OK. Good afternoon, everybody.

Welcome to our next review. This is a review on cellular therapies, and we have, I think, 2 exciting presentations for you this afternoon. The first is going to be with Doctor Iris Isufi. Dr. Isufi is associate professor in the Department of Medicine and Hematology in the Yale Cancer Center and the director of our Cell Therapy research team and our Clinical Care T.
00:00:36.570 --> 00:00:39.150 Program and she’s gonna talk to
NOTE Confidence: 0.837063833333333
00:00:39.150 --> 00:00:41.773 you about some advances in cell
NOTE Confidence: 0.837063833333333
00:00:41.773 --> 00:00:44.233 therapy at the latest ash meeting.
NOTE Confidence: 0.837063833333333
00:00:44.240 --> 00:00:46.766 So, Doctor Suffi, take it away.
NOTE Confidence: 0.861653135
00:00:49.150 --> 00:00:51.358 Thank you Stuart. I’m gonna share my screen.
NOTE Confidence: 0.8588443
00:01:00.170 --> 00:01:02.250 Before you start, can I just
NOTE Confidence: 0.8588443
00:01:02.250 --> 00:01:04.020 remind everybody if you’d like
NOTE Confidence: 0.911925422307692
00:01:04.096 --> 00:01:06.384 to submit questions, there will
NOTE Confidence: 0.911925422307692
00:01:06.384 --> 00:01:09.156 be a question and answer period.
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00:01:09.160 --> 00:01:10.378 Possibly between the
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00:01:10.378 --> 00:01:12.408 presentations and at the end,
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00:01:12.410 --> 00:01:14.885 but you can submit questions
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00:01:14.885 --> 00:01:18.625 through the chat or Q&amp;A during the
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00:01:18.625 --> 00:01:21.550 talk and we’ll possibly answer
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NOTE Confidence: 0.911925422307692
00:01:24.690 --> 00:01:27.590 talks or at the end. OK.
00:01:29.610 --> 00:01:31.608 Thanks. So I’ll take welcome everyone.
00:01:31.610 --> 00:01:35.082 I’ll take the first half of the session
00:01:35.082 --> 00:01:38.940 just to present some of the ash data
00:01:38.940 --> 00:01:42.822 on cell therapies and I know this
00:01:42.822 --> 00:01:45.774 was talked about that the myeloma.
00:01:45.780 --> 00:01:49.280 View as well, but today I’ll focus
00:01:49.280 --> 00:01:52.449 particularly on non Hodgkin lymphomas
00:01:52.450 --> 00:01:59.070 and some also exciting data on AL.
00:01:59.070 --> 00:02:04.350 These are my disclosures. So the 1st.
00:02:07.590 --> 00:02:10.294 Presentation, the first abstract
00:02:10.294 --> 00:02:16.290 Lysol cell, mariluz cell and this
00:02:16.290 --> 00:02:19.242 is a cellular therapy product that is
00:02:19.242 --> 00:02:21.462 different from the prior ones on the
00:02:21.462 --> 00:02:25.583 that’s looking at Lysol cell,
00:02:25.583 --> 00:02:29.034 Lysol catagen, mariluz cell and this
00:02:29.034 --> 00:02:33.082 is a cellular therapy product that is
00:02:33.082 --> 00:02:37.034 different from the prior ones on the
00:02:37.034 --> 00:02:41.034 So I’ll take welcome everyone.
market because it has a defined CD4 to CD8 ratio and this has already been approved in the third line setting. And more recently also in the second line setting for diffuse large B cell lymphoma, so. Here they presented their primary analysis of the randomized phase three transform study where lyso cell was compared to standard of care with salvage chemotherapy alone, so patients had a good performance status. The ones that were randomized to the standard of care arm who had relapsed. Um were randomized to receive 3 cycles of chemo immunotherapy.
These were high risk patients. They were patients who were either primary refractory to their first line or patients who had relapsed within 12 months of their initial therapy. So they took this highest risk group to compare it to stem cell transplant. And so the patients who received salvage chemotherapy and achieved either a complete or a good partial response proceeded to high dose chemotherapy and autologous. Then self rescue a typically with a beam regimen and then. The other arm was randomized to receive
lysis cell and so they underwent lymphodepletion with fludarabine and cyclophosphamide and they were allowed to get some bridging if their disease was rapidly progressing. Importantly, in this trial, crossover was allowed for patients who received standard of care and were not deemed to be good candidates for autologous stem cell transplant. For multiple reasons. So they crossed over and the primary endpoint was event free survival and then they looked at complete response rates, progression free and overall survival.
They do have now a 17.5 month follow up. And you know that's important because we know that the majority of these patients with primary refractory or early relapse disease will again relapse within typically within the first year of salvage. So, uh, with that median follow-up you can see here, there was a significant improvement in the event free survival where the median event free survival was actually not reached compared to a median event free survival of only 2.4 months in.
The standard of care arm with stem cell transplant with a hazard ratio of 0.35. And this was. For a self therapy trial, relatively large trial with about 184 patients, 92 on each arm. So you can see here that for their secondary endpoints there is also statistically significant complete response rate of 68% compared to 40% in the standard of care arm and an improvement in progression free survival that was not reached for the cell. Therapy group versus only 6.2 months in
00:05:48.221 --> 00:05:51.150 the standard of care arm for patients who received chemotherapy and transplant.

00:05:51.150 --> 00:05:53.400 And importantly,

00:05:53.400 --> 00:05:54.670 despite 67% of patients at crossing over from the transplant arm,

00:05:58.480 --> 00:06:01.798 the chemotherapy arm to receive licea cell,

00:06:01.800 --> 00:06:04.887 there was,

00:06:04.890 --> 00:06:05.552 you know,

00:06:05.552 --> 00:06:06.214 there still seem to be a trend favoring overall survival in patients who received licea cell where overall survival was not reached versus about 30 months in the standard of care arm.

00:06:06.214 --> 00:06:08.200 So this primary analysis with almost two year of follow-up confirmed
the significant clinical benefit
NOTE Confidence: 0.830955749
of Lisa cell over the standard of
NOTE Confidence: 0.830955749
care and given these very meaningful
NOTE Confidence: 0.830955749
improvements in complete response rates,
NOTE Confidence: 0.830955749
event free and progression free survival this
NOTE Confidence: 0.830955749
and a trend towards overall survival.
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This has now been approved and is
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considered the standard of care in the
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second line for patients with primary.
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Refractory or early relapsed lymphoma
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and there is another product on
NOTE Confidence: 0.830955749
the market but this was the one
NOTE Confidence: 0.830955749
that had the the updated at ASH.
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At the next one that I was also interested
NOTE Confidence: 0.830955749
in is abstract 154 where they looked
NOTE Confidence: 0.830955749
at really aggressive lymphomas that
NOTE Confidence: 0.830955749
00:07:12.616 --> 00:07:15.624 are high grade with Mick and BCL 2
NOTE Confidence: 0.830955749
00:07:15.624 --> 00:07:18.418 plus or minus BCL 6 rearrangements.
NOTE Confidence: 0.830955749
00:07:18.420 --> 00:07:20.828 So the so-called double or triple hit
NOTE Confidence: 0.830955749
00:07:20.828 --> 00:07:22.741 lymphomas and also double expressor
NOTE Confidence: 0.830955749
00:07:22.741 --> 00:07:24.365 lymphomas with dual overexpression
NOTE Confidence: 0.830955749
00:07:24.365 --> 00:07:26.300 of MYC and BCL two.
NOTE Confidence: 0.830955749
00:07:26.300 --> 00:07:29.380 And we know that those are very
NOTE Confidence: 0.830955749
00:07:29.380 --> 00:07:31.275 inferior responses to frontline
NOTE Confidence: 0.830955749
00:07:31.275 --> 00:07:33.700 and later lines of chemotherapy.
NOTE Confidence: 0.830955749
00:07:33.700 --> 00:07:35.955 They have very poor outcomes
NOTE Confidence: 0.830955749
00:07:35.955 --> 00:07:37.759 with stem cell transplantation.
NOTE Confidence: 0.830955749
00:07:37.760 --> 00:07:40.870 There have already been some
NOTE Confidence: 0.830955749
00:07:40.870 --> 00:07:43.327 presentations in terms of the role of
NOTE Confidence: 0.830955749
00:07:43.327 --> 00:07:45.710 carlee for this patient population,
NOTE Confidence: 0.830955749
00:07:45.710 --> 00:07:48.842 which has led to similar overall
NOTE Confidence: 0.830955749
response rates.

