Will. Occupy some time, which we don’t have a lot of today. Uh, my name is Nicolai Podolski. If I’m associate Professor, Department of Medicine, Hematology section, and I’m joined by Doctor Amir Zadan and Doctor Lourdes Mendez. Today we will be talking about myeloid malignancies and acute leukemias. I will start by talking about ash presentations I have selected on the topic of myeloproliferative neoplasms. Amar will continue and we’ll discuss. Mrs.
Abstracts and finally Lordis will finish, uh this session, uh, by discussion of studies which were presented on the subject of acute myeloid leukemia and all. So without further ado, I will proceed with my presentations. Those who are joining late will be able to get benefit anyway because this presentation is structured and includes quite a few things. So hold on one second, let me just see here we go. Uh, so I’m going to talk about UH-4, uh,
different presentations on the subject of myelofibrosis and then uh I will finish with polycythemia Vera. It is interesting how many drugs are being developed in the area of myelofibrosis taking into consideration relatively low prevalence of the disease in the United States. At any given time, we have about 13,000 patients. Of course, PVR is much more prevalent because these patients survive a bit longer, so maybe 10 times more so, but of course development of
This new drugs are benefiting.

For patients and today I will be talking about four, four different medications and different stages of development. And I just wanna say that none of them are approved by FDA in myelofibrosis at this time. And you know some of them are in the pipeline closer to be approved to others is just at the beginning and phase one development. So this is the table which summarizes currently approved drugs which are Jack inhibitors as well as the drug which is. Uh in the pipeline for approval,
new drug application was submitted by the company developing this drug to the FDA. This is monoethnic, the last and the table and the review is expected to end sometime at the beginning of summer. So very soon we’ll know if this drug is going to be approved and it is expected to be so this drugs called Jack inhibitors, but they actually have slightly different mechanism of action and that’s why they may have slightly different effectiveness as well as different side effects was approved in 2011.
More than 10 years ago and it is Jack one Jack 2 inhibitor used in frontline treatment for high risk patients with myelofibrosis intermediate and high risk patients with main side effects related to cytopenias.

driven in 2019, eight years later.

And this is the drug which can be used in frontline but most of us are using it in second line and it inhibits Jack 2 but also Jack one and some other tising kinase including fleet 3 enhanced GI side effects.

Pacritinib approval was in February of 2022 for patients with.
Myelofibrosis who have low platelet count less than 50 button second line NCC and recommends to use it uh for patients with any platelet count. Again GI side effects can be seen in patients using this drug. Finally momelotinib. Claims fame in the area of anemia which is one of the common manifestations of myelofibrosis and mostly it is expected to be beneficial for patients because of its inhibition not only of Jack, but acvr.
leads to anemia and acvr inhibition

So this is the study momentum phase

three study of MOMELOTINIB versus danazol

in symptomatic patients with anemia.

Who have uh intermediate or high risk myelofibrosis and previously treated with Jack inhibitor.

So these are the patients mostly treated with ruxolitinib who then either were resistant or refractory to this drug

and proceeded with the second line treatment which included monoethnic or danazol in this randomized study.

So as I’ve mentioned inhibits Jack one, Jack two similar to ruxolitinib but
also a CD R1 which is active in a receptor type one and signaling in ACR. One leads to increased production of hepcidin which limits access to iron for hematopoiesis and inhibition of C acvr. One actually decreases hepcidin and improves production of red blood cells. As the result it is expected that anemia can improve. So the phase three trial looked at patients who are Jack experienced and those who are symptomatic as well as an intermediate to high risk disease based on dips and have hemoglobin less than 10.
So with all of this.

Actions anemic to certain degree and platelet count should be more than 25,000.

So the study randomized patients into one fashion and the first group received more melatonin but 200 milligrams per day versus danazol placebo.

The group with Danazol received danazol 300 milligrams twice a day and monolithic placebo.

So the key primary endpoint was told symptoms score response at Week 24, secondary endpoints transfusion independence at Week 24 and splenic response rate at week 24.

This is the results which were
00:05:29.898 --> 00:05:30.844 presented AT-2022.

00:05:30.844 --> 00:05:35.650 So this the top line results at week 24.

00:05:35.650 --> 00:05:38.150 Also the results were published in Lancet Climatology.

00:05:38.150 --> 00:05:39.650 This month, uh, so uh, as you can see, I didn’t start from primary endpoint,

00:05:43.136 --> 00:05:44.936 uh, I didn’t start from primary endpoint,

00:05:44.940 --> 00:05:46.430 I started from transfusion independence here where you can see in the Red Square,

00:05:46.430 --> 00:05:48.837 the response rate for momelotinib group was higher than for danazol group,

00:05:48.840 --> 00:05:51.366 the response rate for momelotinib group was higher than for danazol group,

00:05:51.366 --> 00:05:54.119 was higher than for danazol group,

00:05:54.120 --> 00:05:56.556 30% versus 20% of patients were transfusion independent at Week 24,

00:05:56.556 --> 00:05:58.504 it is actually impressive how well danazol did, 20%.

00:06:00.448 --> 00:06:03.420 So this drug certainly has role in
management of anemia, myelofibrosis, but obviously one Molotov was better. So the other result, the primary endpoint, the symptoms. There are controlled in 25% of patients and splenic reduction by 35% was accomplished in 23% of patients. Certainly you wouldn’t expect much of that happening in Danazol arm. So when the Lightning did reasonably well from the standpoint of symptoms and spleen size reduction in this group of patients previously treated with ruxolitinib. So the data was then looked at in different subgroups based on platelet
count and it looks like it works as well.

The patients got platelet count less than 50 uh hundred,

less than 100 or less than 150

with uh uh better results in

so side effects, uh,

there are not no surprises here uh.

So the Grade 3 or higher adverse

events happened with similar

similarly in 49 and 46% of patients in

Momelotinib Group and Danazol group,

the rate of serious adverse

was very similar.

So just want to highlight obviously you know
cytopenia still a current myelofibrosis, there are some GI side effects which happened similarly in both groups of patients and peripheral sensory neuropathy is highlighted at the bottom. Was there a signal in early phase studies that may be an issue in more melodic treated patients but it didn’t really seem to happen in this particular phase three trial? Moving on uh, so from Jack inhibitors to the drugs which uh have different mechanisms of action and still used and myelofibrosis and this particular drug is called navitoclax and in this
study it was used together works with Jack inhibitor naive patients now. So it’s a frontline treatment for patients with myelofibrosis who have intermediate to high risk disease. And now the study highlights certain things which claim that the results are suggestive of disease modification.

