Welcome everyone to the 2023 Post American Society of Hematology annual meeting. We are starting off the series today with multiple myeloma. Our first two presenters are Doctor Nofar Barr and Doctor Sabrina Browning who will be reviewing abstracts. We will then have a question and answer period at the end of the presentation where we will be joined by two other panelists, Dr. Ellen Gorshin and Doctor Natalia. If you could please appraise.
Hi everyone, I'm just gonna start sharing my screen here.

Alright, it’s good to be here.

Good afternoon.

Today I’m going to be looking at the newly diagnosed myeloma abstracts in Ashes 2022 this past December with a particular focus on subgroups.

So I have no disclosures.

The first subgroup I’m going to be speaking about are the frail patients and why is it important to have...
NOTE Confidence: 0.9029528
00:01:21.990 --> 00:01:23.886 dedicated studies for these folks is
NOTE Confidence: 0.9029528
00:01:23.886 --> 00:01:25.578 that they have different outcomes,
NOTE Confidence: 0.9029528
00:01:25.578 --> 00:01:27.290 they have shorter survival,
NOTE Confidence: 0.9029528
00:01:27.290 --> 00:01:29.438 they have higher rates of toxicity
NOTE Confidence: 0.9029528
00:01:29.438 --> 00:01:31.369 and therefore higher rates of
NOTE Confidence: 0.9029528
00:01:31.369 --> 00:01:32.689 discontinuation of therapy.
NOTE Confidence: 0.9029528
00:01:32.690 --> 00:01:33.262 Traditionally,
NOTE Confidence: 0.9029528
00:01:33.262 --> 00:01:35.550 studies have categorized myeloma
NOTE Confidence: 0.9029528
00:01:35.550 --> 00:01:38.410 patients as either transplant or
NOTE Confidence: 0.9029528
00:01:38.417 --> 00:01:40.417 transplant ineligible patients,
NOTE Confidence: 0.9029528
00:01:40.417 --> 00:01:42.979 but this category really does not
NOTE Confidence: 0.9029528
00:01:42.979 --> 00:01:45.474 capture frail patients because the frail
NOTE Confidence: 0.9029528
00:01:45.474 --> 00:01:47.766 scores are not routinely checked in
NOTE Confidence: 0.9029528
00:01:47.766 --> 00:01:50.349 those non transplant eligible patients.
NOTE Confidence: 0.9029528
00:01:50.350 --> 00:01:52.838 For a long time the standard of care
NOTE Confidence: 0.9029528
for non transplant eligible patients

But since the Maya study, we now have a new standard of care for patients which is Derek Tuma Mab

So what the FM 2017 O3 study analyzed is removal of dexamethasone early.

So they hypothesized if you take dexamethasone away from there, this will still be effective and it will reduce toxicities.

Before we get into the study design, I want to talk about what is a frailty score.
to take a look at this in your clinic,

so I am WG.

Frailty score involves a few things.

Age, activity of daily living,

which involves feeding oneself,

bathing oneself, instrumental activities

of daily living which involve food,

shopping, cleaning the house,

doing your finances and the comorbidity index, which is what it means.

Comorbidity is like lung disease.

Diabetes, liver disease and so forth.

Now, as you can imagine,

this takes time to do this frailty score.

There was a lot of questions involved.
So the IM group devised a simplified score which involves age, which is fairly easy, ECOG performance status, which we do routinely, and then the comorbidity index, which is easily accessible from chart review. And if you had a score of two or more, you’re classified as frail and otherwise you’re fit. So this is the study design. They include a newly diagnosed patients over 65 years of age and I am FM frailty score of two or above. It was a 2 to one randomization with REVLIMID decks or Dara REVLIMID.
I do want to note that with the Dara and Revlimid’s group which ARM B right here, they did receive steroids for the first two cycles along with dexamethasone primarily to avoid infusion reactions. So their primary endpoint was PFS, but this is immature at the moment. So they did an interim analysis and looked at response rate including MRD negative rate and occurrence of grade three or more toxicities. I want to highlight here some of the patient characteristics. So if you look at the median age, they were significantly older,
median age of 81 compared to the Maya study which was 73.

While the inclusion criteria in the study included two or for the frailty score was two or higher, actually the majority of the patients were three and higher. If you look at the risk categories, they were fairly similar in the two groups. So Dara REVLIMID clearly led to deeper response rates than REVLIMID. dexamethasone you can see here first based on just the the response rates, you had higher CR and very good partial response rates and then Dara Rev Group and you also had higher MRD negative rates,
NOTE Confidence: 0.93684912
00:04:54.030 --> 00:04:56.890 attentive negative 5th using next
NOTE Confidence: 0.93684912
00:04:56.890 --> 00:05:00.330 generation sequencing 10 compared to three.
NOTE Confidence: 0.93684912
00:05:00.330 --> 00:05:03.147 MRD was assessed at one year in patients who
NOTE Confidence: 0.93684912
00:05:03.147 --> 00:05:06.067 had a very good posture response or higher,
NOTE Confidence: 0.93684912
00:05:06.070 --> 00:05:07.426 it is important to note that.
NOTE Confidence: 0.93684912
00:05:07.430 --> 00:05:10.944 Any missing data was considered MRD positive.
NOTE Confidence: 0.93684912
00:05:10.950 --> 00:05:13.064 So it’s important because there is a
NOTE Confidence: 0.93684912
00:05:13.064 --> 00:05:14.979 significant group of patients that have
NOTE Confidence: 0.93684912
00:05:14.979 --> 00:05:17.306 missing data and for example, the Dr.
NOTE Confidence: 0.93684912
00:05:17.306 --> 00:05:20.670 Group had 20% missing data and the Rd.
NOTE Confidence: 0.93684912
00:05:20.670 --> 00:05:22.126 had 14% missing data.
NOTE Confidence: 0.93684912
00:05:22.126 --> 00:05:24.310 And I’m not about to compare
NOTE Confidence: 0.93684912
00:05:24.392 --> 00:05:26.797 different studies to one another,
NOTE Confidence: 0.93684912
00:05:26.800 --> 00:05:28.520 but I want to give us a framework
NOTE Confidence: 0.93684912
00:05:28.520 --> 00:05:30.168 of what the Maya study showed.
NOTE Confidence: 0.93684912

