Typically this is a CME event composed of six sessions. We already had the first session for multiple myeloma on January 15th and the lymphoid malignancy session last week. Today will be updating you on the myeloid malignancy and next week we have an update on pediatric leukemia and also adult acute lymphoblastic leukemia. February 12th will be classical or non benign hematology and we will conclude on February 19th with cell therapy and transplantation updates. So as you can tell,
there are many great abstracts that are being presented in ash this year, and it’s very difficult to try to cover all of these, especially with the time limitation. So here the abstracts that have been selected in this session and in the other sessions basically are chosen for their highest impact, and the ones that are most relevant clinically, especially in areas of unmet clinical need with decided to group them basically by the disease area AML MD’s. And my love I almyra preffective neoplasms.
Of course, that doesn’t mean that the other abstracts that are not presented are not as great. It just as time limitation, and also important to remember that a lot of the abstracts contain preliminary information and preliminary data, and they have not been peer reviewed or finalize or published. So these results always have to be taken with that consideration in mind.

We also like to thank all the authors of those abstracts who have shared their slides. With us for this presentation at the end of the entire Series A recording.
NOTE Confidence: 0.8444918
00:01:41.830 --> 00:01:44.216 of this session and the other sessions
NOTE Confidence: 0.8444918
00:01:44.216 --> 00:01:46.806 will be available on the subsequent week.
NOTE Confidence: 0.8444918
00:01:46.810 --> 00:01:49.386 An slice of each presentation that will
NOTE Confidence: 0.8444918
00:01:49.386 --> 00:01:51.844 also be available for your review and
NOTE Confidence: 0.8444918
00:01:51.844 --> 00:01:54.560 for people who cannot make the live event.
NOTE Confidence: 0.8444918
00:01:54.560 --> 00:01:57.264 At the end of the six session series,
NOTE Confidence: 0.8444918
00:01:57.270 --> 00:01:58.965 CME Credit will be provided
NOTE Confidence: 0.8444918
00:01:58.965 --> 00:02:00.660 for those who claim it.
NOTE Confidence: 0.8444918
00:02:00.660 --> 00:02:05.079 You will have to fill a quick form and.
NOTE Confidence: 0.8444918
00:02:05.080 --> 00:02:07.660 Supply some feedback to claim the
NOTE Confidence: 0.8444918
00:02:07.660 --> 00:02:10.990 CME credit at the end of the series.
NOTE Confidence: 0.8444918
00:02:10.990 --> 00:02:12.630 So today we’ll be covering
NOTE Confidence: 0.8444918
00:02:12.630 --> 00:02:13.614 the myeloid neoplasms.
NOTE Confidence: 0.8444918
00:02:13.620 --> 00:02:15.270 As you can see here,
NOTE Confidence: 0.8444918
00:02:15.270 --> 00:02:17.573 I will be updating you for Milo
NOTE Confidence: 0.8444918
Dysplastic syndromes then, Doctor Orish Alice will update us on acute myeloid leukemia and finally doctor, but also full update us on myeloproliferative. Neoplasms will try to stick to the times that you can see here so that we can allow some time for questions in the last 10 minutes. We can stay a few minutes beyond one. For those of you who can stay if there are many questions as well. So I'll start with the updates on my latest ostick syndromes. So these are my disclosures. So I'm just as many of you know,
their management is really highly risk adaptive. It’s somewhat unusual compared to other malignancy’s in which the interventions vary significantly all the way from observation. For patients with lower risk, MDS all the way to recommending a very aggressive intervention, like allogenic bone marrow transplantation for patients who have very aggressive disease, which have a prognosis almost like acute myeloid leukemia. In the most aggressive forms of Andy’s,
this is actually a schema from 2013,
and the reason I’m showing you this one.
From seven or eight years ago is because.
Not much really has changed in
the schema in the management of
Andy as until last year until 2020
and in 2020 we have the first 2
approvers basically since
so we had 14 years without any
approvals for Andy’s until 2020 when we
have two drugs that have been approved.
One of them is last battleship which
is a transforming growth factor beta,
an inhibitor disinhibits. Elegant and.
This is recommended for patients who
have lower risk MD’s who have any
meandering senior class and other drug, was an oral decitabine. An oral version of this item, in that we will be talking about, but this was also approved in late 2024 patients with high risk MD's. So I think it’s important to start the presentation by highlighting that high unmet need for patients with high risk MD's. So these are some real life analysis that showed that despite the introduction of hypomethylating agents in for treatment for high risk MD as the outcomes or me and pull the overall responses is around 40 to 50%.
However, the complete response rate is only around 15% and most of those responses are limited and most patients die from the disease relatively quickly. You can see here previous real life analysis that we conducted for patients who receive is cited in or decide to be in and you can see the median overall survival for older patients. And this was a serious Medicare analysis was eleven months while for patients who were younger and were referred to tertiary big centers in the MD’s Clinical Research Consortium. The median overall survival was 17 months.
So basically it's much lower than what is generally described in the literature. On 24 months, and for patients who progress after receiving those hypomethylating agents, their survival is even worse. This is an important study that was published by our colleague, Doctor to my Propay, showing that the median survival was only five months. Basically after failure of hypomethylating agents and I think all of this data highlight the significant unmet need that we should not just routinely
use hypomethylating agents.

But we should try to improve the outcomes of patients.

So going to some of the major highlights from the ash meeting,

This is a drug that I just mentioned. Oral deci TB in that has just been approved in August 2020,

so decide to be in the reason why you cannot give this ITB in orally

is because it’s highly metabolised

Citadine dominates as well as in the liver,

so you have significant first pass effect.

So what was done here in to develop
this drug which is called in covi.

Is to combine decided being with an inhibitor of this city in Germany is called sisters OR and the combination in phase one.

Phase two trials was shown to result in similar pharmacodynamic and pharmacodynamic.

Activities to the Ivy decided mean,

so this combination was taken to a phase three trial that looked at pharmacokinetic equivalence as a final end point,

and this trial was presented in 2019 and you can see A at the bottom.

The final conclusion, which you have 99% equivalence pharmacokinetic equivalence
between oral and IV decitabine.

However, the follow up from this study was somewhat limited and an important update. Was presented in the American Society of Hematology meeting this year by Doctor Savona, and this trial is actually a trial. We participated in many of you in the care centers, have refer patients for us, so we thank you for that. The update from the certain study showed that the complete response rate was around 22% and the median overall survival after median follow up of 24 months has not yet been reached and the median duration
00:07:26.614 --> 00:07:28.726 of best response was 12 months.

00:07:28.730 --> 00:07:31.350 So I think well.

00:07:31.350 --> 00:07:33.966 The follow up still needs to be longer.

00:07:33.970 --> 00:07:36.546 It’s important to know that for now it

00:07:36.546 --> 00:07:38.974 seems that oral version of Decitabine is

00:07:38.974 --> 00:07:41.808 very similar to how we decide to be in,

00:07:41.810 --> 00:07:43.916 and I think we have a lot of data

00:07:43.916 --> 00:07:46.090 now suggesting that it can be

00:07:46.090 --> 00:07:47.960 completely replacing the IBD side

00:07:48.024 --> 00:07:49.989 been as monotherapy for Andy’s.