Let’s look at the navitoclax itself. So what does this drug so and why would we combine it with ruxolitinib? So rux lithium suppresses transcription through Jack inhibition of jackson pathway.
transcription of pro survival
NOTE Confidence: 0.783701811538462
proteins MCL one and BCL Excel.
NOTE Confidence: 0.783701811538462
So Navitoclax it’s direct inhibitor of
NOTE Confidence: 0.783701811538462
antiapoptotic activity of BCL XLS well
NOTE Confidence: 0.783701811538462
as BCL two and in preclinical studies.
NOTE Confidence: 0.783701811538462
Yeah, they showed this to drug showed
NOTE Confidence: 0.783701811538462
synergistic synergism in inducing
NOTE Confidence: 0.783701811538462
apoptosis in malignant cells that led
NOTE Confidence: 0.783701811538462
to the development of this combination.
NOTE Confidence: 0.783701811538462
And at ASH 2022 Cohort 3 of refined study
NOTE Confidence: 0.783701811538462
phase two trial enrolling Jack Jack
NOTE Confidence: 0.783701811538462
inhibitor naive patients was presented.
NOTE Confidence: 0.783701811538462
So key criteria key endpoint was splenic
NOTE Confidence: 0.783701811538462
volume reduction by 35% at week 24 measured.
NOTE Confidence: 0.783701811538462
Grammarian cat scan and key secondary
exploratory endpoints were changing
bone marrow fibrosis grade from baseline reviewed locally as well as reduction variant frequency for driver mutations determined centrally.
So as we are 35 was achieved in 80% of patients which is pretty good. So you can see that pretty much all the patients had some splenic reduction and again among those who accomplish as CR35 response at 24 weeks about third of patients had achieved. Reduction in marrow fibrosis by at least one grade. So the secondary endpoint
looked at fibrosis itself.

The reduction by one grade was observed in nine out of 32 patients, 28% and among nine patients, two had complete resolution of myelofibrosis.

The mean time to resolution to reduction in bone marrow fibrosis was 12.3 weeks and also there was reduction, 36% of patients had 50% reduction or more.

So this findings uh in improvement of fibrosis as well as reduction of varietal frequency objectives, mutations suggests disease modification with use of this medication combination.
So next drug which also was tried in treatment naive patients. Together with ruxolitinib is called Palabra Zeb. This is again a phase two study and first of all couple of words about collaborative itself. So it’s better. Keep it and that is a family would be genetic proteins which are overexpressed in cancer. Collaborative is novel oral BET inhibitor which belongs to this class of drugs known as epigenetic modifiers. The lab razip selectively inhibits
BD1 and D2 bromo domains of that
proteins and you can see on the
cartoon on the right that it can work
cordantly with Jack inhibitors.
So Jack inhibitors inhibitors jackstadt
pathway that proteins are important in.
Transcriptions which lead to
production of TGF Beta NF, Kappa B,
Those are associated with aberrant
differentiation,
increased cytokines,
bone marrow fibrosis and cell survival.
So if you inhibit Jack as well as
better at the same time you decrease
production of this site okines and
this can lead to the improvement of symptoms and perhaps disease modification. So the study we’re looking at is has four arms, but we’re only looking at. Arm 3 which is a first line uh, treatment for patients not exposed to Jack inhibitors who have intermediate tool to high risk disease and there’s all of these people were in this phase two trade study: received collaborative and ruxolitinib. The primary endpoint was SVR 35, splenic volume reduction by 35% and total symptom score is actioned by 50% at week 24. So as you can see the SVR.
35 was at week 24 was 68.

Some previous study actually 80% again

we can’t come cannot compare apples

and oranges here and TSS 50 reduction

was accomplished by 56% of patients.

Interestingly at any given time as we

are 35 was accomplished again by 80%

are 35 was accomplished again by 80%

of patients similar number to which

was shown previous study I shared with you.

So from the standpoint Ballmer of

fibrosis again about 27% of patients

fibrosis again about 27% of patients

here at had at least one great reduction

in bone marrow fibrosis by Week 24.

Clinical responses were connected

to reduction of variable frequency

inject 2V617-F mutations.
Most adverse events here were low grade and 14% of patients had to discontinue the study participation due to adverse events. So uh, this is to me is one of the more exciting presentations plenary session. You can see this presentation #6 and it looks at completely different mechanism of action. This group of diseases and myeloproliferative neoplasms, so this is the presentation of preclinical data on monoclonal antibody against mutant calreticulin.
So mutant calreticulin is responsible for modification of thrombopoietin receptor before it moves to the surface of the cell. Mutated calreticulin instead of just modifying it attaches itself to the TPO receptor. And moves together with the receptor to the surface, causing dimerization of the receptor and its activation, which doesn't require ligand. When antibody attacks and mutated color electrically and on the surface of the cell it, the reverses this dimerization and activation of jakstadt pathway.
So this study used fully human FC silent IgG 1 antibody again against mutant calreticulin. The binding was selective to mutant calreticulin antagonized mutant calreticulin used signaling and congenic function inhibited cell proliferation. Start 5 phosphorylation in CD34 mutant calreticulin cells. It caused apoptosis of those cells and didn’t affect non mutant. Political in cells once again you know this is the uh preclinical data. The Phase One study is expected to be opened within next few months.
So moving on to polycythemia Vera, much higher incidence and prevalence of this disease and the United States only one study and this is the study for patients with low risk disease. So low risk defined as age less than 60 and no history of Thrombosis, so this patients historically treated with phlebotomies and aspirin and what this study looked at is addition of row peg interferon A2, B to this treatment. So the patients randomized in this phase two trial in one to one fashion standard of care is on the
left phlebotomy plus aspirin and on the right is lobotomy plus aspirin as well as row peg interferon.

It’s at fixed dose of 100 micrograms every two weeks.

Primary endpoint was response and. Response was defined as median chemical less than 45 in the absence of disease progression.

Definition of disease progression for low risk HPV patients includes progressive symptoms and progressive symptomatic thromboctosis, progressive Leukocytosis, vascular and major bleeding complications.
So this is the primary endpoint.

The study was published in 2021.

So at that time the second interim analysis was presented at one year and this is a final results.

So this is observation of patients over a period of two years.

Study was stopped to accrual after second analysis uh because uh significantly better performance of patients who were treated with row peg interferon from the standoff composite primary endpoint.

So you can see that this is schematically control lack of progression which was observed.
in much higher number of patients treated with row peg interferon.