9
So in the Maya study they assess MRD negativity, attend to negative 5th, but they used a different assay so they use flow. So flow tends to have a higher MRD negative rate just by the nature of its assets. So just something to note, but they had in the DRD group 24% MRD negativity versus 7 in the Rd. Group. In terms of toxicity, which is very important, you can see that Grade 3 or above Texas City was higher in the Dr. Group, particularly with hematologic toxicities like anemia or neutropenia.
And in this group, of course you worry about infections with this neutropenia, but they did not see an increase in grade 3 above infections in the Dr. Group compared to the R group and even when looking at patients who are very frail with scores of four and five, there was no difference in grade 3 infections, so this is reassuring. So in conclusion, I think it is time to rethink duration deaths methadone especially for outpatients, longer follow-up of PFS is needed.
but higher MRD rates in the Dr. Group is very promising. I think the better comparator to Dr. like DRD and Maya would have been a better design. However, this was not the standard of care when this was designed. They are going to be there are going to have a retrospective comparison. To the main study in the frail population, I think you know in you know right now when you see patients in clinic when you have that very frail over 80 year old patient where you’re really not sure about triple drug induction
and you’re thinking about a doublets. I would choose Dara Rev with a short duration of steroids as opposed to Rev Deck. So I do think it’s meaningful for our practice today. The next set of subgroups I want to talk about another area of very high unmet need is the high risk population where we really have limited randomized studies guiding our treatment. The only randomized study was a 1, and this was evaluated the addition of ELOTUZUMAB to Velcade REVLIMID index methadone VRD.
Now we know we need to do better than VRD, but how do we do it? One appealing option was switching out the VELCADE with carfilzomib, which is a more potent proteasome inhibitor and outperform VELCADE in the relapsed refractory setting. Additionally, there was phase two studies showing high MRD negative rates in KRD. So it made sense to compare VRD to card and they did this in an endurance study and they actually did not find superiority of care due to the Rd. but they excluded high risk patients.
So that question about how do we better improve our induction in the high risk patients was not really answered by this study. But people have not abandoned care for a variety of reasons. In the Memorial Stone Kettering Group where they are earlier, they were early adapters of Carradine induction. They were able to do a retrospective analysis and this was presented. Doctor Tan in this year's ash of Care versus verdine high risk myeloma.
Their inclusion criteria for high risk included having gain of 1 Q translocations.

They identified 154 patients in this category. About 50% of each of these groups underwent early stem cell transplant.

Their primary endpoint was progression free survival and they also looked at response rate including MRD, negative rate and overall survival.

So this is the patient characteristics.

A few things to highlight.

The carotid group were younger...
and then I want to look at the cytogenetic characteristics here just to see who are dealing with majority of the patients who are high risk or high risk by definition of chromosome 1Q gain or amplification, which is not unusual because this is one of the more common findings we see. The second most common was deletion 17P and importantly about 1/4 of the patients of E in each group had two or more high risk. The genetic abnormalities, and this is now called the double hit or the ultra high risk patients
which really have poor outcomes.

So this is the response rates and the median PFS results.

You see higher CR rates with KRD compared to VRD,

higher MRD negative rates by flow,

but it was not statistically significant.

I think the most impressive results is the PFS,

the KD having a median of 71 months compared to 41 months and this was you know highly statistical significance and they also saw an overall survival benefit.

The five year estimate of 85% compared to 63%.
I want to just point out here in the ENDURANCE study remembers it is non-high risk patients the PFS of both arms was 30-4 months and it’s not quite clear why in this high risk populations that PFS is actually higher. So this was kind of brought up to the presenter and it was not there wasn’t a great explanation but something to think about you know endurance was done in a in a community setting and this. Early as in a single institution, tertiary center. So next they did a multivariate
analysis looking at different factors
that are associated with better PFS and OS.
So first type of inductions, OK,
D is better, early transplant was better,
having revised ISIS one compared to
having revised access one in
this high risk patient population,
it's really those patients that
have gained one cube because
they were not included,
not part of the revised ISS criteria.
So you know who these patients.
And then the number of cycles
having six or more induction
cycles had better PFS and OS.
So to summarize, I think the study is interesting. It does suggest that maybe Cardi could be better than VRD in high risk patients, but it is very limited by the retrospective nature of this design. I also think that they don’t talk about which maintenance strategies they used and that will definitely impact PFS and OS. I think this study continues to support the notion that early transplant in high risk patients is beneficial and it does bring into question. What is the optimal number of induction
treatments in high risk patients? 

Next I want to move to a more modern question, you know, now that we’re using quadruplex, how do high risk patients fare with the most commonly used quadruplets, the Dara VRD. So Dara VRD was studied in the Griffin study, which compared the addition of Dara to VRD in transplant eligible patients. In all patients they saw that there were higher MRD rates and also progression free survival benefit. But again this isn’t all patients. There are only 15% of those patients and study that were high risk
cytogenetics by the traditional high risk features like deletion 17, translocation 414 and four 416. So the Doctor Charity wanted to evaluate this subset group in the Griffin to really hone in on different high risk categories in the Griffin study. And I want to. Really it’s a busy, a little bit busy slide, but let’s just focus in on the side the genetic risk categories here as I highlighted they as I mentioned the initial high risk category were very few in both arms,
but then they revised or high risk category to include chromosome abnormality and that really increased their, patient population from 16 to 42 patients in the Dara VRD and categorize patients having zero. So no high risk features, HCA 1, high risk cell genetic abnormality or two or more as we call the ultra high risk patients. Clearly you can see the PFS in patients who are standard risk didn’t seem to differ much between the two groups. Both of them had were were not reached
Clearly the ultra high risk patients are too small to really make any conclusions about only 10 patients in eight patients. But in the high risk in the one high risk cytogenetic abnormality group there was an improvement in PFS not reached compared to. And this is the only subgroup here that actually does not cross the hazard ratio does not cross one. So a different way of looking at the same data, if you're you know,
a more visual person, is looking at the PFS curves and. What I want to show here in the kind of medium purple line the dare RVD with one high risk staging netic feature. Compare that to this green dotted line here, the derivative with sorry with VRD with one high risk feature there’s a clear separation of the PFS curves, while there is really not a big difference with those patients who are standard risk and clearly the ultra high risk due poorly. Now look at the graph on the right. These are these are the amplification or gain of 1 Q and the grasp is actually
pretty identical to the ones with the one high risk hydrogenic abnormality, which really showed you who those patients are. So in conclusion, I think this analysis shows that Dara VRD seemed to outperform VRD in high risk patients harbouring gain of 1 Q. High risk patients with more than two cytogenetic abnormalities do poorly, and we can’t make any conclusions for this analysis because of the numbers were too small. So this brings me to this category of ultra high risk myeloma and the optimum study was very clever study in
The UK they it was a screening study. So anyone in multiple UK centers who had the who’s being worked up for multiple myeloma or was offered the participation in the study and they screen patients for high risk features. It’s they’re inclusion was to be double hit. So you have to have two of the following translocation 4141416. Station one gain of 1, so deletion one peak gain of 1Q and deletion 17P or high risk gene profile. If you had plasma cell leukemia, which really is these patients are excluded from every study.
they identified 107 patients, ten of which had plasma cell leukemia. So there’s a few things going on in this study.

I want to focus first on the study design of the optimum study, which you talked about up here. On top, they use five drugs in induction. So they added cytotoxin to Dara VRD. They added VELCADE in the Peri transplant period. They used six cycles of Dara VRD induction and then 12 more cycles of Dara RVD in extended consolidation, so basically excluding steroids.
in another year. Of consolidation to and then there are in until progression and notably they're not using a proteasome inhibitor long term. So ideally the authors would love to have done a randomized study, but there was no standard of care for these ultra high risk patients. They thought it was unethical, so they did not do so. So it’s a single arm study, but they were very much interested in understanding how this would compare to a genetically similar group of patients with myeloma.
So they looked at their myeloma experience and had genetic testing for all these patients identified and identical. Population with this ultra high risk phenotype, I’m not going to go into the details of that study because I do think it’s an overall sub par comparator. But it’s just for numerical purposes here that they used cytotoxin. REVLIMID decks or carfilzomib, dexam induction transplant and then either they got no maintenance which is really not what we do.
or REVLIMID maintenance so.