However, until this abstract, there had not been any data or update on the duration of response for these high risk groups and so this multicenter retrospective analysis evaluated survival.

Outcomes with Carti and also what happened to patients who produced double hit lymphoma or dual overexpress or who progressed after court. And there was a large group of patients, they looked at 408, eighty of which had double hit and 328 non double hit.
Some of them received access cells, some Tessa cell and a minority received licea cell and the clinical characteristics were similar between the double hit and the non double hit group. So the median follow-up was also about 18 months for surviving patients. So relatively long follow up. And what? What they saw actually was that patients did very well or whether they had double hits or dual express or lymphoma compared to other subtypes of lymphoma.
In terms of their progression free survival, overall response rates were no different, no statistically significant in the order of 65 to 70% complete response rates also. About 50%, which is what we expect with the run-of-the-mill diffuse large B cell lymphoma and. The median all overall survival was not reached actually for the double hit group versus 21 months in the non double hit and not statistically significant. However, importantly, patients with double hit lymphoma.
who progressed after court had a very poor outcome with overall survival that was very short only in the order of 2.7 months. So this is a group of patients. That you know, if they progress after Carti, where they do need better salvage strategies for. So this was the largest analysis basically that provided some update as to what happens with these patients with double hit or dual overexpress or lymphomas. So those patients should be encouraged to participate in car T trials and and
should be considered to receive it as a part of standard of care without fear that they’re not going to respond as well as the regular DLBCL. So umm, what about patients who progress after CD19 directed cortisol therapy? This is a very challenging group of patients. As you know they die within typically three months of progressing. And so this was a study from Stanford that looked at City 22 directed car T. In patients who had previously received CD19 directed car T cell therapy, this was initially published in Blood where they treated five.
They treated three patients who had had all high-risk features with five prior lines of therapy. Including Carte, in fact one of the patients had had commercial parties and targeting City 19 and then also a by specific City 19 and City 20 core T and had relapsed and all of those patients achieved a complete remission with the city 22 targeted car T so that led to this.

Moving forward to a larger study with 38 participants rate up to 84 years old with a good performance status. They were heavily pretreated.
with three to 8 lines of therapy.
The median was four.
In fact, about 33rd of patients did not have remission to any prior line of therapy.
About 20% had had a transplant
Prior City 19 core T cell therapy.
So the median follow-up has not reached the two year mark for some of the cohorts.
But very importantly the overall response rate and complete response rates were very high, higher than predicted 72% and CR of 53% which is similar to what we see with first line card T and all of the complete responses have actually been very durable with only one patient who achieved the CR having relapsed. And and you can see there the progression free survival and overall survival curves on the left look actually very good for a second line cartee and and compare.
very favourably to first line chart. And as you can see the majority of
the patients experienced grade one or two cytokine release syndrome
and neurologic toxicity associated with immune effector cell therapy.
Interestingly, what they saw in the higher dose level, which was dose level 2 is that there was a significant number of patients that experienced what is a syndrome that’s very much like of falsity claim for histiocytosis. Got a name of its own of carnage LH.
where it’s a syndrome of five ferritin, cytopenia square apathy and liver abnormalities and there was just in general more toxicity in those level 2.

So dose level one had very was the one that had the results I showed you. That’s the dose that they’re moving forward with.

And then one patient developed treatment related MSDS and AML without evidence of lymphoma relapse which again underscores the importance of us following this patients long term.

Um, so another study of interest is actually? Engineered allogeneic core T cell therapy,
all the commercial products are autologous products and also the one that I just presented the city 22 was an autologous product. This is a an aloe gamma delta cortisol therapy and actually it’s a first in class it instead of targeting C19 like the commercial products it targets. It expresses MHC independent gamma delta T cell receptor. So the risk of GVHD is low without
the need for gene editing which is more complex and takes longer. So this is the industry’s most advanced core asset using Gamma Delta and they presented the multicenter phase one trial for relapsed refractory B cell lymphoma. Patients had to have CD20 expression on their tumor cells. They had to have received at least two prior lines of therapy and at ash they presented the data for their first dose cohorts in a three by three dose escalation scheme and in dose Level 3. They did allow patients to be reduced a week later without any lymphodema.
additional lymphodepletion chemotherapy.

So the median number of therapies was four range two to five, they were heavily pretreated. And four of the nine patients who were evaluable had received prior anti CD19 car T cell therapy. It was very well tolerated. There was no reported graph versus host disease and there were no Grade 3 cytokine release syndrome or neurologic toxicity. And this is their preliminary efficacy data. So as you can see there’s six months complete response rate was in the order of 67% and for patients in those Level 3,
actually a small number of three patients, they had a complete response rate of 100%.
So this compares very favorably to autologous products and the advantage being that it’s an off the shelf product, so the turnaround time. It’s extremely short. The cells perhaps are fitter than those obtained from a heavily pretreated patient, without much in the way of toxicity. And then more recently, the company opened a dose level 4 cohort, so now they have a larger number of patients. However, they do not have particularly the higher

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dose levels of three and four do not have very short follow-up and the patients who have been treated so far, a good number of them if you see her in red have actually relapsed and so the durability of responses is still questionable and. You know, it has investors pretty much really worried. You know about how this product is going to do in the long run. But again we just need to see what’s gonna happen to these patients who are getting the higher doses with longer follow up. And you can see that the patients here
highlighted in yellow are patients who all had prior cortisol therapy, anti CD19 cortisol therapy and they all have achieved complete remission and. Some of them are still responding to treatment. So I’m not going to spend a lot of time here, but just to shift gears to bring your attention that car T cell therapy is also approved for patients with follicular lymphoma. In the third line setting and this is based on two trials, Zuma five with the access cell and
Elara with the TISAGENLECLEUCEL.

So this was the Zuma 5 update with a 3 year survival.

You can see here that the overall response rates and the complete response rates with Car T cell therapy are very high in the third line setting in both patients with follicular lymphoma and also in patients with marginal zone lymphoma and progression free survival is very good for these patients.

