00:00:00.000 --> 00:00:03.776 Much for joining us today for another
00:00:03.776 --> 00:00:05.612 edition of the highlights of the
00:00:05.612 --> 00:00:07.205 American State of Hematology meeting
00:00:10.010 --> 00:00:16.389 My name is Ammar.
00:00:16.389 --> 00:00:20.461 Doctor Rory Chalice and we will be together
00:00:20.461 --> 00:00:22.180 presenting on myeloid malignancies.
00:00:22.180 --> 00:00:25.000 I will start by talking about
00:00:25.000 --> 00:00:27.080 MD’s for around 15 minutes.
00:00:27.080 --> 00:00:28.832 Doctor Cialis will follow
00:00:28.832 --> 00:00:30.584 with highlights of XAML.
then Doctor will finish.

Will highlights of Milo proliferative neoplasms?

Feel free to post your questions in the chat.

At the end, we are going to have 10 to 15 minutes. We'll try to finish around 12:50 so that you can ask your questions directly. Or if you want, you can type them during the presentations so that we can also tackle them at the end.

Thank you so much for joining and I'm going to get started.

So for MTS, basically, UM, this has been a very exciting field.
These are my disclosures.

There has been a lot of new developments in MD’s over the last couple of years,

and I think this is an area where we continue to have new drugs approved.

So one of the drugs that has been recently approved is a combination of oral.

Put in so the site being is a standard of care treatment for higher risk MD’s that’s given intravenously.

The problem is that this drug cannot be given orally because it undergoes first passed in the liver and the gut and therefore has not been able to do orally subsequently which inhibits
the enzyme cytidine dominates as you can see in this slide basically allows the desire to be in to be given orally and in a phase three trial. All that certain trial that we participated in at Yale. It was shown to have the same pharmacokinetics, such as intravenous decided and based on this data, the drug was approved in the year 2020. The clinical results have been presented more than once, but the paper has not been published yet, so this is the presentation of the
overall data from 2020 where the complete response rate was shown to be around 20%. And many patients achieved as you can see platelets and erythrocytes. Transition independence around 50% of patients. And you can see the CR was durable around 14 months. The patients are still being followed for. Long term survival I think. Important update that was presented in this ASH in December was the activity in the lower risk. Andy Ashby,
'cause some patients had intermediate tips and as you can see the complete response rate was also seen in those patients around 23%. So it seems that even for lower risk MD SIDEK has activity, which is something we see. However, it's not clear if this is the right dose for these patients, because we certainly see neutropenia and thrombocytopenia and therefore a phase two study randomized phase. Two study was initiated where the Sidik is given in two doses,
lower doses than the approved dose
in patients with lower risk MD’s who are not responding to her therapist stimulating agents.
So this study is open currently at the main campus for any lower risk MD’s patient,
feel free to discuss any patients who might have. For this study.
Another drug that has been also approved in the year 2020 as Los Patterson,
solo spatter said, basically is a transforming growth factor pathway inhibitor.
So these transforming growth
factor pathway proteins have been shown to interfere with. Luis is and what does low specific do its ligand trap so it removes it, removes the inhibitory effect on erythropoiesis and therefore stimulating red blood cell production? The drug has been shown to improve transfusion independence rates. You can see here the pivotal trial results from the MIDDLE'S trial which was published in 2020 yet participated in that around 1/3 of the patients achieved transfusion independence, so this was. Refractory setting after yes, a failure.
We currently have the commands trial which is in the frontline setting, so this is open actually in several of the Cancer Center. Satellite centers basically this is available for a front drawing. Randomization against erythropoiesis, stimulating agents and this is regardless whether you have the patient has rings to drop class or not, so please feel free to refer patients for this or again it’s open in many of the care centers so the patients can be treated on the trial right there. That is another drug first in class.
TELOMERS inhibitor that has shown also good data in the refractory labs. Lower risk MD. As you can see here the presentation from the phase two part of the emerge study which showed a rate of transfusion independence of around 42%. So a good number of patients are achieving transfusion independence with this drug. Also the emerge which has been open at the main part of the study has actually been fully accrued and closed. But there is an extension of this study. So currently if you have patients
who have lower risk MD’s who are. First line, they can be considered for the commands trial if they have received essays and they are not responding. We have two options. I merge trial with that as well as the lower dose of the oral disability being available for these patients. How about higher risk MD’s so many of you are aware of any talk lacks having very good activity in XAML. It’s a standard approved drug. Now it’s an oral pill that’s given for older patients with acute myeloid leukemia,
and we’ve been using it for several years now, so there has been a lot of interest in exploring that in patients who have higher risk MD’s as well with excess players, and we have preclinical data suggesting synergy with. There’s a side to Dean because one of the common resistance mechanisms to Cited in is actually up regulation of PCL two, so trial was two trials were designed basically as early phase trials in the frontline as well as in the relapse refractory setting. After HMA failure,
00:07:14.810 --> 00:07:17.367 combining venetoclax with you

00:07:17.367 --> 00:07:20.146 can see in this slide that those

00:07:20.146 --> 00:07:22.820 escalation design of that study that

00:07:22.820 --> 00:07:25.070 subsequently went to those expansion

00:07:25.070 --> 00:07:27.905 and this is in the frontline setting.

00:07:27.910 --> 00:07:30.016 Very important to note that venetoclax

00:07:30.016 --> 00:07:31.979 here was given for 14 days.

00:07:31.980 --> 00:07:33.655 So it’s not continuously given

00:07:33.655 --> 00:07:36.880 like it is in AML only 14 days and

00:07:36.880 --> 00:07:37.987 doses 400 milligram,

00:07:37.990 --> 00:07:39.754 which is the same dose that

00:07:39.754 --> 00:07:41.589 we do in patients with AML.

00:07:41.590 --> 00:07:44.250 However has a lot of drug interactions

00:07:44.250 --> 00:07:46.718 and it’s important to adjust those

00:07:46.718 --> 00:07:48.818 accordingly and monitor the patient

NOTE Confidence: 0.726456156363636
closely for infections which are common because you get neutropenia, those patients should be on prophylactic antibiotics and should be treated very aggressively if they have an infection. They need a lot of transfusion care as well. Especially during the first one to two cycles. So the patient should be seen at least twice a week and given transitions as needed. With all of that being said, basically we are seeing early activity in with this combination, so the complete response rate is around 35%, which is similar to what
NOTE Confidence: 0.805172283636364
00:08:23.510 --> 00:08:24.990 was observed in XAML.
NOTE Confidence: 0.805172283636364
00:08:24.990 --> 00:08:26.784 However, many of the other patients
NOTE Confidence: 0.805172283636364
00:08:26.784 --> 00:08:28.735 are achieving also more OCR where the
NOTE Confidence: 0.805172283636364
00:08:28.735 --> 00:08:31.554 plants are less than 5% and they are
NOTE Confidence: 0.805172283636364
00:08:31.554 --> 00:08:33.198 achieving hematologic improvement.
NOTE Confidence: 0.805172283636364
00:08:33.200 --> 00:08:35.798 You can see that the response
NOTE Confidence: 0.805172283636364
00:08:35.798 --> 00:08:37.530 is achieved relatively quickly.
NOTE Confidence: 0.805172283636364
00:08:37.530 --> 00:08:39.672 The first response is seen within one
NOTE Confidence: 0.805172283636364
00:08:39.672 --> 00:08:41.918 month and those responses are durable.
NOTE Confidence: 0.805172283636364
00:08:41.920 --> 00:08:44.608 12 months you can see also that
NOTE Confidence: 0.805172283636364
00:08:44.608 --> 00:08:46.922 there is and this is the main update
NOTE Confidence: 0.805172283636364
00:08:46.922 --> 00:08:48.592 that was presented in ASH 2021.
NOTE Confidence: 0.805172283636364
00:08:48.592 --> 00:08:51.616 You can see that many patients achieve
NOTE Confidence: 0.805172283636364
00:08:51.616 --> 00:08:54.637 no molecular clearance where the TP 53
NOTE Confidence: 0.805172283636364
00:08:54.637 --> 00:08:57.560 for example molecular load is decreased.
NOTE Confidence: 0.805172283636364
However, the question in TP 53 in particular is whether overall survival is improved or not. So I think this data is encouraging. Clearly, however, this is a single ARM study. It’s not randomized. Study less than 70 patients were enrolled. And therefore we have an ongoing registration study called DEVARONA. Which is also open at Yale. This is a randomized phase three study in which patients are randomized in a double blind, placebo controlled fashion to receive. Either as a sighted in with venetoclax...
or azacitidine with placebo, and we have presented the schema of this study in ASCO 2021. You can see here 500 patients will be enrolled and this study continues to be open and we encourage you to refer patients who have higher risk MD's. I currently discourage people from using plaques off label in the frontline setting because we still don’t fully understand if it actually is better than is cited in monotherapy. And that’s I think another reason to consider enrolling patients on this study, which is open at yet.
In the refractory relapse setting, Yale has participated in a study that was led by the sponsor, similar design, those escalation followed by those expansion and this was a smaller study than the frontline study. 44 patients were treated same dosing, 400 milligram of Veneto class given for two weeks and venetoclax was added to a society in so the patient had a failure. But the patient continued in the MA so it is. And you can see here that response rate was seen in 39%. However, many of those were more hours.
The CRA was 7%, but those responses were durable. As you can see, the duration was nine months of the CR or the more OCR. But most importantly, we are actually seeing. I think mean clinically meaningful responses.