So the separate endpoints for hematocrit control and disease progression you can see that frequency of phlebotomies was less in experimental arm and uh, you can see that the disease progression was only observed in patients treated with phlebotomies plus aspirin without rollback. In six patients placed count increased to more than a million and baseline was lower than 602 patients planning infarction and transient ischemic attack occurred.
The effect was reasonably durable as you can see and also there was improvement of symptoms as measured by MPN. Off TSS and splenomegaly improved in ROBEC treated patients as well significantly when compared to patients treated without rollback. So Jack 2V617-F very until frequency decreased in ropek treated patients and slightly increased the 12 months in patients who didn’t receive rollback. Obviously people who are treated with row had higher incidence of adverse events.
Related adverse events 55% versus 6%

Grade 3 or 4 adverse events were about the same and adverse events that caused treatment discontinuation were only revealed in rollback treated patients.

In conclusion, I would like to summarize what I presented to you.

Molotov may improve anemia in patients with myelofibrosis and acne due to acvr inhibition.

Ruxolitinib and collaborative, the better inhibitor and light treatment associated with high SVR rates and TSS 50 reductions.
Decrease fibrosis the clustering of megakaryocytes and decrease in Jack 2V617 affair and total frequency may be a sign of disease modification and phase three trial which used the same model of combining roots lithium and collaborative just completed accrual. So waiting for the results Rubidium and Navitoclax and another combination frontline treatment. This BCL two BCL Excel inhibitor also was associated with a significant reduction in spleen volume as well as decreasing fibrosis and Jack. Will be six months there until frequency phase three transform.
one study is ongoing monoclonal antibody against mutant calreticulin is effective in preclinical models. We are looking forward to see how this drug will perform in clinical trials. Finally, row Peg interferon can be considered for selected patients with low risk polycythemia Vera based on the results of phase two study.

Thank you, Nikolai. So I’m going to be talking about MD S right now and let me share my Slides.
So I decided actually talk a little bit more in general about some of the main updates and on integrating some of the ASH abstracts. These are my disclosures. So I’m going to talk about updates in the diagnosis, classification, prognostication and response assessment and then management to flower. On higher risk MD S. I think the first important thing to know is that the diagnostic criteria for MDS were updated by The Who. So right now rather than requiring a hemoglobin of less than 10 and a
00:19:41.683 --> 00:19:43.267 platelet count of less than 100,
00:19:43.270 --> 00:19:44.607 as you can see to the left,
00:19:44.610 --> 00:19:46.370 the thresholds were a little
00:19:46.370 --> 00:19:47.426 bit less restrictive.
00:19:47.430 --> 00:19:49.272 So any anemia which is hemoglobin
00:19:49.272 --> 00:19:52.408 less than 12 in women and 13 in men
00:19:52.408 --> 00:19:53.884 or thrombocytopenia platelet count
00:19:53.884 --> 00:19:56.072 less than 150 can diagnose MSDS
00:19:56.072 --> 00:19:58.300 once you exclude other things that
00:19:58.300 --> 00:20:00.650 can cause MSDS but importantly.
00:20:00.650 --> 00:20:02.522 Certain genetic alterations such
00:20:02.522 --> 00:20:06.670 as as after B1 and B53 one could
00:20:06.670 --> 00:20:09.070 potentially lead to diagnosis
00:20:09.070 --> 00:20:11.598 of MDS in the right context.
00:20:11.598 --> 00:20:13.936 So that will probably mean that you
00:20:13.936 --> 00:20:15.628 are going to see more diagnosis
NOTE Confidence: 0.879195086666667
00:20:15.628 --> 00:20:17.788 on the as among your patients.
NOTE Confidence: 0.879195086666667
00:20:17.790 --> 00:20:20.567 The second I think major change in 2022.
NOTE Confidence: 0.879195086666667
NOTE Confidence: 0.879195086666667
00:20:24.330 --> 00:20:26.070 We have two different classifications
NOTE Confidence: 0.879195086666667
00:20:26.070 --> 00:20:27.114 right now for
NOTE Confidence: 0.8667911825
00:20:29.350 --> 00:20:33.612 MDDS WHO 20222020 and ICC 2022 and
NOTE Confidence: 0.8667911825
00:20:33.612 --> 00:20:36.096 this is important because you there
NOTE Confidence: 0.8667911825
00:20:36.096 --> 00:20:39.295 are some differences between these two
NOTE Confidence: 0.8667911825
00:20:39.295 --> 00:20:43.017 classifications and you are going to start
NOTE Confidence: 0.8667911825
00:20:43.017 --> 00:20:45.856 seeing in your pathology reports some
NOTE Confidence: 0.8667911825
00:20:45.856 --> 00:20:48.386 discrepancies between the two diagnosis.
NOTE Confidence: 0.8667911825
00:20:48.390 --> 00:20:50.256 In some cases a patient could
NOTE Confidence: 0.8667911825
00:20:50.256 --> 00:20:51.189 be diagnosed with.
NOTE Confidence: 0.8667911825
00:20:51.190 --> 00:20:55.465 Animal by one category and MDS by the other.
NOTE Confidence: 0.8667911825
00:20:55.470 --> 00:20:57.350 For the sake of time today I’m not going to
be able to go through the details of this, but the main updates is that certain genetic alteration as I mentioned, such as 3B1 and TB53 mutated now can define genetically.

And the and also the category of 10 to 19% blast in the ICC classification is called MDS/AMD.

So I think this is important to remember as you look at your path reports and one of the ASH abstracts actually compared the two classifications. This was a large effort on behalf of the International Consortium for MDS and I’m not going to go again.
through all these results, but what? Was found is that certain aspects of each classification seem to function well and therefore ideally these two classification should be harmonized, which is an effort that is currently ongoing. But until that happens, feel free to reach out to us and to the pathologist to discuss any aspects of the path report that does confuse you a little bit because it’s going to be a confusing gear in terms of the diagnosis and classification. Now going to prognostication where things a little bit easier. So we still think about MDS in two big
groups, lower risk and higher risk.

Lower risk quality of life is the main goal.

Higher risk you generally would treat with the goal of changing the Natural History, often requiring bone marrow transplantation.

So this is the classical scoring systems, IPS and revised ipss, the two most commonly used ones.

And based on the adding of the blast count, cytogenetics and cytopenias you classify the patient into these lower and higher risk.

And one of the main developments of 2022 was the publication of the ISM.