00:07:49.990 --> 00:08:01.850 That has been approved,
00:08:01.850 --> 00:08:03.806 but this is was only approved
NOTE Confidence: 0.8306338
00:08:03.806 --> 00:08:06.009 in AML on your egg Aurora.
NOTE Confidence: 0.8306338
00:08:06.010 --> 00:08:08.439 Laser sighted is very different in
NOTE Confidence: 0.8306338
00:08:08.439 --> 00:08:10.178 pharmacokinetics. Ann for Neko Dynamics.
NOTE Confidence: 0.8306338
00:08:10.178 --> 00:08:12.260 Then I be decided in an.
NOTE Confidence: 0.8306338
00:08:12.260 --> 00:08:13.078 I'm sorry.
NOTE Confidence: 0.8306338
00:08:13.078 --> 00:08:15.941 Then Ivy is exciting in and therefore
NOTE Confidence: 0.8306338
00:08:15.941 --> 00:08:18.920 should not be used in MD as its only
NOTE Confidence: 0.8306338
00:08:18.920 --> 00:08:21.445 approved for AML and I think it should
NOTE Confidence: 0.8306338
00:08:21.445 --> 00:08:23.708 be used only in that sitting and
NOTE Confidence: 0.8306338
00:08:23.708 --> 00:08:25.784 AML only in the maintenance setting.
NOTE Confidence: 0.8306338
00:08:25.790 --> 00:08:27.146 After achieving remission with
NOTE Confidence: 0.8306338
00:08:27.146 --> 00:08:28.841 intensive chemotherapy and not as
NOTE Confidence: 0.8306338
00:08:28.841 --> 00:08:30.777 a replacement as monotherapy or.
NOTE Confidence: 0.8306338
00:08:30.780 --> 00:08:32.495 In combination with Venator class
NOTE Confidence: 0.8306338
00:08:32.495 --> 00:08:34.580 so this is important to note.
I think another combination that’s attracting a lot of attention as a combination of hypomethylating agents with Veneto class. So this is an update that was presented by Doctor Garcia and her colleagues in the frontline setting, so this is a phase One piece study that looked at combination of SSI tied in with Veneto class and this is a single arm study and they provided an update here in around 78 patients and what you can see is a very high CR rates. So the CR rate is around 40%. Remember that the CR rate would is cited in.
Monotherapy is only around 15% to 20% at best and the overall response rate is around 80%. The responses, as you can see, were durable around 13 months and the median follow up on the study was somewhat short 16 months, but the survival so far, especially for those patients who have complete responses, appear quite significant. However, I think these data are important to take into consideration still early. A single arm. We don’t have randomized data and we have many drugs that
shown excellent data as monotherapy, but when they went to randomized setting they did not basically show improvement in overall survival and I think This is why it’s important to wait for the randomized data before this could be used as a, you know a setting in like in routine clinic. Another I think important study is the one we conducted here at Yale in collaboration with many other centers. And we also provided an update from this data in the American Society of Hematology here.
in the relapsed or refractory setting, and as you can see, the response rate is around 40% total. Around 7% of those have complete responses, but many of those who have more complete responses also achieved significant hematologic improvement transfusion independence of. As you can see. So there are significant clinical benefits. But also as you can see on the right side, the median overall survival of all patients was 12 months, which compares favorably than the four to six months that I showed you earlier.
in the typical refractory relapsed MD setting and even patients who have more OCR have significant survival. As you can see with 15 months. Again, this is single ARM study, not randomized, and I think we need more data before this could be used in routine clinical practice. There are important differences in how financial classes used in real life setting or for Andy as compared to AML for example. Veneto class was given only for 14 days,
not the 28 days that are given in AML. And that’s important because MTS patients might not tolerate the same degree of myelosuppression that their male patients who tend to be somewhat younger than on average and MD’s patients. So we have now around a nice face retrial. The Verona trial, which is looking at, is cited in versus cases cited in with venetoclax in the frontline setting. This study is going to open at Yale. We are also opening at a number of daycare centers and I encourage you to enroll patients on it to see if
this setup we actually will change the standard management of high risk MD’s.
Another update that was prevent presented in the American state of Mythology meeting was on this drug people, and it is that which is the 1st in class need it inhibitor. So this this is an upstream of the proteasome and it was shown in early phase trials in combination with their society into lead to improvement and responses. This trial randomized patients, but this was a randomized phase two trial in which not only patients with
MD as but also patients with illegal plastic, AML and CML were randomized to receive.

Cited in alone or as a sighted in with people needed stat and this trial also was actually open here at at year and what you can see here or the subgroup analysis of the patients who had higher risk and the S which were a total of 67 patients. This paper this this was just also published in Leukemia Journal. What you can see is that there was like a marginal improvement in event free survival, but the primary endpoint of the study the overall survival was not improved. And I think most notable here is that the overall response rate,
but especially the CR rate, was significantly higher with the combination compared to the monotherapy and was more durable. There is a phase three trial of the same. Basically, design of P1 is a sighted in compared to azacitidine alone. This trial, actually called the Panther trial, has fully accrued and we expect results from the study soon. So I think this also could potentially be a practice changing if the if there is us are posted.
Many of you use immune checkpoint inhibitors such as anti PD, One PD, L1, for routinely for management of solid tumors, we've been trying to use these drugs for some time now in high risk MD ASAN myeloid malignancy really and so far a lot of the data has been single arm and. A single center data. This is what I'm showing you is a presentation from ASH 2019 in which we showed with colleagues from other centers in a randomized phase two study that the combination of is cited in with the anti PDL one door
volume app which is approved for several solid tumors did not improve outcomes compared to other sighting. However I think this is probably just related to PD L1. And does not extend necessarily to other classes of immune checkpoint inhibitors. And on that note, another immune checkpoint inhibitor called sabatella mob or MPG 453. Is basically being studied in combination with hypomethylating agents, not only for high risk MD’s, but also for AML patients and the data from what was presented in
This year showed this is a single arm again phase one study, but it showed the CR rate of 23% which is slightly higher than what you expect with monotherapy, but the overall response rate was 64%, and what you can see on the right hand is that there was encouraging durability. Of the combination, especially with patients who have long or very high risk disease, and I would note the side effect profile here it does not seem to add myelosuppression to the exercise again alone, and also importantly, the incidence of immune related
NOTE Confidence: 0.8049437
00:15:16.866 --> 00:15:19.039 effects seems to be low with this.
NOTE Confidence: 0.8049437
00:15:19.040 --> 00:15:20.520 With this particular agent,
NOTE Confidence: 0.8049437
00:15:20.520 --> 00:15:22.370 so appears on this data.
NOTE Confidence: 0.8049437
00:15:22.370 --> 00:15:24.220 There are ongoing several study.
NOTE Confidence: 0.8049437
00:15:24.220 --> 00:15:27.444 We just completed a cruel to a randomized
NOTE Confidence: 0.8049437
00:15:27.444 --> 00:15:30.624 phase two study in higher risk MD S of.
NOTE Confidence: 0.82144034
00:15:30.630 --> 00:15:32.814 Is there with the battle map versus
NOTE Confidence: 0.82144034
00:15:32.814 --> 00:15:35.306 is alone and this study is completed
NOTE Confidence: 0.82144034
00:15:35.306 --> 00:15:37.532 accrual and we expect the results
NOTE Confidence: 0.82144034
00:15:37.601 --> 00:15:39.484 in the next one to two years.
NOTE Confidence: 0.82144034
00:15:39.490 --> 00:15:40.802 There’s another face retrial
NOTE Confidence: 0.82144034
00:15:40.802 --> 00:15:42.770 that will open here as well.
NOTE Confidence: 0.82144034
00:15:42.770 --> 00:15:44.410 Called the stimulus MD S2,
NOTE Confidence: 0.82144034
00:15:44.410 --> 00:15:46.714 which is a randomized phase three
NOTE Confidence: 0.82144034
00:15:46.714 --> 00:15:48.939 of the same combination is with
NOTE Confidence: 0.82144034