You can see that platelets and red blood cell transfusion independence among patients who were transfusion dependent. OK fine, so the patient was needing blood or platelets around 1/3 of those patients are becoming transfusion independent with venetoclax to exercise and you.
can see that many patients achieve hematologic improvement as well, 43% and the median overall survival was 12 months. We know historically that median overall survival after a jammy failure is around six months, so it does seem that. We are seeing promising activity with this combination in the refractory labs setting. I think another important study from this hash meeting was the phase three update using that, so people need this stat. Is it activating enzyme inhibitor? It works upstream of the protein zone so
this is a negative phase three study. The reason why I think this is an important presentation is because there has been a lot of early data with. That we had a randomized phase two study with people instead that showed the CR rate was 50% more than double death of his immunotherapy, and we had durable responses. So there was a lot of excitement about this drug and we did participate in the phase two part of this. Evaluation, but not in the phase three. However, you can see here in the phase
three that there was.

No difference in the event free survival, which was the primary endpoint.

No difference in the overall survival.

And even in the CRA there was no improvement with the combo.

So that I think highlights why it’s very important we enroll patients in phase three trials and not just assume activity based on phase two trials. How about immune checkpoint inhibition? As I’m sure you know, inhibition has led to very important progress in very difficult to treat tumors such as Melanoma and lung cancer.
Early data with immune checkpoint inhibitors in MD's has not been so far particularly great. With this is an example of this study that was conducted at several centers, including Yale, where we showed that there was no difference by adding door volume app, which is an approved PDL 1 inhibitor that already has. Meaningful clinical activity and solid tumors by adding it to a society. However, there are novel inhibitors that seem to.
Early and early results seem to have a promising clinical activity.

One of them is about so sabatelli map works on a receptor called Team Three. So term 3 basically is an inhibitory receptor that is not only expressed on the adaptive cells, such as the T cells, but also it’s expressed in the innate immune cells, including the macrophages, but also importantly on the leukemia stem cells. So this is being. Presented as as an immuno myeloid agent? Because it leads to activation of the T cells and then it immune system.
but also it directly inhibits. A loop of self renewal within the leukemia stem cells by interfering with the ligand called galectin 9 that binds to team three on leukemia stem cells. So this drug was combined with Dean and Decitabine in a phase one trial. You can see here the early data that was presented in actually more than one ASH meeting. However, in certain subsets like TP 53 for example, the CR rate was not very high compared to a similar therapy. The CR was durable.
The median duration of response was 21 months, which again in a very difficult field such as CP3, I think, is very exciting, but we are also seeing hints of durability and other subsets, so clearly there is also excitement about this agent. There is actually a randomized phase two and a randomized phase three trial. Both of them were open at Yale and they are fully enrolled and we have two other studies with this drug, one in combination with oral.
So you can give the sidik the oral decitabine with this drug, and another study of a triplet where is cited in with venetoclax and will be given for patients with high risk MD’s and both of those studies will open at the end. Lastly, the idea inhibitors this is dawn of the precision era in MD’s like other. Malignancies in leukemia, where we do it more so approved clearly and MD’s, but we have seen 2 presentations from the French group and ash where we are seeing basically activity and
responses within a signal for IDH 2

mutated MD’s and I was sitting there

for IDH 1 mutated MD’s so I think

this is an option clearly off label.

But in the absence of a clinical trial,

I do check for IDH mutations for patients

with MD’s and consider using these drugs.

Lastly, CPX 351 or liposomal

daunorubicin was approved for secondary,

AML is also being studied in high

risk patients who have access plus

in particular and we are seeing

encouraging activity.

Again this is single ARM study.

Small number of patients.

Those are not your typical MD’s patients.
Those are younger fit patients who go to transplant. So this probably does not apply to most patients, and this is intensive chemo, so there is high risk of toxicity. Those patients should be monitored the same way you would consider someone who is getting 7 + 3. In summary, a lot of active. Instigation for new agents in MD’s, I think the field is clearly very exciting with looking like a therapeutic revolution similar to what’s happening in XAML.
and I think to continue with that
we need to continue to refer
patients for clinical trials.
So thank you so much.
This is my email.
Many of you have my cell as well and feel free to reach out for any questions about MD’s or any other questions you might have.
Thank you so much and I will move to Doctor Challace who will talk about acute myeloid leukemia updates.
I have to confirm it’s just presenter view or the standard view.
It’s a present, sorry it’s your for you. You need
Such. How’s that look good? Yeah, but.

So alright thanks Doctor Sadanand all of you for joining.

I’ll be reviewing some of the highlights from this past meeting as it relates to similar disease.

Akuma leukemia touching on a few that caught our attention as a community we can start with a retrospective analysis.

First, liposomal done rubison sutera.

been or CPX 351 and hypomethylating agent plus band have shown vantage as frontline therapies for older and we call adverse risk AML.

Although HMA van is approved for
ineligible patients who are ineligible to receive intensive therapy, there’s an increased use of this combo in older intensive therapy. Eligible patients including adverse risk disease. Furthermore, there’s no getting around the fact that CPX is just pretty darn expensive, and we also recently published data on this and listen to classical 7 + 3, but getting back to CPX and ban there have been no randomized trials. So the two treatments have not been appropriately compared. There have been a number of. Retrospective analysis comparing them.
But as upfront therapy for newly diagnosed AML. But this would be the largest thus far, so this was a multicenter retrospective study from 4 centers northwestern, Moffitt, Cornell. And yeah, I think Sloane, presented by Pinkel Desai and included 211 patients treated with CPX 351 and server 220 that got then you could see here the overall population on the left baseline characteristics. The meeting ages were different between.

Groups as expected,
more adverse risk disease in the HM Event group. Like I mentioned, there’s also a trend towards being a more enriched for P53 mutated disease, but the CPX group was more likely to have received prior HMA relevant consideration given these patients probably progressed from MD’s. The study team is also interested on the right here. You could see in patients aged 60 or 75 years, which was the original age group studied for CPX. on the randomized phase three
and differences between groups were about the same as you can see here. With regards to outcomes, more patients achieved CR in the CPX group, but more CRI in the HMA Venn Group as you would expect given the continual the cyclic continuous mouse oppression that’s encountered with phonetic lack specifically. However, these differences appear to offset when looking at the overall or composite. And there was a trend towards better CR I in the TPP related subgroup.
And interestingly, no differences in response rates for patients with prior looking to the right.

You can see that real free survival was longer than CPX group, actually more than doubled but did not meet statistical significance.