So this finally and formally
integrated molecular IPS into the prognostic picture you can see here. On this table a list of the genes. So there are 17 or sorry, there are 31 different genes that are part of the molecular classification and this is becoming the standard of care risk tool assessment. Again, why is that important for your practice is now it’s having the molecular data affects both the diagnosis classification as well as prognostication of MD S and I still see many path reports or when the World Cup for Ms. is done in Community settings.
Many times people are just sending karyotype and fish and they are not sending molecular assessment. So it’s really important that an exigency sequencing, which is readily available in our impact department should be run on those patients because it can affect all of these. Assessments which subsequently can influence therapy. The ISM now uses 6 categories rather than five categories, 3 lower risk ones and three high risk ones. And the good news is that this good thread of the intermediate ISR,
which used to be a problem because it was never clear whether you treat it as lower risk or higher risk. There are different ways to do that, but in the molecular IPS the patient is either lower risk or high risk, and I think that makes it somewhat easier. Now this model is a bit complex and it’s not easy to clearly remember all the different variables, but the good news is that you have this website. And the as riskmodel.com you can see to the left side and all what you need to do is just enter the variables plus count,
platelet count and what molecular alteration the patient has.
And then you can see that the ISM score for example for this patient was .24 moderate high.
Also, this gives you the revised ISS score, so you can get both the molecular and revised IPS in the same in the same snapshot when you enter the data.
So one of the important presentations from ASH 2022 was comparing the molecular IPS which was just published in 2022 again against the revised IPS.
And what you can see here is that the C index,
which is a measure of the prognostic utility or the model accuracy is better for the molecular IPS as in this large European cohort.

There were a number of presentations looking at this from different cohorts and all of them showing the same thing is that the molecular IPS is better.

And therefore I think we should really try to get it calculated on all of our patients, but of course that’s going to require you to give them molecular data.

So we talked about diagnosis classification and the response criteria. And response criteria have been somewhat problematic in MD S because
they have contributed to some of the delayed drug development in my opinion by introducing data, molecular response responses that are sub optimal such as model. PR which has never been correlated with long term survival and at the same time used very high cutoff for hemoglobin, for example of 11 to denoise donate complete response which is very difficult to obtain in an Ms. And there's this is beyond the scope of discussion today about all the issues that come with the response criteria.
But finally an international panel, the IWG has revised the criteria so we have a new criteria for higher risk. Mrs. and I think this is going to address several shortcomings of the 2006 criteria. How about some of the clinical development abstracts? There were several important ones for both lower risk and higher risk. For lower risk MD as the treatment continues to be ESA erythropoiesis stimulating agents for most patients with lower risk MD S. How about for patients who have deletion? 5Q Lenalidomide is an important drug.
Lenalidomide is currently approved for lower risk deletion 5Q DS patients who are transfusion dependent. So this important abstract, this is a randomized phase three trial looked at giving Lenalidomide in patients with Delphi Q lower risk who are not yet transfusion dependent. As you can see the criteria eligibility anemia of less than 12. So if you have a hemoglobin of 10 or 11 and you are symptomatic. Even if you are not needing transfusions, you would be eligible for this trial. Patients were randomized to
Lenalidomide in a time limited fashion, meaning that you are getting the drug only for two years, it's not continuous versus placebo. And then the patient who are monitored and this is the top line result of this study is that Lenalidomide has significantly lower the chance of needing regular transfusions as well as delayed the time to transition dependency significantly more than six years. For patients who are only related to mild compared to patients who are getting a placebo and also induced a lot of cytogenetic responses and their safety profile,
both hematological and non-hematological was generally well tolerated. So I think this could potentially lead to a major change in practice in earlier initiation of Lenalidomide and this is one thing that I think is important to consider in patients with deletion 5Q who are anemic but not yet transfusion dependent. The Middle East trial which many of you have contributed to when it was ongoing. This trial led to the approval of Los Battleship the transforming growth factor pathway drug that is illegal trap that has been shown in
patients with RingCentral Plast Mrs.

with ring sideroblasts to improve transition independence.

You can see this is the New England Journal of Medicine,

a paper that led to the approval 38% transfusion independence we.

Published an update from that study in 2022 showing that the responses would lose better ship, were long lasting and not only limited to transfusion dependence, but there was a lot of improvement in hematologic parameters as well as significant reduction in the red blood cell transfusion among those who did
not fully achieve transfusion independence. However, the approval was after SF failure for patients who have Ms. with ring sideroblasts, so the commands trial this is a phase three. Well, uh of less partnership versus ESA, so this is a frontline treatment where patients were randomized to receive either lose partnership or erythropoietin in the frontline setting first treatment and not only in patients with RingCentral Press, but also in patients without ring syndrome.
Last and this trial was a large international trial, more than 350 patients were enrolled including here at TL and data were not presented from this trial in ASH, but there was a press release from the manufacturer. Uh, basically declaring positive results for the primary endpoint. So this is I think could be an important development in the management of lower risk MD S in 2023. We are hoping to see the data later this year describing the impact of Los leadership in the frontline setting.
Another free trial that was open here. TL is the trial that looked at the imetelstat which is a first in class telomerase inhibitor. This is an IV drug that’s given every four weeks and phase two data single arm. Phase two data previously published have shown that among patients who are heavily transfused without deletion 5Q but had lower risk. MD S 38 patients have higher rates of transfusion independence. With this drug 40% achieve transfusion independence.
What was presented in ASH is an update on the patients who had transfusion independence on the drug, which lasted more than one year and there were eleven out of the 3829%. And you can see here that among those patients there was significant durability of the transition independence, 92 weeks of transfusion independence, but also the mean change in the hemoglobin was quite impressive. The median increase was almost 3 grams. The median increase was almost 3 grams. So those are not patients. Going from hemoglobin 8 to 9, this is someone going from 8 to 11. So that’s certainly is a meaningful benefit.
But importantly there was a press release also this was a year of press releases, all our risk and bias, the Immerge phase three trial, the top line results also confirmed that advantage of the phase two showing transition independence with the loss would initially start in 40% of patients who have received this drug and this drug is now in front of the. They are also in consideration for approval. We are hoping to see the data also later this year. But between these two drugs, I think there could be a significant
change in the landscape of management of lower risk MDs about higher risk MDs.

So at Jamies have been a significant. Basically in terms of helping patients with high risk MDs but real life data such as the one I’m showing you here showed that the benefit from HM is is suboptimal. The median survival is only 11 to 17 months. Once they stop working, the survival is 5 to six months. So we certainly need improvements. However, many of the drugs that were added to HMA’s have not unfortunately shown any benefit. We have a big graveyard of drugs. You can see some of them listed here.
Once combined with HM, it is initially shown to have good data in single arm trials, but once you have the phase three trials or the randomized phase two trials, the results were negative.

However, we have other drugs that are now in phase three trials and we are optimistic about some of those.

You can see here 6 randomized phase three trials ongoing in the high risk MD S sitting in combination with HMS. The two trials that you see the drug listed in black people need to start and APR 246.
those two threads have read out as negative for the primary endpoint.

