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 Basically are focused on preliminary data and subsequently some of those results might be modified and they are still not peer reviewed,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
00:00:45.466 --> 00:00:49.962 think about the data that will be presented.
00:00:49.970 --> 00:00:52.147 That there will be a recording of
00:00:52.147 --> 00:00:54.209 this session and all the sessions.
00:00:54.210 --> 00:00:56.744 This will be available and accessible as
00:00:56.744 --> 00:01:01.710 in during material in addition to the
00:01:01.710 --> 00:01:03.552 the six sessions you’ll be able
00:01:03.552 --> 00:01:05.290 to claim your CME credit.
00:01:05.290 --> 00:01:08.224 For those of you who wants to claim it.
00:01:08.230 --> 00:01:10.384 After you answer a brief evaluation
00:01:10.384 --> 00:01:12.744 and some feedback about how we can
00:01:12.744 --> 00:01:14.746 improve the format of the series.
00:01:17.160 --> 00:01:19.115 So today it’s a pleasure
00:01:19.115 --> 00:01:20.679 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
00:01:42.976 --> 00:01:44.991 update us and I think some of the
NOTE Confidence: 0.8310966
00:01:44.991 --> 00:01:47.828 most important updates from the
NOTE Confidence: 0.8310966
00:01:47.830 --> 00:01:49.542 ASH meeting on pediatric leukemias,
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
00:02:01.020 --> 00:02:03.974 talks that will be presented our the.

00:02:03.980 --> 00:02:04.824 Abstractly presented,

00:02:04.824 --> 00:02:07.356 but also about any other additional

00:02:07.356 --> 00:02:09.480 questions about pediatric hematology,

00:02:09.480 --> 00:02:12.056 and in general so we look forward

00:02:12.056 --> 00:02:14.970 to a very exciting discussion,

00:02:14.970 --> 00:02:18.099 and I would like to start by

00:02:18.099 --> 00:02:20.010 introducing Doctor Nikolai Bodos.

00:02:20.010 --> 00:02:22.758 If our associate professor of medicine,

00:02:22.760 --> 00:02:25.050 here in the hematologist auction,

00:02:25.050 --> 00:02:28.249 who focuses on Accutane for blastic leukemia.

00:02:36.010 --> 00:02:37.229 Nicola, you’re on mute.

00:02:36.010 --> 00:02:37.229 Nicola, you’re on mute.

00:02:43.690 --> 00:02:47.670 He would go so almost there next.

00:02:47.670 --> 00:02:51.132 Let me see. Looking for

00:02:51.132 --> 00:02:52.556 my PowerPoint here ago.