With relatively long term follow-up, because in the third line setting, typically what we would expect
NOTE Confidence: 0.90459693375
00:19:46.310 --> 00:19:48.970 from a third line therapy is a
NOTE Confidence: 0.90459693375
00:19:48.970 --> 00:19:51.179 shorter duration of response that
NOTE Confidence: 0.90459693375
00:19:51.179 --> 00:19:53.402 is typically less than two years
NOTE Confidence: 0.90459693375
00:19:53.402 --> 00:19:55.250 and sometimes less than one year
NOTE Confidence: 0.90459693375
00:19:55.318 --> 00:19:57.098 depending on the product used.
NOTE Confidence: 0.90459693375
00:19:57.100 --> 00:19:59.404 But here you can see that the median
NOTE Confidence: 0.90459693375
00:19:59.404 --> 00:20:01.291 PFS for follicular lymphoma was
NOTE Confidence: 0.90459693375
00:20:01.291 --> 00:20:03.769 fourteen months and was not reached
NOTE Confidence: 0.90459693375
00:20:03.769 --> 00:20:05.890 for a marginal zone lymphoma.
NOTE Confidence: 0.90459693375
00:20:08.460 --> 00:20:12.892 Umm. And then uh, similar data from the
NOTE Confidence: 0.764501193846154
00:20:12.892 --> 00:20:17.148 Elara study looking at Tisagenlecleucel,
NOTE Confidence: 0.764501193846154
00:20:17.150 --> 00:20:20.214 so also targeting CD19, but if with a
NOTE Confidence: 0.764501193846154
00:20:20.214 --> 00:20:22.673 different Co stimulatory molecule that
NOTE Confidence: 0.764501193846154
00:20:22.673 --> 00:20:29.104 is 41B with over two years of follow-up,
NOTE Confidence: 0.764501193846154
00:20:29.110 --> 00:20:31.480 patients who achieved complete response
NOTE Confidence: 0.764501193846154
represented here in the top curve have not reached their median progression free survival and the anticipated. For all two year progression free survival is about 60%. Umm. So umm. There was also this additional presentation that compared access cell to other third line standard of care therapies for relapse refractory follicular lymphoma and this was retrospective in nature but compared to scholar five study that does show a substantial improvement with axicom tagen with the cellular therapy compared to other third line.
00:21:17.850 --> 00:21:20.360 Therapies.
00:21:20.360 --> 00:21:21.436 But again,
00:21:21.436 --> 00:21:24.664 it's not a randomized study and
00:21:24.664 --> 00:21:26.120 it's different to.
00:21:26.120 --> 00:21:28.395 There may be differences in
00:21:28.395 --> 00:21:30.215 baseline characteristics that do
00:21:30.215 --> 00:21:32.318 restrict cross study comparisons,
00:21:32.318 --> 00:21:34.816 but this is what the progression
00:21:34.816 --> 00:21:37.314 free overall survival and time to
00:21:37.314 --> 00:21:39.974 next treatment look like in blue for
00:21:39.974 --> 00:21:41.921 patients who had cortisol therapy
00:21:41.921 --> 00:21:44.615 versus at the bottom in red for
00:21:44.615 --> 00:21:47.800 patients who have who would have had
00:21:47.800 --> 00:21:51.610 other third line standard of care therapies.
00:21:51.610 --> 00:21:54.666 And this was published recently in in blood.
And then I want to also bring attention to the study published by our very own group led by Kunal under the mentorship of Scott Huntington where the cost effectiveness of car T cell therapy was compared in adults with relapsed refractory follicular lymphoma and. The cost of core T cell therapy is about $730,000 as opposed to $450,000 for the standard of care with an eyesore of about 80,000 for quality adjusted life years. But I think considering the risks associated with car T cell therapy in terms of cytokine release...
syndrome and neurologic toxicity.

We need to do a better job and have a longer follow-up and randomized comparisons to other lines of therapy. So that we subject these patients to who have the majority of them have long progression free survival so that we subject them to minimal toxicity as we can. And particularly now we have a new bispecific antibody approved for follicular lymphoma which is not. A part of these? Cost effectiveness comparison here, but I think that’s also going to play.
00:23:27.919 --> 00:23:30.966 a role and we need to see how in the
NOTE Confidence: 0.839117332222222
00:23:30.966 --> 00:23:33.642 long run we’re going to best sequence
NOTE Confidence: 0.839117332222222
00:23:33.642 --> 00:23:35.807 these these therapies based on.
NOTE Confidence: 0.877115921428571
00:23:38.250 --> 00:23:40.140 The the way of administration
NOTE Confidence: 0.877115921428571
00:23:40.140 --> 00:23:42.030 you know multiple times versus
NOTE Confidence: 0.877115921428571
00:23:42.102 --> 00:23:43.870 one time patient preference,
NOTE Confidence: 0.877115921428571
00:23:43.870 --> 00:23:47.262 toxicities and cost effectiveness.
NOTE Confidence: 0.877115921428571
00:23:47.262 --> 00:23:50.360 So um. I’m going to switch gears
NOTE Confidence: 0.877115921428571
00:23:50.360 --> 00:23:51.760 now to mantle cell lymphoma.
NOTE Confidence: 0.877115921428571
00:23:51.760 --> 00:23:55.440 This is abstract 623 which is phase
NOTE Confidence: 0.877115921428571
00:23:55.440 --> 00:24:01.901 by specific anti CD20, anti CD 19.
NOTE Confidence: 0.877115921428571
00:24:01.901 --> 00:24:04.463 We do have a product that’s
NOTE Confidence: 0.877115921428571
00:24:04.463 --> 00:24:07.065 Brexit prapta gene that’s already
NOTE Confidence: 0.877115921428571
00:24:07.065 --> 00:24:10.650 approved but it is very toxic and.
NOTE Confidence: 0.83040595
00:24:13.070 --> 00:24:16.566 There are. There’s the hypothesis
of this study was that if we use a bispecific tandem targeting product targeting both City 20 and city 19 with.

Expansion with the I7 and I-15 that we might get less exhausted car products with more durable, even more durable clinical activity.

And this product actually is manufactured using climax prodigy device. It’s a fresh infusion and the manufacturing time is quite short, somewhere between 8:00 and 12 days.

So for patients with rapidly progressive mantle cell lymphoma. It’s a great product to have that we
can infuse rapidly and you can see here

that the manufacturing rate was very high,

There were no Grade 3 cytokine release syndrome cases and there was only one patient with grade three eye cans.

They were patients that had at least 4 lines of therapy.

They were all exposed to BTK inhibitors and you can look at a long term progression free survival.

Looks excellent and we already have the diffuse large B cell lymphoma study but we’re gonna go ahead and open this for mantle cell lymphoma at Yale.

And then finally,
I’m going to switch gears to talk a little bit about T cell and B cell leukemia. This was published in Blood this year. As we know, finding a target for T cell lymphomas and leukemias has been challenging. City 7 is a very commonly expressed antigen, but it is expressed in the T cells and there is concern that there’s going to be fratricide the way this is a Chinese group that they actually developed. A novel methyl method of CD7 antigen masking that makes the cells fratricide resistant and this was their initial study was published earlier of these.
naturally selected core T cells without genetic modification and then abstract looked at 53 patients that had. Relapse refractory T cell all or T cell lymphoblastic lymphoma treated with this therapy you can see they were very heavily pretreated group of patients about half of them had more than 5% blast and their mayoral some of them had extramedullary disease even and. They had. Very decent overall end event free survival in this relapse refractory setting. So the median follow-up is pretty long, 206 days. Some of the data is here.
I’m not going to go into it in detail, but suffice it to say that the 18 month overall survival 75% and event free survival of 53% and. Some patients were bridged to an allogeneic stem cell transplant, but many patients were not and the ones that achieved CR were able to maintain the CR. So umm, this was highly effective. They including in patients with extramedullary involvement or patients with have prior cart and they did identify a patients with the SIL tile one having a Porter response.
and early relapses and when relapses occur they did see loss of city 7 expression.