28
00:15:48.939 --> 00:15:51.109 the battle map versus Asia and we
NOTE Confidence: 0.82144034
00:15:51.109 --> 00:15:53.143 have our as well a frontline study
NOTE Confidence: 0.82144034
00:15:53.143 --> 00:15:55.390 with a 7 is events a battle map.
NOTE Confidence: 0.82144034
00:15:55.390 --> 00:15:57.572 All of those are open at at
NOTE Confidence: 0.82144034
00:15:57.572 --> 00:15:59.192 yet another interesting immune
NOTE Confidence: 0.82144034
00:15:59.192 --> 00:16:01.480 checkpoint inhibitor is the CD 47.
NOTE Confidence: 0.82144034
00:16:01.480 --> 00:16:03.965 Anti CD 47. They don’t eat me.
NOTE Confidence: 0.82144034
00:16:03.970 --> 00:16:05.690 Signal inhibitor mag rolling up
NOTE Confidence: 0.82144034
00:16:05.690 --> 00:16:07.778 what was presented in ash this
NOTE Confidence: 0.82144034
00:16:07.778 --> 00:16:09.892 year was an update and what the
NOTE Confidence: 0.82144034
00:16:09.892 --> 00:16:11.851 authors shown the significant plus
NOTE Confidence: 0.82144034
00:16:11.851 --> 00:16:13.575 reduction among all patients.
NOTE Confidence: 0.82144034
00:16:13.580 --> 00:16:16.002 But the data was most impressive in
NOTE Confidence: 0.82144034
00:16:16.002 --> 00:16:18.251 patients who have TP 53 mutations
NOTE Confidence: 0.82144034
00:16:18.251 --> 00:16:20.525 in which the median overall survival
NOTE Confidence: 0.82144034
00:16:20.525 --> 00:16:22.480 among patients who had TP 50.
Three was 12 months, which is higher than what we typically expect it to nine months. Generally in patients who have this mutation. So this drug now is being studied. In a randomized trial called the enhance in high risk MD’s whether they have TP 53 or not, magherally map with laser versus is alone, but also there are efforts to study it in acute myeloid leukemia patients as well, especially those with TP 53. This is a transplant abstract and as I mentioned, there is a separate transplant.
presentation that will happen at the end of the series, but I just wanted to highlight this the conclusion from this because this is in my view, one of the most important abstracts from this because it showed in a randomized trial data, so here this was randomized. All the data that we have about MD's improving survival in high risk MD's patients compared to hypomethylating agents alone is based on Markov decision analysis and modeling, but this is the first randomized trial to actually show.
An absolute improvement in overall survival and the three year survival for donor versus no donor arm. And I think what is very important is this study allowed patients after the age of 75. And this is important to get out there, that because we still see patients who are like 72 who come to us very later and their scores and being told they were not candidates for transplant. So I think it’s important to know that even patients up to the age of 75 could be considered for curative therapy and they should be referred for big Centers for clinical trials.
as transplant consideration

in the last couple of minutes.

I will talk about lower risk MD’s

as I mentioned was partnership has been approved after ESA failure.

For patients who have RingCentral plastic anemia from lower risk MD’s now, this drug is being studied in the commands trial, so this is it’s being studied compared to low Earth roelle powerton and this or a potent procrit and this or whether you have ringstad or plus or not, you could be randomized to either a proton or low spatter set and this trial
is open in the care centers as well.

So many of you will be able to enroll in it.

Another interesting drug is the emitted step, which is the 1st in class telomerase inhibitor which has been shown also to improve transfusion independence.

Regardless of having RingCentral Plus or not and some of those responses which occur in 42% of patients were at durable.

Now we have actually an open study here. The High Merge study the phase three randomized study after so this is a randomized study after he has a failure so frontline we have the commands in lower risk and be as.

Refractory, we have the Hymer study.
for patients after failure of PSA

In which patients are randomized to him until a stat versus placebo.

In the last minute I wanna show you another like non interventional study that we did in patients with MD S who have lower who have anemia and as you know one of the open questions in MDSS. When do you transfuse patients with MD S and many people use different cut off seven or eight of hemoglobin? Here we used verified quality of life instrument in a investigator initiated effort led by Doctor Go in Table. Go on Dana Farber. And we looked at the quality of life
00:19:45.835 --> 00:19:47.835 improvement before and after transfusion
00:19:47.835 --> 00:19:50.843 and what we have shown is that most patients 2/3 of patients did not experience an improvement in their quality of life after transfusion.
00:19:50.843 --> 00:19:52.889 So I think that puts into question our practice of Troy.
00:19:52.889 --> 00:19:54.434 Using patients based on hemoglobin cut offs of aid,
00:19:54.434 --> 00:19:56.340 and I think it’s important to try to study this in more extensive sitting about what is the right cut for transfusions in,
00:19:56.340 --> 00:19:58.755 especially in the outpatient setting.
00:19:58.755 --> 00:20:00.210 For patients with ambius rather than
00:20:00.210 --> 00:20:01.880 especially in the outpatient setting.
00:20:14.808 --> 00:20:16.909 using random cut offs of hemoglobin.
NOTE Confidence: 0.7745304
00:20:16.910 --> 00:20:19.295 So this is my last slide and I will
NOTE Confidence: 0.7745304
00:20:19.295 --> 00:20:21.735 give the floor now to my colleague
NOTE Confidence: 0.7745304
00:20:21.735 --> 00:20:23.987 Doctor Rory Challis who will update
NOTE Confidence: 0.7745304
00:20:23.987 --> 00:20:25.927 us on acute myeloid leukemia.
NOTE Confidence: 0.7745304
00:20:25.930 --> 00:20:27.302 Updates from the ash.
NOTE Confidence: 0.7745304
00:20:27.302 --> 00:20:29.778 Thank you and we'll be happy all
NOTE Confidence: 0.7745304
00:20:29.778 --> 00:20:31.836 of us will be taking questions.
NOTE Confidence: 0.7745304
00:20:31.840 --> 00:20:34.280 At the end of that seminar at 12:50,
NOTE Confidence: 0.7745304
00:20:34.280 --> 00:20:34.590 thanks.
NOTE Confidence: 0.78832996
00:20:52.070 --> 00:20:53.700 OK, How are we looking?
NOTE Confidence: 0.78832996
00:20:53.700 --> 00:20:55.646 Every seeing a full slide who
NOTE Confidence: 0.78832996
00:20:55.646 --> 00:21:00.100 screens two screens again? Sorry.
NOTE Confidence: 0.78832996
00:21:00.100 --> 00:21:01.828 Standard technical difficulties.
NOTE Confidence: 0.80935025
00:21:07.370 --> 00:21:09.786 Yeah, I think you need to swap your
NOTE Confidence: 0.80935025
00:21:09.790 --> 00:21:11.310 screens. Let’s try this again.

37

Yes.

Looks good.

You're seeing one. Yes, one scream.

You're good to go alright? Do this by then.

Sorry bout that.

OK.

Alright one screen we're good to go so.

Thanks for the introduction.

I'll be specifically focusing on the highlights presented this past meeting as they pertain to AML.

I have no disclosures, so.

Again, you're still seeing one screen, right?
OK, it’s a bit hard to really focus in on really a select few updates from an entire years worth of. I would say progress in the field. So I’ll try to really focus on agents with which we already have some familiarity, but also some new combinations or regiments, some of which you can guess we’re going to include the BCL two inhibitor of medical acts. All of these are all the studies I’ll be discussing are going to be interventional of only really try to give some minimal background so it’s really focused on the updates themselves.
So jump right in. As many of you are. Aware Gilteritinib is a flip through inhibitor, which in the Admiral trial was shown to improve survival when compared with classical salvage chemotherapy in their refractory setting. So its approval for such over the outcomes for these patients treated with guilt, or it never guilt are still quite poor. The preclinical data does support some synergy when Gilteritinib is combined with a BCL two inhibitor.
and those data prompted the launch of the trial that I'll be talking about.