Their objectives of the studies to look at MRD, to look at PFS and toxicity.

I do want to note this is quite an intensive treatment and they did have several fallouts dropouts.

So out of 107 patients, only 74 patients completed consolidation too.

The dropouts in the induction transplant section was due to intolerance and dropout and consolidation was due to progression of disease.

You can see that the MRDD deepened as you move from end of induction to end of transplant at 63%.
I don’t want you to be discouraged by the lower percentage after end of consolidation because they mentioned there are dropouts. So you can see here 30% of the patients didn’t reach that endpoint. What is important we know sustain MRD is actually more. Relevance than just one time point of emerging negativity is that had sustained MRD negativity at the end of consolidation.
Now this is the PFS course again.

I'm not surprised that the PFS is better with this optimum regiments than the comparator.

They did spread out in the myeloma X the ones that got prophesied that were not to secularism seemed to be a little bit better than not.

Again not very surprising with produce some inhibitor but regardless I think it's very impressive the 30 month PFS estimate of 77% and this does fare favorably to other.

Other data out there for this really high risk patient population.

In terms of toxicity,
which is very relevant when people are getting this intense prolonged treatment, they showed you here the consolidation to adverse events. So there are some grade three side effects. There are not that many, most of them are hematological like neutropenia. There were some Grade 3 infections, about 12%, most of them being respiratory tract infections and they don’t separate out, you know, the viruses from the bacteria, but that I think that would be relevant. Especially in the era of a pandemic.
So it seems to be fairly toggled.

They did.

One thing to note, they did allow for very flexible dose reductions, even for Grade 1 toxicity to allow patients to continue on treatment for longer.

In conclusion, I think these type of single ARM studies can serve as comparators for future randomized studies and of course balancing the efficacy and toxicity in this patient population.

Now the last study I’m going to go into, I’m going to shift gears to a different subtype of high risk patients and these are the functional
high risk myeloma and these are not the patients you know that they’re high risk when you first see them, they demonstrate themselves because they or they relapse early. So patients who have early relapse after transplant within one year have horrible prognosis. You see here 26 months overall survival compared to 91 months if you didn’t have this early. About relapse, So what this Karma 2A study analyzed is the use of either cell or abukuma, which is the first CMA directed
They used it in this patient population. The inclusion criteria includes elapse 18 months after initiation of frontline therapy. And you had to have revilement based maintenance. The primary endpoint was a CR and secondary endpoints include duration of response, progression free survival and toxicity. Patient characteristics are presented here, few things to highlight in terms of high risk features. There were 32% high risk disease in
this functionally high risk patients.

There were 40% with missing data. It they did have information about their response to upfront therapy and 24% of the patients have CR to their first line of therapy. Most patients have progression of disease within 12 months of transplant and no patients were refractory to an anti CD 38 like there are two now. This is the efficacy data. The CRH which I think is the most relevant in terms of the response rate is 45%.

Just put here in Gray,
this agent in the relapse that heavily pretreated population which is 33%? Just like the other car T products, we see the deeper response, the longer duration of response. Overall, the median duration of the responder responding patients was 15 months, but if you had a CR then it goes to 23 months and if you had a PR for example, it’s as short as three months. So really depth of response is extremely important. PFS is roughly a year, so 11 months here which is quite similar to what was seen in the relapse refractory patient population and
you know I think again this includes all those non responders as well. I think it would be interesting to see the PFS for those who are responding. In terms of toxicity, there was initial concern that when you’re using these cartee products earlier in the line of treatment that the T cells might be fitter, they might be healthier and actually have higher toxicities like CRS and the neurotoxicity icams, but they didn’t see that in this study. So there were roughly the same amount of percentage of events in
the CRS and the neurotoxicity group

as was seen in the prior study

and actually there were lower.

Or at least numerically lower number

of high grade events like grade 3/4 in

both groups compared to the prior study.

I do want to mention infections

is still an issue of post party.

There was a grade 3-4 infections at 22%

and in fact 2 deaths from this with

pneumonia and another from studemont sepsis.

So in conclusion,

in this functionally high

risk patient population,

either cell achieved 45% CR rates

and this was higher than what was
00:24:58.970 --> 00:25:01.112 seen in the first line of therapy.

NOTE Confidence: 0.770254851538461

00:25:01.120 --> 00:25:02.341 For these patients.

NOTE Confidence: 0.770254851538461

00:25:02.341 --> 00:25:05.190 It seems that there are less grade

NOTE Confidence: 0.770254851538461

00:25:05.273 --> 00:25:08.148 3-4 toxicities compared to the

NOTE Confidence: 0.770254851538461

00:25:08.148 --> 00:25:09.873 relapse refractory population.

NOTE Confidence: 0.770254851538461

00:25:09.880 --> 00:25:12.424 The PFS seems similar to what was seen

NOTE Confidence: 0.770254851538461

00:25:12.424 --> 00:25:15.260 in the heavily pretreated population,

NOTE Confidence: 0.770254851538461

00:25:15.260 --> 00:25:17.255 but these patients are very high risk,

NOTE Confidence: 0.770254851538461

00:25:17.260 --> 00:25:18.890 they they are very difficult

NOTE Confidence: 0.770254851538461

00:25:18.890 --> 00:25:20.520 to treat and salvage so.

NOTE Confidence: 0.770254851538461

00:25:20.520 --> 00:25:22.344 I think we really need randomized

NOTE Confidence: 0.770254851538461

00:25:22.344 --> 00:25:24.719 study to see what is the best

NOTE Confidence: 0.770254851538461

00:25:24.719 --> 00:25:26.539 treatment for these patients and

NOTE Confidence: 0.770254851538461

00:25:26.539 --> 00:25:28.147 ideally identify those that have

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00:25:28.147 --> 00:25:29.779 that will have a CR rate.

