00:00:00.000 --> 00:00:03.776 Much for joining us today for another edition of the highlights of the American State of Hematology meeting that was held in December 2021.

00:00:10.010 --> 00:00:13.150 My name is Ammar. I’m joined today by Doctor Nicola and Doctor Rory Chalice and we will be together presenting on myeloid malignancies.

00:00:20.461 --> 00:00:22.180 Doctor Rory Chalice and we will be together presenting on myeloid malignancies.

00:00:27.080 --> 00:00:28.832 Doctor Cialis will follow with highlights of XAML.

00:00:32.180 For another 15 minutes and
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.

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,
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.
'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. Also the intravenous decide. 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,
00:03:37.180 --> 00:03:39.250 lower doses than the approved dose
00:03:39.250 --> 00:03:41.361 in patients with lower risk MD’s
00:03:41.361 --> 00:03:43.887 who are not responding to her
00:03:43.887 --> 00:03:45.150 therapist stimulating agents.
00:03:45.150 --> 00:03:46.866 So this study is open currently
00:03:46.866 --> 00:03:49.045 at the main campus for any lower
00:03:49.045 --> 00:03:50.080 risk MD’s patient,
00:03:50.080 --> 00:03:52.162 feel free to discuss any patients
00:03:52.162 --> 00:03:55.109 who might have. For this study.
00:03:55.110 --> 00:03:57.336 Another drug that has been also approved
00:03:57.336 --> 00:03:59.709 in the year 2020 as Los Patterson,
00:03:59.710 --> 00:04:01.165 solo spatter said,
00:04:01.165 --> 00:04:03.105 basically is a transforming
00:04:03.105 --> 00:04:05.376 growth factor pathway inhibitor.
00:04:05.376 --> 00:04:07.968 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 designed basically as early phase 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
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
00:08:23.510 --> 00:08:24.990 was observed in XAML.

00:08:24.990 --> 00:08:26.784 However, many of the other patients are achieving also more OCR where the plants are less than 5% and they are achieving hematologic improvement.

00:08:31.554 --> 00:08:33.198 You can see that the response is achieved relatively quickly.

00:08:35.798 --> 00:08:37.530 The first response is seen within one month and those responses are durable.

00:08:41.920 --> 00:08:44.608 12 months you can see also that there is and this is the main update that was presented in ASH 2021.