However, meeting OS was better in the arm at 17.3 months. Among patients aged 60 to 75 years, similar to the overall cohort but neither in this case was OS in multivariable analysis. After adjusting for things like age,
Ellen Risk, history of permanency and importantly prior receipt of HMA, there was an advantage favoring CPX for with regards to P53. Sorry TP. 50 mutated cohort. However, it should be noted that among this population age 60 or 75 years. The shy 50% of patients in the CPX arm went to transplant compared to just 520. More than double in this is important because you know, transplant was a significant predictor of RFS and OS.
They conducted another MVA in patients that were aged 65 years who did not receive a transplant and found no difference in OS. So, in conclusion, this was a significant difference favoring CPS and the overall cohort and in several subgroups, although in no difference in C. However, this is very likely related to a better rate of outlook transplant in the CPX group or likely had. As you'd imagine, if you were morbidities and thus you know CPX could still be the standard for younger fit patients, even with at risk disease. Switching gears to some clinical trial...
updates starting with targeted agents.

Given the dawn of a new era, Doctor Zaidan had appropriately mentioned and specifically starting with frontline trials, we could talk about each one mutated disease, which are found so mutations in IDH 1 mutations are found at about 5 to 10% really diagnose patients. Ibis Sydney is an oral IDH 1 inhibitor that’s FDA approved for two population, specifically adults with factory mutated disease and those with newly diagnosed disease, but are just. Older 75 years plus,
or if commodities that quote UN quote

preclude the use of intensive therapy

there already data from a phase.

One study of think it was 2425 patients

showed a favorable safety profile

and pretty encouraging clinical

activity for the combination of

either sitting in a society and for

that reason and also for the fact

that this trial started enrolling.

I think I wanna say March or April 2018,

before we had the valley a data.

This prompted a double blind randomized,

placebo controlled phase three study

where patients were randomized 1 to
one to receive Asia or Asia plus. I've acid nip with the primary endpoint. 
As you can see in the right here of event free survival, which was defined as a time frame randomization until treatment failure. 
146 patients have been enrolled as of this day to cut with the data. Cutoff was March of 2021 and as shown here, these were older patients with a median age of 75 to 76 years, a third with Anika performance status of two. Also about 1/4 of patients had defined poor risk disease. In looking at responses,
which was not the primary end point,
there was a statistically significant
difference in CR as well as composite CRH
favoring the Asia plus I've Sydney more,
which namely demonstrated a 53% rate of CRC,
RH, and half of these patients
experienced a mutational clearance
which is increasingly becoming.
Is being recognized as a predictor
of a durability of response and
improvement in event based outcomes
in the intent to treat population
in line with the better rates of
response and deep response by.
There was a better EFS in the
Asia plus Ivy Sydney farm.
This is also translated into better OS for that arm as well. Quite striking at 24 months compared with eight months. As you can see here for patients just getting as alone and this is generally what we expect for patients getting a zoumana therapy. Did it come at the cost of more toxicity? Not really in looking at human logic talks, but perhaps a little more neutropenia. Pina Nonheme talks was also about the same, but the frequency of all grade differentiation syndrome, but concerned with. Ibis Sydney Pomona.
Couple other targeted agents as assessed by investigators, was about 14% in the combo arm, compared to 8%. Think 70% on the monotherapy arm, although grade 3 differentiation syndrome was only about 4%. However, in both arms, you can see that Ivo plus Asia appear to be a bit more favorable, and measurements of quality of life. You can see that Ivo plus Asia appear to be a bit more favorable, so in some there wasn’t. Recommendation that further enrollment
00:25:41.736 --> 00:25:44.106 be prematurely discontinued given the evidence of a benefit for the combination.

00:25:44.106 --> 00:25:46.475 So I would say, how does this translate into clinical practice?

00:25:46.480 --> 00:25:48.531 In short, as yet it remains to be determined for the patient with ID terminated disease, whether he or she is best served with a so plus van or a soap.

00:25:52.570 --> 00:25:54.640 I am personally aware of any randomized trial at the moment, but suspect that is a that is coming soon.

00:26:02.330 --> 00:26:06.038 but suspect that is a that is coming soon. Sticking with the same theme for frontline randomized trials, we should discuss the LACEWING trial,
which was just presented by Eunice Wang at the meeting and this is a trial that randomized patients with newly diagnosed AML and who were inappropriate to receive intensive therapy to either get a Cerezo plus gilteritinib which is a footer inhibitor that demonstrated efficacy and safety and patients with refractory for the mutated disease and what’s known as the atom whole trial. Similarly, this trial was launched before the results of the alley A. Were known the primary endpoint of this trial was overall
Survival, so not FS and not or more of a response based endpoint.

Patients were originally randomized 1 to 1, either get ASA or acea alone. But due to the website preference, it was modified to randomize patients 2 to 1, either guiltless ASA or acea alone.

Baseline characteristics are shown here and demonstrate that this was as expected and. Older population with mean ages 77 years and also a good proportion with any card performance status of two plus with perhaps some imbalance in.
In favor of the Asian monotherapy arm.

As expected, there were about 80% IT mutations and similar rates of it.

High disease without at least from my eyes.

Clear imbalances.

It's pretty much up for this slide with regards to responses CR rates, which is OS like I mentioned, we're somewhere between arms, but the rates of CRI and CRP which are less than CR response is still to be clinically meaningful were higher in the combination are nearly three times actually for a composite C area of about 58% for the combo.
and the 26% for as a monotherapy.
However, it is pretty clear from this KM curve that overall survival was not different between arms at about nine months. It should be noted, however, and this was discussed at the meeting and I believe it that this may be explained by a couple things. Subsequent email therapy was received by 20% of patients on ASA and just shaved half of patients on the ASA monotherapy arm, meaning time to that next therapy was a bit longer in the ASA.
Sorry, the combination arm.

It was like 8 versus 5 months.

So this might have influenced OS in addition to the imbalance and performance status that I showed you earlier on the right here.

Looking at unplanned subgroup analysis, improved overall survival with guilt.

Although some trans were noted for patients that were more fit and also here with higher delir ratio.

I didn’t show any adverse event data because they were largely similar between arms including grade 3 plus events.

So in some,
although a negative trial
still an informative 1.
Supporting the contention that
a zevan as based on the alley a
may be the preferred combination
for older patients who were
inappropriate to receive intensive
therapy with mutated disease.
At the moment, I guess I can always change.
Last year I had reviewed the data for
Asia and McGraw map which is an anti
CD 47 antibody that blocks the quote.
Don’t eat these signal on
macrophages and specifically.
Pretty robust efficacy for patients
that have both P fitted mutated disease and wild type disease. Actually, for the pilot for the mutated cohort, I just over 12 months would be the longest meeting OS reported for that particular subgroup. But like everything else, this has to be combined with a zven, right? But I will say there are a number of preclinical studies which do support synergy for this combination, so this leads to the trial, which was a phase 1B2 trials divide with the triplet and patients with both. Newly diagnosed disease but restricted to P footage.
Mutated disease as well as factory disease.
Regardless of Peachtree status, the latter being the only cohort for the phase one portion and the primary endpoint for this trial was a composite rate of.

Here are some baseline characteristics to date. I should mention that.
It's basically nothing out of the ordinary.
In line with what I mentioned as how the kind of codes were divided up.
You could see that you know the ages, maybe a bit younger in the mutated cohorts and the rips or factories specifically,
then naive cohorts, as you would imagine. But other than that, no major surprises from a baseline characteristics standpoint and looking well. Just go over some safety data. No DLT’s were observed in the Phase 1B portion and the RP 2 randomized phase. Two dose recommended phase two dose was established at 30 milligrams per kick with about a two week kind of priming dose ramp up and then eventually gets a bit easier for the patient every two weeks. Cycle 3 going forward. So getting to some efficacy data.
Global findings first.

The rate of CR being based on 14 patients with TP50 mutated disease with 64% double what you would expect with a sub N alone, and this has been attributed to at least at the meeting.

