So today will be the second part of our series about updates from the American Society of Hematology, with the highlights today focusing on lymphoid malignancy’s. As you probably know, we have six sessions within this series. We had the myeloma session last week and this is actually has been recorded and available on the website. For those who could not attend last week, so feel free to check their website and we will also be including the slides for your own reference next week on
January 29th will be the update on my malignancy’s. February 5th will be pediatric leukemia and acute for plastic leukemia and pediatric oncology. February 12 will be the classical or benign hematology and February 19 will be cell therapy and transplantation. All of those are on Fridays and at 12:00 PM noon. All of those sessions will be recorded and the slides will be available along with the recordings after the sessions. There will be CME credit for those who submit for it at the end of the entire series, and they’ll be a form for feedback.
where we would love to get your input about what you like and what you don’t like about the series and how we can improve it going forward. This is the first time we’re doing the hematology post ash highlights, and I hope to keep this going for the next few years with a combination of virtual and in person. It’s a pleasure to have three of our faculty presenting and we will be starting with Doctor Schelling, Kothari or Assistant Professor of Medicine who will go over aggressive lymphoid malignancy’s B cell type.
Doctor Francis Commentary will cover for us the indolent B cell malignancies and Doctor Turchin City.

Also Assistant Professor of Medicine will be covering the T cell malignancies, both indolent and aggressive.

At the end we will have a Q&A. The talks will be around 40 to 45 minutes in total and the last 15 minutes will have a question and answer session and this will be moderated by our Assistant Professor of Medicine Doctor Scott Huntington, who will be joining at the panel.
at the panel at the end.

So without further ado, I'd like to introduce Doctor Schelling Kothari, who will start us off. Thank you. Thank you Amar.

So today I'm going to talk about updates from Astronium 20 focusing on aggressive B cell informers. One very heavily participated and we were one of the top accruing sites of oral triple combination of BTK number M, or inhibitor animite, and relapse refractory Richter’s transformation and Dean over DL BCL and then
I'll talk about more sooner to Zoom app, which is a T cell engaging bispecific antibody in aggressive lymphomas. I will not cover the other 3 T cell engaging bispecific antibodies, but they were also presented at. Lastly roll off CNS prophylaxis in high risk DLP CL.

So this is the first study is the once daily ordered triple combination of the three agents that I talked about in Richter’s transformation and in over.
diffuse large B cell lymphoma. This was presented at ASH 2020 by Doctor Mato.

Other preclinical studies. This was a national combination based on synthetic synthetic lethality.

As you can see on the left, the tumor volume of in mice drastic drastically reduced in the triple combination arm in comparison to the vehicle or a single agent.

On the right you just see the B cell receptor pathway and other pathways that further help.

In Onco Genesis an how the triple combination therapy could help prevent tumor resistance by targeting
different pathways together, namely employment pathway AKT, mtor pathway, BTK pathway, and I have four inhibition.

The key eligibility criteria for this 3 + 3 design is age more than 18. Life expectancy more than 12 weeks, with other standard inclusion criteria. The stage one, which is what we are presenting today is the BTK monotherapy, like not in combination in one pill but three separate pills of DRM 12 which is the BTK inhibitor. Novel became a bitter in combination with.

Letter from Little Mind and...
everolimus and then eventually. We are will start accruing
the Stage 2 instead of three, which is a single pill with
two different drugs, and then eventually all three
drugs in one pill for patient convenience and ease of use.
This is these other patient characteristics. Here you can see that in
Richter’s transformation panel, most patients had gotten our chop while in
DLB seal all patients had gotten our job. So these patients were heavily treated.
Median prior therapies were three in
Victor’s transformation into Indy.
LBC, Elko hurt, so these were in general. The point is that they were heavily pretreated patients. At this is the data, so overall response rate in Richter’s transformation is 46%, which is quite phenomenal in such an aggressive disease, Indian over DLB sell, it was 45%. These are the CRN PR’s. This is the waterfall plot, essentially looking at the percentage of tumor reduction. Yellow being the LBC, Ellen blue being Richter’s transformation.
You see that there is a significant tumor reduction in both the cohorts.

Cytopenias were present for sure. Given the triple combination neutropenia, 33% grade, 321% grade, 429% grade 3 thrombocytopenia, and 8% Grade 4 thrombocytopenia.

The non heme toxicities were low. You know 4% odds are only in one patient and there were no grade for side effects.