00:02:51.132 --> 00:02:52.556 my PowerPoint here ago.
Right, and do you see a single screen? Yup 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, 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
NOTE Confidence: 0.88896275
against conventional chemotherapy.
NOTE Confidence: 0.88896275
And as you can see,
NOTE Confidence: 0.88896275
there was a survival difference
NOTE Confidence: 0.88896275
of 7.7 versus four months,
NOTE Confidence: 0.88896275
which was statistically significant.
NOTE Confidence: 0.88896275
Response rate was 44%,
NOTE Confidence: 0.88896275
with 76% achieving mean negative,
NOTE Confidence: 0.88896275
minimal residual disease.
NOTE Confidence: 0.88896275
So this is all control study
NOTE Confidence: 0.88896275
also blinatumomab it’s an.
NOTE Confidence: 0.88896275
It’s a phase two study single arm
NOTE Confidence: 0.88896275
looking at BLT amount for Peach paused,
NOTE Confidence: 0.88896275
available patients and again you can
NOTE Confidence: 0.88896275
see that the survival here for this
NOTE Confidence: 0.88896275
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 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.
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, negative B cell, 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. These 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 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.
NOTE Confidence: 0.78378654
00:09:43.036 --> 00:09:44.410 CD 20 antibody.
NOTE Confidence: 0.78378654
00:09:44.410 --> 00:09:46.993 As well as use of prophylactic it chemotherapy sectarian metrics 8 so
NOTE Confidence: 0.78378654
00:09:46.993 --> 00:09:48.850 after finishing this intensive phase,
NOTE Confidence: 0.78378654
00:09:48.850 --> 00:09:50.580 patients would go to blender two
NOTE Confidence: 0.78378654
00:09:50.580 --> 00:09:52.596 more phase where they would receive
NOTE Confidence: 0.78378654
00:09:52.596 --> 00:09:54.790 6 four cycles of blinatumomab,
NOTE Confidence: 0.74640524
00:09:54.790 --> 00:09:56.750 four weeks on continuous infusion,
NOTE Confidence: 0.74640524
00:09:56.750 --> 00:10:00.146 two weeks off and.
NOTE Confidence: 0.74640524
00:10:00.146 --> 00:10:02.116 Go to maintenance phase which
NOTE Confidence: 0.74640524
00:10:02.116 --> 00:10:04.956 is actually 18 as opposed to 36
NOTE Confidence: 0.74640524
00:10:04.956 --> 00:10:07.929 months and the blender two map is
NOTE Confidence: 0.74640524
00:10:07.929 --> 00:10:11.814 incorporated between the cycles of pomp,
NOTE Confidence: 0.74640524
00:10:10.560 --> 00:10:11.814 chemotherapy and additional
NOTE Confidence: 0.74640524
00:10:11.814 --> 00:10:13.486 3 cycles of blinatumomab.
NOTE Confidence: 0.74640524
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. 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
accomplished a CR and MRD, negativity was 71%.
After induction and 97% at anytime during the study, early mortality was at 0.
So. I relapse free. Survival was not one of the endpoints of the study, and as you can see, relapse free survival at two years is 71%.
At one year, 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.
00:11:32.569 --> 00:11:34.970 included younger patients 17 and older.
00:11:34.970 --> 00:11:37.376 So this is comparing the results
00:11:37.376 --> 00:11:39.986 of current study in blue with
00:11:39.986 --> 00:11:42.764 another study done in the same
00:11:42.764 --> 00:11:44.230 institution earlier hyper.
00:11:44.230 --> 00:11:47.016 See what with over to Mumbai think
00:11:47.016 --> 00:11:49.485 60 plus patient 69 patients and
00:11:49.485 --> 00:11:52.271 you can see that both studies show
00:11:52.352 --> 00:11:54.820 comparable to overall survival,
00:11:54.820 --> 00:11:57.214 but the plateau of no mortality
00:11:57.214 --> 00:11:59.885 after two years for the current
00:11:59.885 --> 00:12:01.869 study is very encouraging.
00:12:01.870 --> 00:12:05.956 adverse events of interest.
00:12:04.140 --> 00:12:07.910 Related to Blender two map
00:12:07.910 --> 00:12:09.470 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 a 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 second 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 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 CR CR I. And now this actually, you know, for patients receive three cycles. So there were some haematological and molecular responses. So there were some haematological and molecular responses.
As you can see 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, it persisting one marrable us after two cycles went into some of 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?

We sell LL as well as T cell LL. We’re 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 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 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, four.
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. 

NOTE Confidence: 0.7981414

MRD response on the 21 I was observed in 

NOTE Confidence: 0.7981414

78% and overall in 96% of the patients. 

NOTE Confidence: 0.7981414

So the reason that why numbers 

NOTE Confidence: 0.7981414

are all different, there’s been. 

NOTE Confidence: 0.7981414

Five patients were enrolled in 

NOTE Confidence: 0.7981414

CR on this 

NOTE Confidence: 0.812878906363636

study. This is the patients who received 

NOTE Confidence: 0.812878906363636

one cycle before they were enrolled 

NOTE Confidence: 0.812878906363636

because they have to make it to MD 

NOTE Confidence: 0.812878906363636

Anderson to start their treatment. 

NOTE Confidence: 0.812878906363636

So these are grade three adverse 

NOTE Confidence: 0.812878906363636

events and I just highlighted here 

NOTE Confidence: 0.812878906363636

being occlusive disease, which was 

NOTE Confidence: 0.812878906363636

seen only in nine percent of patients. 

NOTE Confidence: 0.83798635

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%.

margin negativity in 96%.

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
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. My so the point of Phase one studies of
course to identify maximal tolerated dose of another class in combination with platinum and dexamethasone.

There are secondary endpoints including CMR 8 Relapse free survival, overall survival and of course, safety. The patients who were included on the study were patients with relapsed refractory Ph+ positive LL with CML in lymphoid space and they have to be treated by at least one desirable 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, 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.
00:25:02.821 --> 00:25:05.249 that the issue is 26 to 73.

00:25:05.250 --> 00:25:07.452 There were no patience with the

00:25:07.452 --> 00:25:09.370 with performance status of three,

00:25:09.370 --> 00:25:12.370 so half of the patients had T315I mutations.

00:25:12.370 --> 00:25:15.258 And as you can see it was very

00:25:15.258 --> 00:25:16.500 heavily pretreated group.

00:25:16.500 --> 00:25:18.435 17% order received platinum probably

00:25:18.435 --> 00:25:21.370 going to my treatment and 56% of patients

00:25:21.370 --> 00:25:23.988 and prior transplant in 67% of patients.