A quick depth of response with more than half being negative by flow and a first response in less than a month without really any. As you can see here, any early mortality and what I would consider to be a reasonable time to blood count recovery felt to be
meaningful and really landing with the definition of what we call CRH. Frontline treatment for wild type patients was even more impressive with a CR CRA of 90%. Conversely, and this is, you know, one of the downsides. This doesn’t appear to be a meaningful option for patients who’ve already been failed by vanetta klax based regimen with the CRA. As you can see here, based on 15 patients, but still zero and only 20% rate of CRI and at the bottom here you can see a 20% mortality here.
Look at this plot that was presented at the meeting. Much of what the last slide kind of showed, but also including data demonstrating that. There was 100% six month OS so short follow up as you could see here as well. For patients that had mutated disease and five of the 14 that were able to get to. Some form of response. We’re able to get the transplants about 35% of course. Again short follow up, so maybe more will get the transplant. We’ll get a better sense of the median OS and see how it stacks up to 12.
months noted for the Asian Macro Delta

NOTE Confidence: 0.898801785

data that I presented to you last year.

NOTE Confidence: 0.898801785

Frequent I share some more toxicity

NOTE Confidence: 0.898801785

data frequente, ease of all grades.

NOTE Confidence: 0.898801785

Hypokalemia, hypophosphatemia, about half of patients,

NOTE Confidence: 0.898801785

hyperbilirubinemia, about half of patients,

NOTE Confidence: 0.898801785

and some otherwise.

NOTE Confidence: 0.898801785

He talks you would expect

NOTE Confidence: 0.898801785

with as event itself,

NOTE Confidence: 0.898801785

not necessarily mad or attributable.

NOTE Confidence: 0.898801785

Among 17 patients that were newly diagnosed,

NOTE Confidence: 0.898801785

and thus TP50 mutated,

NOTE Confidence: 0.898801785

the median drop was just about

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gram per deciliter this after

NOTE Confidence: 0.552926056153846

the first dose,

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and even lesser after the second dose.
So with close monitoring, this anemia was manageable and the anemia, which just to give a refresher. There is some target hemolytic anemia, just that you know was a bit troublesome early on in the trial, but appears to be manageable with no SAS, no interruptions or discontinuations due to this anemia specifically, so this is promising and position to possibly be a new standard. I mean maybe a little ambitious, but for frontline treatment both for TP 53 mutated disease.
and even wild type disease. But of course need more data and more follow up and of course randomized trials to confirm this added benefit they are underway. One last combination and this one is one that’s restricted to patients with RIPS or factory disease and that of interest and maybe patients who have been failed by better clocks today to critical area of need after patients are failed by then, it’s essentially. A black hole Blackstone ever
metaphor you want to use. This is another combination that adds to an event, but for which there is sound clinical rationale. This is a therapy that targets CD123, which is the alpha subunit of the aisle 3 receptor and is overexpressed on leukemic blasts Immunogen 632. It’s a CD123 targeting ADC comprised of a high affinity anti CD123 antibody coupled to a novel DNA alkylating payload. Linedata Goodyear in PDX modeling or experiments good synergy between
00:34:12.623 --> 00:34:14.717 Immunogen 632 in Asia and Dwarven,
NOTE Confidence: 0.552926056153846
00:34:14.720 --> 00:34:17.155 including being able to overcome
NOTE Confidence: 0.552926056153846
00:34:17.155 --> 00:34:18.616 a certain resistance.
NOTE Confidence: 0.552926056153846
00:34:18.620 --> 00:34:20.654 So For these reasons, this is a phase one.
NOTE Confidence: 0.552926056153846
00:34:20.660 --> 00:34:22.466 Two trial of that product combined with
NOTE Confidence: 0.552926056153846
00:34:22.466 --> 00:34:25.280 a 7 and patients with as you’d have guessed,
NOTE Confidence: 0.552926056153846
00:34:25.280 --> 00:34:28.822 CD one or three positive AML to date.
NOTE Confidence: 0.552926056153846
00:34:28.822 --> 00:34:30.226 The triple combo escalation
NOTE Confidence: 0.552926056153846
00:34:30.226 --> 00:34:32.200 is consists of five cohorts,
NOTE Confidence: 0.552926056153846
00:34:32.200 --> 00:34:34.475 4 with the investigational product
NOTE Confidence: 0.552926056153846
00:34:34.475 --> 00:34:36.776 dosed on day, seven of each cycle,
NOTE Confidence: 0.552926056153846
00:34:36.776 --> 00:34:38.180 and one cohort where it’s dosed
NOTE Confidence: 0.552926056153846
00:34:38.225 --> 00:34:38.989 on the first day.
NOTE Confidence: 0.552926056153846
00:34:38.990 --> 00:34:40.341 Each cycle make it a bit more
NOTE Confidence: 0.552926056153846
00:34:40.341 --> 00:34:41.952 convenient for the patient at the
NOTE Confidence: 0.552926056153846
00:34:41.952 --> 00:34:43.707 time of this analysis presented.
Obviously at the last meeting, 35 patients have been enrolled based on characteristics are shown here in meeting age was about 65, so it was somewhat younger population with median 2 lines or prior therapy up to three, so not relatively terribly pretreated, but half of patients did receive prior medical acts important to know the talks profile was manageable, and this inherently goes factory population with multiplier therapies become an S were. Infusion related reactions.
About 1/3 of patients with only two

One patient in the day one cohort had to discontinue because of an infusion reaction was considered DLT,

So my last slide among the 29 percent 29 patients who are valuable efficacy was seen across kind

The response rate was 55%.

And looking at the composite remission rate, it’s about 30%, you know,
dose cohorts of no patients prior
van had good Angeliki make activity
as seen here on the right, waterfall plot and overall response rate of 40%.
Other subsets of note flipper mutated disease.
Even more striking.
I’ll be at 9 patients,
but certainly.
Like the other studies I presented
more data to assure these values
don’t regress to the mean like
unfortunately many other similar studies.

That’s my last slide.

There are a few more presentations

from match that I wish I could discuss,

but last only 15 minutes and

I’m sure I’m over that already,

so I apologize to Doctor Podolsky and

look forward to your questions at the end.

Can you unshare? Sure can.

Go. Still cannot share the screen.

Right here we go. Thank you alright,

so let me find my presentation here.

Sorry about this technical difficulty.

Here we go. Alright, here’s my view OK?

Alright, here’s my view OK?

Yes, OK, so this is my disclosures,

so I’m going to go onto the outline.
So I’m going to present four studies which I selected based on disease. Talk about devera, myelofibrosis and one other condition which is infrequent. Myeloid lymphoid neoplasm is in Affilia and FGFR 1 rearrangement, so the first study I would like to talk about is the study which is. So the rationale for the study is. Which is looking at Hillside and medic. Right is the fact that in patients with polycythemia Vera. So the rationale for the study is.
polycythemia Vera iron is necessary to make red blood cells in the marrow, which is affected by Jack. So as you can see on the left, ferroportin is the main transporter of the iron from outside, from inside the macrophage to the circulation and then delivered by transparent to the bone marrow which is utilized to make excessive amounts of red blood cells by Jack. So the hepcidin as well as restricted which is hepcidin. Medical shut down the gates ferroportin
and decreases the amount of iron which is available for transparent to transport to the bone marrow so it’s kind of shutting down the door but perhaps not the window. A little bit of line is available and the idea is that there is no iron deficiency state which is otherwise created by phlebotomies. Patients with PD diagnosis based on increased quality of life of this patients due to tissue and efficiency. So this is a phase two trial over spare type in patients requiring phlebotomy.
on 2016 W criteria were included. At least three phlebotomies in the last six months were necessary. Patients were treated with or without sector. Reductive therapy and therapy, so the primary endpoint was proportion of patients in randomized withdrawal period. Who schematic rate is maintained. Without the need for phlebotomy, the secondary endpoints is the response of 29 weeks. Absence of liberty eligibility, and that’s what I’m going to talk about today, as well as total symptom score for those patients who are
The idea is that symptoms will get better while they’re receiving this treatment because planning deficiency state, which is otherwise present in patients treated with therapeutic phlebotomies, will be gone, so the study.