00:08:48.592 --> 00:08:51.616 You can see that many patients achieve molecular clearance where the TP 53 molecular load is decreased.
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,
In the refractory relapse setting, Yale has participated in a study that was led by the sponsor. The sponsor organized the study with a similar design. Those escalation followed by those expansion and this was a smaller study than the frontline study. 44 patients were treated with 400 milligram of Veneto class given for two weeks and venetoclax was added to a society in so the patient had a failure. However, many of those were more hours. And you can see here that response rate was seen in 39%.
00:10:46.010 --> 00:10:47.730 The CRA was 7%,
NOTE Confidence: 0.8713487
00:10:47.730 --> 00:10:49.880 but those responses were durable.
NOTE Confidence: 0.8713487
00:10:49.880 --> 00:10:52.776 As you can see, the duration was nine
NOTE Confidence: 0.8713487
00:10:52.776 --> 00:10:56.140 months of the CR or the more OCR.
NOTE Confidence: 0.8713487
00:10:56.140 --> 00:10:57.364 But most importantly,
NOTE Confidence: 0.8713487
00:10:57.364 --> 00:10:58.996 we are actually seeing.
NOTE Confidence: 0.8713487
00:10:59.000 --> 00:11:02.306 I think mean clinically meaningful responses.
NOTE Confidence: 0.8713487
00:11:02.310 --> 00:11:05.094 You can see that platelets and red blood
NOTE Confidence: 0.8713487
00:11:05.094 --> 00:11:06.889 cell transfusion independence among
NOTE Confidence: 0.8713487
00:11:06.889 --> 00:11:09.464 patients who were transfusion dependent.
NOTE Confidence: 0.8713487
00:11:09.470 --> 00:11:11.990 OK fine, so the patient was needing
NOTE Confidence: 0.8713487
00:11:11.990 --> 00:11:14.073 blood or platelets around 1/3
NOTE Confidence: 0.8713487
00:11:14.073 --> 00:11:16.408 of those patients are becoming
NOTE Confidence: 0.8713487
00:11:16.408 --> 00:11:18.302 transfusion independent with by
NOTE Confidence: 0.8713487
00:11:18.302 --> 00:11:20.886 adding venetoclax to exercise and you
NOTE Confidence: 0.8713487
00:11:20.886 --> 00:11:23.514 can see that many patients achieve
NOTE Confidence: 0.8713487
00:11:23.514 --> 00:11:24.989 hematologic improvement as well,
NOTE Confidence: 0.8713487
00:11:24.990 --> 00:11:26.990 43% and the median overall
NOTE Confidence: 0.8713487
00:11:26.990 --> 00:11:28.590 survival was 12 months.
NOTE Confidence: 0.8713487
00:11:28.590 --> 00:11:30.995 We know historically that median
NOTE Confidence: 0.8713487
00:11:30.995 --> 00:11:33.400 overall survival after a jammy
NOTE Confidence: 0.8713487
00:11:33.483 --> 00:11:35.698 failure is around six months,
NOTE Confidence: 0.8713487
00:11:35.700 --> 00:11:37.510 so it does seem that.
NOTE Confidence: 0.8713487
00:11:37.510 --> 00:11:41.731 We are seeing promising activity with this
NOTE Confidence: 0.8713487
00:11:41.731 --> 00:11:46.018 combination in the refractory labs setting.
NOTE Confidence: 0.8713487
00:11:46.020 --> 00:11:48.290 I think another important study
NOTE Confidence: 0.8713487
00:11:48.290 --> 00:11:51.076 from this hash meeting was the
NOTE Confidence: 0.8713487
00:11:51.076 --> 00:11:53.031 phase three update using that,
NOTE Confidence: 0.8713487
00:11:53.031 --> 00:11:54.036 so people need this stat.
NOTE Confidence: 0.8713487
00:11:54.040 --> 00:11:56.360 Is it activating enzyme inhibitor?
NOTE Confidence: 0.8713487
00:11:56.360 --> 00:11:58.208 It works upstream of the protein zone so
00:11:58.208 --> 00:12:00.117 this is a negative phase three study.

00:12:00.120 --> 00:12:03.168 The reason why I think this is an important presentation is because there has been a lot of early data with.

00:12:03.168 --> 00:12:04.917 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,

00:12:04.917 --> 00:12:07.470 and we had durable responses.

00:12:07.470 --> 00:12:09.582 So there was a lot of excitement about this drug and we did participate in the phase two part of this.

00:12:09.582 --> 00:12:11.736 Evaluation, but not in the phase three.

00:12:11.736 --> 00:12:14.981 However,

00:12:14.981 --> 00:12:17.566 we had durable responses.

00:12:17.570 --> 00:12:20.730 and we had durable responses.

00:12:20.730 --> 00:12:22.942 So there was a lot of excitement about this drug and we did participate in the phase two part of this.

00:12:22.942 --> 00:12:25.203 Evaluation, but not in the phase three.

00:12:25.203 --> 00:12:27.460 However,
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, in solar tumors immune checkpoint 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 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. Typo methylating agents.
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 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. So 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 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
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 S in the 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. So 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 there 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
NOTE Confidence: 0.619771994
00:23:35.078 --> 00:23:37.190 one to receive Asia or Asia plus I've
NOTE Confidence: 0.619771994
00:23:37.190 --> 00:23:39.277 acid nip with the primary endpoint.
NOTE Confidence: 0.619771994
00:23:39.280 --> 00:23:40.648 As you can see in the right here
NOTE Confidence: 0.619771994
00:23:40.648 --> 00:23:41.619 of event free survival,
NOTE Confidence: 0.619771994
00:23:41.620 --> 00:23:44.070 which was defined as a time frame
NOTE Confidence: 0.619771994
00:23:44.070 --> 00:23:45.630 randomization until treatment failure.
NOTE Confidence: 0.795475042142857
00:23:48.090 --> 00:23:49.428 146 patients have been enrolled as
NOTE Confidence: 0.795475042142857
00:23:49.428 --> 00:23:51.189 of this day to cut with the data.
NOTE Confidence: 0.795475042142857
00:23:51.190 --> 00:23:54.382 Cutoff was March of 2021 and as shown here,
NOTE Confidence: 0.795475042142857
00:23:54.382 --> 00:23:55.922 these were older patients with
NOTE Confidence: 0.795475042142857
00:23:55.922 --> 00:23:58.046 a median age of 75 to 76 years,
NOTE Confidence: 0.795475042142857
00:23:58.050 --> 00:24:00.666 a third with Anika performance status of two.
NOTE Confidence: 0.795475042142857
00:24:00.670 --> 00:24:03.400 Also about 1/4 of patients had
NOTE Confidence: 0.795475042142857
00:24:03.400 --> 00:24:06.468 defined poor risk disease.
NOTE Confidence: 0.795475042142857
00:24:06.470 --> 00:24:07.438 In looking at responses,
NOTE Confidence: 0.795475042142857
which was not the primary endpoint,