So the conclusion of this study was that the primary endpoint was met, that the triple combination therapy has an acceptable study safety profile. The main safety findings were expected and manageable, and currently we are...
00:07:25.036 --> 00:07:28.270 accruing for the phase two study.
00:07:28.270 --> 00:07:30.085 It is underway targeting patients
00:07:30.085 --> 00:07:32.430 with novel agents exposed to relapse,
00:07:32.430 --> 00:07:34.735 refractory CLL and other non Hodgkin lymphoma’s. Um?
00:07:34.735 --> 00:07:37.660 The next study I will talk about is
00:07:37.660 --> 00:07:40.452 the single agent motion resume AB,
00:07:40.452 --> 00:07:45.584 which is a T cell engaging bispecific antibody and this was presented by Doctor Adam Orlowski from Brown University.
00:07:45.584 --> 00:07:48.574 And this was studied in the frontline setting, so treatment naive elderly unfit patients with diffuse large B cell lymphoma.
00:08:00.530 --> 00:08:02.651 Up to 30% of patients aged more
than 25 years do not receive standard chemo immunotherapy, so there is a lot of unmet need and there is need to develop therapies which are less toxic more sooner to some apples in IgG, one CD20 CD. Three bispecific antibody that redirects T cells to engage and eliminate malignant B cells. So here Doctor ourselves keep presented early clinical data with single agent most Natuzzi my best first line therapy. The key inclusion criterias, treatment, naive, ideal BCL,
patients or high grade B cell informers for patients who were 60 to 79 they would have to have impairment in adls or inability to tolerate full. Those immunotherapy for whatever reason. Just like with all other bispecific antibody trials, typically it’s done in a ramp up fashion to decrease the chances and severe of cytokine release syndrome. Study design allowed pre face therapy with Prednisone and vincristine and responses estimates were done at interim. Cycle four in Cycle 8 and every six months. There are two doors.
Levels are studied 13.5 and 30 at day 15. So you start with one milligram in 13.5 or 1, and then there was continued every 21 weeks.

Patient population is shown here. So 29 elderly unfit patients were enrolled in this study of eight patients less than 80 years old. Five patients had impairment in renal function. As you can see here, we do see clinically patients who have worse performance status, but given the clinical trial design,
it isn’t. It is quite understandable that they were enrolling 022. Almost 50% of Asia. With stage four disease and 50% with elevated LDH, so overall a good real world characterization of patients here. Side effects were present, but relatively easy to manage, so rash, fatigue, abdominal pain, infusion related reaction, decreased appetite and dry mouth. Cytokine release syndrome was also present, but the grade three and four CRS events were very low.
The best oral response rate was seen in 63.5% of patients and in the highest dose cohort, 30 milligrams. 50% of the patients achieved complete response. This is still sure the durability of response. The ones in green are the patients with complete response and most of them continue to enjoy the durable response rate. Immediate duration of response was not reached and this is only a 5.4 months of median follow-up, so clearly very early data and we need to wait for the data too much or.
So these are the authors conclusions. Early clinical data indicates that single agent is manageable and acceptable. Has acceptable safety profile. Encouraging efficacy was seen in this setting, although they did some correlated studies and they did not find any clear association with peripheral T cell activation and response. This paves way for either single agent or combination therapies with most senators. Mab in frontline setting, especially in elderly unfit. Patients. The third study I would like to...
talk about is the predictive power of early sequential MRD monitoring in mental cell lymphoma following autologous stem cell transplantation with or without rituximab maintenance. This was presented by Doctor Callanan on behalf of the Lisa Group. The study was designed so the patients with classical mantle lymphoma had baseline MRD analysis followed by 4 cycles of our dehab followed by pre autologous tense, transplant, MRD analysis and then you know high dose chemotherapy and then again post autologous transplant MRD analysis and
then patients were either randomized to trucks or maintenance or observation. That type of MRD that was done was. Yeah, so IGHQ PCR. Looking at VDJ recombination region. Am the only talk about the first name given in interest of time is the prognostic impact of MRD status pre and post autologous stem cell transplant. This is the survival curve for pre autologous stem cell transplant, autologous stem cell transplant, MRD status, so the one in red is MRD, negative green, blue is MRD positive so you can see that there is clear split.
in PFS and OS with improvement in PFS in patients with MRD negativity.

And hence essentially, this figure shows that there is a prognostic value in doing MRD analysis. The next question that the authors looked at was to look at impact of maintenance therapy and MRD negative patients so the one the curve in red is patients who got Rituxan. Mab were but were not MRD negative and in blue is patients who are an observation and were MRD negative so you can see that even though these patients. MRD negative that is a clear split and MRD negative that is a clear split and that is you know statistically significant.
00:13:55.225 --> 00:13:58.217 difference with PFS OS benefit in

00:13:58.217 --> 00:14:00.707 patients who got rituximab maintenance.