But the other four trials with venetoclax, sabatelli map, negroli Mab and Tammy paroxetine, all of those are ongoing and I’m going to tell you a little bit about them. However, none of those four trials have yet reported. But I think those are trials that are important for the field because they potentially, if any of them are positive, it could change the landscape of treatment of high risk MD so another important reminder is that.
Patients with MDD should be considered for transplant when they have higher risk disease. If you just keep the patient on HMA alone the long term survival is very poor, 4% for higher risk Ms. patients. And now we have randomized data. This is biological assignment trial. If you have a donor versus no donor and that showed up to the age of 75 that your overall survival could be doubled. The three-year survival for patients who had a donor was 50% compared to 26% and again this is up. At the age of 75,
many patients are being told they are not candidate for transplant because they are late 60s or early 70s. But if the patient is otherwise good shape, I would strongly recommend that you refer them to discuss transplant. Venetoclax is approved for all their unfit patients with AML. However, the data in frontline in high risk MD S has been promising. But this is single arm trial. We have previously published a trial that Yale participated in in the relapse refractory setting where venetoclax has been added after HMA.
failure and the Verona trial which also was open at TL randomized patients to receive Asia versus Asia when this trial has fully accrued. And we are waiting for the results of this trial to. Look at the role of venetoclax in high risk MD. Another I think interesting molecule that we’ve been part of is sabatelli map and item 3. So tem three basically is an inhibitory receptor that is not only present on T cells like regular immune checkpoints, but this is also present on some of
the leukemia stem cells and the blast.

So Sabato Lima could basically be targeting both the immune system as an immune checkpoint inhibitor, but also directly attacking the plus and the leukemia stem cells. Early data have suggested activity in the clinical setting and based on this around the phase two trial which we had open here at TL, the stimulus MS1 randomized patients to receive Sabato Lima with HMA versus HMA alone and the primary endpoint was CR and PFS. We presented this data in ASH. This was the only randomized phase
Two trial presented in ASH 2022. Unfortunately the primary endpoint on this randomized. This too was not reached. There was still no significant difference in CR and PFS. But what I attract your attention to is that there was late separation of the curves and the PFS was eleven months compared to 8.5 months, which would be potentially consistent with delayed onset of action seen importantly among patients who achieve CR. So the CR rate was not increased,
but those who achieved CR, the duration of the CR was doubled for the combination compared to. I mean one of therapy again suggesting potentially that there could be a deeper response and more durable response with with the combination. But of course these are exploratory analysis. The phase three trial is already also fully accrued. It was open at Yale. Some of the care centers have contributed patients to this royal which randomized patients to receive trial is fully accrued and we
are waiting for the results.

Negroli Mab is another drug that had attracted a lot of attention in AML.

This is this works on the on CD47 but don’t Eat Me Signal CD

Can evade phagocytosis so inhibiting it with the anti CD 47 agent can lead to increased phagocytosis.

This is a phase two study of margaroli map with azacitidine showing promising responses,

but this was a single arm trial.

They are ongoing phase three trials.
00:37:34.816 --> 00:37:36.640 with this drug margaroli map.
NOTE Confidence: 0.783587409090909

00:37:36.640 --> 00:37:39.772 And we also have a study coming ATL where
NOTE Confidence: 0.783587409090909

00:37:39.772 --> 00:37:43.157 oral HMA is being combined with Negroli map.
NOTE Confidence: 0.783587409090909

00:37:43.160 --> 00:37:45.827 This is a trial in progress abstract
NOTE Confidence: 0.783587409090909

00:37:45.827 --> 00:37:47.865 presented in ASH that discusses
NOTE Confidence: 0.783587409090909

00:37:47.865 --> 00:37:49.920 the design of this trial.
NOTE Confidence: 0.783587409090909

00:37:49.920 --> 00:37:52.769 And we have another anti CD 47
NOTE Confidence: 0.783587409090909

00:37:52.769 --> 00:38:03.187 agent that is being tested and for
NOTE Confidence: 0.783587409090909

00:38:03.190 --> 00:38:05.398 MSDS and AML after HMA failure.
NOTE Confidence: 0.783587409090909

00:38:05.398 --> 00:38:07.848 So a lot of drugs are being tested
NOTE Confidence: 0.783587409090909

00:38:07.848 --> 00:38:10.514 in MD S This is showing them of
NOTE Confidence: 0.783587409090909

00:38:10.514 --> 00:38:12.584 some of the trials that we had open
NOTE Confidence: 0.783587409090909

00:38:12.590 --> 00:38:15.788 Tammy protein which is Arara agonist,
NOTE Confidence: 0.508897156666667

00:38:15.790 --> 00:38:18.070 super agonist.
NOTE Confidence: 0.508897156666667

00:38:18.070 --> 00:38:20.020 Aurora is basically over expressed in
around half of the patients with MDS.

So this is a phase three trial that randomizes patients to Asia Tami paroxetine versus Asia.

This is an activation in addition to the single arm oral decitabine with macro for higher risk MDS.

And then for the lower risk we have an extension of the imetelstat sub study that I mentioned to you.

So this is a single arm study that gives patients initially stat and this includes patients with HMA.

Earlier or Lenalidomide failure. So I encourage you to refer patients.
00:38:52.629 --> 00:38:54.829 who are transfusion dependent who
NOTE Confidence: 0.508897156666667
00:38:54.829 --> 00:38:57.100 have not responded or benefited
NOTE Confidence: 0.508897156666667
00:38:57.100 --> 00:38:59.280 from standard of care drugs.
NOTE Confidence: 0.508897156666667
00:38:59.280 --> 00:39:01.128 So this is my last slide and I'm
NOTE Confidence: 0.508897156666667
00:39:01.128 --> 00:39:03.058 happy to take any questions later.
NOTE Confidence: 0.508897156666667
00:39:03.060 --> 00:39:03.800 Thank you so much.
NOTE Confidence: 0.88455987
00:39:14.110 --> 00:39:16.868 OK, this will present now
NOTE Confidence: 0.88455987
00:39:16.868 --> 00:39:18.556 updates on acute leukemias.
NOTE Confidence: 0.831800535
00:39:20.060 --> 00:39:22.832 OK. So I'm going to start with
NOTE Confidence: 0.831800535
00:39:22.832 --> 00:39:25.320 AML and then move to a LL.
NOTE Confidence: 0.831800535
00:39:25.320 --> 00:39:27.268 I have no disclosures.
NOTE Confidence: 0.831800535
00:39:27.268 --> 00:39:29.703 So AML remains a disease
NOTE Confidence: 0.831800535
00:39:29.703 --> 00:39:32.160 with suboptimal outcomes.
NOTE Confidence: 0.831800535
00:39:32.160 --> 00:39:35.406 The five year relative survival is 30.5%
NOTE Confidence: 0.831800535
00:39:35.406 --> 00:39:38.814 and this is a disease of older adults.
NOTE Confidence: 0.831800535
00:39:38.820 --> 00:39:40.292 Median age at diagnosis