As the three parts, the first one is those findings part that 28 weeks, then there is blinded withdrawal and then open label part is part three, so we’re talking about 63 patients currently enrolled enrollment.
between October 2019 and May 2021, and patients were treated up to 18 months between 8:00 and 92 weeks. So you can see here that initial period is describing six months preceding the first dose of the drug. Yeah, and patients are getting phlebotomy is that by you can see this by red triangles right after those there are very few red triangles, so this is going to be for optimization. That’s what we looking for. 84% of patients did not require 14% of patients did not require 14% and only 2% required 2 phlebotomists so very significant we self
eliminating phlebotomies in almost all of the patients within the first 28 weeks.

Treatment, so this was actually true for both patients who received such a reductive therapy and who didn’t on the left.

31 patients who didn’t require center adaptive therapy on the right put in two patients who did so from the standpoint of assessment of symptoms. Scoring system was used weekly and you can see on the left at baseline the score as well as the score after 2020 weeks of therapy. There is significant reduction of treatment out of symptoms with this
treatment and specifically 1/3 of patients reported at least 40% reduction of symptoms based on MPN soft TSS at 28 weeks. So it is the drug is effective at the eliminating the need of phlebotomy. This is a continuous injection which patients self inject once a week. So from the standpoint Bruce of basically the main side effect was injection reaction. 20% of patients and it was transient and did not require discontinuation. In summary, research type war that PTG 300 is hepcidin, mimetic subcutaneously injected
for PV patients, leading to elimination of therapeutic phlebotomy needs of majority of patients within the 1st 28 weeks of treatment. Also, reversing iron deficiency, which was evident by increasing MCV MHC and 13 of those patients that was positive impact on PV related symptoms, perhaps because of. Negating some of the iron deficiency related to therapeutic phlebotomies, it was safe and well tolerated without grade 3-4 adverse events and we are planning to open phase three randomized
control study at Yale for this patients.

NOTE Confidence: 0.78128789

So the second study is for my

NOTE Confidence: 0.78128789

love fibrosis patients and it’s

NOTE Confidence: 0.78128789

gone collaborative wanna therapy

NOTE Confidence: 0.78128789

for patients with myelofibrosis?

NOTE Confidence: 0.78128789

This is update of ongoing study.

NOTE Confidence: 0.78128789

I presented this study last year so

NOTE Confidence: 0.78128789

it uses it utilizes this knowledge

NOTE Confidence: 0.78128789

that promo domain and extra terminal

NOTE Confidence: 0.78128789

domain proteins promote myelofibrosis.

NOTE Confidence: 0.78128789

You can see the activation of NF

NOTE Confidence: 0.78128789

Kappa B targeted genes leading to

NOTE Confidence: 0.78128789

increased inflammatory response.

NOTE Confidence: 0.78128789

Aberrant,

NOTE Confidence: 0.78128789

or through a differentiation

NOTE Confidence: 0.78128789

and aberrant megakaryocytic
NOTE Confidence: 0.78128789
00:43:48.210 --> 00:43:49.251 differentiation manifestations.
NOTE Confidence: 0.78128789
00:43:49.251 --> 00:43:51.906 So far my love fibrosis,
NOTE Confidence: 0.78128789
00:43:51.910 --> 00:43:54.250 inflammatory response causes systemic
NOTE Confidence: 0.78128789
00:43:54.250 --> 00:43:56.945 symptoms as well as cytopenias,
NOTE Confidence: 0.78128789
00:43:56.945 --> 00:43:58.720 including an email from both.
NOTE Confidence: 0.78128789
00:43:58.720 --> 00:44:00.656 Cytopenia conceit can be seen in my life.
NOTE Confidence: 0.78128789
00:44:00.660 --> 00:44:02.432 I prove this difference,
NOTE Confidence: 0.78128789
00:44:02.432 --> 00:44:04.660 so collaboration is the subject of
NOTE Confidence: 0.78128789
00:44:04.660 --> 00:44:07.450 this study, also known as CPI 0610,
NOTE Confidence: 0.78128789
00:44:07.450 --> 00:44:10.498 which is a first in class selective oral,
NOTE Confidence: 0.78128789
00:44:10.500 --> 00:44:12.135 small local inhibitor,
NOTE Confidence: 0.78128789
00:44:12.135 --> 00:44:13.770 bit bad proteins.
NOTE Confidence: 0.78128789
00:44:13.770 --> 00:44:15.966 Got it modifies the expression of
NOTE Confidence: 0.78128789
00:44:15.966 --> 00:44:19.218 genes and Bolton Kappa B signaling.
NOTE Confidence: 0.78128789
00:44:19.218 --> 00:44:21.314 Decreasing the cytokines.
NOTE Confidence: 0.78128789
Also promoting erythrocyte differentiation and normalizing megakaryocytic differentiation. So that’s the background for this study. The study is currently ongoing. It’s manifest trial, global study and at this pace to trial. So there are three arms and the arm. I’m going to focus on this patients who are receiving. A collaborative and second line so they were previously treated with rock solid nib treated with rock solid nib or were not able to take Luke Slim for some reason so the dosing is an oral drug so this is given
00:44:56.841 --> 00:44:59.297 to its one one week off schedule and
00:44:59.368 --> 00:45:01.685 there are two cohorts in this arm.
00:45:01.690 --> 00:45:03.190 One part of the study,
00:45:03.190 --> 00:45:05.549 one of them is transfusion dependent cohort,
00:45:05.550 --> 00:45:08.378 36 out of 60 patients accrued and
00:45:08.378 --> 00:45:10.374 there’s ongoing enrollment and the
00:45:10.374 --> 00:45:12.498 2nd cohort cohort one be finished.
00:45:12.500 --> 00:45:14.980 Enrollment 50 patients. So the.
00:45:14.980 --> 00:45:16.472 Primary endpoint for transfusion
00:45:16.472 --> 00:45:18.337 Dependent Court court is transfusion,
00:45:18.340 --> 00:45:21.917 independence for patients and one cohort 1B.
00:45:21.920 --> 00:45:25.820 It’s it’s splenic volume response,
00:45:25.820 --> 00:45:27.476 35% reduction spleen volume.
00:45:27.476 --> 00:45:29.546 So the patients were enrolled
00:45:29.546 --> 00:45:31.799 were either Ching knowledgeable,
00:45:31.800 --> 00:45:32.667 jacked to intolerant,
NOTE Confidence: 0.844425436363636
00:45:32.667 --> 00:45:34.401 and the biggest group is jacked
NOTE Confidence: 0.844425436363636
00:45:34.401 --> 00:45:36.299 to refractory resistant patients.
NOTE Confidence: 0.844425436363636
00:45:36.300 --> 00:45:38.722 56% this is a group of patients
NOTE Confidence: 0.844425436363636
00:45:38.722 --> 00:45:39.760 with poor outcomes.
NOTE Confidence: 0.844425436363636
00:45:39.760 --> 00:45:42.280 Median survival is about 14 months,
NOTE Confidence: 0.844425436363636
00:45:42.280 --> 00:45:45.976 so the SDR 35 response at week 20.
NOTE Confidence: 0.844425436363636
00:45:45.980 --> 00:45:48.038 War was a primary endpoint for
NOTE Confidence: 0.844425436363636
00:45:48.038 --> 00:45:50.363 group 1D which is non transfusion
NOTE Confidence: 0.844425436363636
00:45:50.363 --> 00:45:52.944 dependent cohort and it was 18%.
NOTE Confidence: 0.844425436363636
00:45:52.944 --> 00:45:54.864 Most of the patients had
NOTE Confidence: 0.844425436363636
00:45:54.864 --> 00:45:56.016 some splenic response,
NOTE Confidence: 0.844425436363636
00:45:56.020 --> 00:45:58.810 18% had reduction by 35%.
NOTE Confidence: 0.844425436363636
00:45:58.810 --> 00:46:04.659 So the symptom reduction by 50% at
NOTE Confidence: 0.844425436363636
00:46:04.659 --> 00:46:07.291 the end of the 24 week period was
NOTE Confidence: 0.844425436363636
00:46:07.291 --> 00:46:09.504 observed in 20% among all study

80
participants transfusion dependent and not transfusion dependent participants.