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 line with the better rates of response and deep response by.

There was a better EFS in the

Asia plus Ivy Sydney farm.
00:24:42.210 --> 00:24:43.872 This is also translated into better
00:24:43.872 --> 00:24:45.960 OS for that for that arm as well.
00:24:45.960 --> 00:24:47.560 Quite striking at 24 months
00:24:47.560 --> 00:24:48.840 compared with eight months.
00:24:48.840 --> 00:24:50.646 As you can see here for patients
00:24:50.646 --> 00:24:52.369 just getting as alone and this
00:24:52.369 --> 00:24:54.145 is generally what we expect for
00:24:54.145 --> 00:24:55.899 patients getting a zoumana therapy.
00:24:55.900 --> 00:24:58.447 Did it come at the cost of more toxicity?
00:24:58.450 --> 00:25:00.426 Not really in looking at human logic talks,
00:25:00.430 --> 00:25:02.248 but perhaps a little more neutropenia.
00:25:02.250 --> 00:25:05.300 Pina Nonheme talks was also about the same,
00:25:05.300 --> 00:25:07.628 but the frequency of all grade
00:25:07.628 --> 00:25:09.259 differentiation syndrome, but concerned with.
00:25:09.259 --> 00:25:10.108 Ibis Sydney Pomona.
00:25:10.108 --> 00:25:10.108
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
NOTE Confidence: 0.795475042142857
00:25:41.736 --> 00:25:44.106 be prematurely discontinued given the
NOTE Confidence: 0.795475042142857
00:25:44.106 --> 00:25:46.475 evidence of a benefit for the combination.
NOTE Confidence: 0.795475042142857
00:25:46.480 --> 00:25:48.531 So I would say, how does this
NOTE Confidence: 0.795475042142857
00:25:48.531 --> 00:25:49.970 translate into clinical practice?
NOTE Confidence: 0.795475042142857
00:25:49.970 --> 00:25:50.478 In short,
NOTE Confidence: 0.795475042142857
00:25:50.478 --> 00:25:52.510 as yet it remains to be determined for
NOTE Confidence: 0.795475042142857
00:25:52.570 --> 00:25:54.640 the patient with ID terminated disease,
NOTE Confidence: 0.795475042142857
00:25:54.640 --> 00:25:57.146 whether he or she is best served
NOTE Confidence: 0.795475042142857
00:25:57.146 --> 00:25:59.929 with a so plus van or a soap.
NOTE Confidence: 0.795475042142857
00:25:59.930 --> 00:26:01.178 I am personally aware of any
NOTE Confidence: 0.795475042142857
00:26:01.178 --> 00:26:02.330 randomized trial at the moment,
NOTE Confidence: 0.795475042142857
00:26:02.330 --> 00:26:06.038 but suspect that is a that is coming soon.
NOTE Confidence: 0.795475042142857
00:26:06.040 --> 00:26:07.645 Sticking with the same theme
NOTE Confidence: 0.795475042142857
00:26:07.645 --> 00:26:08.929 for frontline randomized trials,
NOTE Confidence: 0.795475042142857
00:26:08.930 --> 00:26:11.456 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
one to one either get filter written at
monotherapy built plus as a or as alone.
But due to the website it as
it was modified to randomize patients 2 to
one to get either guiltless ASA oracea alone.
Baseline characteristics are shown here and
demonstrate that this was as expected and.
Older population with meaning ages 77
and also a good proportion with
any card performance status of two
plus with perhaps some imbalance in
00:27:14.578 --> 00:27:16.572 favor of the Asian monotherapy arm.
NOTE Confidence: 0.839955340909091
00:27:16.572 --> 00:27:19.542 As expected, there were about 80% IT
NOTE Confidence: 0.839955340909091
00:27:19.542 --> 00:27:21.414 mutations and similar rates of it.
NOTE Confidence: 0.839955340909091
00:27:21.420 --> 00:27:23.828 High disease without at least from my eyes.
NOTE Confidence: 0.839955340909091
NOTE Confidence: 0.688259697142857
00:27:27.260 --> 00:27:29.269 It’s pretty much up for this slide
NOTE Confidence: 0.688259697142857
00:27:29.270 --> 00:27:31.760 with regards to responses CR rates,
NOTE Confidence: 0.688259697142857
00:27:31.760 --> 00:27:32.856 not the primary endpoint,
NOTE Confidence: 0.688259697142857
00:27:32.856 --> 00:27:34.500 which is OS like I mentioned,
NOTE Confidence: 0.688259697142857
00:27:34.500 --> 00:27:35.860 we’re somewhere between arms,
NOTE Confidence: 0.688259697142857
00:27:35.860 --> 00:27:38.148 but the rates of CRI and CRP which
NOTE Confidence: 0.688259697142857
00:27:38.148 --> 00:27:39.921 are less than CR response is still
NOTE Confidence: 0.688259697142857
00:27:39.921 --> 00:27:41.536 to be clinically meaningful were
NOTE Confidence: 0.688259697142857
00:27:41.536 --> 00:27:43.433 higher in the combination are nearly
NOTE Confidence: 0.688259697142857
00:27:43.433 --> 00:27:45.071 three times actually for a composite
NOTE Confidence: 0.688259697142857
00:27:45.071 --> 00:27:47.990 C area of about 58% for the combo
and the 26% for as a monotherapy. However, it’s 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 guilt 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.
00:28:17.700 --> 00:28:19.100 Sorry, the combination arm.
NOTE Confidence: 0.879116239523809