68
00:39:40.292 --> 00:39:43.672 is 68 and at death is 73.
00:39:43.672 --> 00:39:46.932 And so treatments that are
efficacious either new agents or.
00:39:46.932 --> 00:39:49.980 New combinations,
particularly that are tolerated
by this age group are needed.
00:39:49.980 --> 00:40:02.618 The addition of an edit flex to
hypomethylating agents improved CR
rates to 65 to 70% in the frontline
setting and older unfit AML.
00:40:02.618 --> 00:40:07.560 However.
00:40:07.560 --> 00:40:12.206 Longer term data from the Viale study
has shown that only a minority of
patients experience durable remission
and survival such as it two years
and in high risk groups such as TP53, mutant JML, but also flip three mutant AML. Particularly in older and unfit AML patients, they’re continued to be very poor outcomes. As an example, in TP53 mutant AML, the median overall survival is 5 to 7 months. With our standard of care therapies, there’s also a great need in relapsed refractory AML where the median overall survival and the unfit subgroup is 3 to 7 months. And so turning to the TP 53 mutated group, it is occurring this mutation in five to 10% of patients with the Novo AML and its enriched in therapy related
AML and as noted before with standard of care the survival is poor less than one year including post transplant. And so doctor Zaiden discussed this agent Mike Roll Amab which targets CD-47 which has been called amyloid checkpoint and is a do not eat me signal and naval daver presented results from the phase one two study of the triplet of megola map on the venetta claxson, azacitidine backbone and newly diagnosed patients with. A group of in a group of patients that was heavily enriched for TP53 mutated AML and still for TP53 mutated AML and still.
what’s being shown here and what was presented was a frontline cohort and separated into de Novo AML and secondary AML that was untreated secondary meaning having antecedent hematologic malignancy that could have been. T reated but not with hypomethylating agent and so you can see the age is older individuals and almost exclusively I’m heavily weighed in terms of being adverse risk group. ELN 2017 classification system. And further separated into by the TP 53 status mutant versus wild type and as I mentioned heavily enriched for TP53 mutated patients given
that there’s hope for a grolla mab

for the subtype of AML and.

These are the response rates again

separated into the de Novo group and

the untreated secondary AML group and

separated by the status of TP53 mutation.

And so there is a CR CRI rate of

63% with TP53 mutated patients in
de Novo and untreated secondary.

In a higher CRI CRI rate in the wild

type patients ranging from 80 to 90%.

And on the left is the survival

curves for the de Novo population alone.

You can see a separation in the

curves between TP53 wild type and
TP53 mutant patients.

The 12 month overall survival of the TP53 mutant patients was 53% which compared to historical data is encouraging because I’ll remind you that the median overall survival is on the order of six months.

On the right is the median overall survival in the combined frontline groups, which is less favorable because the secondary AML patients did not respond as well and had short responses as well.

So moving on to a separate high risk group, the FLIP 3 mutated group. Nicholas Short reported updated results from a phase one two study
NOTE Confidence: 0.827654426
00:44:46.781 --> 00:44:48.560 of another triplet,
NOTE Confidence: 0.827654426
00:44:48.560 --> 00:44:51.446 gilteritinib added on to the backbone
NOTE Confidence: 0.827654426
00:44:51.446 --> 00:44:53.830 of venetoclax and azacitidine for
NOTE Confidence: 0.827654426
00:44:53.830 --> 00:44:56.110 patients with FLIP 3 mutated AML.
NOTE Confidence: 0.899006091428571
00:44:58.130 --> 00:45:00.426 And there were two groups of patients,
NOTE Confidence: 0.899006091428571
00:45:00.430 --> 00:45:02.035 those who were newly diagnosed
NOTE Confidence: 0.899006091428571
00:45:02.035 --> 00:45:03.934 with split three mutated AML and
NOTE Confidence: 0.899006091428571
00:45:03.934 --> 00:45:05.806 this could be ITD or TKD who were
NOTE Confidence: 0.899006091428571
00:45:05.806 --> 00:45:07.568 unfit for intensive chemotherapy.
NOTE Confidence: 0.899006091428571
00:45:07.570 --> 00:45:10.516 And then there was also a
NOTE Confidence: 0.899006091428571
00:45:10.516 --> 00:45:11.989 relapsed refractory group.
NOTE Confidence: 0.899006091428571
00:45:11.990 --> 00:45:14.654 And in the middle you see the schedule
NOTE Confidence: 0.899006091428571
00:45:14.654 --> 00:45:16.845 of treatment notably with triplets
NOTE Confidence: 0.899006091428571
00:45:16.845 --> 00:45:18.785 myelosuppression is a concern.
NOTE Confidence: 0.899006091428571
00:45:18.790 --> 00:45:21.940 And so built into the treatment schedule
NOTE Confidence: 0.899006091428571
Of venetoclax, Gilteritinib was given at one of two doses and the recommended phase dose was ultimately selected to be 80 milligrams of gilteritinib. And on the right you see the consolidation treatment plan. So these are the responses for the frontline and the relapse refractory group. You can see the composite CR rates are quite high, 100% in the frontline group and 70% in the relapse refractory group and there were no early deaths and it
was considered to be well tolerated.

These are the overall relapse rate survival on the left and the overall survival curves on the right and you can see that the one year overall Survival rate is 85%, which is again very encouraging and.

So I just briefly want to touch on men and inhibitors and the concept behind these drugs. There are several minute inhibitors under development and the men in KMT 2A previously known as ML interaction.
Is it critical dependency in ML

mutated rearranged leukemias as well

as interestingly in NPM 1 mutated leukemias where it’s responsible?