In brief, you can see here, so this was done in the context of the following trial schema patients, as you guessed it, had relapsed refractory disease, including wild type patients. In the dose escalation phase, without you know, a low white counts. They really had controlled proliferation. They received standard phonetic lacks 4 milligrams in combination with either guilt 80 or 120 milligrams, which the latter of which is the standard dose that was studied in Phase
testing, and this was later expanded, so the demographics were, for the most part, I would say, expected with regards to age, set of genetic risk given the inclusion criteria that I mentioned before, a majority of patients. Did have ITD mutations? Of note, 65% of patients received prior therapy with the flip three inhibitor and a third enrolled after they had a relapse after allogeneic transplantation. All patients experienced an adverse
event in nearly all grade three, with unsurprisingly, was being cytopenias. You know, given the combination with medical access, you know a very well known Milo toxic amount suppressive agent, but perhaps some contribution of guilt. And as well, three patients were reported as having laboratory tumor lysis syndrome with only one of these having clinical TLS, only 60% of patients, at least as of last follow-up, discontinued the drug due to adverse events. Of note, no patients died within a month of dosing,
but six died with up to 60 days out. Amongst 41 adult patients, only three achieved CR or 7% specifically. However, 27% of patients achieved a less than CR remission, which here was inclusive of CR or CR P. Half of patients achieved MFS or morphologic leukemia Free State again, in the context of the Netflix related mileage suppression. Amongst responders, the median time to response was one month, but best responses were observed up to four months out.
No more could differences in response or the types of response for that matter were apparent after accounting for prior flip three inhibitor exposure other than maybe a little less or chance of CR. As you can see here, 7.3 versus one quote versus 3.6%. The median overall survival for the overall cohort was 12.3 months and specifically not reached, including an unreached lower limit of the 95% confidence interval for ITD patients. Clear differences in survival were noted based on prior filter exposure, so I would say in some the addition of
attacks appears to augment the efficacy of guilt monotherapy in this situation, which based on the Admiral trial I had mentioned before, predicts a median survival around 9 nine and a half months. This is at the expense of near double hematologic toxicity, which I think we can all agree is attributable to the phonetic LAX, but of course. Just hearing some caution and saying it appears to increase the efficacy outside of a randomized clinical trial, so this isn’t of course need.
to at least confirm this.

This likely benefit here.

Jump into the next update.

I have 40 or so older patients with AML.

Have generally a poor outcomes,

but there there is some variance

noted to improve these outcomes.

Ventures like the following are underway,

so next I’d like to discuss the

interim results of a striking study

of cladribine and lodosa Terrapin,

which is essentially a double

cladribine backbone and Aza,

both with the addition of an ethics course.

The double clad plus Ldac backbone

has been previously studied this.
This isn’t showing here in this slide with alternating decide to be as treatment for newly diagnosed.

Older patients with AML and this led to a composite CR of 68%, including CR 50%.

Quite nice with a median OS of well over a year. It appears 14.8 months with quite low mortality.

So this is the actual trial. This scheme is a little complex, but essentially like I mentioned,

newly diagnosed patients with AML received clad plus ldac with van with.
As you can see here, the standard dose reductions for CYP 3A four inhibitor use receive this for cycle one, with cycle to being the same three drugs but less clad and a little bit less fanatical acts with cycle three switching the nucleoside backbone for Asia on the standard schedule, again with phonetic lacks for 14 days, similar to cycle two. So basically patients received. Part A, as you can see here and they can move. I don’t. I don’t know how to use a
00:27:59.334 --> 00:28:00.319 highlighter or whatever, but patients received a * 2 then
00:28:00.320 --> 00:28:02.318 B * 2 and then back and forth back
00:28:02.318 --> 00:28:05.304 and forth for up to 18 cycles.
00:28:05.304 --> 00:28:07.978 So here the patient characteristics
00:28:07.980 --> 00:28:10.225 as of the first day to cut of
00:28:10.225 --> 00:28:13.440 note 40% of patients for older.
00:28:13.440 --> 00:28:15.638 Sorry older than 70 years,
00:28:15.638 --> 00:28:17.648 25% were had disease characterized
00:28:17.650 --> 00:28:19.665 by porous I, generally expected given this population,
00:28:19.665 --> 00:28:20.874 although nearly half were ellenor European leukemia net poor risk
00:28:20.880 --> 00:28:23.100 genetics ANAN would be would be
00:28:23.100 --> 00:28:25.310 generally expected given this population,
00:28:25.310 --> 00:28:27.675 although nearly half were ellenor
00:28:27.675 --> 00:28:30.040 after accounting for the relevant
molecular features on top of genetics.

Amongst the 54 patients that today have been accrued and are in fact invaluable with a median one cycle or month to responses, striking 78% achieved CR and basically all except three achieved MFC MRD negativity. Basically, MRD negativity by flow centric analysis including CRIA composite CR rate of 93% was rendered which is simply amazing and perhaps I really should have saved this safest route for the end so.

One of the more striking updates from ASH with regards to the response rates.
However, it's not all about response rates for the patient not proceeding to therapy, really care about event-based outcomes like survival in evaluating survival and a medium median of 14.2 months. The OS and RFS curves were essentially the same, meaning OS was reached was not reached. Sorry, and 60% of patients were still alive at two years after starting therapy again. Quite amazing considering the fact that half of patients were.
Yellen adverse risk. Sorry

NOTE Confidence: 0.64456517

hadelin adverse risk disease.

NOTE Confidence: 0.8340789

However, this is just some.

NOTE Confidence: 0.8340789

You know, some smaller kind

NOTE Confidence: 0.8340789

You can see that when accounting for

NOTE Confidence: 0.8340789

set of genetic risk and Dylan risk,

NOTE Confidence: 0.8340789

not surprising differences

NOTE Confidence: 0.8340789

are in fact observed.

NOTE Confidence: 0.8340789

I would note that 11 patients

NOTE Confidence: 0.8340789

or 2524% of the 45 responding.

NOTE Confidence: 0.8340789

Patients proceeding to

NOTE Confidence: 0.8340789

transplant with these patients,

NOTE Confidence: 0.8340789

patients really enjoying more

NOTE Confidence: 0.8340789

than 90% survival at one year,

NOTE Confidence: 0.8340789

which when compared with the
folks not getting to transform with 69% but a difference, did not reach statistical significance. Likely in the setting of just, you know, obviously a small early phase study.

So just going to switch gears a little bit with AML, gears a little bit with AML, one of the first decision we have to make is whether patient is quote unquote intensive therapy eligible or not. The first 2 trials I mentioned were really geared towards patients that are intensive therapy ineligible.
intensive therapy generally felt to be the standard of care for those who are eligible with some specific exceptions? Of course if prompted debate, but that’s a discussion for another. Here is the schema for a trial also out of MD Anderson and evaluating the addition of genetic lacks. To CPX, 3/5 one or the brand name being fix EOS which is standard of care for patients with AML MRC and therapy quote unquote related AML. The design included cohort for adults with newly diagnosed AML as well as looks. Factory disease, with the latter
allowing prior phonetics exposure.

Quite important criterion.

A dose escalation phase or safety

Of course, all the patients,

irrespective of whether they

were Dinovo slash,

newly diagnosed or realtor factory.

Of note CPX 3/5 one was given

at the standard dose on label.

Essentially event began fairly

quickly on day two with a three day

ramp up to a target dose of 400,

again with the standard dose

reductions you would expect or should
00:31:37.620 --> 00:31:39.235 be considering with concurrency 3A
NOTE Confidence: 0.7932578
00:31:39.235 --> 00:31:41.230 four inhibition as well as toxicities
NOTE Confidence: 0.7932578
00:31:41.230 --> 00:31:42.522 prompted prompting dropping to
NOTE Confidence: 0.7932578
00:31:42.522 --> 00:31:44.741 lower dose levels as they came up.
NOTE Confidence: 0.7932578
00:31:44.741 --> 00:31:46.890 Essentially this was then was given for
NOTE Confidence: 0.7932578
00:31:46.957 --> 00:31:48.769 three weeks during induction as well
NOTE Confidence: 0.7932578
00:31:48.769 --> 00:31:51.428 As for 20 three weeks during each cycle.
NOTE Confidence: 0.7932578
00:31:51.430 --> 00:31:51.808 Consolidation.
NOTE Confidence: 0.7932578
00:31:51.808 --> 00:31:55.210 In this case they allowed up to four cycles.
NOTE Confidence: 0.7932578
00:31:55.210 --> 00:32:00.600 Of consolidation,
NOTE Confidence: 0.7932578
00:32:00.600 --> 00:32:02.950 In contrast to the standard on label CPX 351.
NOTE Confidence: 0.7932578
00:32:02.950 --> 00:32:04.570 Monotherapy consolidation.
NOTE Confidence: 0.7932578
00:32:04.570 --> 00:32:06.554 Here the characteristics of the
NOTE Confidence: 0.7932578
00:32:06.554 --> 00:32:08.384 patients who had a broad range
NOTE Confidence: 0.7932578
00:32:08.390 --> 00:32:10.707 I’ll call your attention to the right
where you can see that 30% of patients had disease characterized by the presence of a TP 53 mutation and after including ASL one and runx one mutations, the majority of patients did in fact have guillain adverse risk disease. Only 6% of patients achieved CR, but CR CRA was the rate of CRC. I was 39% still fairly low with a median one cycle time to response. The most common reason for coming off of study was actually proceeding to transplant. This occurred in 31 patients were but generally 50 half of the patient population. The most common grade 3 plus
ease were human logic in nature,

NOTE Confidence: 0.79286337

pneumonia amongst other infections didn’t.