00:28:19.100 --> 00:28:21.770 It was like 8 versus 5 months.
NOTE Confidence: 0.879116239523809

00:28:21.770 --> 00:28:23.318 So this might have influenced OS
NOTE Confidence: 0.879116239523809

00:28:23.318 --> 00:28:25.055 in addition to the imbalance and
NOTE Confidence: 0.879116239523809

00:28:25.055 --> 00:28:26.685 performance status that I showed
NOTE Confidence: 0.879116239523809

NOTE Confidence: 0.879116239523809

00:28:28.912 --> 00:28:30.877 Looking at unplanned subgroup analysis,
NOTE Confidence: 0.879116239523809

00:28:30.880 --> 00:28:32.140 improved overall survival with guilt
NOTE Confidence: 0.879116239523809

00:28:32.140 --> 00:28:34.159 as it was really not observed in any.
NOTE Confidence: 0.879116239523809

00:28:34.160 --> 00:28:36.008 Although some trans were noted for
NOTE Confidence: 0.879116239523809

00:28:36.008 --> 00:28:37.972 patients that were more fit and
NOTE Confidence: 0.879116239523809

00:28:37.972 --> 00:28:41.044 also here with Hihget delic ratio,
NOTE Confidence: 0.879116239523809

00:28:41.050 --> 00:28:43.024 I didn’t show any adverse event data
NOTE Confidence: 0.879116239523809

00:28:43.024 --> 00:28:44.934 here because they were largely similar
NOTE Confidence: 0.879116239523809

00:28:44.934 --> 00:28:47.279 between arms including grade 3 plus events.
NOTE Confidence: 0.879116239523809