NOTE Confidence: 0.909416426
So I want to close with this one last slide. This is what I think is the future. It’s this risk adaptive therapy directed according to response type of study. This is the radar study that was presented by Doctor Wong from the UK. We don’t want to go into the details of all this is a busy slide but the concept here is extremely important that you separate out the standard risk from the high risk, high risk patients. We don’t want to stop treatment on, we need better treatments standard risk that have. MRD negative disease can maybe even stop treatment and standardized patients.
00:26:03.984 --> 00:26:05.554 who don’t achieve MRD negativity
NOTE Confidence: 0.909416426
00:26:05.554 --> 00:26:07.991 how is how are we going to deepen
NOTE Confidence: 0.909416426
00:26:07.991 --> 00:26:10.058 their response how are we going to
NOTE Confidence: 0.909416426
00:26:10.058 --> 00:26:12.326 get them together MRD negative state
NOTE Confidence: 0.909416426
00:26:12.326 --> 00:26:14.953 so you know when and randomizing
NOTE Confidence: 0.909416426
00:26:14.953 --> 00:26:17.313 doing a randomized fashion so.
NOTE Confidence: 0.909416426
00:26:17.320 --> 00:26:19.721 The this and other type studies like
NOTE Confidence: 0.909416426
00:26:19.721 --> 00:26:22.470 this are ongoing and I think the next
NOTE Confidence: 0.909416426
00:26:22.470 --> 00:26:25.034 decade hopefully we’ll have an answer to
NOTE Confidence: 0.909416426
00:26:25.034 --> 00:26:27.758 how to personalize treatments for myeloma.
NOTE Confidence: 0.909416426
00:26:27.760 --> 00:26:30.950 And with that I will close my section of the
NOTE Confidence: 0.909416426
00:26:31.028 --> 00:26:34.148 talk and we’ll move on to Doctor Brownings.
NOTE Confidence: 0.885277639166667
00:26:39.870 --> 00:26:41.802 OK, great. Well, thank you Doctor
NOTE Confidence: 0.885277639166667
00:26:41.802 --> 00:26:44.050 Barr and and welcome again everyone.
NOTE Confidence: 0.885277639166667
00:26:44.050 --> 00:26:46.378 My name is Sabrina Browning and with the
NOTE Confidence: 0.885277639166667

45
remainder of our time that we have left, I'm going to review with you data on relapse refractory myeloma and we'll also briefly touch upon a new therapeutic in light chainer ALE amyloidosis. And I have no disclosures to report. So a major focus in myeloma at Ash this year was the diverse and advancing immunotherapeutic landscape for relapse and refractory disease. And as you all are familiar B cell maturation antigen or BCM A has been a critical target on myeloma cells. And as Doctor Barr mentioned we now have two approved anti BCM a car T cell products eye to cell and cell.
to cell as well as an anti BCM A
by specific antibody articles amab
and while I won’t cover this today.
There was promising early phase data
presented on the combination of teclis
tamil with daratumumab and Lenalidomide
and there are other combinations
with this by specific antibody that
are also actively being studied.
As well as the number of new BCM ART
invites but importantly the abstracts
that I will focus on today with with
you all highlight some T cell to
redirection therapies that harness
new myeloma cell antigen targets.
And these include G protein coupled receptor family C Group 5 member D or what’s referred to as GPRC 5D and SC receptor homologue 5 or FCR H5 as well as some non cellular therapies that help reverse tumor mediated immune paralysis that occurs in myeloma, the novel cereblon, Eli Gaze modulators, or what is referred to as cell months. So to start we will discuss the phase two results from the monumental study which was represented by Doctor Ajai Chari and this evaluates talked amab. Talked Amab is a first in class T cell bispecific antibody that targets GPRC 5D.
And as previously discussed this is highly expressed on myeloma cells and thought to have limited expression on normal cells cells and that includes hematopoietic stem cells and in December of this past year the phase one data from the monumental study were published in the New England Journal and demonstrated an impressive overall response rate of 64 to 70% with both weekly and every other weekly dosing. And so for the phase two portion patients had to have an ECOG of zero to two with measurable disease and
three or more lines of prior therapy.

And this included a PROTEOSOME inhibitor, an imid and an anti CD 38 antibody.

And the three cohorts in this portion of the study that you see outlined here included a 0.4 milligram.

In this group 0.8 milligrams per kilogram every other week subcutaneous dosing where 109 patients were enrolled.

And then a third group of patients who had received prior T cell redirection therapy and were administered either of the two mentioned dosing schedules.
And the aim of this study was to assess efficacy and safety of this novel agent. And so the table on the left here on the slide outline some of the key patient and disease characteristics from the phase two cohorts of this study. Median age was 67 and 8.4% of the 0.4 milligram per kilogram group and 6.2% of the 0.8 kilogram milligram per kilogram group were black or African American. And as one would expect in a heavily pretreated population with an average of five prior lines of therapy high risk features including extramedullary disease.
three disease were observed in about 1/4 to 1/3 of patients as documented here in the table and approximately 3/4 of the patients have triple class refractory disease. However despite this population again with high risk disease and there wasn’t an impressive overall response rate as seen in the figure here on on the right at 74.1% and 73.1% in the two dosing. Groups and VGPR are better was achieved in approximately 60% of patients which also indicates a high depth of response with this agent. These responses were maintained across subgroups except for those.
00:31:02.533 --> 00:31:04.277 with Extramedullary disease where

00:31:04.277 --> 00:31:06.893 the overall response rate was reduced

00:31:06.954 --> 00:31:09.062 some at 50% and responses were rapid

00:31:09.062 --> 00:31:11.538 with the median time to response of

00:31:11.538 --> 00:31:13.650 a little over a month and a median

00:31:13.650 --> 00:31:16.046 time to best response of approximately

00:31:16.050 --> 00:31:18.150 2.5 months and thus far responses

00:31:18.150 --> 00:31:19.550 have also been durable.

00:31:19.550 --> 00:31:21.752 Of the median progression free survival

00:31:21.752 --> 00:31:24.674 at the time of presentation was 7.5

00:31:24.674 --> 00:31:27.026 months and 11.9 months in the 22 cohorts

00:31:27.026 --> 00:31:29.294 with a median duration of of response

00:31:29.294 --> 00:31:31.677 that was not reached in patients who

00:31:31.677 --> 00:31:33.765 had achieved a complete response or

00:31:33.765 --> 00:31:35.920 better and median overall survival was

NOTE Confidence: 0.818111631724138

53
not reached for the study cohort to date.

Importantly for the patients who had received prior T cell redirection therapy which included 70%,

seventy .6% of patients who had received prior car T and 35.3%.

The overall response rate was still high at 62.7%.

Responses were higher in those that received prior car T compared to buy specifics,

although the number of patients in in the study that received prior price by specifics was small with an end of 18.