NOTE Confidence: 0.79286337

Did also occur 30 and 60 day

NOTE Confidence: 0.79286337

mortality were weren’t nominal

NOTE Confidence: 0.79286337

10% at 30 days and 20% at 60 days,

NOTE Confidence: 0.79286337

so a fairly toxic regimen with again

NOTE Confidence: 0.79286337

relatively limited efficacy in comparison

NOTE Confidence: 0.79286337

to the other guys I’ve presented.

NOTE Confidence: 0.79286337

The median overall survival was six months

NOTE Confidence: 0.79286337

with a 6 month OS rate of about 53%.

NOTE Confidence: 0.79286337

Just to be specific and 46% at one year.

NOTE Confidence: 0.79286337

So not terribly different.

NOTE Confidence: 0.79286337

6 versus 12 months among responders,

NOTE Confidence: 0.79286337

the median OS and RFS were not reached,

NOTE Confidence: 0.79286337

and the six month OS and RFS

NOTE Confidence: 0.79286337

were essentially about 8590%.
You can see that patients without prior medical exposure did better. However, again, given the small numbers, this did not reach statistical significance. Sticking with this is another trial. Sticking with intensive therapy eligible patients. What about adding then to other intensive backbones beyond CPX 351, here's a schema which demonstrates that patients with both newly diagnosed disease and relapse refractory disease received a fairly standard flag. Ida regimen and dosing with Medical X added, especially specifically during days.
one through 14 at a target dose

but not without a ramp up and then high
debt consolidation had been incorporated.
Days one through 14.
So a complex slide,
but hopefully that kind of summed it up.
Here are the patient demographics or sorry
patient characteristics specifically,
noting that the relapse refractory
cohorts were a bit more enriched
for adverse risk disease.
And as you would otherwise expect and
had received prior allogeneic
Amanda poetic stem cell transplant.
The toxicity was what you would
00:34:40.328 --> 00:34:42.303 expect with intensive therapy and
00:34:42.303 --> 00:34:44.313 addition of class including based on
00:34:44.313 --> 00:34:48.838 what I just presented. For C PX351.
00:34:48.840 --> 00:35:00.998 CRC is 90% and in the newly diagnosed cohort
00:35:01.000 --> 00:35:04.664 So and fairly good rates of MRD negativity.
00:35:04.670 --> 00:35:06.390 Based on their disease, the disease cohort specifically.
00:35:07.834 --> 00:35:10.689 So I’ll just kind of wrap it up
00:35:06.390 --> 00:35:07.834 with just promise two more slides.
00:35:07.834 --> 00:35:10.689 with just promise two more slides.
00:35:10.689 --> 00:35:12.555 with just promise two more slides.
00:35:12.560 --> 00:35:14.270 So those updates for therapies
00:35:14.270 --> 00:35:15.296 we already had.
00:35:15.300 --> 00:35:17.190 But what about just one update
00:35:17.190 --> 00:35:19.080 on an agent or regimen?
We do not yet really have. This is Google Map or the this is the humanized anti CD. 47 IgG, four monoclonal antibody product from Gilead Sciences, relevant as tumor expression of CD 47 prompts evasion from an 80 minute surveillance. Specifically macrophage mediated. Microcytosis and in fact pre clinical data support that AML, leukemic blast doing factor, or enriched for CD 47 Express expression. So this was studied in combination with Asia and a phase one. B2 trial that armored actually touched on
earlier most in the context of high risk

MD S but I’ll just focus on the AML cohort. Specifically,

90 except sorry,

70% porous surgeon attics 70% P

three mutations with a robust

median vaf which would otherwise

predict biallelic loss of function.

So essentially a very, very, very poorest population and not the
toxicity profile was generally what

other than I’d say a mild transient

on targeting me that was reversible.
Know whether grade 3/4 plus 80s and no immune related AE’s given.

This is a slide hammer showed you this is the AML cohort,

essentially a 20% rate of see better in comparison to generate 20% rate of expected as a monotherapy.

60 ish percent, essentially with essentially in the waterfall plot.

Here nearly all patients experiencing Meryl Blast percentage reduction with many being robust reductions.

The median OS at last day to cut off of patients in the trial was
NOTE Confidence: 0.79211825
00:36:51.025 --> 00:36:53.557 18.9 months and even after isolating
NOTE Confidence: 0.79211825
00:36:53.557 --> 00:36:56.317 patients that had a P3 mutation.
NOTE Confidence: 0.79211825
00:36:56.320 --> 00:36:57.940 And we still 12.9 months,
NOTE Confidence: 0.79211825
00:36:57.940 --> 00:36:59.781 which to be honest is the longest
NOTE Confidence: 0.79211825
00:36:59.781 --> 00:37:01.867 median OS I believe ever reported
NOTE Confidence: 0.79211825
00:37:01.867 --> 00:37:03.097 for this population,
NOTE Confidence: 0.79211825
00:37:03.100 --> 00:37:05.354 so quite striking as you can see,
NOTE Confidence: 0.79211825
00:37:05.360 --> 00:37:07.274 four or five patients are still
NOTE Confidence: 0.79211825
00:37:07.274 --> 00:37:09.240 alive more than two years out,
NOTE Confidence: 0.79211825
00:37:09.240 --> 00:37:10.143 so quite impressive.
NOTE Confidence: 0.79211825
00:37:10.143 --> 00:37:12.674 So I am a little bit over and
NOTE Confidence: 0.79211825
00:37:12.674 --> 00:37:14.090 I apologize to Nikolai.
NOTE Confidence: 0.79211825
00:37:14.090 --> 00:37:15.410 Mostly this is raw,
NOTE Confidence: 0.79211825
00:37:15.410 --> 00:37:17.060 conclude my section and look
NOTE Confidence: 0.79211825
00:37:17.060 --> 00:37:18.929 forward any questions at the end.
NOTE Confidence: 0.79211825

66
00:37:18.930 --> 00:37:20.850 So next I'd like to introduce
Doctor Nikolai Pedulla civilly
00:37:20.850 --> 00:37:22.130 discussing the ash 2020 updates
00:37:22.187 --> 00:37:23.787 in there almost perfect NPS.
00:37:29.040 --> 00:37:31.374 Alright, thank you Oriel let
me share my slides with you.
00:37:31.374 --> 00:37:34.260 How does it look?
00:37:34.260 --> 00:37:35.228 Does it look like one screen?
00:37:35.228 --> 00:37:36.680 We don’t see slides head.
00:37:40.950 --> 00:37:42.830 Sadly you don’t see slides OK,
00:37:42.830 --> 00:37:45.080 just a second. We just see you.
00:37:45.080 --> 00:37:48.244 just a second. We just see you.
00:37:48.244 --> 00:37:57.949 And so I’ll do this. How about now?
00:37:57.950 --> 00:38:01.950 Do you see two right and I need to swap?
00:38:01.950 --> 00:38:03.558 No, we still don’t see them.
00:38:03.558 --> 00:38:04.630 You don’t see them.