Finally the group 1B. Primary endpoint the transfusion dependence converting to transfusion independence occurred in 16% of patients overall in the whole population there was observed improvement in hemoglobin levels. As you can see on the right hand side and among transfusion independent patients, 38% had improved hemoglobin level by 1.5 grams per deciliter. At the end of the 24 week period. So there are some exploratory
Endpoints including evolution.

Fibrosis in the marrow, and about quarter of patients had improvement, including about 6.7% of patients who had improvement by two grades of fibrosis.

Improvement in fibrosis correlated with improvement in hemoglobin levels, so the side effects are summarized.

For the sake of time, 19% of patients reported adverse events which led to discontinuation. Most of the side effects were great.

One and two.
So, in conclusion, this is manifest on one looking at 64 patients planned enrollment, 110 patients, there was a decent reduction of the spleen volume among transfusion dependent patients, and there was an improvement in hemoglobin, including among patients who are transfusion dependent and the 16% of them became transfusion independent. Marrow fibrosis and I didn’t present this data. Plasma cytokines decrease suggested potential disease modification by...
00:47:51.560 --> 00:47:53.780 majority of the most common treatment.
NOTE Confidence: 0.844425436363636

00:47:53.780 --> 00:47:55.850 Emergent adverse events were low grade
NOTE Confidence: 0.844425436363636

00:47:55.850 --> 00:47:58.453 and we are planning to participate in
NOTE Confidence: 0.844425436363636

00:47:58.453 --> 00:48:00.944 manifest 2 study randomized phase.
NOTE Confidence: 0.844425436363636

00:48:00.944 --> 00:48:01.996 Three study,
NOTE Confidence: 0.844425436363636

00:48:02.000 --> 00:48:03.590 double blinded between
NOTE Confidence: 0.553255013571428

00:48:05.840 --> 00:48:07.933 CPI 0610 and looks lit new versus
NOTE Confidence: 0.553255013571428

00:48:07.933 --> 00:48:09.827 placebo and looks lit nip at Yale.
NOTE Confidence: 0.553255013571428

00:48:09.830 --> 00:48:13.410 So the next step is and this is
NOTE Confidence: 0.553255013571428

00:48:13.410 --> 00:48:16.169 about the symbol of the drug which
NOTE Confidence: 0.553255013571428

00:48:16.169 --> 00:48:18.478 was recently approved for patients
NOTE Confidence: 0.553255013571428

NOTE Confidence: 0.553255013571428

00:48:21.310 --> 00:48:24.495 People who were enrolled in the study
NOTE Confidence: 0.553255013571428

00:48:24.500 --> 00:48:27.923 received at least two TCR’s and the
NOTE Confidence: 0.553255013571428

00:48:27.923 --> 00:48:30.865 presentation I’m focusing on today is
NOTE Confidence: 0.553255013571428

00:48:30.865 --> 00:48:33.643 update of what was previously presented.
So this is the drug which is in which hits BCR ABL on core protein. Activity specifically targeting able marstall pocket. It’s a different way of inhibiting BCR ABL, as you can see, even with key for one point, 9 mutation. Weighty people get this changed, and regular guys cannot attach a synonym, was able to inhibit people one kinase activity. Study is a phase three trial which randomizes patients. Between pursuit net 500 milligrams once a day and a 740 milligrams twice a day.
Once again, there's a patients who were previously treated for chronic phase CML with at least two different keys and the initial presentation at previous ASH meeting looked at primary endpoint, which is major molecular response at 24 weeks. This presentation updates the results by expanding. Observation period for additional 7 1/2 months. So basically in 19.2 months So the key secondary endpoint is Mr rated 96 weeks is not presented yet,
so this is the first. Presentation in 20 Dash 2020, which was also the data was also published in Blood. Last year, so the synonym was better than pursuit nip from the standard primary endpoint, which is major molecular response at 24 weeks by 12.2%. So the updated 48 week results continue to show the higher major molecular response rate. So basically at one year is 29.3% which is 16% higher than with pursuit nip. Also the reduction of desirable
transcript to less than one. OR something blood is seen more frequently in a semi warm 42% versus 19% more than double. So the deep responses are also better in a synonym as you can see on our 4.57 point 6 versus 1.3% and Mr. 410.8 versus 3.9% when compared to episode. So we’re all adverse events that were less common in patients with severe then with mood dip. So nevertheless pretty much everyone had some kind of adversity. But adverse events leading to discontinuation again less frequent in a similar treating patients treated patients,
so this is the most common all

NOTE Confidence: 0.553255013571428

great adverse events as seen

NOTE Confidence: 0.553255013571428

in more than 20% of patients.

NOTE Confidence: 0.553255013571428

You can see that a synonym is better

NOTE Confidence: 0.553255013571428

than other than cytopenia switch.

NOTE Confidence: 0.553255013571428

I seen more frequently among patients

NOTE Confidence: 0.553255013571428

who are treated with a similar,

NOTE Confidence: 0.553255013571428

but this was transient fact at

NOTE Confidence: 0.553255013571428

the beginning of treatment,

NOTE Confidence: 0.553255013571428

usually related to the disease itself

NOTE Confidence: 0.553255013571428

rather than to the treatment so.

NOTE Confidence: 0.553255013571428

Adverse arterial occlusive events

NOTE Confidence: 0.553255013571428

that were comparable in both groups,

NOTE Confidence: 0.553255013571428

but it is challenging to say

NOTE Confidence: 0.553255013571428

what would happen to the certain

NOTE Confidence: 0.553255013571428
00:51:41.914 --> 00:51:43.364 patients because they were observed
NOTE Confidence: 0.553255013571428
00:51:43.364 --> 00:51:45.177 a lot less than a similar patient.
NOTE Confidence: 0.789190589090909
00:51:45.180 --> 00:51:47.644 So, in conclusion, this is the first
NOTE Confidence: 0.789190589090909
00:51:47.644 --> 00:51:50.016 control study comparing tiki for resistant,
NOTE Confidence: 0.789190589090909
00:51:50.016 --> 00:51:51.540 intolerant patients using
NOTE Confidence: 0.789190589090909
00:51:51.540 --> 00:51:54.080 first and class specific drug,
NOTE Confidence: 0.789190589090909
00:51:54.080 --> 00:51:55.588 which is specifically targeting
NOTE Confidence: 0.789190589090909
00:51:55.588 --> 00:51:57.096 able one restoril pocket.
NOTE Confidence: 0.789190589090909
00:51:57.100 --> 00:51:59.348 Superior efficacy was demonstrated
NOTE Confidence: 0.789190589090909
00:51:59.348 --> 00:52:01.932 for synonym against BOSUTINIB, and.
NOTE Confidence: 0.789190589090909
00:52:01.932 --> 00:52:03.592 More patients remain the treatment
NOTE Confidence: 0.789190589090909
00:52:03.592 --> 00:52:05.928 at the end of 48 week period,
NOTE Confidence: 0.789190589090909
00:52:05.930 --> 00:52:07.748 so it has favorable safety profile.
NOTE Confidence: 0.789190589090909
00:52:07.750 --> 00:52:10.020 Now this is the drug which is available as a
NOTE Confidence: 0.789190589090909
00:52:10.080 --> 00:52:12.408 standard of care option for our CML patients,
NOTE Confidence: 0.789190589090909
00:52:12.410 --> 00:52:14.546 particularly with resistant with
resistance and influence to two TK eyes or more so finally, the.

They got me up for patients with the nominee and rearrangement of GFR one.

So just to map that this is one of the myeloid malignancies.