It’s important to consider safety
as we discussed and fortunately as you can see outlined here, high grade adverse events were uncommon but when they were present they were mostly hematologic in nature. And with that being said, still there was less than 1/3 of patients that had high grade heme toxicities and most of the toxicity was limited to the first few cycles of treatment. High grade infections were also uncommon in this study and as you can see that included a low number of opportunistic infections. COVID infections occurred in
approximately 10% of patients with COVID-19. Only two deaths from COVID and actually no deaths reported in the phase one portion that was published in the New England Journal back in December. As mentioned, rates of IVIG use were also relatively low with less severe and this is somewhat distinct from our anti-BCM a targeted by specific antibodies that are now in utilization. The most common adverse events were cytokine release syndrome or CRS as well as altered taste.
00:33:20.600 --> 00:33:23.372 Or discuss Jia skin and nail
NOTE Confidence: 0.855970994347826
00:33:23.372 --> 00:33:26.399 related events as well and and the.
NOTE Confidence: 0.855970994347826
00:33:26.400 --> 00:33:28.962 The CRS events appear to be restricted
NOTE Confidence: 0.855970994347826
00:33:28.962 --> 00:33:31.431 largely to step up dosing and full
NOTE Confidence: 0.855970994347826
00:33:31.431 --> 00:33:33.736 first full dose with a median time
NOTE Confidence: 0.855970994347826
00:33:33.736 --> 00:33:36.020 to onset of two days immune effector
NOTE Confidence: 0.855970994347826
00:33:36.020 --> 00:33:37.760 cell associated neurotoxicity or
NOTE Confidence: 0.855970994347826
00:33:37.760 --> 00:33:40.479 what we refer to as icans occurred
NOTE Confidence: 0.855970994347826
00:33:40.479 --> 00:33:43.056 in about 10 to 11% of patients,
NOTE Confidence: 0.855970994347826
00:33:43.056 --> 00:33:46.254 but again we’re mostly low grade.
NOTE Confidence: 0.855970994347826
00:33:46.260 --> 00:33:47.337 So in conclusion,
NOTE Confidence: 0.855970994347826
00:33:47.337 --> 00:33:50.973 tell Ketama B which is a a first in
NOTE Confidence: 0.855970994347826
00:33:50.973 --> 00:33:53.558 class by specific antibody again
NOTE Confidence: 0.855970994347826
00:33:53.558 --> 00:33:56.168 targeting novel GPRC 5D on myeloma
NOTE Confidence: 0.855970994347826
00:33:56.168 --> 00:33:57.736 cells demonstrated an impressive
NOTE Confidence: 0.855970994347826
overall response rate of more than 70% in patients with heavily pretreated relapsed and refractory myeloma. And high overall response rates were also seen in those who had received prior T cell redirection therapy which is an important cohort to learn more about responses have been durable and the agent. Because generally been overall well tolerated with CRS that seems to be manageable and fewer infections. Although it does have unique safety profile and those include things like skin and nail related events as well as taste alteration or dusia
as previously mentioned. Although these were generally managed with supportive care and there was a low overall rate of discontinuation due to the adverse events and and therefore there are additional studies that are now ongoing to looking at the look at talked amab both in combination. In combination with a variety of different anti myeloma agents. And so next I want to briefly share with you the following abstract. This was presented by Doctor Jesus Berdeja and this is now a novel car T cell therapy therapy that’s
targeting GPRC 5D and this has a this car T construct as seen in the figure here on the right.

And this data came from a phase one multicenter open label study and the data was presented on 33 patients enrolled in the part a dose escalation cohort eligible patients had relapsed refractory myeloma. With three or more prior lines of therapy and prior BCMA therapy was allowed, there were five dose levels that were tested from ranging from 25 to 450 million car T cells and thus far the state the overall safety and efficacy have profiles have been favorable.
Treatment emergent adverse events were seen in close to 88% of patients and 73% of patients had grade 3 or 4 adverse events. And in comparison to Cal talk tamag, hematologic adverse events and particularly neutropenia and thrombocytopenia. Thrombocytopenia seemed to be more common with a dose limiting toxicity of prolonged grade 4 neutropenia and thrombocytopenia in two patients. Again CRS was the most common non hematologic. Reverse advent at 63.6% and the median time to onset with this cartee was three days.
Although grade three and four CRS events were only observed in 6% of patients. Icans was infrequent with only two patients and was reversible in both instances. Instances with steroid treatment, again because of the GPR, the unique target that this car T targets there were skin and nail related. Adverse events as well as taste alterations, but these seem to be less common than talked amab and all were low grade and the majority did not require any sort of treatment. The maximum tolerated dose has not yet been exceeded in this study and
there have been no deaths thought to be related to study treatment. Importantly, the overall response rate of the total cohort was high at 89.5% with a complete response rate of 47.4. Percent and there were four patients that were evaluated for minimal residual disease or MRD and all four of those were MRD negative. So in conclusion, responses with this novel cartee seem durable and also deepen over time, making this a promising
treatment moving forward, including those patients that are already exposed to a treatment.
The next abstract I will present was discussed by Doctor Susan Trudell and it looked at a cohort in a safety and efficacy trial of savasta amab and SAVASA. Amab is a bispecific antibody seen here on the right that targets ye another new myeloma antigen known exclusively expressed in B cell lineage and is thought to be near ubiquitous on myeloma cells and at ASH in 2021 there was initial data presented.
On the phase one dose finding study of savasta mab and revealed a favorable efficacy and safety profile in those patients with heavily pretreated relapsed and refractory myeloma. This year’s abstract reviews reviewed a cohort in this study who received a single dose of the IL 6 receptor blocker to Solus amount at 8 milligrams per kilograms. And this was given 2 hours prior to the first of Austin maps step up dose which is 3.6 milligram and these patients were then compared retrospectively. To a previously enrolled group who.
did not receive tocilizumab and the objective which was based on preclinical data was to determine whether there’s this would reduce the frequency of cytokine release syndrome or CRS which as we’ve discussed now in several abstracts is one of the most common adverse event with bispecific antibody treatment and it’s thought to be mediated by IL sex and other cytokines. And as you can see here on the the bottom savasa amab is its administered with a single step up dose. Initially at 3.6 milligrams and then to a target dose of 90 milligrams, and it’s given intravenously.
every three weeks.
So 31 patients were enrolled in the total amount pretreatment arm with 44 patients in the comparator arm and in both groups as you can see in the table here on the left included heavily pretreated patients with a median time, excuse me, a median line of therapies being four and six respectively with fairly similar patient and disease characteristics except for those that I’ve highlighted for you here on the in the table on the left and as you can see the tocilizumab pretreatment group did. Have somewhat less extramedullary
disease as well as less penta,

NOTE Confidence: 0.84287700875

00:39:49.910 --> 00:39:52.538 refractory penta drug refractory disease and
NOTES Confidence: 0.84287700875

00:39:52.538 --> 00:39:55.690 fewer patients in the tocilizumab are arm.
NOTES Confidence: 0.84287700875

00:39:55.690 --> 00:39:59.029 Had received prior anti BCM cell therapy
NOTE Confidence: 0.84287700875

00:39:59.030 --> 00:40:00.938 and the most commonly observed adverse
NOTE Confidence: 0.84287700875

00:40:00.938 --> 00:40:03.170 events in both groups were neutropenia,
NOTE Confidence: 0.84287700875

00:40:03.170 --> 00:40:05.606 anemia, thrombocytopenia and CRS and of
NOTE Confidence: 0.84287700875

00:40:05.606 --> 00:40:08.517 no neutropenia which is a known side
NOTE Confidence: 0.84287700875

00:40:08.517 --> 00:40:10.547 effect of tocilizumab with significantly
NOTE Confidence: 0.84287700875

00:40:10.547 --> 00:40:13.299 higher in the Tosi pre treatment group,
NOTE Confidence: 0.84287700875

00:40:13.300 --> 00:40:15.156 but was said by the authors to be
NOTE Confidence: 0.84287700875

00:40:15.156 --> 00:40:16.788 reversible and manageable with growth.
NOTE Confidence: 0.84287700875

00:40:16.790 --> 00:40:19.177 Doctor um when appropriate and this did
NOTE Confidence: 0.84287700875

00:40:19.177 --> 00:40:22.220 not lead to Savasta Amab discontinuation.
NOTE Confidence: 0.84287700875

00:40:22.220 --> 00:40:24.110 The infection rate was also reportedly
NOTE Confidence: 0.84287700875