00:14:00.710 --> 00:14:02.640 The same thing holds true

00:14:02.640 --> 00:14:04.184 for post autologous stem,

00:14:04.190 --> 00:14:06.438 cell transplant, MRD also.

00:14:06.438 --> 00:14:09.430 Hence, the data is a bit humbling.

00:14:09.430 --> 00:14:11.726 Where we would you know would love

00:14:11.726 --> 00:14:14.680 to use MRD for therapeutic decisions,

00:14:14.680 --> 00:14:17.648 but it is pretty clear that maintenance

00:14:17.648 --> 00:14:19.891 rituximab still remains gold standard

00:14:19.891 --> 00:14:22.597 in classical mental cell lymphoma and

00:14:22.597 --> 00:14:24.860 it’s definitely a proof of concept

00:14:24.860 --> 00:14:27.198 that MRD is a good prognostic tool

00:14:27.198 --> 00:14:29.984 and should be used in addition to

00:14:29.984 --> 00:14:32.458 other tools such as pet imaging.

NOTE Confidence: 0.80789965

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Lastly, I will talk about CNS prophylaxis in aggressive non-Hodgkin lymphoma’s. There were two abstracts presented in the oral session at ASH 2020 and both kind of guide us in different directions in terms of what we do in clinics as of today, but there is a big caveat that both are retrospective studies and I would say that we need more prospective data before we change our or practice patterns. Traditionally, the CNS relapse risk is calculated as CNS IPI scoring, which includes age, stage of the patient, LDH, and each status. The number of external sites and kidney and adrenal involvement.
So patients who have intermediate or high CNS IPI score are thought to benefit from CNS prophylaxis, mainly high dose Ivy methotrexate. Rather than intrathecal methotrexate. The first study that I’ll talk about here. Their objective was to determine if high dose methotrexate reduced CNS relapse rates and this was based in Alberta, Canada. The design was retrospective. Patients were 18 to 70 years of age with DL BCL treated between 2012 and 2019. These patients CNS involvement at diagnosis were excluded, as evident here.
00:16:12.468 --> 00:16:14.324 site where they had identified
NOTE Confidence: 0.683736
00:16:14.324 --> 00:16:17.075 high risk patients only out of 326
NOTE Confidence: 0.683736
00:16:17.075 --> 00:16:18.780 identified high risk patients,
NOTE Confidence: 0.683736
00:16:18.780 --> 00:16:21.496 only 115 had gotten high dose methotrexate
NOTE Confidence: 0.683736
00:16:21.496 --> 00:16:24.156 for unknown reasons to under 911 patients
NOTE Confidence: 0.683736
00:16:24.156 --> 00:16:26.298 did not get high dose methotrexate,
NOTE Confidence: 0.683736
00:16:26.300 --> 00:16:28.788 so right off the bat you know since
NOTE Confidence: 0.683736
00:16:28.788 --> 00:16:31.558 we are analyzing only 115 patients,
NOTE Confidence: 0.683736
00:16:31.560 --> 00:16:33.985 it’s difficult to make any
NOTE Confidence: 0.683736
00:16:33.985 --> 00:16:34.955 strong conclusions.
NOTE Confidence: 0.683736
00:16:34.960 --> 00:16:37.234 But here high dose methotrexate was
NOTE Confidence: 0.683736
00:16:37.234 --> 00:16:39.579 used was associated with younger age,
NOTE Confidence: 0.683736
00:16:39.580 --> 00:16:41.920 more the next one external site
NOTE Confidence: 0.683736
00:16:41.920 --> 00:16:43.480 could bring additional involvement
NOTE Confidence: 0.683736
00:16:43.548 --> 00:16:44.968 and double hit lymphoma.
NOTE Confidence: 0.83204776
00:16:47.040 --> 00:16:49.615 Multivariate analysis is shown here
where you can see that the. There was no. Reflected high dose methotrexate did not show any improvement in CNS relapse and the same holds true for intensive immunochemotherapy such as our dose adjusted epoch or are high perceive. Add in comparison to R. Chop consolidative autologous stem cell transplantation was definitely showed more impact, although it did still cross the. Hazard ratio of 1. Here I’m showing multivariate analysis for PFS and OS. You can see that prophylactic high
dose methotrexate and intensive immunochemotherapy did not show any statistically significant difference, although there was difference in PFS and OS in consolidative, autologous stem cell transplanted patients. Authors conclusions were there CNS relapse affect 6% of DCL patients and as a proof of concept similar to rates reported in prior publications. Consolidative autologous stem cell transplantation or intensive immunochemotherapy trended to reduce CNS relapse of finding that is worthy of
further study in a prospective setting.