We spoke about MPN’s pH positive and negative so far,

but this is the myeloid lymphoid neoplasm with is an affiliate affiliates.

Hallmark feature of this group of malignant myeloid malignancies.

I’m going to focus on this particular one, which is, I mean, all of them are not very common,
but nevertheless it’s an interesting disease which is due to translocation of eight P.  
11 leading to constitutive activation of FGFR, one that’s 16 known partners.  
Chronic phase of this disease may present as MPNMS or MDSMPN.  
That’s why it is important to check if patient has an affiliate for this rearrangement, 
usually treated with hydroxyurea and keys, including non selective ponatinib and might historian.  
50% of patients are in blast phase after 12 months and meeting all survival
00:53:18.738 --> 00:53:20.323 and unfortunately only nine months
NOTE Confidence: 0.789190589090909
00:53:20.323 --> 00:53:22.117 without stem cell transplant one term.
NOTE Confidence: 0.789190589090909
00:53:22.120 --> 00:53:24.120 Oceans are possible with transplants.
NOTE Confidence: 0.789190589090909
00:53:24.120 --> 00:53:26.958 Las Vegas may present as a
NOTE Confidence: 0.789190589090909
00:53:26.960 --> 00:53:28.540 MLTOB cell and mix phenotype.
NOTE Confidence: 0.789190589090909
00:53:28.540 --> 00:53:30.825 Acute leukemia once again important
NOTE Confidence: 0.789190589090909
00:53:30.825 --> 00:53:34.056 test to do to select this patients
NOTE Confidence: 0.789190589090909
00:53:34.056 --> 00:53:36.608 and there is treatment with
NOTE Confidence: 0.789190589090909
00:53:36.608 --> 00:53:38.174 specific induction chemotherapy,
NOTE Confidence: 0.789190589090909
00:53:38.180 --> 00:53:40.108 perhaps with the tiki with one year survival,
NOTE Confidence: 0.789190589090909
00:53:40.110 --> 00:53:41.232 one with 30%.
NOTE Confidence: 0.789190589090909
00:53:41.232 --> 00:53:43.476 Those who achieve CR will abduction,
NOTE Confidence: 0.789190589090909
00:53:43.480 --> 00:53:45.780 Kima have superior survival obviously,
NOTE Confidence: 0.789190589090909
00:53:45.780 --> 00:53:47.355 and long term remissions are
NOTE Confidence: 0.789190589090909
00:53:47.355 --> 00:53:48.615 reported with transplanted patients.
NOTE Confidence: 0.789190589090909
So this disease is rare.
And also not very good to have because of lack of specific treatments.

The drug inhibits FGFR 1/3 and that led to its study in this flight.
Two or three trial.
So this is a swimmer sport showing ongoing responses for majority of patients with chronic phase. There are 18 of them and then there is. This is the 13 patients with blast phase. Unfortunately less responses here. A lot of patients, especially in the black box who died from this disease in the blast based. Nevertheless, some were breached to allogeneic stem cell transplant. So in conclusion. Is the first therapy to demonstrate durable and high rates of CR&CCYR in this group of patients.
Previously, these patients were treated with other treatments. Majority of them progressed, including intensive chemotherapy and chemotherapeutic stem cell transplant. Kaplan Meier median duration of CR and overall response have not been reached in those treated with Pamela Gardner clinical and cytogenetic. Responses were less frequent in and durable and blood space, but nevertheless some patients were able to breach too. Collagen in stem cell transplant.

See if there were no surprises and safety profiles and die of this
treatment consistent with Jeff Gordon condition and this may be a good option for long term treatment for patients with Melanie with FGFR rearrangement ineligible for transplant or facilitate bridging tool transplant.

Thank you, Doctor Badasci, thank you, Doctor Cialis. Great comprehensive presentations and.

We are going to take a few questions from the audience if any has, so please feel free if you want to type your question or if you want to ask directly, you can.
I think Lenny can mute you and you can ask the question.

I'm gonna actually start one question for Doctor Sheraz where we are waiting so Rory treatment of AML historical. 7 + 3 or really not much aside from that, so can you walk us through your thinking of the different options for a patient that potentially could be seen in any of the care centers. 74 year old male. Walks with a cane, but otherwise in good shape. Who comes with acute myeloid leukemia outpatient? And the patient has a flip 3.
see certainly in some patients. So how do you work through the different treatment options as you consider what to do with this patient? Well, I could think my practices is fairly evidence based with some rare exceptions, and you know, I’d say this is a double edged sword. I mean, it’s very fortunate that the field is moving very quickly with novel agents, novel combinations with. You know a recent preference for randomized trials, but by the time a trial is launched, let alone completed,
maybe the reference standard, the comparator arm is obsolete, so.

At the moment, you know a 74 year old is, age isn’t all ages, more of an imperfect surrogate for other patient specific factors like end organ reserve.

And I’d say maybe I put a bit more emphasis on the disease biology and with two troubling mutations and intensive therapy appropriate eligible candidate.

I mean, I would probably say this is a patient that probably would be treated with...
an intensive backbone plus midostaurin.

But I think we can all agree this is probably a patient best served with that triplet regimen.

You know at the patient was not intensive,

they would be eligible in the clinic.

You know, you know,

eyes in the beholder.

Then it’s a it’s dealers choice.

As event is probably still appropriate just based on the Lacewing data,

you know that Eunice Wang had presented and until we have a randomized trial looking at sequencing.
00:58:13.320 --> 00:58:14.064 Just flip three.
NOTE Confidence: 0.851500112857143

00:58:14.064 --> 00:58:15.800 I think the question is still unanswered,
NOTE Confidence: 0.851500112857143

00:58:15.800 --> 00:58:17.000 but it’s hard to stray from
NOTE Confidence: 0.851500112857143

00:58:17.000 --> 00:58:18.066 what we know from the belly.
NOTE Confidence: 0.851500112857143

00:58:18.066 --> 00:58:19.770 I think as of them still be the
NOTE Confidence: 0.851500112857143

00:58:19.824 --> 00:58:21.637 standard if the patient is need to
NOTE Confidence: 0.851500112857143

00:58:21.637 --> 00:58:23.043 not be intensive therapy appropriate
NOTE Confidence: 0.851500112857143

00:58:23.043 --> 00:58:25.066 and maybe in the next couple of
NOTE Confidence: 0.851500112857143

00:58:25.066 --> 00:58:26.600 years you might have a randomized
NOTE Confidence: 0.851500112857143

00:58:26.600 --> 00:58:28.402 trial that looks at that and maybe
NOTE Confidence: 0.851500112857143

00:58:28.402 --> 00:58:30.173 a seven could be superior to even
NOTE Confidence: 0.851500112857143

00:58:30.173 --> 00:58:31.339 classical intensive therapy,
NOTE Confidence: 0.851500112857143

00:58:31.340 --> 00:58:32.894 but at the moment that’s the
NOTE Confidence: 0.851500112857143

00:58:32.894 --> 00:58:33.930 dichotomy I would say.
NOTE Confidence: 0.758994072

00:58:36.740 --> 00:58:38.805 Perfect so clearly a lot of options
NOTE Confidence: 0.758994072

00:58:38.805 --> 00:58:40.394 for this patient. This patient
Some patients can still do IDH 2 monotherapy could be aids with IDH 2 inhibitor could be. 10 + 3 could be 7 + 3 with middle story and you still could consider transparent or not. So clearly many many different options. And clearly the best option is always a clinical trial, which we always encourage. So I’m pretty sure you know in the care centers these patients are seen all the time and I encourage people even if the patient does not want to come to the main campus or cannot travel to call one of us and go through some of the
potential options that we have Nikolai.

So fibrosis things are also clearly changing

issue that some of the clinical trials

Doctors in.

In practice,

one of the most common I think tough

situations is patients with myelofibrosis

who are on rock solid and anemic.

So the patient basically

has controlled spleen.

They are not having constitutional

symptoms but they are needing

transfusions and they are on.