00:38:14.660 --> 00:38:18.670 Did you share a video girl OK?

00:38:18.670 --> 00:38:20.916 Yep, now we see alright.

00:38:20.916 --> 00:38:23.604 You see this one slide right?

00:38:23.610 --> 00:38:24.766 Alright, OK,

00:38:24.766 --> 00:38:28.234 alright so I’ll be talking about.

00:38:28.240 --> 00:38:30.844 Milo proliferative neoplasms and I had to

00:38:30.844 --> 00:38:33.108 be selective because of the time frame,

00:38:33.110 --> 00:38:35.510 so this are my disclosures.

00:38:35.510 --> 00:38:37.830 I’ll go over 4 studies and the first

00:38:37.830 --> 00:38:40.552 one was presented as a late breaking

00:38:40.552 --> 00:38:43.076 abstract is not the interventional study

00:38:43.076 --> 00:38:45.729 I thought would be important to mention.

00:38:45.730 --> 00:38:48.285 I just have one slide about it.

00:38:48.290 --> 00:38:50.110 This is about driver mutation,
acquisition in pH, negative MPs, and this study managed to show that this mutations are quite as early as in utero until disease develops decades later. So the goal of the study was timing of driver, mutation, acquisition, and clonal expansion evolution. The methods used by UK investigators included studying 10 patients with Jack. Two mutations of this is Jack. Two mutation for Stevens. This patients were between H20 and 76. The single cell derived hematopoietic colonies were studied.
using whole exome sequencing. There was targeted resequencing of longitudinal blood samples from the stem patients and something which is still not clear very clear to me, but they were able to create those. Polygenetic trees or of hematopoiesis, allowing them to understand when initial driver mutation occurred as the result it was found that mpanza originate from driver mutation quite very early in life, including before birth, and then there is lifelong clonal expansion and evolution.
So this.

Results are quite amazing because they tell us that this Jack two mutation, which eventually leads to development of MPN late at life, is present in utero and perhaps if we can understand how it develops and evolves, we may use some preventative strategies in the future to prevent expansion of this clone or its evolution.

Moving onto interventional studies, first of all, I will talk about CML and again another late breaking abstract second.

I will talk about one study using new drug for Milo fibrosis patients,
and finally I'll finish with the study for PVR patients. So the second study I would like to talk about looked at a synonym also known as able 001. This is the first class stamp inhibitor. An stamp is specifically targeting the allosteric BSL, Belmira stole pork it so its allosteric BSL, one BSL BCR ABL one inhibitor which is different to advertising kinese inhibitors which targeting ATP pocket on April 1. So as you can see on the cartoon from New England Journal Medicine article discussing Phase One.
results with this medication.

There is Mr Lated and terminal which auto inhibits able one

an with BCR ABL translocation.

This N terminal piece of.

Peace is gone,

so you have PCR and now there is

no auto inhibition and there is

constitutive activation of ABL kinase

Aciman app targets that fork it and

can allosterically inhibit PCR able?

So as you can see,

the other tiki eyes we have currently

in practice and use in practice

go to ATP binding site and the

Aciman app actually affects able
one kinase inhibits able one kinase

using this mirror style pocket, hence the name specifically targeting the able Morris to pocket. So it works even when mutations like T315Y inhibit ability of the tiki eyes to inhibit able one. Like in this particular situation, in the cartoon you can see that the teising kinase inhibitor cannot attach to the pocket due to change of its confirmation, but a synonym still able to attach to Bristol Pocket inhibiting able one kinase. So this is a phase three study was
Simonette versus Design IP in patients with chronic phase CML previously treated with at least two tiki eyes, two different guys and this is an important study because the drug is now undergoing review for approval and I'm hoping that. It will be available as yet another medication to treat chronic myeloid leukemia later this year. So the selection criteria listed and patients were included had chronic phase two or more GIS used before and patients have to change treatment either because they were intolerant or resistant to treatment and so
The patients were 2315 I mutation or V299L mutations were excluded because pursuit Nip is not. So this is specifically the study which didn’t include T315I mutated patients. This particular group of patients was addressed by the Phase One study and the drug is active against the BCR. ABL with this particular mutation, so patients were randomized. As you can see in two to one fashion, and the demographics were slightly different in two groups I highlighted. In yellow here that a similar patients
there were more men than women.

Also in a similar patients, the switch of therapy was less likely to be due to lack of efficacy and more likely due to taller ability and that basically is characteristic of a group of patients which may be more responsive to the next line of treatment.

And finally also in a similar barman less patience than in pursuit. Newbomb received three or more tikis. So this is the primary endpoint of this study which showed improved major molecular response rate at 24 weeks at six months, and the difference between two
groups was twelve point 2%.

So taking into consideration the differences between two groups I showed on previous slide that the logistic regression analysis was done and showed that odds ratios adjusted for those things which were different in two groups were quite similar towards ratios without adjustment, which gives us hope that the improved outcome in a similar treated patients is not related to the difference in the population.

So the side effect profiles a lot of patients get different side effects,
but overall a similar patients have less side effects than positive treated patients. 

One thing I would like to highlight here that a similar group there were two deaths related to arterial embolism won an ischemic stroke. Another Iman positive patients. One patient died due to septic shock, so the side effect profile was different, so anemia and thrombocytopenia. Sorry, Trump said opinion neutropenia were similar in both groups and then GI side effects in the left abnormalities were more common in bosutinib treated patients. 

So in conclusion, this assemble study was the first control study.
00:45:48.012 --> 00:45:50.220 comparing tikis for treatment.

00:45:50.220 --> 00:45:51.753 Assistant Intolerant CML

00:45:51.753 --> 00:45:53.286 population and assimilate,

00:45:53.290 --> 00:45:56.356 which is first class stamp inhibitor,

00:45:56.360 --> 00:45:58.875 showed superior efficacy compared with

00:45:58.875 --> 00:46:02.000 bosutinib with favorable side effect profile,

00:46:02.000 --> 00:46:06.130 so this is upcoming hopefully.

00:46:06.130 --> 00:46:08.040 Approved in the near future

00:46:08.040 --> 00:46:09.950 treatment option for CML patients,

00:46:09.950 --> 00:46:11.474 particularly with resistant and

00:46:11.474 --> 00:46:12.236 intolerant disease.

00:46:12.240 --> 00:46:14.526 After treatment with two different guys.

00:46:14.530 --> 00:46:16.690 Also, the drug is effective in

00:46:16.690 --> 00:46:18.740 treating patients with T315I mutation,

00:46:18.740 --> 00:46:21.407 so moving on to the next study.

NOTE Confidence: 0.800081
I wanted to present today you will understand towards the end why pick this particular one? There are a number of drugs where there are a number of drugs being developed in patients with myelofibrosis. I think they’re up to 10. A phase three randomized phase three studies in this field. So this particular study presented by John Mascarenhas is about CPI, 0610. Bromodomain angusta terminal domain protein or BET inhibitor in combination with reflective for Jack inhibitor naive Milo fibrosis patients or manifest study. So one word about bet so bromodomain and
extra terminal domain protein promote.

Symptoms of Milo fibrosis by activating bet targeted genes leading to increase production of cytokines responsible for inflammation, extramental hematopoiesis, and bone marrow fibrosis. All manifestations of patients with primary myelofibrosis as well as modify process after PD and 80 so the other influence of bat is activations of target genes leading to aberrant erythroid differentiation as well as aberrant megakaryocytic differentiation. And this patients may have an email.
Thrombocytopenia, as you know. So CPI 610 inhibits bat and may suppress cytokine production as well as promote erythroid differentiation as well as normalized megakaryocytic differentiation. So let’s see how this drug did in this phase two studies. Today’s I’m three which looked at Jack inhibitor naive patients and use the combination of CPI 610 and Rosslyn. If the other two arms were add on CPI, six dental clinic patients
who didn’t have full benefit.