The other study that I will quickly go over before I hand over to Doctor said he is the CNS relapse by prophylaxis route.

So the this study was a US multi center retrospective study where they found that from all the centers with patients 100 and 1000 patients total 5.5% had overall CNS relapse rate of the patients who got intravenous prophylaxis, 5.3% had CNS relapse and of the patients who got intravenous prophylaxis, 7% had CNS relapse.

So there there are many other...
findings from this study, but in interest of time, I'll briefly discuss their conclusions. What I found interesting from this study was that not only CNS IPI scoring is important, but they also found a significant CNS relapse rate in patients who had involvement of testis or liver. So that’s something that we should keep in mind in our clinics, but overall, you know CNS relapse rates were similar, following prophylaxis, either intrathecal or high dose methotrexate. They are going to do comparisons of single versus dual route so intra fickle.
compare pro flexes and no pro flexes, which would I think be of interest to all of us?

But overall outcomes for following CNS relapse remain poor without clear benefit from existing treatment options.

Thank you and please use the chat window for questions while we go along with more presentations.

Hi everyone. So I’ll be presenting the update on primarily focusing on the Salem farmers. And. So just one at a couple of abstracts for indolent lymphoma. I have no relevant disclosures.
So just starting with a brief overview.

You know, dealing with the challenging field of T cell informers.

You know there were a few studies that were presented that are off.

Note that I’d like to highlight it in frontline peripheral T cell lymphoma.

A couple of studies including the combination romidepsin job and as I said in chapter.

Presented in relapsed refractory PTCL we had an update.

On developer and relapsed refractory CDCR.

There was a novel interleukin antagonist BNZ one,

and then I will shift gears in touch on a couple of CLL studies.
At the end.

So talking about property selling former really the frontline treatment of this aggressive disease is a major area of clinical need and.

You know, we most of us have been using CHOP or chop like regiments as the backbone chemotherapy backbone of frontline therapy. However, unfortunately, unlike diffuse large B cell lymphoma where our job has almost doubles, the CR rates that are seen with PTCL. So with PCL, which job we’re looking at CR rates of just 35 to 40% in the setting of an aggressive lymphoma.
This is really a very challenging situation. Chip has been studied and shown to be of some limited success in certain in subtypes of patients in a subset of patients, specially those younger than 60 years of age. Much higher toxicity was seen in higher age group and those adjusted are. Suggested the bug is really considered for more aggressive subtypes like ATL and clinically aggressive presentations of PTCL. It’s only recently that no one study has changed the standard of care in CD. 30 positive TCL primarily in LCL Septics,
where which where there was the most robust data for the combination of brentuximab, CHP from the Echelon two trial. But outside of this you know other studies that have tried to build on the chop backbone have not been very successful. So with this I’m going to present two frontline trials for PTCL, frontline treatment and so starting with Rd shop.

A study conducted by the Lisa Group and again a frontline treatment of PTCL. It was presented by Doctor Vashi. So this study was based on the
Phase 1B prior Phase 1B data.

That showed. Basically a phase two dose of 12 milligram per meter squared was the one that was associated with, you know, but the best safety data given on day one and data for 21 day cycle with CHOP given on day one. This particular this is this prior study did have. Basically they give 8 cycles and a total of about 37 patients were studied. So in this present study presented by Doctor Bashi, this was a randomized controlled trial phase three data where the army was chop alone,
and then I’m be had romidepsin, given in addition to chop again days 121 and eight at a dose of 12 milligram per meter squared. The recommended phase two dose from the Phase 1B study. So in the study population, I do want to highlight that like many T cell lymphoma trials, it did include a very heterogeneous population of all aggressive histologies and then also looking at. One thing that is relevant really here is that patients undergoing autologous or allogeneic transplant.
planned as a consolidation

were excluded from this study, which is really important to note because.

A lot of people, even based on controversial data

you consider autologous stem cell transplant for most patients who are eligible in first remission after frontline treatment of PCL.

The primary endpoint of this study was progression free survival and was progression free survival and secondary endpoints included safety as well as additional efficacy endpoints.