Let’s say 20 milligram P opyd.

Now we have a drug approved that we
have a drug nib and there's another
drug in front of the FDA molet nib.
And you know a bunch of other things,
he says androgens and potentially.
So how do you think about these
different options as you approach
your patient like this?
So from the standpoint
of FDA approved therapy,
we have right now for awhile and
looks like name is obviously
dominating the market since 2011,
so I think that was approved for
similar group of patients from 2019
and usually considered as a second
01:00:29.125 --> 01:00:31.065 line for those patients who are
NOTE Confidence: 0.5364392455
01:00:31.065 --> 01:00:33.375 not satisfied with that rock solid.
NOTE Confidence: 0.5364392455
01:00:33.380 --> 01:00:35.680 Networx limp is not working
NOTE Confidence: 0.5364392455
01:00:35.680 --> 01:00:37.415 anymore with variable results,
NOTE Confidence: 0.5364392455
01:00:37.415 --> 01:00:39.965 So what we have approval is.
NOTE Confidence: 0.5364392455
01:00:39.970 --> 01:00:41.860 A grid Neb out on the 1st of March
NOTE Confidence: 0.5364392455
01:00:41.860 --> 01:00:43.428 was FDA approved for patients
NOTE Confidence: 0.5364392455
01:00:43.428 --> 01:00:45.403 who have low platelet count so
NOTE Confidence: 0.5364392455
01:00:45.403 --> 01:00:47.118 called cited piknic Milo fibrosis
NOTE Confidence: 0.5364392455
01:00:47.118 --> 01:00:49.454 and perhaps this drug can be used
NOTE Confidence: 0.5364392455
01:00:49.454 --> 01:00:51.260 not only for patients who have
NOTE Confidence: 0.5364392455
01:00:51.260 --> 01:00:52.928 platelet count less than 50 so,
NOTE Confidence: 0.5364392455
01:00:52.930 --> 01:00:55.821 but maybe between 50 and 100 because
NOTE Confidence: 0.5364392455
01:00:55.821 --> 01:00:57.694 effective dose sometimes is not
NOTE Confidence: 0.5364392455
01:00:57.694 --> 01:00:59.782 feasible for this group of patients.
NOTE Confidence: 0.5364392455
01:00:59.790 --> 01:01:02.954 So none of these drugs address anemia
sore from momentum study which was just presented that you know the data was presented as a company release, so there’s no publication about that at the end of January. So this drug is geared towards patients with anemia, who are progressing after sliding. Now this was a randomized study against Danazol, which you argue may not be the best randomization strategy. So there is some improvement in patients who have anemia there, but the drug is for symptom control.
more just for anemia.

Fix the patient you were talking about at the beginning.

Looks solid, treated, patient with anemia.

There is a study called Independents trial looking at luspatercept.

This group of patients we know that was part of Sept is approved for and perhaps some people can get it off label to treat these patients, but I think it is a little premature.

We have to see how this results are going to bend out.

So what would you do so you know, for patients who first
01:02:03.148 --> 01:02:05.673 of all don’t give up slip to patients
01:02:05.673 --> 01:02:08.024 whose main problem is an email, right?
01:02:08.024 --> 01:02:10.148 So because an email becomes worse,
01:02:10.150 --> 01:02:12.474 is the drug to fix the symptoms,
01:02:12.480 --> 01:02:15.301 and some patients would be happy to
01:02:15.301 --> 01:02:17.390 take crooks because they have bad
01:02:17.390 --> 01:02:18.670 symptoms and receive transfusions
01:02:18.670 --> 01:02:20.110 because their quality of life,
01:02:20.110 --> 01:02:21.832 even though transfusions may be a little
01:02:21.832 --> 01:02:23.590 bit more frequent, becomes better.
01:02:23.590 --> 01:02:27.160 So we can sometimes try to give
01:02:27.160 --> 01:02:29.390 everything like Derby Poitin 150 weekly
01:02:29.390 --> 01:02:31.790 or 300 weekly to those patients.
01:02:31.790 --> 01:02:33.815 In conjunction with within those
01:02:33.815 --> 01:02:34.625 country intuitive.
Because rooks, lithium is a Jack stat pathway inhibitor and worth reporting. Actually activates that pathway, but Bruce Lipton was not there 24/7, so we allow some hematopoiesis in between. So by doing that and some of the patients may have less transfusion requirement, so it’s either supportive, or trying to give darbepoetin to those patients who need or trying to decrease the looks lit nap, which of course is a you know may lead to. Reoccurrence of some of the symptoms and worsening of symptomatology in those patients.
So no perfect solution to this group of patients at this time.

Would you consider adding danazol also or so danazol would be one of the options with Retropulsion doesn’t work with overall response rate of about 20%, which may last up to two years.

Again, monitoring of liver function, test PSA and man would be important for this group of patients.

Yes, this is the second line option for an email management.

Can I ask you a question? So because we have to move to the tumor board.
I just have this question so if there is no clinical trial and your patience and your patient with MD’s didn’t respond to HMA, would you try to do off label addition of donetta clocks two weeks on, two weeks off to this patient? If you can get it covered by the insurance? No clinical trial available. Yeah, so that’s again like the dilemma we have with those patients because we don’t have anything that’s FDA approved for those patients, so I would consider it. However, I would, you know, be very clear with the patient about
the limitations of this being off label and we don’t have a lot of data.
I do think it’s quite a suppressive regimen, so for some patients you have to expect that they are going to need to come three times a week to the clinic,
need frequent transitions they will need to be on prophylactic antibiotics. So I consider it more in the setting where I’m thinking about bridging the patient to a transplant.
If the patient does not have a transplant option.
Think about it, but not as strongly,
except in situations where the patient is in relatively good shape.

The problem is that many of those patients are very old and they have a lot of comorbidities and therefore supportive care could be. Also, I think appropriate in some patients, but just take one last question because I see it from doctor to doctor Szeles about. Why do you think there was no overall survival advantage with 5% Neb with guilt in in the agile. I actually answered in the trap, but I guess in brief I mean there were some imbalances between the
groups were only talking about the
you know the Lacewing trial which
which is the gold ribbon trial.
More patients on the ASA monotherapy arm were able to proceed to subsequent therapy which of course could influence any OS for that group as well.
I think it was 40 versus 20%.
It was almost double and there is also about a four month difference in time to next therapy.
So patients who already committed so that could probably.
You know, explain some of that.
There were also striking imbalance in the performance status, which is more of a surrogate for frailty, which is again debated itself, but more patients on the ASIC guilt arm were just higher performance status you talked to was I think I wanna say 30% wallpaper so you know I thought the second line treatment with guilt in those who were treated with ASA you know so would be also the main reason why there was no at the end of all survival difference in this too. And they were, you know.
01:06:11.040 --> 01:06:12.390 So it’s just very difficult

01:06:12.390 --> 01:06:13.470 to show overall survival.

01:06:15.830 --> 01:06:17.486 Yeah, I think with all of

01:06:17.486 --> 01:06:19.338 these trials I know, I,

01:06:19.338 --> 01:06:21.546 I think doing this postmortem is,


01:06:23.690 --> 01:06:24.747 But at the end of the day,

01:06:24.750 --> 01:06:26.454 all of this should be thought

01:06:26.454 --> 01:06:27.962 before the trial and what we

01:06:27.962 --> 01:06:29.450 have is what we need to go with.

01:06:29.450 --> 01:06:30.727 So thank you so much. Again,

01:06:30.727 --> 01:06:32.869 if anybody has any additional questions,

01:06:32.870 --> 01:06:35.781 feel free to send us an

01:06:35.781 --> 01:06:37.107 email or call any of us.

01:06:37.110 --> 01:06:38.573 Thank you so much and I think

01:06:37.110 --> 01:06:38.573 Thank you so much and I think
01:06:38.573 --> 01:06:40.300 we have the tumor board. Yes,
NOTE Confidence: 0.71855441
01:06:40.310 --> 01:06:42.998 tumor board please.