From Brooklyn balloon treatment and monotherapy with CPI,

this study was also presented as an abstract as a poster during ash meeting,

so I’m three, basically Jack inhibitor naïve Milo fibrosis patients who need treatment.

They received two drugs, rock Solid Nap standard of care but in additional CPI 0610 better hitter.

So this drug better hitter was administered two weeks on two weeks, one week off and.
The endpoints which we were looked at was.

Spleen volume response 35% spleen.

World in response at 24 weeks as well as total symptom score 50%.

Reduction of symptoms by 24 weeks.

This is primary endpoint which basically it was achieved by 67% of patients so again the drug probably worked a little bit better for patients who are low risk but it was compatible 72-73% for intermediate 160.

Four 66% for intermediate to high risk based on the IP SS and IP address.

Most of the patients cadres, reduction of spleen volume only one had increased.

This is out of 70 patients studied,
so the second endpoint at the symptoms decreased by 50%. Again, this was seen in 57% of patients. Most of the patients get this clinical benefit in the study at week 24, so one of the interesting finding when you start looks lit up in patients with myelofibrosis you expect a dip in hemoglobin about three points, so here the dip was not as deep. And then, as you can see, hemoglobin improved overtime. In fact, baseline increased a little bit higher than the baseline, so this. Awful actually looks at patients who had
hemoglobin more than 10 and less than 10, but didn’t require transfusions. And as you can see, after initial small dip there is improvement in anemia in this subgroup of patients, which is quite impressive. So one other thing, at the bone marrow’s, their biopsies were done at the beginning as well as during the study and there was improvement in fibrosis. Great in 1/3 of patients and most of the improvements observed were observed during the first six months of treatment. Only two patients get worsening of fibrosis and you can see that there
00:50:35.338 --> 00:50:38.292 is also a sign that there is improved air throughout differentiation and
normalization of megakaryocytic histopathology.

00:50:47.418 --> 00:50:50.036 combination with Link was generally well tolerated.

87% reported at least one treatment emergent adverse event.

44% reported, one grade, treatment emergent adverse event.

So the most common ones were haematological and an email from both cytopenia.

Of course this may be manifestations of megakaryocytic histopathology.
of the disease itself,
NOTE Confidence: 0.8362344

the most common and non human to
NOTE Confidence: 0.8362344

logic was diarrhea or which was
NOTE Confidence: 0.8362344

mild moderate Grade 1 two so.
NOTE Confidence: 0.8362344

Great five were two events.
NOTE Confidence: 0.8362344

Multiorgan failure with due to
NOTE Confidence: 0.8362344

sepsis times two.
NOTE Confidence: 0.8362344

So overall the drug was pretty
NOTE Confidence: 0.8362344

reasonably well tolerated.
NOTE Confidence: 0.8362344

The combination of drugs I have
NOTE Confidence: 0.8362344

to say because we’re looking at
NOTE Confidence: 0.8362344

the side effect profile of two
NOTE Confidence: 0.8362344

drugs administered together.
NOTE Confidence: 0.8362344

So finally conclusions 67% of patients
NOTE Confidence: 0.8362344

achieve CVR 35 comparing to historical phase,
NOTE Confidence: 0.8362344

three studies simplifying comfort studies.
This looks better even though we cannot compare apples to oranges in those studies with ruxolitinib alone, the response was 28 to 42%. 57% in the study achieved improvement and symptoms. 50% reduction of symptoms and there were improvement in bone marrow findings suggestive of potential disease modification. So it was well tolerated combination and phase three study is planned and this would be a randomized study for treatment. Naive patients looks lit up against ruxolitinib Sir, plus CPI six 110 versus wrestling.
plus placebo, which allows crossover down the road. We are planning to open it at Yale this year. So the final study I want to present is PG 300 study hepcidin mimetic as you know, hepcidin was discovered about 20 years ago, master regulator why and metabolism with high hepcidin level shutting down for a port and transport of ferritin. And so the reason to use it in polycythemia is of course this patient need phlebotomies as the main part of their treatment which lead to iron deficiency. Perhaps keep citing analog PG 300? Can do this instead by shutting down availability of iron to every throw pesis so
eligibility requirement PV diagnosed based on most recent to double check criteria, three phlebotomies in the last six months or more necessary primary endpoint is proportion of patients randomized withdrawal period whose cymatic Rick is maintained without need for phlebotomy. Secondary endpoint response at Week 29 as well as improvement in symptoms using MP NTSS. So complicated schema. What we're looking at is just initial phase of this study. First 18. Patients enrolled who went through the first part of the study.
Those finding at 28 weeks.

There's those escalation,

trying to identify how much

subcutaneous injections once a week.

You need to control phlebotomy

and you know when you identify it.

You kind of continue with that dose.

Then you reach the second part of

the study blinded withdrawal.

Some patients continue real thing others

and switch to placebo to see how it's

going to affect the phlebotomy requirement.

And finally,

there is open label extension so

that the report only dealt with

this red part of the study.
And as you can see in the red dots are phlebotomy requirements. Before initiation of the study, the first was only three patients required one phlebotomy Chen, those were getting the low level of the medication with which was further escalated. So pretty impressive effectiveness. As you can see, ferritin increasing significantly, showing that iron deficiency is gone. Total symptom score improving with time. And this is subset you know you can see improved concentration,
fatigue, itching for writers,
and though this is.
The scoring system used to assess MPN scores MPN symptoms.
We can say that perhaps some of it is related to the fact that iron deficiency is gone because I am deficiency can cause the symptoms as well was well tolerated.
More than 90% had drug related adverse events, but all of them were sorry, so I would like to conclude by summarizing this study.
It was PG 300 subcutaneously
00:54:55.015 --> 00:54:56.419 administered once a week,
00:54:56.420 --> 00:54:59.509 was safe and well tolerated, no Grade 3/4.
00:54:59.509 --> 00:55:01.724 Adverse events related to treatment.
00:55:01.730 --> 00:55:04.145 It was effective in eliminating
00:55:04.145 --> 00:55:06.077 the therapeutic phlebotomy’s and
00:55:06.077 --> 00:55:08.405 reversing iron deficiency impact on
00:55:08.405 --> 00:55:10.620 previous symptoms is being studied,
00:55:10.620 --> 00:55:13.380 and this study is also planned
00:55:13.380 --> 00:55:16.239 for opening at Yell this year.
00:55:19.670 --> 00:55:21.806 Thank you Nikolaj and Rory great
00:55:21.806 --> 00:55:24.299 talks and I think very important
00:55:24.300 --> 00:55:26.232 updates from from the meeting
00:55:26.232 --> 00:55:28.548 since we’re a little bit overtime,
00:55:28.550 --> 00:55:30.300 will actually take 10 minutes
00:55:30.300 --> 00:55:32.790 beyond 1:00 PM for any questions,
NOTE Confidence: 0.8375762
00:55:32.790 --> 00:55:36.264 but I will start with a question for Doctor.
NOTE Confidence: 0.8375762
00:55:36.270 --> 00:55:38.918 But also as he needs to go out
NOTE Confidence: 0.8375762
00:55:38.918 --> 00:55:41.667 at 1:00 PM for another meeting.
NOTE Confidence: 0.8375762
00:55:41.670 --> 00:55:42.828 Actually two questions.
NOTE Confidence: 0.8375762
00:55:42.828 --> 00:55:44.758 So one of them is.
NOTE Confidence: 0.8375762
00:55:44.760 --> 00:55:47.460 Are there any immediately practice changing
NOTE Confidence: 0.8375762
00:55:47.460 --> 00:55:50.790 updates you take from from the ash meeting?
NOTE Confidence: 0.8375762
00:55:50.790 --> 00:55:54.040 In terms of what we do day today and the
NOTE Confidence: 0.8375762
00:55:54.128 --> 00:55:57.140 second question is from Doctor Isufi,
NOTE Confidence: 0.8375762
00:55:57.140 --> 00:55:59.185 she’s asking whether the ampion
NOTE Confidence: 0.8375762
00:55:59.185 --> 00:56:00.821 driver mutations were acquired
NOTE Confidence: 0.8375762
00:56:00.821 --> 00:56:02.699 that were acquired in nutri,
NOTE Confidence: 0.8375762
00:56:02.700 --> 00:56:04.460 worthy, germline or somatic.
NOTE Confidence: 0.8375762
00:56:04.460 --> 00:56:07.100 Also please free to type your
NOTE Confidence: 0.8375762
00:56:07.179 --> 00:56:09.183 questions and if you want to
00:56:09.183 --> 00:56:11.429 ask live or any can unmute,
00:56:11.430 --> 00:56:13.018 you just just indicating
00:56:13.020 --> 00:56:15.402 the chat Nikolai so no immediate
00:56:15.402 --> 00:56:16.593 practice changing presentations.
00:56:16.600 --> 00:56:19.060 I think a similar but the
00:56:19.060 --> 00:56:21.090 drug for CML will be.
00:56:21.090 --> 00:56:22.835 Changing our practice when the
00:56:22.835 --> 00:56:25.479 drug and if the drug is approved,
00:56:25.480 --> 00:56:27.694 which I think should be you
00:56:27.694 --> 00:56:29.870 know towards the end of 2021,
00:56:29.870 --> 00:56:32.250 so you know I presented two studies
00:56:32.250 --> 00:56:34.506 where the drugs are very interesting
00:56:34.506 --> 00:56:37.215 and for that reason this studies will
00:56:37.288 --> 00:56:39.759 be available to our patients at Yale.
00:56:39.760 --> 00:56:43.046 So in regards to the mutations in utero, no.
Those are somatic mutations. Those are not germline mutations. This is somatic mutations which acquired. So Doctor God actually follows up on the CML presentation and he’s asking if this drug is actually approved. Does that change your calculation and whether you transplant patients would like you put this drug ahead of assertive in your kind of lines of therapy? If the drug is approved? Or how would you approach it? Yeah, so you know.
if this is going to eliminate transplant for some of our patients. So, but yes, you know, based on the study which I presented today, it may be before positive for patients who had two tiki eyes prior. You know, looking at the results here. So unless there are other questions for doctor adults, if I will go to Doctor Challace. So Rory, any immediate practice changing abstracts for what people do to leukemia in their practices right now, whether in the community or in the academic centers that you
take out from the ash meeting.