00:25:23.988 --> 00:25:26.202 So nine but very heavily pretreated


00:25:28.670 --> 00:25:30.650 So we’re not even look like

00:25:30.650 --> 00:25:32.484 Sundecks didn’t cause any deal

00:25:32.484 --> 00:25:34.276 tease those limited toxicities.

00:25:34.280 --> 00:25:36.518 Maximal tolerated dose was not reached.
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

NOTE Confidence: 0.7313096

in place with recovery,

NOTE Confidence: 0.7313096

but was not counted as responded because

NOTE Confidence: 0.7313096

Blacks were still about 5% in the marrow.

NOTE Confidence: 0.7313096

So this is to highlight that phonetic

NOTE Confidence: 0.7313096

likes those 800 milligram patients

NOTE Confidence: 0.7313096

are the only patients who responded.

NOTE Confidence: 0.7313096

None of the three patients

NOTE Confidence: 0.7313096

who received an attic LAX

NOTE Confidence: 0.8183674

at 400. Those responded, but five out of 6.

NOTE Confidence: 0.8183674

Our patients in those two with 800

NOTE Confidence: 0.8183674

milligrams of another class had response,

NOTE Confidence: 0.8183674

so this is of course 9 patients.

NOTE Confidence: 0.8183674

Potassium plus fanatical X

NOTE Confidence: 0.8183674

one year old survival, 63%.

NOTE Confidence: 0.8183674

Only two patients died and those were
nonresponders they were not relapse patients.

They did not respond to the magnet and Vene tic lacks combination.

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

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

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 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
overnight as a mob induction, followed by Glenna to map consolidation for patients with newly diagnosed or relapse refractory CD. I have to say that CD 19 and CD 22 positivity is seen in more than 90% of patients with SLE, so this cohort one includes patients older than 60 and older and we will be looking at event free survival, one event free survival. For this transplant in eligible patient group with newly diagnosed LL, the cohort two is for younger
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
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 Netuma 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. 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 intermediate risk or very high risk. Based on that and the backbone 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 tire 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
00:34:21.257 --> 00:34:23.682 do have patients throughout that
NOTE Confidence: 0.8259487
00:34:23.682 --> 00:34:26.920 range so the majority are under 18.
NOTE Confidence: 0.77742743
00:34:29.620 --> 00:34:33.176 This time is expected to accrue 1400
NOTE Confidence: 0.77742743
00:34:33.176 --> 00:34:36.404 patients over 4.4 years, most powered
NOTE Confidence: 0.77742743
00:34:36.404 --> 00:34:40.580 for a 5% difference in four year EFS.
NOTE Confidence: 0.77742743
00:34:40.580 --> 00:34:43.700 However, it only enrolled 847 patients
NOTE Confidence: 0.77742743
00:34:43.700 --> 00:34:47.383 because went at that point to the
NOTE Confidence: 0.77742743
00:34:47.383 --> 00:34:50.401 results of the precursor study was
NOTE Confidence: 0.77742743
00:34:50.401 --> 00:34:53.108 available in that precursor study.
NOTE Confidence: 0.77742743
00:34:53.110 --> 00:35:00.408 AALL 0434 randomized to know Larabee
NOTE Confidence: 0.77742743
00:35:02.800 --> 00:35:06.424 Very much an advantage to having
NOTE Confidence: 0.7045952
00:35:06.424 --> 00:35:10.490 allara been with event free survival.
NOTE Confidence: 0.7045952
00:35:10.490 --> 00:35:13.730 Advantage of about 5% and also
NOTE Confidence: 0.7045952
00:35:13.730 --> 00:35:16.500 at lower CNS recurrence rate.
NOTE Confidence: 0.7045952
00:35:16.500 --> 00:35:20.005 So that’s the study was

56
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, the. 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, four, 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 case.
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 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
NOTE Confidence: 0.7734715
the first 2 blocks patients were
NOTE Confidence: 0.7734715
randomized to blend into mmap or two.
NOTE Confidence: 0.7734715
Third block and then they went to
NOTE Confidence: 0.7734715
stem cell transplant if they could.
NOTE Confidence: 0.7734715
And this study also ended early.
NOTE Confidence: 0.7734715
It was supposed to enroll 202
NOTE Confidence: 0.7734715
patients and only 100 patients or
NOTE Confidence: 0.7734715
so were enrolled because there was
NOTE Confidence: 0.7734715
a clear result that there was an
NOTE Confidence: 0.7734715
advantage of blended to mmap both in.
NOTE Confidence: 0.7734715
Add.
NOTE Confidence: 0.7734715
Event free survival and in time
NOTE Confidence: 0.7734715
from diagnosis to relapse.
NOTE Confidence: 0.7734715
There is also an advantage.
NOTE Confidence: 0.7734715
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 arm overall and it was more remarkable 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 there weren’t. events in CR S and there weren’t. There was really not an increase in severe events or moderate or severe events,
so the third study that also relates to blend into my map has to do with whether Blend into my map. Treatment prior to car affects car outcomes. And this is a multi site study. I’m so just there will be a separate car session, but this slide is here if people want to look at this later. But basically a patients T cells are harvested and then they are expanded and then they are transfected to T cells via viral vector 2. Have T cell receptor gamma and
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.