00:28:47.280 --> 00:28:48.651 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
NOTE Confidence: 0.898801785
the definition of what we call CRH.
NOTE Confidence: 0.898801785
Frontline treatment for wild type
NOTE Confidence: 0.898801785
patients was even more impressive
NOTE Confidence: 0.898801785
with a CR CRA of 90%.
NOTE Confidence: 0.898801785
Conversely, and this is,
NOTE Confidence: 0.898801785
you know, one of the downsides.
NOTE Confidence: 0.898801785
This doesn’t appear to be a
NOTE Confidence: 0.898801785
meaningful option for patients
NOTE Confidence: 0.898801785
who’ve already been failed by vanetta
NOTE Confidence: 0.898801785
klax based regimen with the CRA.
NOTE Confidence: 0.898801785
As you can see here, based on 15 patients,
NOTE Confidence: 0.898801785
but still zero and only 20% rate of CRI
NOTE Confidence: 0.898801785
and at the bottom here you can see a 20%.
NOTE Confidence: 0.898801785
It gets phone numbers but 20%
NOTE Confidence: 0.898801785
rate of pearly 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
data that I presented to you last year.
Frequent I share some more toxicity
data frequente, ease of all grades.
Hypokalemia, hypophosphatemia,
about half of patients, and some otherwise.
He talks you would expect
with as event itself,
not necessarily mad or attributable.
Among 17 patients that were newly diagnosed,
and thus TP50 mutated,
the median drop was just about
1 gram per deciliter this after
the first dose,
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 on target hemolytic anemia, just that you know was a bit troublesome early on in the trial, but appears to be manageable with you know 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.

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 as event, but for which there is sound clinical rationale. This is a therapy that targets CD 123, 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 CD 123 antibody coupled to a novel DNA alkylating payload. Linedata Goodyear in PDX modeling or experiments good synergy between
Immunogen 632 in Asia and Dwarven, including being able to overcome a certain resistance. So for these reasons, this is a phase one. Two trial of that product combined with 7 and patients with as you'd have guessed, CD one or three positive AML to date. The triple combo escalation is consists of five cohorts, 4 with the investigational product dosed on day, seven of each cycle, one cohort where it’s dosed and one cohort where it’s dosed on the first day. Each cycle make it a bit more convenient for the patient at the time of this analysis presented.
00:34:43.710 --> 00:34:45.520 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 percent being grade 3 and otherwise things you would expect with a Savannah loan. One patient in the day one cohort had to discontinue because of an infusion reaction was considered DLT, but early mortality defined it at the bottom here 30 days with zero percent. 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, with maybe higher rates in the higher.
00:35:48.200 --> 00:35:50.594 dose cohorts of no patients prior

00:35:50.594 --> 00:35:52.992 van had good Angeliki make activity

00:35:52.992 --> 00:35:55.626 as seen here on the right, waterfall

00:35:55.626 --> 00:35:58.818 plot and overall response rate of 40%.

00:35:58.820 --> 00:36:00.252 Other subsets of note

00:36:00.252 --> 00:36:01.326 flipper mutated disease.

00:36:01.330 --> 00:36:01.951 Even more striking.

00:36:01.951 --> 00:36:02.986 I’ll be at $9$ patients,

00:36:02.990 --> 00:36:04.886 but 80% rate of composite emission.

00:36:04.890 --> 00:36:07.256 So in some encouraging in some molecular

00:36:07.256 --> 00:36:09.339 subsets and then treated patients,

00:36:09.340 --> 00:36:09.968 but certainly.

00:36:09.968 --> 00:36:11.852 Like the other studies I presented

00:36:11.852 --> 00:36:13.665 more data to assure these values

00:36:13.665 --> 00:36:15.357 don’t regress to the mean like

NOTE Confidence: 0.699811161538462
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 

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? 

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 looking at Hillside and medic. Right is the fact that in patients with polycythemia Vera. So the rationale for the study is. Which is looking at Hillside and medic. Right is the fact that in patients with polycythemia Vera.
polycythemia Vera iron is necessary to make red blood cells in the marrow, which is affected by Jack. Two V 617 FM PM. So as you can see on the left, ferroportin is the main transporter of the iron from outside 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. 2 mutated. Red blood cell precursors. 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 otherwise created by therapeutic phlebotomies. Leading to decreased 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. Patients with PD diagnosis based
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% required one and only 2% required 2 phlebotomists so very significant we self...
eliminating phlebotomies in almost all of the patients within the 1st 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 30 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. So 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 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 adverse events and we are planning to open phase three randomized
control study at Yale for this patients.

So the second study is for my

love fibrosis patients and it’s

gone collaborative wanna therapy

for patients with myelofibrosis?