00:40:24.110 --> 00:40:25.620 higher than the comparator arm,
although compared to other cohorts in the study there was a similar infection rate and grade three infections also occurred at a similar rate between these two study groups. And as you can see in the figure here on the right, the overall rate of CRS was significantly lower in the Tosi Pre treatment group at 38.7%. Compared to the non Tosi group, CRS was limited to grade one and grade two events in both, the median time to onset of one day.
And the beneficial effects of Tosi on CRS were continued with subsequent doses in cycle one. In the tocilizumab pretreatment arm, I can’t was seen in frequently in both groups occurred in only two patients in the Tosi arm and six patients in the non-toxic arm and interestingly the authors demonstrated in the toasty. Pretreatment arm that after the 1st 3.6 milligrams of fastmac dose, there were higher peak levels of IL 6 which were hypothesized to be due to inhibition of IL 6 clearance by tocilizumab. However,
there was also near complete suppression of CRP which is produced by IL 6 receptor binding and thereby suggesting that there was effective blockade or blockage of the IL 6 inflammatory signal signaling pathway, also importantly pretreatment with tocilizumab. Did not appear to negatively impact clinical response rates with an overall response rate rate of 54.8% and a very good partial response or a VGR or better rate of 32.3% observed in the Tosi group. And that was compared to an overall
response rate of 37.2% and VG,

VG PR or better of 25.5% in the non-toxic arm and median time to best response as well as median duration of response was similar between the two groups.

So in conclusion, pretreatment with a single dose of tocilizumab significantly reduced the rate of CRS in patients with relapsed refractory myeloma likely thought to be through suppression of the IL 6 signaling pathway, but did not seem to negatively impact the
NOTE Confidence: 0.7604757118
00:42:37.212 --> 00:42:39.380 anti myeloma activity of this Asia agent.
NOTE Confidence: 0.7604757118
00:42:39.380 --> 00:42:41.662 And so the authors noted that two
NOTE Confidence: 0.7604757118
00:42:41.662 --> 00:42:43.765 salesman may may play an important
NOTE Confidence: 0.7604757118
00:42:43.765 --> 00:42:46.229 future role in CRS mitigation as pre
NOTE Confidence: 0.7604757118
00:42:46.299 --> 00:42:48.910 dosing and may potentially help us move.
NOTE Confidence: 0.7604757118
00:42:48.910 --> 00:42:50.558 By specific treatment to
NOTE Confidence: 0.7604757118
00:42:50.558 --> 00:42:51.794 the outpatient setting.
NOTE Confidence: 0.7462215285
00:43:03.445 --> 00:43:05.989 and Messi is a a potent novel.
NOTE Confidence: 0.7462215285
00:43:05.990 --> 00:43:07.929 Sarah Blunt Eli Gaze modulator or what
NOTE Confidence: 0.7462215285
00:43:07.929 --> 00:43:10.718 we know as a cell mod and this was looked
NOTE Confidence: 0.7462215285
00:43:10.718 --> 00:43:12.670 at in combination with dexamethasone.
NOTE Confidence: 0.7462215285
In this abstract Messi is an oral agent and as could be seen in the figure here, it binds and activates Sarah blown and it leads to what happens is it leads to maximal degradation. Of important transcription factors and that includes ICAROS and ilos that are both really important in myeloma pathophysiology and pathobiology. And this results in enhanced myeloma cell killing and immune stimulatory activity when compared to our common immunomodulatory drugs such as Lenalidomide. And in this phase one two trial, Messi was evaluated alone and in combination with dexamethasone and
the recommended phase two dose for Messi was selected at 1 milligram daily for 21 days. Out of a 28 day cycle with a notable overall response rate in the phase one portion of 54.5% and to be eligible for the phase two dose expansion portion of the study that was reported in this abstract. patients had to be relapsed refractory and have had received three or more prior lines of treatment and be refractory to at least one immunomodulatory agent. Again prior exposure to CMA therapy was allowed and dexamethasone was
administered at 20 to 40 milligrams.

Dependent on age in combination with Mezzi,

the main objectives of the study included advocacy and safety

of this novel combination.

So 101 patients were included in the MEZZI plus DEX cohort and they're patient characteristics are outlined in the table on the left.

Median age as expected was 67 years and these were heavily pretreated patients with a median time since initial diagnosis of myeloma of 7.44 years, a median of 6 lines of prior treatment and 100% of patients were triple class refractory.
There were only approximately 20% of patients with Stage three disease although 39.6 had extramedullary disease and this included in their study soft tissue bone related plasmacytoma in addition to true soft tissue extramedullary disease and 36.6% of patients had high risk cytogenetics. 29.7% of patients had received prior anti BCMH treatment mostly in the form of antibody drug conjugates. And in terms of clinical activity, as you can see on the figure here on the right.
00:45:38.920 --> 00:45:42.280 the overall response in the total
NOTE Confidence: 0.769961027307693
00:45:42.280 --> 00:45:46.233 population of what what’s 40.6% with a
NOTE Confidence: 0.769961027307693
00:45:46.233 --> 00:45:49.659 high quality responses that included a
NOTE Confidence: 0.769961027307693
00:45:49.659 --> 00:45:53.139 stringent CR complete response and VGPR.
NOTE Confidence: 0.769961027307693
00:45:53.140 --> 00:45:55.055 And in those with Extramedullary
NOTE Confidence: 0.769961027307693
00:45:55.055 --> 00:45:57.327 disease overall response rate was still
NOTE Confidence: 0.769961027307693
00:45:57.327 --> 00:45:59.976 notable at 30% and patients who had
NOTE Confidence: 0.769961027307693
00:45:59.976 --> 00:46:02.196 received anti BCH treatment although
NOTE Confidence: 0.769961027307693
00:46:02.196 --> 00:46:04.826 small in in number with 30 patients.
NOTE Confidence: 0.769961027307693
00:46:04.830 --> 00:46:07.238 Portal had an overall response rate of of
NOTE Confidence: 0.769961027307693
00:46:07.240 --> 00:46:11.280 50% and while follow-up is short to date,
NOTE Confidence: 0.769961027307693
00:46:11.280 --> 00:46:13.365 the median progression free survival
NOTE Confidence: 0.769961027307693
00:46:13.365 --> 00:46:15.800 observed was 4.4 months and median
NOTE Confidence: 0.769961027307693
00:46:15.800 --> 00:46:18.600 duration of response was 9.2 months
NOTE Confidence: 0.769961027307693
00:46:18.600 --> 00:46:21.600 when patients achieved VGPR better.
NOTE Confidence: 0.769961027307693
00:46:21.600 --> 00:46:23.875 And Doctor Richardson presented some
correlative data from this abstract as well, showing that Messi is active in patients who are either refractory to pomalidomide or POMALYST and in those receiving pomalidomide as in their last regimen. As their last regimen of treatment. At a median follow-up of 7.5 months, 90.1% of patients had discontinued treatment, although the majority due to progressive myeloma. 5 patients were reported to have adverse events. Related events, excuse me. 5 patients were reported to have adverse events.
adverse event related deaths, including two with PJP pneumonia, an additional with pneumonia and one due to COVID-19 infection and one due to septic shock. And while a majority of patients did require dose interruptions due to adverse events. Those reductions were less common and a few patients discontinued drug due to adverse events as is outlined here and as you can see in the tables here on the bottom, treatment emergent adverse events were primarily hematologic in nature with neutropenia being the
most common although this was felt to be manageable again with those adjustments and growth factor support. Additionally infections were the most common non hematologic adverse event with infections of any grade seen in about 2/3 of patients. Other observed side effects are listed here in the tables, although they were less common and less severe. So to summarize, Mazda Magnemite or Messi is an oral potent novel cell mod which in preclinical studies has a distinct
profile from our immunomodulatory agents.