Now the Stephan Grupp group at Penn presented this abstract.

17 patients were infused.

All of them had sitting negative disease that had relapsed.

Postcard T and some of them had received blinatumomab and inotuzumab and nine had had a prior transplant including
three with multiple prior transplants.

They the bone marrow blasts pre infusion were high and you can see here that the probability of survival for this group of patients getting city 22 therapy. Is is pretty good the 18 month? Uh, overall survival, actually they have been even longer follow-up for this study, but. You can see here that the probability of survival. At 18 month at 18 month Mark is still relatively decent for patients who otherwise most of them as you all know would have very poor outcomes.
and would succumb to their disease.

So now they have almost 30 months of follow-up and the median relapse free survival is about five months and overall survival is about 16 months.

So there were two patients that also worried treated with this for city 22 relapse disease after initial infusion and one of them went into remission again. So there is a possibility of retreating these patients and all of that data is here. But I just want to emphasize that we can salvage a portion of patients who fail CD 19. You can see here 77% achieve CR and including undetectable MRD by flow.
So you know, they do develop toxicity and particularly.
The risk of infections is extremely high and cytopenias after back-to-back Carter cell therapies like this. So they had successful manufacturing again with an autologous product and there were high initial response rates but there are later recurrences and I think what was being looked at now is how to combine City 19 and City 22 to to decrease the risk of relapse. I’m not gonna. I know we’re running out of time, so I’m not going to spend too
much time on on this abstract,

but it did compare.

Car T cell therapy in both patients

who had received a blinatumomab and

patients who had not

this propensity score matching analysis.

And what they actually find found

received blinatumomab and this is

in the adult population where they did

this propensity score matching analysis.

And what they actually find found

is that the group that received car

t cell therapy with access cell had

much higher complete response rates

of 85% versus patients who had.

Other standard of care approaches also

predominantly chemotherapy of 35% with

a median overall survival that was
higher at 16 months versus about five months. And this was true in both patients who were treated with blue 99-O2 zimat before, but also patients who were treatment naive that they both of those groups. For both of those groups we should consider car T because patients do respond. And and may have improved outcomes compared to other standard of care approaches. The relapse phenotype is very important and it informs our therapeutic decisions. So about 22% of patients will relapse with City 19 positive disease, about 15% with city 19 negative AL and about 3% have lineage switched.
And the group that has lineage switch actually is the group that has the poorest outcomes and they have quite poor. Outcomes, even with cartee cell therapy. And then post Cartee there is even more increasing complexity of the relapse immunophenotype and the most difficult of all group to deal with is the group that postcard team now have both city 19 and CD20 negative AL and again the patients with this lineage switch, So what? This is uh the group from the NCI new Rally that published recently and also presented at ASH that patients who get blinatumomab prior to car T cell therapy and do not achieve a
00:33:41.782 --> 00:33:44.503 complete response to blinatumomab have
00:33:44.503 --> 00:33:47.701 the have very poor outcomes postcard
00:33:47.701 --> 00:33:52.194 T and and that again having city 19
00:33:52.194 --> 00:33:55.342 damn disease pre Carty will influence.
00:33:55.342 --> 00:33:58.078 The postcard T cell relapse phenotype
00:33:58.078 --> 00:34:01.193 that a lot of those patients will
00:34:01.193 --> 00:34:03.630 have city 19 negative disease at,
00:34:03.630 --> 00:34:05.639 at the time of relapse and they
00:34:05.639 --> 00:34:07.749 will also have very poor outcomes.
00:34:07.750 --> 00:34:10.423 So it’s very important in a L for us
00:34:10.423 --> 00:34:13.347 now to really break down the groups
00:34:13.347 --> 00:34:15.911 and follow these patients not just
00:34:15.911 --> 00:34:18.275 with B cell aplasia but actually
00:34:18.275 --> 00:34:22.202 follow them even more closely with
00:34:22.202 --> 00:34:26.117 MRD by NGS techniques because.
Some patients. May still have some persistent B cells there, but still relapse early and we really need to move those patients toward clinical trials or doing an urgent allogeneic stem cell transplant. So I think that perhaps we'll leave questions at the end to allow doctor Gowda to present. All right. That was an awful lot of exciting information. There is one question. Doctor Gowda is presenting.
So next is Doctor Lohith Gowda. He’s assistant professor in the transplant room. Cell therapy program here at Yale, and he’s going to go over some new and exciting transplant results from the ASH meeting.

Hello everyone and it’s a Friday afternoon. I promise I’ll get you guys out for lunch in time. No conflicts of interest.

Here are my thoughts comments for the study investigators, from the study investigators, the study groups, and different.
individuals who shared their slides.

The main objective of today’s talk is largely club under three main headings.

Yeah, as we all know, allergenic transplantation as a 70 year track record of cure, but relapses do happen.

So I’m going to present you some data about the role of preemptive maintenance post transplant.

One of the Achilles heel of alleged extract point has been graph to source disease normally would present under 2 headings, acute and chronic graft resource disease.

Based on the most recent data.
that I'm going to present, looks like you might have one drug which is taking care of both of that. So that's the phase three study. And finally, I know it's the last talk of our CME series, but throughout my life group discussion, we've learned that, you know, there are many novel, exciting advances that drugs are coming through. But I'm here to convince you guys that despite those drug advances, allergic stem cell transplant.
is actually at the forefront and we anticipate a high number of patients going forward to receive other transplant because outcomes have gotten significantly better.

And I’ll bring about some data to support that statement. Alright. And the first study that I’m going to be talking to you is, a study that was done across is a study that was done across from CFO which was using ID, its two mutation sub group which happens in about 20% of the cases, 20% of patients. We all know that Doug Anderson name is approved in mutant ideas
00:36:58.998 --> 00:37:01.658 plus two types index subgroup.

00:37:01.658 --> 00:37:04.202 Those with the last refractory AML

00:37:04.202 --> 00:37:06.867 D or R is about 40% but there are

00:37:06.867 --> 00:37:08.400 responses do not last long with the

00:37:08.451 --> 00:37:10.512 median duration of response about 5.8 months.

00:37:10.512 --> 00:37:12.258 So the group here actually tried

00:37:12.258 --> 00:37:14.535 to do a maintenance concept post

00:37:14.535 --> 00:37:16.167 transplant wherein they introduced

00:37:16.167 --> 00:37:18.548 the drug post transplant from days 50

00:37:18.548 --> 00:37:21.174 to 18120 at about 100 milligrams per day.

00:37:21.180 --> 00:37:22.776 The plan was to give for about

00:37:22.776 --> 00:37:24.334 two years and each cycle would

00:37:24.334 --> 00:37:25.694 last for about 20-8 days.

00:37:25.700 --> 00:37:26.800 It’s a small group study.

