell disease, 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 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
01:01:35.008 --> 01:01:36.100 a very pertinent issue,
NOTE Confidence: 0.76860124
01:01:36.100 --> 01:01:37.630 which puts a lot of pressure
NOTE Confidence: 0.76860124
01:01:37.630 --> 01:01:38.997 on giving out chemotherapy in
NOTE Confidence: 0.76860124
01:01:38.997 --> 01:01:40.467 adequate numbers to those patients.
NOTE Confidence: 0.76860124
01:01:40.470 --> 01:01:41.830 As we don’t know really,
NOTE Confidence: 0.76860124
01:01:41.830 --> 01:01:44.006 you know about the effects of the tool.
NOTE Confidence: 0.7827345
01:01:46.830 --> 01:01:49.990 My last question to Doctor Nikolai and
NOTE Confidence: 0.7827345
01:01:49.990 --> 01:01:52.560 I’m I’m pediatric transplant are so,
NOTE Confidence: 0.7827345
01:01:52.560 --> 01:01:54.765 but looking at this good
NOTE Confidence: 0.7827345
01:01:54.765 --> 01:01:56.529 day to our financials,
NOTE Confidence: 0.7827345
01:01:56.530 --> 01:01:58.294 demandment cleaner to ma’am.
NOTE Confidence: 0.7827345
01:01:58.294 --> 01:02:00.940 Would you consider this in this?
NOTE Confidence: 0.7827345
01:02:00.940 --> 01:02:04.468 You’re more than 60 year old older adult,
NOTE Confidence: 0.7827345
01:02:04.470 --> 01:02:06.997 so how you see in changing your
NOTE Confidence: 0.7827345
01:02:06.997 --> 01:02:08.648 practice or your treatment
NOTE Confidence: 0.7827345
01:02:08.648 --> 01:02:11.582 algorithm for those group of LL
patient highly scalable patients

so you know I think 4.

Older patients, the question about transplant is more difficult because you know the outcomes are worse.

And the administration of this new drugs give hope that some of these patients may be cured without transplant.

Having said that, I don’t think we know yet how many of them will be cured, so that’s why I cannot clearly answer that question.

And I apologize.

I have to leave because I’m running that your board,
01:02:43.750 --> 01:02:45.420 which starts at 1:00 o’clock.

NOTE Confidence: 0.79139125

01:02:45.420 --> 01:02:48.076 When on that note, thank you so much.

NOTE Confidence: 0.79139125

01:02:48.080 --> 01:02:50.446 Tower speakers at Doctor Baddour said doctor

NOTE Confidence: 0.79139125

01:02:50.446 --> 01:02:52.155 catalytic and overloaded and moderate

NOTE Confidence: 0.79139125

01:02:52.155 --> 01:02:54.069 are Doctor Nikita Shad excellent talks.

NOTE Confidence: 0.79139125

01:02:54.070 --> 01:02:56.506 And if you have any additional questions.

NOTE Confidence: 0.79139125

01:02:56.510 --> 01:02:59.065 Feel free to follow up directly with

NOTE Confidence: 0.79139125

01:02:59.065 --> 01:03:02.061 the speakers and we look forward to our

NOTE Confidence: 0.79139125

01:03:02.061 --> 01:03:04.386 next session next Friday about benign

NOTE Confidence: 0.79139125

01:03:04.386 --> 01:03:06.924 hematology and have a great weekend.

NOTE Confidence: 0.79139125

01:03:06.930 --> 01:03:08.088 Everyone take care.

NOTE Confidence: 0.82131004

01:03:09.760 --> 01:03:10.240 Bye bye.