Um for enacting an aberrant leukemia

genic gene expression program so the inhibitors bind a well defined pocket

and this disrupts the interaction between ML and MENNEN and causes an abnormal transcription complex to disassemble and through down regulation of Hawks, A and mice, mice, transcription and other targets. Allows differentiation of the leukemia cells as well as apoptosis. And so as I mentioned,
there’s more than one of these inhibitors that’s being developed and. Doctor Isa reported results from the Phase one study of the men and inhibitor review Munib in patients with KM22KMT2A rearranged or MPM One mutant AML. And for the sake of time that trial is the AUGMENT 101 trial and what was notable in terms of adverse events were frequent QTC prolongations and there were two dose limiting toxicities because of QTC prolongation, but there was. Lesser rate of grade, three or more QTC prolongation and
in a heavily pretreated group with a median of four prior lines of treatment, there was encouraging activity with 30% CRC RH meaning incomplete hematologic recovery rate. In these genetic subgroups and MLL rearranged and NPM 1 mutated leukemias and the response rates were different by each genotype. Doctor Harry Erba presented on another minute inhibitor Dominic in the same type of AML and also in the relapsed refractory setting, the comment 001 trial and. Here differentiation syndrome was observed as was and with the
prior men and inhibitor, but there were no drug induced QT or QTC Prolongations reported. And again, particularly at the 600 milligrams dose, which was the recommended phase two dose, there was in heavily pretreated population evidence of encouraging activity with a 30% CR rate in the NPM 1 mutated group. The CR rate was much lower in the ML group and it remains to be seen whether in fact there’s differential activity in different genotypes. With these agents.
So in conclusion for the AML section, men and inhibitors are showing promising activities and relapsed NPM one and MLL rearranged or mutated patients. And the two triplets that I touched on with gilteritinib on a backbone showing promising safety and efficacy in the upfront but also relapse setting. Whereas Megola map added to azacitidine shows promising activity. TP 53 mutated AML's and their randomized trials ongoing. For magala map. So turning to ALAL is evenly split in
the in between the pediatric and the adult groups, roughly half and half. However, whereas the median age at diagnosis is 17, the median age at death is 58 and so the outcomes are far inferior in adults and this is a particular problem in older adults. And here you see a summary of overall survival at the three and five year marks. Which on average is about 20%. And if you consider individuals that are elderly 70 or above, they’re really dismal rates and just as a kind of
a reminder of the importance of measurable residual disease.

In L, the two outcomes, event free survival and overall survival, you see, you know, dramatic split between those patients who have no measurable residual disease and those who do. But importantly, there’s also relapse and mortality even in the situation of no measurable residual disease. And so one of the strategies that’s been taken to try and improve outcomes, particularly in older adults, is the integration of novel agents.
00:52:01.717 --> 00:52:03.729 into the frontline setting.

00:52:03.730 --> 00:52:07.190 focusing on blinatumomab and inotuzumab.

00:52:07.190 --> 00:52:09.830 Inotuzumab is an antibody drug conjugate against CD22 Lina.

00:52:11.694 --> 00:52:14.910 Tuma Mab is a bi-functional T cell engaging antibody that directs cytotoxic T cells to CD19 expressing cells.

00:52:15.003 --> 00:52:17.227 And notably, the trials that led to the approval of Blinatumomab and Inotuzumab in relapse refractory Bal demonstrated that I Natuzzi Mob has activity across all levels of disease burden, suggesting that it could be suitable for induction.

85
whereas blinatumomab has higher efficacy with lower burden of disease. I'm suggesting that its role may be primarily in a setting where there's already been side a reduction. So there's multiple trials that are studying the combinations of inotuzumab with chemotherapy. Particularly in older individuals and this is one that Gmall initial one trial. And in this trial it's the sequential strategy and the choose amab is given for three cycles followed by conventional chemotherapy and patients greater than 55 years of age. In this trial a primary event free,
the primary endpoint was 12 month event free survival with a goal of seeing better than 60% and and you can see on the left that this was met at one year it was 88% and the two years it was 73%. But you’ll also note though is the downward slope of this curve indicating that there are. Ongoing events after year one suggesting that there may be a need to improve on the consolidation strategy. There was a similar in terms of approach study that was presented by Chevalier the result of the Ewal Ino
study and here I know choose Amab is

intercalated with chemotherapy from

the beginning and these are only two

Presentation that perhaps received

the most notoriety at ASH 2022 was

by in the space of L was by Mark

Lizzo reporting the results of

E1910A phase three randomized trial

BLINATUMOMAB for newly diagnosed

pH negative Bal in adults.

And these adults were age ages ranging

from 30 to 70 and they received.

Two cycles of induction intensification

and were then randomized either to the

experimental arm or to the standard
consolidation chemotherapy arm.

The experimental arm had four cycles of blood and blinatumomab intercalated with chemotherapy consolidation and MRD was defined as greater than or equal to 1 in 10,000 cells as assessed by 6 color flow cytometry.

It was actually the outcomes in MRD negative patients was the focus of the study and.

MRD was defined as greater than or equal to 1 in 10,000 cells as assessed by 6 color flow cytometry.

And so these are the results. These are this is overall survival.