00:37:26.800 --> 00:37:28.064 The total was 15.
They included patients and had a transparent CR1CR2 onward MRD positive cases post alert CT as well. In this study, the median time to start the drug was 105 days. Various GVHD and various transparent relative conditionings. The median age is population with about 58 years and all great adverse events during the study was reported for the first two cycles, whereas for grade 3 or higher for subsequent cycles were reported. In the first two cycles, it’s usually all of them was included.
The methodology used to monitor for DS2 was a digital doctor PCR. And as has been shown here, if you focus on the right and one of the commonest concern that we have of using these drugs is cytopenias. The risks of cytopenias, lymphopenia, anemia and neutropenia is was pretty modest and it's not really significant for those of you use the drug in the pre transplant context that's a major issue but those are usually the people that have an abnormal marrow and the disease in association.
So I was surprised to see the side opinions although existing wasn’t significantly high and GI side effect was rather common side effect interestingly at least as was presented with the median follow-up of 17 months the one and two are progression free survival was about 100%. Common when we talk about maintenance, we talk about flip 3 limited studies. We’re waiting on the full data of the BMT that used the three Nevada. But I think outside of that idea as to where we have targeted agents is an important subgroup and I thought this would be of meaningful practical
00:38:58.250 --> 00:38:59.758 use as we treat our patients.

00:39:02.270 --> 00:39:03.680 The other maintenance stadium going

00:39:03.680 --> 00:39:05.989 to talk about is a phase one study.

00:39:05.990 --> 00:39:08.470 Some of you might be aware that when

00:39:08.470 --> 00:39:10.502 the clients has also been integrated

00:39:10.502 --> 00:39:12.267 in the transplant preparative regimens.

00:39:12.270 --> 00:39:14.718 The study was published by Garcia

00:39:14.718 --> 00:39:16.350 and colleagues from Boston.

00:39:16.350 --> 00:39:17.885 What they're now presenting is

00:39:17.885 --> 00:39:19.746 when you integrate whether class to

00:39:19.746 --> 00:39:21.685 flow data and cell phone which is

00:39:21.685 --> 00:39:23.020 appropriate regiment that’s commonly

00:39:23.020 --> 00:39:24.830 used in the transplantation context.

00:39:24.830 --> 00:39:27.845 There are trying to add the HMM and when

00:39:27.845 --> 00:39:31.539 it reflects as a maintenance post transplant.
The last ticket put on really is focused on using is a Satanism maintenance and there are many many interesting reports in that regard. But the combination as you realize the doublets and triplets are making forays in the non transparent context. And I also see this now coming in the post transplant context. And this is one of those phase one study to identify the doses. So they started out with 400 milligrams from Day 1 to 14 is the cycling was used at 36 milligrams per meter square on days one to five. A lot of user trials in the
00:40:00.631 --> 00:40:01.600 past have tried different.

00:40:01.600 --> 00:40:03.408 This is different days and and I think

00:40:03.408 --> 00:40:05.236 at least in this study they kind of

00:40:05.236 --> 00:40:06.948 narrowed it down to a slightly lower

00:40:06.948 --> 00:40:08.761 dose which with the hope that perhaps

00:40:08.770 --> 00:40:11.730 the combination is well tolerated.

00:40:11.730 --> 00:40:12.954 As was expected.

00:40:12.954 --> 00:40:15.624 You know, cytopenias worst thing.

00:40:15.624 --> 00:40:17.249 Neutropenia was 95%,

00:40:17.249 --> 00:40:18.416 thrombocytopenia was 91%.

00:40:18.416 --> 00:40:20.361 So cleverly the DLT definition

00:40:20.361 --> 00:40:21.929 that study was grateful.

00:40:21.930 --> 00:40:23.518 Looping or thrombocytopenia greater

00:40:23.518 --> 00:40:25.882 than two weeks with a median follow-up

00:40:25.882 --> 00:40:27.347 of 12 months follow-up regardless
00:40:27.347 --> 00:40:29.070 of the patient got maintenance.
NOTE Confidence: 0.772969496923077
00:40:29.070 --> 00:40:30.715 The one year progression free
NOTE Confidence: 0.772969496923077
00:40:30.715 --> 00:40:32.690 survival was in relapse report here.
NOTE Confidence: 0.772969496923077
00:40:32.690 --> 00:40:35.724 The OS was 70%, PFS was 57%.
NOTE Confidence: 0.772969496923077
00:40:35.724 --> 00:40:37.608 There was no non relapse mortality
NOTE Confidence: 0.772969496923077
00:40:37.608 --> 00:40:39.457 suggesting it’s it’s a safer combination
NOTE Confidence: 0.772969496923077
00:40:39.457 --> 00:40:41.910 to push you in the post transplant context.
NOTE Confidence: 0.772969496923077
00:40:41.910 --> 00:40:44.310 But relapse was still of concern
NOTE Confidence: 0.772969496923077
00:40:44.310 --> 00:40:45.910 despite using a doublet.
NOTE Confidence: 0.772969496923077
00:40:45.910 --> 00:40:47.788 Nomination in the post transplant context.
NOTE Confidence: 0.67735497125
00:40:50.530 --> 00:40:53.666 Now let’s switch gears and talk about GVHD.
NOTE Confidence: 0.67735497125
00:40:53.670 --> 00:40:56.855 Now many of you know that calcination
NOTE Confidence: 0.67735497125
00:40:56.855 --> 00:40:58.684 based combination tachyons for
NOTE Confidence: 0.67735497125
00:41:01.372 --> 00:41:04.068 methotrexate has been a standard of care
NOTE Confidence: 0.67735497125
00:41:01.372 --> 00:41:04.068 for the last four decades.
NOTE Confidence: 0.67735497125
00:41:04.070 --> 00:41:06.206 So in order to explore more on how
we can optimize and identify the best combination BMT CTN 1203 study ran A3 ARM study where in the check to conventional arm track methotrexate with Bortezomib tack methotrexate with the chemokine inhibitor. Versus a full side arm, the phase two study and the winner of that study was the post I am which we call the PCI. This was then taken to a phase three study where PCI tackled Amos and microphone. It was compared against the historical control which is stacked and methotrexate. The study allowed reduced intensity.
conditioning for individuals 18 years or older that have controlled disease and peripheral blood stem cell grafts were chosen. Donors could be 6 out of 6 matched or 7 to 8 or 8, six out of 6 actually matched donors or 11 antigen mismatched. Unrelated donors were also aligned. The primary endpoint of the study was one year GRFS has been defined here, even being defined as grade three to four Q GVHD, chronic GVHD. Requiring systemic must suppression, relapse, progression, adapt, and there were a few traditional
NOTE Confidence: 0.67735497125
00:42:11.764 --> 00:42:12.680 standard transplant,
NOTE Confidence: 0.67735497125
00:42:12.680 --> 00:42:15.450 Putin and secondary endpoints chosen.
NOTE Confidence: 0.67735497125
00:42:15.450 --> 00:42:19.517 Here’s just a summary of what happened.
NOTE Confidence: 0.67735497125
00:42:19.520 --> 00:42:21.280 There was slightly more men.
NOTE Confidence: 0.67735497125
00:42:21.280 --> 00:42:23.574 The median Asia was about 66%.
NOTE Confidence: 0.67735497125
00:42:23.574 --> 00:42:26.332 Almost half of the people had kind
NOTE Confidence: 0.67735497125
00:42:26.332 --> 00:42:28.578 of performance score less than 90.
NOTE Confidence: 0.67735497125
00:42:28.580 --> 00:42:31.135 It had a wide range of hematologic
NOTE Confidence: 0.67735497125
00:42:31.135 --> 00:42:35.196 malignancies.
NOTE Confidence: 0.67735497125
00:42:35.200 --> 00:42:37.064 And and here’s the percentage
NOTE Confidence: 0.67735497125
00:42:33.810 --> 00:42:35.196 of related unrelated,
NOTE Confidence: 0.67735497125
00:42:35.200 --> 00:42:37.064 unrelated donors with unrelated
NOTE Confidence: 0.67735497125
00:42:37.064 --> 00:42:39.394 donor being the Communist platform.
NOTE Confidence: 0.67735497125
00:42:39.400 --> 00:42:41.325 They did allow different regiments
NOTE Confidence: 0.67735497125
00:42:41.325 --> 00:42:42.480 to be chosen.
That is blue flu, flu, mail.