Again, baseline characteristics I want to highlight about half of the patients
were of an ITL subtype and then, as expected, PCL and LCL where the other common subtypes. So here, unfortunately, like many other studies. But that have used chopped backbone. This was a this study did not meet its primary endpoint of improved progression free survival. The hazard ratio. For Rd shop versus R Chop Chop was appointed one with a P value of .096. And again, a subgroup analysis based on where this IPI factors.
As well as histologies did not really show any significant subsets that were that achieve greater benefit from this regimen. But patients with AI TL did have. There was a trend too. Some benefit in this particular population, again looking at the overall and the complete response rates, the complete response rate was 41% compared with 37%, which is consistent with historical data that we have from. Again, without. Fighting any increase, additional efficacy. Rd job was more toxic.
A substantial number of patients were not able to receive all doses of romidepsin as well as job and also significant number of patients are received. Had to undergo jobs reduction or interruption because of increased toxicity, which is primarily increased. Haematological toxicity so really, in summary for this study, Roach up increase toxicity without improving efficacy in frontline treatment of PTCL possible future directions really is based on whether CHOP is the right backbone.
We do notes there.

Drugs like romidepsin are more active in certain subtypes of PTCL like PTCL with T follicular helper, cell subtype and AI TL and so maybe’s patient selection.

And based on Histology and then there is another trial that is being.

And that is yet to start accruing.

But it’s basically has been proposed by NCI where they’re looking at the combination of Doxorubicin 5 as a sighted in oral and then romidepsin a sighted in T cell lymphoma.

So those would be, you know, interesting things to look forward to.
Our next study that was presented in Frontline PTCL was oral, cited in CC-486 plus job. This was presented by Doctor Rowan from Kernel. So again, this particular study actually highlighted the point that an oral PCL with T follicular helper cell subtype is associated with. These mutations are not only present in the two T follicular helper cell and this was the rational. These mutations are not only present in the two T follicular helper cell and this was the rational.
00:29:47.567 --> 00:29:50.941 subtype AI TL but also some PTCL,
NOTE Confidence: 0.69032043
00:29:50.950 --> 00:29:55.248 PTCL nosc and so that was the
NOTE Confidence: 0.69032043
00:29:55.248 --> 00:29:58.730 rationale for using is cited in.
NOTE Confidence: 0.69032043
00:29:58.730 --> 00:30:01.244 As an epigenetic.
NOTE Confidence: 0.69032043
00:30:01.244 --> 00:30:03.758 Timer with chop.
NOTE Confidence: 0.69032043
00:30:03.760 --> 00:30:05.950 So this they proceeded straight to
NOTE Confidence: 0.69032043
00:30:05.950 --> 00:30:08.559 a phase two study because there was
NOTE Confidence: 0.69032043
00:30:08.559 --> 00:30:11.065 Phase one data for safety of this
NOTE Confidence: 0.69032043
00:30:11.140 --> 00:30:13.460 combination from B cell lymphoma.
NOTE Confidence: 0.69032043
00:30:13.460 --> 00:30:15.364 Uh, the they do.
NOTE Confidence: 0.69032043
00:30:15.364 --> 00:30:18.220 They do include all PTCL subsets.
NOTE Confidence: 0.69032043
00:30:18.220 --> 00:30:21.100 However they did prioritize enrollment
NOTE Confidence: 0.69032043
00:30:21.100 --> 00:30:24.432 of the T follicular helper cells
NOTE Confidence: 0.69032043
00:30:24.432 --> 00:30:27.699 upset and as you will see of the 20
NOTE Confidence: 0.69032043
00:30:27.791 --> 00:30:31.067 patients 17 where of TFH subset here?
NOTE Confidence: 0.69032043
00:30:31.070 --> 00:30:33.535 The primary endpoint was complete
NOTE Confidence: 0.69032043
00:30:33.535 --> 00:30:36.000 response rate and secondary endpoint
NOTE Confidence: 0.69032043
00:30:36.079 --> 00:30:38.689 was overall response rate and safety.
NOTE Confidence: 0.69032043
00:30:38.690 --> 00:30:41.690 They also looked at some genomic
NOTE Confidence: 0.69032043
00:30:41.690 --> 00:30:44.830 markers so this was an. Interesting.
NOTE Confidence: 0.80174625
00:30:47.220 --> 00:30:50.286 Study design and treatment regimen where
NOTE Confidence: 0.80174625
00:30:50.286 --> 00:30:53.726 initially CC 486 was given as a lead
NOTE Confidence: 0.80174625
00:30:53.726 --> 00:30:57.128 in from day minus 6 two day one for
NOTE Confidence: 0.80174625
00:30:57.128 --> 00:30:59.840 the first cycle and then subsequently
NOTE Confidence: 0.80174625
00:30:59.840 --> 00:31:03.848 from and subsequently four cycles.
NOTE Confidence: 0.80174625
00:31:03.850 --> 00:31:09.160 125 they received CC-486 on.
NOTE Confidence: 0.80174625
00:31:09.160 --> 00:31:14.509 so every so for cycle one.
NOTE Confidence: 0.80174625
00:31:14.510 --> 00:31:17.331 So this present this acted as priming
NOTE Confidence: 0.80174625
00:31:17.331 --> 00:31:20.760 phase for the next cycle of chemotherapy.
NOTE Confidence: 0.83863452
00:31:23.600 --> 00:31:27.744 So. After 21 patients that were enrolled,
20 were evaluable for response and of these almost half of them. These patients actually did go on to receive autologous stem cell transplant or one patient who received Alo. Here we see the overall CR response rate in these patients, and of all patients considering all patients as well as patients with PTCL default color helper cell subtype. It was seen that. CR rate was seen in TFs subtype compared with 75% all comers. Really, majority of the patients were of TFs subtype.
Here are the results from the here.
The survival curves, so the median follow up of 15 months.