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.

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 cell constructs, and it was a seven site study. Their median post infusion follow-up was 2.3 years and this occurred over seven years. Um, 75 of the 420 patients had had prior blennorrhea, 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 blennorrhea and those who did not in terms of MRD status.
whether they had an empty or M3 marrow

CNS status, extramedullary disease,

or circulating glass.

There was a higher rate in those who had
prior brunette with the KM T2A R mutation,
maybe indicating that there were more younger
patients 'cause that occurs more in infants.
And the overall response to the
car was great in these 120 patients,
91% achieved CR,
88% were MRD negative and the
relapse rate was 39.8%,
however.
Blender patients are the ones
who had previously know were more
likely to have residual disease.
00:45:43.610 --> 00:45:45.378 Post CD 19 car,
NOTE Confidence: 0.78015244
00:45:45.378 --> 00:45:49.365 so it was 18% if one had prior blina
NOTE Confidence: 0.78015244
00:45:49.365 --> 00:45:52.910 and only 7% if there was previous blender.
NOTE Confidence: 0.78015244
00:45:52.910 --> 00:45:55.574 This also corresponded to worse relapse
NOTE Confidence: 0.78015244
00:45:55.574 --> 00:45:58.230 free survival both at six months.
NOTE Confidence: 0.78015244
00:45:58.230 --> 00:46:01.324 Anna, 12 months and the median relapse.
NOTE Confidence: 0.78015244
00:46:01.330 --> 00:46:03.540 Free survival was twenty months.
NOTE Confidence: 0.78015244
00:46:03.540 --> 00:46:07.236 If one had had previous planner and 45
NOTE Confidence: 0.78015244
00:46:07.236 --> 00:46:08.930 months. If there had been no blender.
NOTE Confidence: 0.8373493
00:46:11.940 --> 00:46:13.760 So we’re not is associated.
NOTE Confidence: 0.8373493
00:46:13.760 --> 00:46:16.259 Also was also associated with a higher
NOTE Confidence: 0.8373493
00:46:16.259 --> 00:46:18.859 incidence of CD 19 modulation pre car.
NOTE Confidence: 0.8373493
00:46:18.860 --> 00:46:21.038 So the incidents of CD 19,
NOTE Confidence: 0.8373493
00:46:21.040 --> 00:46:22.768 negative, dim or partial
NOTE Confidence: 0.8373493
00:46:22.768 --> 00:46:25.360 expression prior to the car was.
NOTE Confidence: 0.8373493
Was higher in prior blender patients, 13% versus 6% and in patients in which there was a pre and post Lena CD 19 expression 11% had evolution to CD.

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.

00:47:28.474 --> 00:47:31.272 of Dana Farber consortia patients

00:47:31.272 --> 00:47:34.042 who were up to 50 years and initially

00:47:34.042 --> 00:47:37.750 they were true with the coli based

00:47:37.750 --> 00:47:40.715 ones and had 30 weeks of asparagine
depletion and then later,

00:47:40.715 --> 00:47:43.634 this changed to PEG.

00:47:43.634 --> 00:47:46.219 And steroid Dennis Progenies associates

00:47:46.220 --> 00:47:48.276 Austin across is glucose corduroy,

00:47:48.276 --> 00:47:50.846 And steroid Dennis Progenies associates

00:47:50.846 --> 00:47:53.517 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. 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 a 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,
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 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.

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 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

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

But I think the challenges and what wanted to highlight the toxicity issue.