To go with which perhaps in modern day or some of the commonest options used.

Planned post transplant maintenance therapies was used in about approximately 25% of the people in the post I am orsus, 22% in the non Siam.

The study did meet the primary endpoint, the one year graft also source disease relapse with survival was superior with the post transplant cyclophosphamide as has been shown here with that has a ratio of 0.64.

The rates of great three to four Q GVHD was 6.3% versus 14.7% suggesting post
NOTE Confidence: 0.67735497125
00:43:18.315 --> 00:43:21.185 size able to decrease graph resource
NOTE Confidence: 0.67735497125
00:43:21.185 --> 00:43:24.599 disease and same with chronic graft
NOTE Confidence: 0.67735497125
NOTE Confidence: 0.67735497125
00:43:26.310 --> 00:43:28.940 The Posi arm had about 12.5%
NOTE Confidence: 0.67735497125
00:43:28.940 --> 00:43:30.900 methotrexate armor 25% basically
NOTE Confidence: 0.67735497125
00:43:30.900 --> 00:43:34.072 halving the risk of chronic GVHD
NOTE Confidence: 0.67735497125
00:43:34.072 --> 00:43:36.440 requiring suppression and importantly
NOTE Confidence: 0.67735497125
00:43:36.440 --> 00:43:38.600 GVHD prelapsarian survival was
NOTE Confidence: 0.67735497125
00:43:38.600 --> 00:43:41.780 almost 62% compared to 45% off.
NOTE Confidence: 0.67735497125
00:43:41.780 --> 00:43:43.844 Is concerned that when using your
NOTE Confidence: 0.67735497125
00:43:43.844 --> 00:43:45.840 depleting agents there’s the GL impact.
NOTE Confidence: 0.67735497125
00:43:45.840 --> 00:43:48.066 Gmail is impacted as is shown here.
NOTE Confidence: 0.67735497125
00:43:48.070 --> 00:43:50.415 It seems to be disentangled and
NOTE Confidence: 0.67735497125
00:43:50.415 --> 00:43:52.125 relapse and progression was not a
NOTE Confidence: 0.67735497125
00:43:52.125 --> 00:43:53.957 concern with the application of
NOTE Confidence: 0.67735497125
post transplant cyclophosphamide compared to methotrexate.

- Treatment related mortality:
  - 12% if you all read our books back about 10-15 years or treatment later mortality transplant used to be about 25-30%. Now that number has come down significantly and the overall survival in this arm was overall survival at this time point actually didn’t change,

- 77% of interest to note here about 17.827 is that overall survival at this time point actually didn’t change, it was 77%, also 72%.

But remember the study endpoint was GRFS.
So then people tend to ask what...

what about the secondary outcomes...

in highlighted in purple are the ones that were not significant...

...in the dark bright yellow is the ones that are significant.

When your survival didn’t change, when your disease with survival didn’t change, TRM did not change.

Statistically, cumulative incidence or Q GVHD grades two to four did not change.

But what did change though is cumulative incidence of acute GBS day 100 grades three to four.
You know if you have grade one and two GSD most times it’s not of a significant concern, the higher grade. It’s the other one we are concerned about with the post. I was 6.3% compared to about 14.7%. Similarly chronic GVHD at 12 months was 21% compared to 35%. The salary carrier was slightly slower both for neutrophils and platelets and as is commonly expected and the risk of breakthrough infections will not not significantly higher at 12 months now is the risk of CMV reactivation, importantly immunosuppression. free survival at one.
Yeah, was better off as has been shown here.

The other other question people ask is about, you know, what’s the risk of graft failure or how does the chimerism play out?

As shown here, they have definitions for what’s the full chimerism? Mixed graph projections. There’s really no significant differences based on that between the two treatment arms.

Specifically people ask that, you know, this is making significant progress in the field of acute and chronic GVHD.
Does it have any other side effects?

Well, you know the risk of acute or chronic GVHD was significantly lower, but they did come up a concern about some organ failure and we're looking for the full manuscript to see which particular organs were affected as it was slightly higher in the post transplant cyclophosphamide arm compared to the conventional care. There was no increase in relapse slash progressive, which is critical importance to our people.
There was slightly delayed hematopoietic recovery. There was more grade 2 GI events in the infection forms, but they're mostly in the first month. Based on the findings, the field is slowly moving towards the option of using postai as a reduced intensity conditioning GVS 3 prophylactic options going forwards in patients who are well matched. There are ongoing studies to look and look for suitable biomarkers and those will be coming out over the next few months.
In that is available, one of our leaders in the leukemia program asked me to condense some of the TCP slides with the ash. Hematology slides because those are really practice changing here. I’m presenting a study that’s called the CRF study that Seropian was the principal investigator on site for this. This was a multicenter pivotal phase three study of ISOMAP which is going to talk to you about prior to allogeneic stem cell transplant versus conventional care in older patients with acute relapse refractory leukemia. Remember the majority of the patients
actually don’t get to transplant.

Look at the median age for these patients that developed leukemia is somewhere around late 60s, early 70s. And they’re transplant ineligible. So in that patient population while we were at multiple new drug developments transplanted historically considered not suitable. So into that domain, this trial is trying to now make headways with some interesting results as I’m going to show to you all here. Emilyn generally has got poor prognosis.
On top of that, if you add old rays it makes it complicated. There are several reasons for that. Historically always believed intensive induction and accessory to keep permission going for long term. But most of these patients are not able to tolerate it and even if they tolerate it, the toxicities are higher if you continue to long terms and that leads to substantial treatment related mortality. Now since transplant is a higher intensity of treatment compared to the non transparent option, the term tends to go up in the population. However we are able to get some of those.
Patients who have relapsed or practicing at back into remission and one of the conventions that we tend to fall in relapse refractory AML is we we tend not to transplant those patients in active disease because you know back maybe prior to 2000 when we used to do labs attracts AML who had active disease when the data is normal drugs though you know risk of relapse was pretty high in the Tiana was high. So based on that there are multiple novel drug development strategies that have come on. But what I have is not trying to do
is trying to address the question
So first of all, what is our map?
Ahmad is basically a combination of things.
They have a CD45 antibody that’s conjugated to radioactive iodine and it is designed to deliver targeted myeloablative radiation dose to the hematopoietic cells and immune cells and then supplemented with reduced intensity conditioning priority analogy and stem cell transplant.
Remember good old days when we used to do transplant, we used to use radiation based regimens, TBI kind of.
While it’s useful to suppress your immune system and radical Kenya and the narrow, it can cause significant argument toxicity because it’s a total body radiation. Here they’re trying to develop targeted radiation to leukemia cells, bone marrow stem cells, to address the primary problem of cute myeloid leukemia. With induction and conditioning, the hope here is that usage of this drug would allow rapid access to bone marrow transplant for multiple patients who relapsed refractory phenotype. So this was a prospective randomized
strains study which is a phase three study exclusively for patient populations greater than 55 to compare rates of durable complete remissions that would last greater than 180 days following initial complete remission between the two arms. So the study was randomized for IMAP followed by transplant versus physicians choice of conventional care for transplant and physicians. The Commission came included more than 20 different drugs that reflect contemporary practice, including the BCL 2 inhibitor, etc.
Ohh here’s how the study design goes.