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00:55:27.086 --> 00:55:29.626 with the addition of BLINATUMOMAB.
NOTE Confidence: 0.774469366923077
00:55:29.630 --> 00:55:32.045 The median overall survival is 71 months.
NOTE Confidence: 0.774469366923077
00:55:32.050 --> 00:55:34.479 It with chemotherapy alone and with the
NOTE Confidence: 0.774469366923077
00:55:34.479 --> 00:55:37.080 addition of Lena Tuma Mab is not reached.
NOTE Confidence: 0.774469366923077
00:55:37.080 --> 00:55:39.224 And so this was,
NOTE Confidence: 0.774469366923077
00:55:39.224 --> 00:55:42.440 this is a landmark study and.
NOTE Confidence: 0.774469366923077
00:55:42.440 --> 00:55:46.336 Showed for the first time a benefit of
NOTE Confidence: 0.774469366923077
00:55:46.336 --> 00:55:49.358 blinatumomab and MRD negative patients.
NOTE Confidence: 0.774469366923077
00:55:49.360 --> 00:55:50.750 Not I’m not showing here,
NOTE Confidence: 0.774469366923077
00:55:50.750 --> 00:55:52.282 but MRD positive patients.
NOTE Confidence: 0.774469366923077
00:55:52.282 --> 00:55:54.580 There’s also a separation in the
NOTE Confidence: 0.774469366923077
00:55:54.652 --> 00:55:57.262 curves that did not reach statistical
NOTE Confidence: 0.774469366923077
00:55:57.262 --> 00:55:59.992 significance and it’s unclear if this is
NOTE Confidence: 0.774469366923077
00:55:59.992 --> 00:56:04.068 due to smaller numbers or for other reasons.
NOTE Confidence: 0.774469366923077
00:56:04.068 --> 00:56:07.640 So very briefly for pH positive,
NOTE Confidence: 0.774469366923077
00:56:07.640 --> 00:56:09.990 AL.
Nicholas Short presented for upfront treatment the combination of panic and blinatumomab and here the rationale is that with second generation tyrosine kinase inhibitors the majority of patients will relapse with T315I mutated BCR abl which put nibr is active against and in pH positive AML chemotherapy. Free induction has been pioneered with publications on dissent and Prednisone, ponatinib and Prednisone and the Dealba trial reporting Dasatinib and BLINATUMOMAB. And just very briefly, they’re very striking results.
00:56:57.200 --> 00:57:00.398 in 40 patients in the frontline
NOTE Confidence: 0.619180544705882
00:57:00.398 --> 00:57:03.716 setting CR CRI rates of 96%,
NOTE Confidence: 0.619180544705882
00:57:03.716 --> 00:57:09.152 complete molecular response of 87% with an.
NOTE Confidence: 0.619180544705882
00:57:09.152 --> 00:57:12.372 Equally striking event free survival
NOTE Confidence: 0.619180544705882
00:57:12.372 --> 00:57:16.214 and overall survival curves with a
NOTE Confidence: 0.619180544705882
00:57:16.214 --> 00:57:20.590 medium follow-up of 18 months with the
NOTE Confidence: 0.619180544705882
00:57:20.590 --> 00:57:26.460 two year overall survival being 95%.
NOTE Confidence: 0.619180544705882
00:57:26.460 --> 00:57:27.321 So in summary,
NOTE Confidence: 0.619180544705882
00:57:27.321 --> 00:57:29.790 for the abstract shown for ALS into choose,
NOTE Confidence: 0.619180544705882
00:57:29.790 --> 00:57:32.286 the map is an effective induction
NOTE Confidence: 0.619180544705882
00:57:32.286 --> 00:57:35.568 agent with acceptable low toxicity and
NOTE Confidence: 0.619180544705882
00:57:35.568 --> 00:57:38.016 promising early survival outcomes.
NOTE Confidence: 0.619180544705882
00:57:38.020 --> 00:57:41.218 And in the late breaking abstract
NOTE Confidence: 0.619180544705882
00:57:41.218 --> 00:57:43.350 presented by Doctor Litzow,
NOTE Confidence: 0.619180544705882
00:57:43.350 --> 00:57:46.205 the addition of Blinatumomab to
NOTE Confidence: 0.619180544705882
00:57:46.205 --> 00:57:48.489 chemotherapy consolidation in adult
92
00:57:48.489 --> 00:57:51.024 patients with MRD negative Bal has
00:57:51.024 --> 00:57:54.310 shown for the first time in overall and
00:57:54.310 --> 00:57:57.411 relapse free survival in a randomized study.
00:57:57.420 --> 00:58:00.108 And so blinatumomab as a part of post
00:58:00.108 --> 00:58:01.783 remission therapy represents a new
00:58:01.783 --> 00:58:04.580 standard of care for this group of patients.
00:58:04.580 --> 00:58:07.572 And one of the challenges in the field
00:58:07.572 --> 00:58:10.848 will be how to incorporate this in
00:58:10.848 --> 00:58:15.084 regiments in addition to E 1910 since
00:58:15.084 --> 00:58:17.808 that is not too frequently used.
00:58:17.810 --> 00:58:19.910 And the combination of Panaginip
00:58:19.910 --> 00:58:22.010 and Blinatumomab is a promising
00:58:22.083 --> 00:58:24.079 chemotherapy free potentially transplant
00:58:24.079 --> 00:58:27.073 sparing regimen for pH positive AL.
00:58:32.140 --> 00:58:35.356 Alright, so we’re open for questions.
Um, uh, please go ahead. We will stay a few minutes late if necessary. I know it’s end of the hour already.

Any questions? I probably can ask question while we are waiting for people like to talk to poor Mendez, so for ALS treatment, do you foresee moving away to chemo free regimens even in younger patients in the near future? Clearly the progress has been quite impressive with those novel agents.

I think so, especially I mean one of the hesitancies in terms of bringing ponatinib to the front line is its toxicity profile.
which I didn’t have a chance to discuss and the concern for that would be less in younger patients.

And the efficacy at least that we’re seeing is so high that I think that would be a reasonable approach, especially I mean in combination with BLINATUMOMAB so. One can envision a chemotherapy free approach there and I think the difficult question is the role of stem cell transplant and we need longer, more mature data to guide us on that.
Uh, to you I’m almaas.
No, it’s it’s to Lord us.
T o the.
Mab drug substitute of chemotherapy and a LL or AML.
So any, I guess you know any of those drugs,
hich you know will lead to be 3 like.
Going to have actually maps.
Ohh so so it’s a similar question about chemotherapy free treatment of ALS and AML.
And AML, that’s an interesting question.
And I, I took notice of a comment by Naval Daver who was saying that there’s a trial exploring magrou,
and a drug I didn’t have a chance to touch on,
which is I think now been given the name provoke evoke. You could correct me if either of you knows how to pronounce that antibody drug conjugate. I don’t know, but for CD123 and so that’s one that we’re going to explore. I think chemotherapy free, you know, there’s other possibilities, sorry. Umm. You know, if we talk about TT’s and and vanetta clacks, umm, you know, those are other possibilities as well, but I think there’s a lot of hope.
in the triplets and I don’t

On terms of, I actually actually have a question to Amir. So there was nothing mentioned about

So what do you think is the role of

So I mean I talked a little bit about Sabato, Olimov and Margaroli maybe.

I mean I think as immune checkpoint inhibitors I would put them in that category.

But I think the other drugs we did not mention or approaches were

Karti cells as well as by specific.
So the cortices are going to be covered by the cell therapy talk which I think is later in the series. However, in the myeloid space, both of those approaches have been quite challenging mostly because of cytokine release syndrome and prolonged cytopenias. B says you can apply it as much as you can without and you can live with no immunoglobulins generally, OK. But in myeloid space it’s has been a very difficult development. So it it remains to be seen. There are some phase one trials that are going both with Carti sales and by specifics,
but this particular area I think has struggled a lot the antibody drug conjugates. And you could debate whether this is immunotherapy or not. I tend to think of them more as targeted delivery of agents rather than immunotherapy. I think there is more progress. We clearly have gemtuzumab ozogamicin already approved and then the CD 123 agent that took tremendous mention and in the transplant session which I encourage everybody to attend, there is this I map drug. There was a just a couple of days presentation in the tandem transplant meetings.
This is a radio immuno conjugate, so it’s radioactive iodine conjugated to CD45 and there was an improvement in overall survival when it’s given as part of the conditioning for transplant. So there is some movement with the ADC, but bytes and drug cartels for myeloid malignancies have been a bit of a challenge. So I think we’re going to wrap it up. Uh, uh, hematology tumor board is coming up. So I have to say goodbye to everyone. And if you guys have any questions, you can certainly e-mail us and
01:04:14.442 --> 01:04:16.680 contact us after this meeting.
NOTE Confidence: 0.877488686666667
01:04:19.080 --> 01:04:19.779 Thank you, thank
NOTE Confidence: 0.749152685