This is update of ongoing study.

I presented this study last year so

it uses it utilizes this knowledge

that promo domain and extra terminal

domain proteins promote myelofibrosis.

You can see the activation of NF

Kappa B targeted genes leading to

increased inflammatory response.

Aberrant, or through a differentiation

and aberrant megakaryocytic
differentiation manifestations.
So far, my love for fibrosis,
inflammatory response causes systemic symptoms as well as cytopenias,
including an email from both.
Cytopenia conceit can be seen in my life.
I prove this difference,
so collaboration is the subject of this study, also known as CPI 0610,
which is a first in class selective oral, small local inhibitor,
it modifies the expression of genes and Bolton Kappa B signaling.
Decreasing the cytokines.
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. 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 or were not able to take Luke Slim for some reason so the dosing is an oral drug so this is given
to its one week off schedule and there are two cohorts in this arm.

One part of the study, one of them is transfusion dependent cohort, 36 out of 60 patients accrued and there’s ongoing enrollment and the 2nd cohort cohort one be finished. Enrollment 50 patients. So the.

Primary endpoint for transfusion Dependent Court court is transfusion, 35% reduction spleen volume. So the patients were enrolled 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
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 Milo 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 collaborative discontinuation. Most of the side effects were great.
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
majority of the most common treatment. 
Emergent adverse events were low grade and we are planning to participate in manifest 2 study randomized phase. 
Three study, double blinded between CPI 0610 and looks lit new versus placebo and looks lit nip at Yale. 
So the next step is and this is about the symbol of the drug which was recently approved for patients with CML as a third line treatment. People who were enrolled in the study received at least two TCR’s and the presentation I’m focusing on today is 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 marshall pocket. It’s a different way of inhibiting BCR ABL, as you can see, even with key for one point, eighty 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 great adverse events as seen in more than 20% of patients. You can see that a synonym is better than other than cytopenia switch. I seen more frequently among patients who are treated with a similar, but this was transient fact at the beginning of treatment, usually related to the disease itself rather than to the treatment so. Adverse arterial occlusive events that were comparable in both groups, but it is challenging to say what would happen to the certain
patients because they were observed a lot less than a similar patient. So, in conclusion, this is the first control study comparing tiki for resistant, intolerant patients using first and class specific drug, which is specifically targeting able one restoril pocket. Superior efficacy was demonstrated for synonym against BOSUTINIB, and. More patients remain the treatment at the end of 48 week period, so it has favorable safety profile. Now this is the drug which is available as a standard of care option for our CML patients, 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
malignancies 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. I’m due to translocation of eight P. leading to constitutive activation of FGFR, one that’s 16 known partners. Chronic phase of this disease may present as MPNMD 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
and unfortunately only nine months

without stem cell transplant one term.

Oceans are possible with transplants.

Las Vegas may present as a

MLTOB cell and mix phenotype.

Acute leukemia once again important

test to do to select this patients

and there is treatment with

specific induction chemotherapy,

perhaps with the tiki with one year survival,

one with 30%.

Those who achieve CR will abduction,

Kima have superior survival obviously,

and long term remissions are

reported with transplanted patients.
So this disease is rare.
And also not very good to have because of lack of specific treatments as well as poor outcomes with available therapy at perhaps other than transplant which is available for limited number of patients.
So is this drug which is currently approved by FDA as well as in some other countries for patients with cholangiocarcinoma previously treated was FGFR 2 fusion and rearrangements.
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 and 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. 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 mutation and mutation which we can
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,

00:57:15.840 --> 00:57:18.863 the comparator arm is obsolete, so.

At the moment,

00:57:19.952 --> 00:57:22.490 you know a 74 year old is,

00:57:22.490 --> 00:57:24.650 you know, age isn’t all ages,

00:57:24.650 --> 00:57:26.205 more of an imperfect surrogate

00:57:26.205 --> 00:57:27.449 for other patient specific

00:57:27.449 --> 00:57:28.909 factors like end organ reserve.

00:57:28.910 --> 00:57:31.526 And I’d say maybe I put a bit

00:57:31.526 --> 00:57:33.649 more emphasis on the disease

00:57:33.649 --> 00:57:35.969 biology and with two troubling

00:57:35.969 --> 00:57:38.054 mutations and intensive therapy

00:57:38.054 --> 00:57:39.668 appropriate eligible candidate.