And when combined with dexamethasone

Overall response rate was notable

Is manageable with most higher grade

Is manageable with most higher grade adverse events being hematologic in

Given these findings,

Mezi is now being evaluated in

combination with standard myeloma therapies including in phase three trials with Bortezomib and carfilzomib
and this appears to be a promising agent in patients with heavily pretreated relapsed refractory myeloma including those who may be refractory to imids including POMALYST.

So I’ll shift gears a bit now with this last abstract and discuss like Chainer ALE amyloidosis, which as you guys likely know is a rare progressive disorder where clonal plasma cells in the bone marrow produce immunoglobulin light chains that misfold and form amyloid fibrils that become insoluble and deposit in
extracellular tissues and organs
resulting in significant dysfunction.
And we have made advances in the treatment of AL amyloid with exciting data from last year’s ASH on the Andromeda trial. Uh which showed improved team hematologic and organ responses with the addition of daratumumab to cyber deem. However, these available therapies target the clonal plasma cells in order to stop or halt production of light chains, new light chains but they don’t address the amyloid that’s already been deposited and in and organs that lead to significant morbidity.
And in patients with advanced cardiac disease, high mortality with a median overall survival in patients with Mayo stage four disease of only 5.8 months and the abstract. We’ll discuss was presented by Doctor Morie Gertz from the Mayo Clinic on Beartown bertam amount, which is a humanized monoclonal antibody administered intravenously every 28 days and binds conserved epitopes on both Kappa and Lambda immunoglobulin light chains and that leads to neutralization of circulating...
light chain aggregates as well as depletes the insoluble amyloid deposited in the organs thought to be through phagocytosis by macrophages. And the study schema here on the top outlines the phase three vital study which is a multi center double-blind placebo-controlled trial in patients with newly diagnosed treatment naive AL amyloid. All patients enrolled had cardiac involvement and were stratified by Mayo stage, renal stage and six minute walk test. Patients total were enrolled and randomized to receive birtamod in addition to standard of care.
00:50:35.193 --> 00:50:37.390 or placebo with standard of care.

00:50:37.390 --> 00:50:39.530 There was an interim futility analysis back in 2018.

00:50:41.191 --> 00:50:43.046 That actually resulted in early study termination given concern that the primary endpoint which was all cause mortality or time to all cause mortality would not be met in a reasonable amount of time.

00:50:44.911 --> 00:50:46.819 And so afterwards a post hoc analysis was performed on 77 patients that had Mayo Stage 4 cardiac amyloid.

00:50:48.839 --> 00:50:50.626 cause mortality would not be met in a reasonable amount of time.

00:50:52.490 --> 00:50:55.829 And so afterwards a post hoc analysis was performed on 77 patients that had Mayo Stage 4 cardiac amyloid.

00:51:00.600 --> 00:51:02.430 And this has previously been reported.

00:51:04.859 --> 00:51:06.581 Kaplan Meier curve here a survival.
benefit with significant reduction in time to all cause mortality in this cohort. With 74% of patients in the Bertambah group being alive at month nine with only compared to only 49% in the placebo arm with the hazard ratio that you see listed here. So in this year’s abstract Dr. Gerson is coauthors showed using the data from the post hoc analysis that reduction in time to all cause mortality at nine months. I’m favoring the pertama amab arm persisted in these Mayo stage four patients ever even after adjusting for a variety of demographic
and disease characteristics.

As you can see in the forest plots here that come from small numbers but have again impressive hazard ratios.

There was also in the post tech analysis. Patients who received Birtamod had less deterioration in quality of life and improved 6 minute walk test.

And so with the available data for Tim Amab has been safe and well tolerated even in these patients with advanced cardiac disease and it has this data has served as the foundation for the Affirm ALS trial and we have this trial open here.
at Yale as well as in a number of our care centers in Trumbull.

Saint Francis and a female is looking to enroll patients with newly diagnosed treatment naive al amyloid with Mayo stage four disease and looking again to see if we see this survival benefit that was demonstrated in the post hoc analysis. And patients will be randomized 2 to one to receive vertamae in addition to standard care. And I do think this is an incredibly important trial for a very complex very hard to treat population and I
00:52:54.108 --> 00:52:56.138 would be happy to talk with anybody.

00:52:56.140 --> 00:52:58.642 Interested who might have eligible patients

00:52:58.642 --> 00:53:01.248 or have questions about the the trial?

00:53:01.250 --> 00:53:01.551 So,

00:53:01.551 --> 00:53:02.454 so in summary,

00:53:02.454 --> 00:53:04.725 we saw many exciting abstracts at ASH

00:53:04.725 --> 00:53:07.155 looking at new myeloma target antigens

00:53:07.155 --> 00:53:08.998 from biospecific antibodies and car

00:53:08.998 --> 00:53:10.979 T as well as abstract looking at

00:53:10.979 --> 00:53:12.806 improved manufacturing and management

00:53:12.806 --> 00:53:15.366 of side effects including CRS.

00:53:15.370 --> 00:53:17.660 I I will end so that we can move to

00:53:17.735 --> 00:53:20.021 the questions and answers by just

00:53:20.021 --> 00:53:22.530 saying that although not covered today,

00:53:22.530 --> 00:53:24.700 there were up to 30 abstracts on
looking at health disparities in multiple myeloma which remains really a critical unmet need and ongoing.

Investigation is really imperative.

The QR code I’ve included here links to a video by Doctor Joel McHale and the International Myeloma Foundation addressing some of these really important abstracts.

So thank you again all for your time and I look forward to answering some questions.
As we wait for questions, I will start by asking a few. Maybe we’ll start with Elon and Natalia. We heard a lot about side effects from the bispecific T cell engagers, the cartes and even the cell mods in relationship to infections. So how would you propose we manage that risk to help keep our patients safe as these therapies move forward? I mean I guess I can start. We know that there’s a risk of hypogammaglobulinemia with this patient.
So I think that keeping a close signing IG level, making sure that it’s you know consistently at least 400 or even 500 compliance with you know antiviral anti microbial prophylaxis and I think also just educating you know the various colleagues, And members of the community and the oncology team about the, the risk for infection complications in these novel agents. I think they tell you you’re a mute. Help, you’re still muted. And Natalia, you were still on mute. So unfortunately we’re not been
00:55:52.240 --> 00:55:54.300 able to hear what you have said.

00:55:56.170 --> 00:55:57.418 And we can move on. We did have one question from the audience which is asking if calcium deficiency is seen in multiple myeloma.