I think what we want to learn

Even in patients in their 20s who
00:54:13.510 --> 00:54:15.705 we call the older patients rather,
NOTE Confidence: 0.8807261
00:54:15.705 --> 00:54:17.895 they have higher rates of infection.
NOTE Confidence: 0.8807261
00:54:17.900 --> 00:54:20.096 They have higher rates of AVN.
NOTE Confidence: 0.8807261
00:54:20.100 --> 00:54:21.930 They have had higher rates
NOTE Confidence: 0.8807261
00:54:21.930 --> 00:54:23.028 of pancreatitis and,
NOTE Confidence: 0.8807261
00:54:23.030 --> 00:54:25.226 and it’s not clear how to
NOTE Confidence: 0.8807261
00:54:25.226 --> 00:54:26.690 balance those two things,
NOTE Confidence: 0.8807261
00:54:26.690 --> 00:54:28.772 but they would be treated very
NOTE Confidence: 0.8807261
00:54:28.772 --> 00:54:30.618 differently and they would have
NOTE Confidence: 0.8807261
00:54:30.618 --> 00:54:32.178 good disease free outcomes.
NOTE Confidence: 0.7732424
00:54:33.590 --> 00:54:35.500 So we just want comment.
NOTE Confidence: 0.7732424
00:54:35.500 --> 00:54:37.420 We do use pediatric protocols.
NOTE Confidence: 0.7732424
00:54:37.420 --> 00:54:38.928 Pediatric like protocols become
NOTE Confidence: 0.7732424
00:54:38.928 --> 00:54:40.436 backbone protocols and we’re
NOTE Confidence: 0.7732424
00:54:40.436 --> 00:54:42.397 participating in Lion study which
NOTE Confidence: 0.7732424
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 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
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. 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 investigation that study discussed in this session afterwards with the questions. Is that they would like to understand what was their response to the
00:58:54.168 --> 00:58:56.588 blender and weather because it
NOTE Confidence: 0.8002771
00:58:56.588 --> 00:58:59.939 may be that even with the karty.
NOTE Confidence: 0.8002771
00:58:59.940 --> 00:59:03.804 I'm sorry even with the CD 19 expression,
NOTE Confidence: 0.8002771
00:59:03.810 --> 00:59:05.970 there’s something different about
NOTE Confidence: 0.8002771
00:59:05.970 --> 00:59:08.670 those individuals that needs to
NOTE Confidence: 0.8002771
00:59:08.670 --> 00:59:11.680 be recognized and then the other.
NOTE Confidence: 0.8002771
00:59:11.680 --> 00:59:14.008 Thing is that I think just pairing it
NOTE Confidence: 0.8002771
00:59:14.008 --> 00:59:16.448 with that other study that I presented
NOTE Confidence: 0.8002771
00:59:16.448 --> 00:59:19.050 where the outcomes are better if one
NOTE Confidence: 0.8002771
00:59:19.050 --> 00:59:20.905 receives blina prior to transplant.
NOTE Confidence: 0.8002771
00:59:20.910 --> 00:59:23.689 So one can think about I definitely
NOTE Confidence: 0.8002771
00:59:23.689 --> 00:59:25.250 agree about having car.
NOTE Confidence: 0.8002771
00:59:25.250 --> 00:59:27.644 T in the arm and it arium.
NOTE Confidence: 0.8002771
00:59:27.650 --> 00:59:29.798 But whether one should think about
NOTE Confidence: 0.8002771
00:59:29.798 --> 00:59:32.110 transplant versus party as the next step,
NOTE Confidence: 0.8002771
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. Disease of course. Most of the patients have diesel L 85% only.
01:00:03.910 --> 01:00:06.499 need as not a lot of studies
01:00:06.499 --> 01:00:08.399 addressing this patients right
01:00:08.400 --> 01:00:10.776 now, especially adults, and one of
01:00:10.776 --> 01:00:13.117 the questions which Lloyd is just
01:00:13.117 --> 01:00:15.175 asking with regard to this discussion
01:00:15.175 --> 01:00:17.849 of car T versus other newer regions.
01:00:17.850 --> 01:00:20.489 Can these new region across the CNS?
01:00:20.490 --> 01:00:23.109 Yeah, you know.
01:00:23.110 --> 01:00:24.886 It’s challenging questions,
01:00:24.886 --> 01:00:27.846 so you know we know.
01:00:27.850 --> 01:00:29.494 That you know we’re not counting
01:00:29.494 --> 01:00:31.910 on Blender to my boy Natuzzi map to
01:00:31.910 --> 01:00:33.794 address CNS disease in these patients
01:00:33.850 --> 01:00:35.700 were excluded from those studies,
01:00:35.700 --> 01:00:37.674 so we don’t really have those
01:00:37.674 --> 01:00:40.000
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,

and 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 practice or your treatment 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 --> 01:02:19.300 Older patients, the question about

01:02:19.300 --> 01:02:22.130 transplant is more difficult because

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

01:02:24.770 --> 01:02:29.356 And the administration of this new drugs

01:02:26.961 --> 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,
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.