People have relapsed phenotype greater than 55, randomized 1 to 1.

Well then look for whether they’re here or not and if it’s a CR, what’s the duration of CR whether the last six months.

Whereas with the conventional care arm depends whether they get into CR no CR.

If they’re the CR then they could go to the standard of care transplant.
Our standard of care physicians choice. This concept of drug delivery needs hospitalization slightly earlier than what we would normally do in the context of a bone marrow transplant. Those patients were admitted around day 19 to get a test dose. After radioactive iodine and then they have to be kept in the hospital for a few days until the body eliminates all the radioactive doses. The data is then sent across to develop a therapeutic dose of the ILAB which is then given around day minus 12. You wait for about 8 days for that to take effect.
00:51:31.960 --> 00:51:33.976 Remember these are people who have
00:51:33.976 --> 00:51:35.669 active glass and activities coming
00:51:35.669 --> 00:51:37.678 into this this drug would you know
00:51:37.678 --> 00:51:39.292 Oblate most of those patients and
00:51:39.292 --> 00:51:41.324 then you go and use the principles of.
00:51:41.324 --> 00:51:43.298 Transplant just to use low dose of
00:51:43.298 --> 00:51:45.128 immuno ablation with fludarabine and
00:51:45.128 --> 00:51:46.993 TBI which lymphodepletion and also
00:51:46.993 --> 00:51:48.981 eradicate some of the disease followed
00:51:48.981 --> 00:51:50.940 by hematopoietic stem cell rescue and
00:51:50.940 --> 00:51:53.670 the option of GST prophylaxis is tactile
00:51:53.670 --> 00:51:57.760 limus cyclist form with microphone.
00:51:57.760 --> 00:51:59.040 Here’s the concept now.
00:51:59.040 --> 00:52:00.640 Equal number of patients randomized.
00:52:00.640 --> 00:52:02.760 I’m unconventional.
Case 767766 patients received therapeutic dose. 66 were able to get a transplant. Per protocol analysis, 59 were eligible. In contrast, a number of people in the conventional care that were able to get to CR was 14. For those who got to CR and were fourteen of them were all fourteen. Not able to get to CR was 62. For those who got to CR and were fourteen of them were all fourteen. Not able to get to CR was 62. Likely went on to receive what you call palliative care options.
00:52:31.440 --> 00:52:32.768 or no further treatment.

00:52:32.770 --> 00:52:33.866 Crossed over to IMAP.

00:52:33.866 --> 00:52:35.822 The costs over was allowed for people

00:52:35.822 --> 00:52:37.593 who did not reach CR after having

00:52:37.593 --> 00:52:39.529 been in the conventional care arm,

00:52:39.530 --> 00:52:41.756 but 44 crossed over to MMA.

00:52:41.760 --> 00:52:42.514 Of those,

00:52:42.514 --> 00:52:44.399 4440 did get to allergenic

00:52:44.399 --> 00:52:45.530 stem cell transplant,

00:52:45.530 --> 00:52:48.392 and 38 were protocol and were

00:52:48.392 --> 00:52:50.300 eligible for protocol analysis.

00:52:50.300 --> 00:52:50.970 I’m interested,

00:52:50.970 --> 00:52:53.315 I’m trying to run through this past.

00:52:53.320 --> 00:52:55.804 The median age is about in the mid 60s.

00:52:55.810 --> 00:52:57.218 We had favorable intermediate
and adverse risk.

It included primary induction failure earlier relapse,

relapse,

refractory second plus relapse

emphasis because those of you are familiar with asset trial did not include later relapses and only with their earlier relapses, all of them at about 3 lines of medium therapies, people had already exhausted targeted therapies.

About 60% of the patient actually had a KPS score performance score.
less than 90% and the matter presented and the matter of last percentage was around 30% and 28% which is significantly high truly reflecting active disease population. And I'm here are the doses that are being presented, whether you got amab or crossover doses of the matter was about Gray here where the divided the crossover time to UTC from the randomization was 29 days. With the standard of care on the median time was 66 days. In the crossover arm the median
days was 61 days.

NOTE Confidence: 0.7668775975

Engraftment was very good.

NOTE Confidence: 0.7668775975

The median time was 14 days

NOTE Confidence: 0.7668775975

which is what we normally see

NOTE Confidence: 0.7668775975

with our standard transplant.

NOTE Confidence: 0.7668775975

Somewhere around there for platelet

NOTE Confidence: 0.7668775975

was about 19 days and the standard

NOTE Confidence: 0.7668775975

HCT the kind of matching up nicely

NOTE Confidence: 0.7668775975

and the comorbidity index as I was

NOTE Confidence: 0.7668775975

showing here approximately 5050.

NOTE Confidence: 0.7668775975

When when you look at durable yards.

NOTE Confidence: 0.7668775975

Here’s the number.

NOTE Confidence: 0.7668775975

About 22% of the patients that I

NOTE Confidence: 0.7668775975

had durable CR on the study endpoint

NOTE Confidence: 0.7668775975

versus none in the conventional

NOTE Confidence: 0.7668775975

curriculum in the crossover arm,
91% received transplant with
52% of those receiving CR.

Posted city maintenance with the TK,
I was only allowed for a more
patient with three mutations,
those toward BCR able
TRANSLOCATIONS that screening.
And these are the the survival cost.
The oral survival was doubled with Irma Bomb.
It was 6.4 months compared to 3.2 months.
One year survival was almost doubled,
26 months was 13 months.
In the crossover covert showing,
the blue line was about 7.1 month and
the survival there was about 3535.8%.
First, sorry. 

Forest plots essentially showing hazard ratios was applicable across most group except the KPS of 9200.

I relapsed. Refractory now those are the ones where they crossed the line. And and when you look at evently survival and intent to trade group,

Specifically, when you follow these patients for long term survival,

six months survival is 100%, twelve months, 92 percent,

eight months survival is 100%, twelve months, 92 percent,

18 months 71% are two years.

Almost 60% of the patients that had remission were alive and ongoing.
Here are some of the adverse events. As you can see here, we were anticipating a high dose of chemotherapy might cause problems and neutropenia was on similar rates both sides. The mucositis was almost similar on both sides. The rates of GVHD was not really different, but sepsis was lower in the conventional compared to conventional now. So in summary, in patients greater than 55 years with active disease, I'm not followed immediately by reduced intensity transplant in his population.
that’s typically not transplant eligible
is now made feasible and possible.
As a result of the study I am having
general was well tolerated and resulted
in engraftment in all those patients
and had a high rate of durable CR
lasting greater than six months.
And for those who have CR lasting
more than six months about 60% of
our life on the long run the rates
of serious adverse events were small.
I am at office of very normal solution
to increase access to transplant
and improve outcomes in patients
that are relapsed and refractory.
You know,
I have two more slides and I'm going to, I'm going to wind up with that. Some of you who were at Ash probably heard of this trial ASAP trial, which is kind of trying to gain access for alternate transplant for those who have primary induction failure, trying to make a case saying that the need for further intensification chemotherapy to achieve CR is perhaps not needed as long as you can sequentially give chemotherapy and take them to transplant if you have a donor available. Thereby the kind of trying to show that.
you probably don’t need to achieve CR if you have a donor availability. But some of the practices in that study might not be applicable in the United States. But for the purposes of discussion I’ve left it here. I would end my talk by summarizing this for those of you who are interested. Since ARMA but ASAP are now trying to advance transplant in the context of relapse refractory study, ASAP Trap was predominantly looking into fit early relapsed patients. Let’s let’s see what they both talked about. ASAP Trap was predominantly looking into fit early relapsed patients. They’re faster laps.
It uses intensive sequential conditioning.