00:57:39.670 --> 00:57:40.192 I mean,

00:57:40.192 --> 00:57:42.280 I would probably say this is a patient

00:57:42.343 --> 00:57:44.455 that probably would be treated with
an intensive backbone plus midostaurin

you didn’t give me a fits it high or.

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
00:58:40.394 --> 00:58:42.506 could go with his even potentially.

00:58:42.510 --> 00:58:46.714 Some patients can still do IDH 2 monotherapy

00:58:46.714 --> 00:58:51.520 could be aids with IDH 2 inhibitor could be.

00:58:51.520 --> 00:58:53.945 10 + 3 could be 7 + 3 with middle story and

00:58:53.945 --> 00:58:56.157 you still could consider transparent or not.

00:58:56.160 --> 00:58:57.918 So clearly many many different options.

00:58:57.920 --> 00:59:00.360 And clearly the best option

00:59:00.360 --> 00:59:01.676 is always a clinical trial,

00:59:01.676 --> 00:59:04.648 which we always encourage.

00:59:04.648 --> 00:59:06.825 So I'm pretty sure you know in the care

00:59:06.888 --> 00:59:09.424 time and I encourage people even if the

00:59:09.424 --> 00:59:11.482 patient does not want to come to the

00:59:11.482 --> 00:59:13.784 main campus or cannot travel to call

00:59:13.784 --> 00:59:16.980 one of us and go through some of the

103
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
NOTE Confidence: 0.758994072
00:59:57.120 --> 00:59:59.500 have a drug nib and there’s another
NOTE Confidence: 0.758994072
00:59:59.500 --> 01:00:02.259 drug in front of the FDA molet nib.
NOTE Confidence: 0.758994072
01:00:02.260 --> 01:00:04.028 And you know a bunch of other things,
NOTE Confidence: 0.758994072
01:00:04.030 --> 01:00:09.240 he says androgens and potentially.
NOTE Confidence: 0.758994072
01:00:09.240 --> 01:00:10.808 So how do you think about these
NOTE Confidence: 0.758994072
01:00:10.808 --> 01:00:12.051 different options as you approach
NOTE Confidence: 0.758994072
01:00:12.051 --> 01:00:13.087 your patient like this?
NOTE Confidence: 0.5364392455
01:00:13.580 --> 01:00:15.200 So from the standpoint
NOTE Confidence: 0.5364392455
01:00:15.200 --> 01:00:16.820 of FDA approved therapy,
NOTE Confidence: 0.5364392455
01:00:16.820 --> 01:00:19.074 we have right now for awhile and
NOTE Confidence: 0.5364392455
01:00:19.074 --> 01:00:21.001 looks like name is obviously
NOTE Confidence: 0.5364392455
01:00:21.001 --> 01:00:23.089 dominating the market since 2011,
NOTE Confidence: 0.5364392455
01:00:23.089 --> 01:00:25.182 so I think that was approved for
NOTE Confidence: 0.5364392455
01:00:25.182 --> 01:00:27.130 similar group of patients from 2019
NOTE Confidence: 0.5364392455
01:00:27.130 --> 01:00:29.062 and usually considered as a second
NOTE Confidence: 0.5364392455
line for those patients who are not satisfied with that rock solid. Networx limp is not working anymore with variable results, So what we have approval is. A grid Neb out on the 1st of March was FDA approved for patients who have low platelet count so called cited piknic Milo fibrosis and perhaps this drug can be used not only for patients who have platelet count less than 50 so, but maybe between 50 and 100 because effective dose sometimes is not feasible for this group of patients. 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 MDS with doing Super Blast right so 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 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, care with transfusions 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 Lacewing trial 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 like 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.
There were also.

There was 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.
So it’s just very difficult to show overall survival.

Yeah, I think with all of these trials I you know, I, I think doing this postmortem is, a good thinking exercise. But at the end of the day, all of this should be thought. All of this should be thought before the trial and what we have is what we need to go with. So thank you so much. Again, if anybody has any additional questions, feel free to send us an email or call any of us. Thank you so much and I think
we have the tumor board. Yes,
tumor board please.