Great question. Thanks

I guess I'll kind of piggyback,

but Nikolai said I mean at the
moment I would say nothing imminent.

Clearly some interesting interim data,
although not yet practice changing.

I'm most interested in the data for Kinetic lacks added to the dual nucleoside therapy.

I know that the data phrase event you know 15

You know, it's hard to argue with 93%

CRC or I rate with you know meeting one

cycle response and meeting OS not reached.

This compares very favorably with you.

Know that the data phrase event you know 15
months OS on the median OS on Bailey a trial.

However, we've learned this year a few times over.

Unfortunately, that single arm studies of agents,

despite great clinical

preclinical rationale, a priority.

Or excellent similar data can fall short, so this needs to

be confirmed in a randomized study.

The same goes for Magnolia Map,

which is currently being evaluated

in phase three in comparison days,

amount of therapy, but the double edged sword you know, pretty
00:58:54.310 --> 00:58:55.540 exciting preclinical data is
NOTE Confidence: 0.733859
00:58:55.540 --> 00:58:56.156 very exciting.
NOTE Confidence: 0.733859
00:58:56.156 --> 00:58:57.696 Single arm data begets more.
NOTE Confidence: 0.733859
00:58:57.700 --> 00:58:59.560 Add on therapy notes with Phase
NOTE Confidence: 0.733859
00:58:59.560 --> 00:59:01.408 one trial of triplet with days
NOTE Confidence: 0.733859
00:59:01.410 --> 00:59:02.956 of medical acts makrolon map.
NOTE Confidence: 0.733859
00:59:02.956 --> 00:59:03.880 Now Aizen Gilteritinib
NOTE Confidence: 0.733859
00:59:03.880 --> 00:59:05.430 phonetic lacks, so I mean
NOTE Confidence: 0.733859
00:59:05.430 --> 00:59:06.970 there’s kind of divergent goals
NOTE Confidence: 0.733859
00:59:06.970 --> 00:59:07.900 here. But to
NOTE Confidence: 0.733859
00:59:07.900 --> 00:59:09.140 answer your question directly,
NOTE Confidence: 0.733859
00:59:09.140 --> 00:59:10.740 I’d say nothing that’s immediately
NOTE Confidence: 0.733859
00:59:10.740 --> 00:59:11.850 practice changing, but.
NOTE Confidence: 0.733859
00:59:11.850 --> 00:59:13.960 Excited for this to be a
NOTE Confidence: 0.733859
00:59:13.960 --> 00:59:14.640 different conversation,
NOTE Confidence: 0.8116402
00:59:14.640 --> 00:59:17.027 maybe a few months to a year.
Yeah, look a lot of exciting agents in development.

This is a question from Doctor Isufi about Sabbato Lima.

Basically, she’s asking whether this targets the leukemia stem cell or does it work as an immune activator and this is a great question arrested.

There’s a lot of ongoing research on this issue, but currently the thinking is that it’s a dual targeting drug, meaning that there is direct evidence that it affects the leukemia stem cells by interfering with.
One of the legs and that is important for self renewal of the leukemic stem cells, and I think this is an interesting differentiator from other immune checkpoint activators, but there is also clearly data that also activates the immune response at the level of the T cells. How do we dissect the clinical efficacy in terms of being related to one or the other? I think it’s a question that we are currently exploring and ongoing clinical trials, but I think this would be very important to explore.
I think there’s a question here from Doctor Gowda about CD 447. Inhibition is asking whether CD 47 inhibition does not cause many immune side effects. Thoughts, this is actually a good question. I will let also really give his his insight. I think this is one of the important things in terms of like single arm studies and needing to know more data. So CD 47 is actually expressed in most of their cells in in the normal body. However, they seem to be overexpressed by the leukemia cells and the idea here is that you’re exploring a therapeutic
window where using the CD 47 you are preferentially targeting the leukemia cells. However, because City 47 is also expressed on red blood cells. We do see hemolytic anemia, and some of those patients which can be actually quite severe and it has to be managed quite carefully, especially during the initial phases. And this is why they prime this drug and carefully monitor patients, etc. But I think it’s a very good question about why no activity against other CD 47 expressing cells are being seen. I think what’s gonna tell us really? The answer is once we see randomized
data and try to. You know, explore whether some of the things that get attributed to the disease, for example, are really disease related or some kind of subtle immune related adverse events. But I think what is clear. Is we are not seeing the typical immune adverse effects that are seen with the PD one or CTL A4 type of drugs such as pneumonitis colitis. It doesn’t seem that this is commonly seen or do you have any additional insights on this that was very well said?
I mean, I think the key points are the transient, presumed immune mediated hemolytic anemia, which really is why do you know the priming dose is sort of incorporated, but I think you’re right. I mean, there’s some element of specificity for those cells on which CD 47 is just enriched. Which happens to be within cells, and I mean outside of like you said, and I mean outside of like you said, subtle or maybe even delayed immune IR A ES that sort of thing. And I think we have what median fourteen 1516 months of follow up?
I mean, maybe there are delayed events that did not yet occurred, but I think it comes down to specificity and more of a different mechanism of action comparison. So you know more of a direct cell effect.

Thank you so much for a few minutes past hour. Be very cognizant of the time. On a Friday afternoon, I’d like to thank everybody who joined us for this session and if there are any additional questions, feel free to.
email their speakers directly.

Thank you so much and looking forward to seeing you next week with their next session next Friday.

Have a great weekend everyone.

Thank you.