00:56:00.926 --> 00:56:03.902 Umm. I don’t know if anyone wants to take the question regarding calcium and multiple myeloma.

00:56:03.902 --> 00:56:06.926 I mean I think that usually with myeloma we see hypercalcemia and I think if it’s poorly controlled we can see hypercalcemia. You know the bisphosphonates and the bone modifying agents can cause hypocalcemia.

00:56:14.630 --> 00:56:16.590 You know the bisphosphonates and the bone modifying agents can cause hypocalcemia, but but typically we would see hypercalcemia.

00:56:20.110 --> 00:56:24.440 I mean I think that usually with myeloma we see hypercalcemia.
Thank you, Elon.

So I may ask a question that’s a little bit unfair to the group. And we can have each of the panelists answer with all of these new targets and they relapsed refractory setting. How do you propose that we sequence them and most of these studies have been done after potentially BCM a. But again, I would be interested in everyone’s thoughts as far as they’re optimal. And maybe we can start with Elon and Natalia and then go to no farms, Sabrina. Another Natalia sorted out her mute option, but. I guess not.
So I think obviously that’s an ongoing area of evaluation and research with these novel agents. We are looking at them in earlier lines of therapy, you know in clinical trials, cartoon etcetera. I think that it depends on a couple of factors. You know how did the patients respond to prior treatments, respond to prior treatments have they had. You know, high risk, standard risk, I think that the
data is pretty encouraging and promising for biospecifics and cartes. So I think that. You know, if they’re candidates for that, we should try to push for that. But a lot, a lot will be. Coming and we’ll have a lot more information in the upcoming, you know, months and annual meetings. Thank you, Ellen, and no far Sabrina. Yeah. So I think at the end of the day the answer is we don’t know as they’re quite effective and we don’t really know which subtypes of patients would do better. But we do have some information that
patients who have gained 1Q have high expressions of the FC RH 5.

So perhaps you know being a little bit more specific in terms of patient selection to some of these again more studies really need to be done in subgroup. Populations.

I think it is encouraging that the infection risk is is lower with tell kalamas supposed to Tequesta amab.

So for patients where you’re more worried about that maybe in a post transplant setting where you know there’s other additives infection complications.

So I think more to come we don’t know.
00:59:04.910 --> 00:59:06.470 You know, I would completely,
NOTE Confidence: 0.79330085
00:59:06.470 --> 00:59:07.040 completely agree.
NOTE Confidence: 0.79330085
00:59:07.040 --> 00:59:09.035 You know, I think there’s a question
NOTE Confidence: 0.79330085
00:59:09.035 --> 00:59:10.400 of not only how to sequence
NOTE Confidence: 0.79330085
00:59:10.400 --> 00:59:11.980 our car T and by specifics,
NOTE Confidence: 0.79330085
00:59:11.980 --> 00:59:13.695 but now sequence in terms of targets.
NOTE Confidence: 0.79330085
00:59:13.700 --> 00:59:15.542 So, you know, I agree with
NOTE Confidence: 0.79330085
00:59:15.542 --> 00:59:17.250 Doctor Barr that I think.
NOTE Confidence: 0.79330085
00:59:17.250 --> 00:59:18.996 You know thinking about choosing a
NOTE Confidence: 0.79330085
00:59:18.996 --> 00:59:21.053 carte or by specific I think depends
NOTE Confidence: 0.79330085
00:59:21.053 --> 00:59:23.013 a little bit on the patient’s disease
NOTE Confidence: 0.79330085
00:59:23.069 --> 00:59:25.211 at that time and the time that it may
NOTE Confidence: 0.79330085
00:59:25.211 --> 00:59:28.208 require for them to get the the treatment.
NOTE Confidence: 0.79330085
00:59:28.210 --> 00:59:29.842 I think you know it’s exciting
NOTE Confidence: 0.79330085
00:59:29.842 --> 00:59:31.580 now to have different targets that
NOTE Confidence: 0.79330085
00:59:31.580 --> 00:59:33.350 do have a unique safety profile.
You know and I think a lot of these newer targets are showing response in patients who had prior BCM a cell therapy. So you know I think we have the most data obviously from our CMA products, but I think there are going to be patient populations where these new targets I think are going to be important and perhaps. You know, our first choice moving forward. Wonderful. Thank you all.
00:59:59.029 --> 01:00:02.382 how do you see MRD driving transplant
NOTE Confidence: 0.830471895454545
01:00:02.382 --> 01:00:05.137 and sequencing of therapies in general?
NOTE Confidence: 0.830471895454545
01:00:05.140 --> 01:00:06.508 So I don’t know if Natalia
NOTE Confidence: 0.830471895454545
01:00:06.508 --> 01:00:08.050 or Nofar you have a response?
NOTE Confidence: 0.925201375
01:00:09.340 --> 01:00:11.920 Yeah, I can talk about this.
NOTE Confidence: 0.925201375
01:00:11.920 --> 01:00:15.456 So I think MRD is going to be
NOTE Confidence: 0.925201375
01:00:15.456 --> 01:00:18.400 driving how we treat patients.
NOTE Confidence: 0.925201375
01:00:18.400 --> 01:00:20.311 I think what we see is in
NOTE Confidence: 0.925201375
01:00:20.311 --> 01:00:21.760 both of those studies,
NOTE Confidence: 0.925201375
01:00:21.760 --> 01:00:23.745 patients who are MRD negative
NOTE Confidence: 0.925201375
01:00:23.745 --> 01:00:28.360 just do better in the IM 2009.
NOTE Confidence: 0.925201375
01:00:28.360 --> 01:00:31.139 30% of patients who had VRD in
NOTE Confidence: 0.925201375
01:00:31.139 --> 01:00:33.828 transplant and one year only one
NOTE Confidence: 0.925201375
01:00:33.828 --> 01:00:35.708 year maintenance still remain
NOTE Confidence: 0.925201375
01:00:35.708 --> 01:00:38.510 in remission 8 years after. So.
NOTE Confidence: 0.925201375
01:00:38.510 --> 01:00:40.490 So clearly we are over treating
some patients and we need to figure out who those patients are and I think even with transplant, right. So if we achieve MRD negativity with quadruplets, I think we need to assess this transplant better. What is the marginal benefit of transferring those patients? These studies are underway. We will find out, but it will take many years. Right now, I do discuss costs, you know risk benefit with patients when I talk about transplant.
especially in standard risk MRD

negative patients as patients who

are considered that presumably

transplant and relying.

And I’m sorry, I had difficulties

with odd earlier, but I

do agree with what’s been said.

MRD does have a value and its primary

significances in predicting progression

free survival and overall survival.

So we do use it in practice

as a prognostic tool and with

enough data with more mature data, we,

we, we will most likely in the

future use the data to discontinue

certain patients with low risk cytogenetics
and durable sustained MRD negative state.

Hey, wonderful. Well,

we are after time as it is one of three.

So I will like to thank all of our

panelists for their presentations and input

today and thank you all for joining us.

Please tune in next Friday

for the next in the series.

Have a good afternoon everyone.

Thank you.