Our chemotherapy rather followed by transplant preparation regimen which is bluemel TB in an eighth grade.

The flip side to that is one of the novel therapies that we used to treat relapsed refractory leukemia was allowed.

So you can argue maybe that’s not suitable for practicing in the United States.

And even then if you know when we’ve known in the past that we use repeated chemotherapy for labs refractory disease to make them get into see how the transparent perhaps that’s only about 15 to 20% of the patients.
We think that might impact even if you are if you decide to give a sequential therapy maybe about 700 to 1000 patients as you’re Gerald summarized it beautifully and may be eligible to become transparent using that intensive chemo approach. In contrast, Sierra included fit or unfit patients both with primary induction failure or first relapse who have traditionally been considered transplant ineligible. And also included second of later. Encompassing a extensively relapse cases including those who are relapsed with contemporary available.
medications but most people might have gone into palliative care and are now getting eligible to consider as an extension of transplant. And I think as Doctor Gerard mentioned he thinks with this concept approximately 8000 patients who were historically considered not transparent eligible may be eligible for other transplant if you have a donor ready and be available. And I posted this drug being explored for different donors conditioning regimen. Both in a hematologic, both neoplastic and non neoplastic conditions.
Going forwards with that I’m going to invest and thank you all for your attention.

I’ll open up the platform provider questions.

Thank you so much.

You muted Stewart. Sorry.

So we have just a few minutes to field some questions if people want to submit.

I’ll just start with a quick one that came through the chat that we couldn’t respond to and this is for Doctor Sophie,

can you just comment on the use of corticosteroids and card T patients?

Are these allowed?

Do they impact therapy?

On paraphrasing the question,
but the question was really what is the impact of using steroids in these patients?

Yeah. So we generally try to limit the use of steroids before cartee collection. It’s critical that they have at least one week window before Cartee.

We do know that steroids are very lymph depleting and the early postpartum period when they developed toxicity. Though it has been shown that giving a short course of either steroids or other antibodies like tocilizumab to treat cytokine release syndrome or neurologic toxicities does not impact.
the long term outcome of these patients.

But again the steroid tapers are.

Rather quick, typically less than a week.

OK, thanks. And I see one other one

Doctor Zeiden and that’s regards.

The whole issue of remission status

prior to transplant and asking if in

So is the short answer is no.

iMac was part of the transplant conditioning.

So these are people who relapse,

refractory disease had bone marrows

with an average of 30% blasts who

instead of our paradigm of going to
salvage therapy and requiring remission

that was the control arm.

They just went right to the transplant.

So they got the therapeutic dose

and the 12 days before the

transplant and that’s ablative.

So there’s no doing a bone marrow to look.

You saw the average delivery of

radiation there was 16 Gray,

that’s about 3 to 4 Gray higher

total body radiation dose that

we can safely give any patient.

So this is a very ablative

dose of radiotherapy.

And and then marrows are not done
prior to delivering the transplant you have to rescue the patient with the graft and the high CR rate confirms the efficacy of that agent.

I think how much? How much?

So in America's asking about acquiring CR in one arm and not the other, so the other arm was to choose conventional treatment, you're right.

And then those patients don't go to transplant. Remember this is a group restricted age 55.

And we don't have, if you're referring to the ASAP study, we don't have flame PSA regimen, which is the popular German regimen.
And if one looks over 40 years of evaluations of outcome for allograft, being the single most predictive variable for treatment failure is disease status. It’s an increase in blasts in the marrow pre transplant. So remember these were people with actively. These weren’t people with just 6% blasts in their marrow. So they, they, they were allowed to to crossover, but these are people who are conventionally don’t go to transplant.
around around the world really,

NOTE Confidence: 0.763167

unless they’re on a clinical

NOTE Confidence: 0.763167

trail like that German study.

NOTE Confidence: 0.762104

There’s actually an excellent review,

NOTE Confidence: 0.762104

but Zeidan armor and Dan Polia

NOTE Confidence: 0.762104

Dan Polio about even the need

NOTE Confidence: 0.762104

for CR after induction therapy.

NOTE Confidence: 0.762104

I’m sure Rama can extrapolate

NOTE Confidence: 0.762104

that into labs refractory setting.

NOTE Confidence: 0.762104

How CR one came into the foreplay,

NOTE Confidence: 0.762104

whether it’s of essence.

NOTE Confidence: 0.762104

I’ll refer him back to his own

NOTE Confidence: 0.762104

publication with that which tells you

NOTE Confidence: 0.762104

the real utility of CR in modern times.

NOTE Confidence: 0.702696867857143

Yeah, what’s probably a good subject for

NOTE Confidence: 0.702696867857143

further discussion in our transplant

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leukemia meetings. I slept see guard also just wanted to say that this type of therapy is also very exciting for other forms of adoptive cell therapy because I know that they are looking at giving non myeloablative doses of this type of radioimmunotherapy actually at lower doses rather than ablative for patients pre adoptive cell therapy and we already have data on how radiation might actually. Decreased T Reg populations for example, and that may be actually important in the postcard T setting as well. One last question for Doctor Isufi in

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the Q&A, how to choose between car T cell therapy or immunotherapy, very appropriate question not just for lymphoma, but iris what do you think? Yeah, so I mean I think that’s a very valid question. Unfortunately you know immunotherapy in terms of PD1 PDL one access has not had very good outcomes in the setting of non Hodgkin lymphoma. Particularly aggressive lymphoma and so. And you know that those particular drugs are not are not have very low CR rates as single single agents and they do not add much to combination. So I think a court would be preferred.
in terms of antibody drug conjugates.

I mean I think that’s that’s a whole other class of drugs that is competing with car T cell therapy in all fronts including non Hodgkin lymphoma, AML and multiple myeloma and I think we have to look at the targets. To make sure that when we give these therapies the patients retain the target and how to sequence them is actually a matter of very hot debate and ongoing trials right now, what the best approach might be with these by specifics I know.
For example, in patients who for leukemia, the use of blinatumomab precarity. You know how do those patients fare and that because both of those are city 19 targeting therapies and so sequencing is very important there. And the interpretation of the data so far is that if they have a good response to blinatumomab and they maintain their CD 19 status, they do well. However, if they do not have a good response to blinatumomab,
they will also respond poorly to car T unfortunately that’s a high risk group and if they lose City 19 after blina then they actually have very poor responses to court. So we have to be careful about how we sequence these therapies and we have to really monitor. I mean I know many academic centers now when they look at city 19 and C22, they do not just report for example whether it’s dim positive, or they will actually report a number for the level of expression.
And that becomes very important in terms of I know that’s what the NCI does and that becomes very important in terms of what the next therapy that they use is going to be. You know if I can add to that comment that you know the nature of drug development was such that we had to go with enabling and then Karti, despite having heavily treated population had highest CR and MRD negative data rates. So that kind of tells you that it’s a potential drug just that we may not be able to get it in time whereas other
drugs may be dispensing it off the shelf.
In terms of the potential, it's clearly there despite a heavily treated population the rates of CR compared to Unism. Under Marty negatively, there is something that we need to look into it if we're looking into that.
OK. I think we're out of time.
Thanks, Doctor Sophie and Doctor Garin, thanks for all the good questions. I hope everybody has a good weekend. Thank you.