One year PFS was 66% for all patients and one year overall survival was 80% and the corresponding numbers for TF subtype were almost 70% and 94%.

This was a relatively well tolerated regimen with expected side effects of. Aside opinion, specially neutropenia, but other than the hematological toxicity, there were no additional significant unexpected side effects.

This study also looked at mutational analysis,
and it’s worth mentioning that they found that tattoo was associated with a favorable prognosis in this cohort of patients and DMD MT3. Oh was associated with worse overall survival. So this was a surprisingly promising study and of this combination. Again, this is very early data of only 20 patients. So this is a, you know, a combination that is being tested further. One particular study that is worth highlighting is this alliance study, which is actually going to be rich is going to include patients with a C30 negative.
00:33:41.420 --> 00:33:44.087 PTCL non alc else Histology and it
00:33:44.087 --> 00:33:47.652 has it had three comparator arms one
00:33:47.652 --> 00:33:50.572 including CC 4861 including development
00:33:50.572 --> 00:33:54.493 and the third one is Chopper show up here
00:33:54.493 --> 00:34:00.400 with these combination they are using
00:34:00.400 --> 00:34:04.636 It’ll be worth looking at the.
00:34:04.640 --> 00:34:10.930 We can see. Of this these combinations.
00:34:10.930 --> 00:34:13.695 Next, I'd like to go onto a
00:34:13.695 --> 00:34:15.830 study with Dibella sub again,
00:34:15.830 --> 00:34:17.458 another promising new agent
00:34:17.458 --> 00:34:19.086 and T cell lymphoma.
00:34:19.090 --> 00:34:21.255 This was in relapsed refractory
00:34:21.255 --> 00:34:23.420 peripheral T cell lymphoma and
00:34:23.496 --> 00:34:25.758 this was updated data from the
phase two Premier trial where they looking at those optimization and I’ll go over that a little bit.

This was presented by Doctor Pro from Northwest.

So dualism is a dual appear three kindness Delta inhibitor.

We know that is FDA approved in relapsed refractory, follicular lymphoma and CLL and the doors in these patients in

test this dosin T cell lymphoma. the Mac the MTD was 75 milligram

PID vid and that was the dose
00:35:01.324 --> 00:35:03.574 tested in T cell lymphoma which

00:35:03.651 --> 00:35:05.726 showed an overall response rate

00:35:05.726 --> 00:35:07.688 of 50% in relapsed refractory,

00:35:07.688 --> 00:35:10.988 PTCL and 33% in cutaneous T cell.

00:35:10.988 --> 00:35:11.530 Former.

00:35:11.530 --> 00:35:14.202 So the reason that was the reason for

00:35:14.202 --> 00:35:16.155 designing this dose optimization study

00:35:16.155 --> 00:35:18.585 was to see whether these patients

00:35:18.585 --> 00:35:20.727 truly need 75 milligrams pob ID.

00:35:20.730 --> 00:35:24.250 Or are we overtreating them?

00:35:24.250 --> 00:35:25.778 So the study design.

00:35:25.778 --> 00:35:28.045 Again, there was a dose optimization

00:35:28.045 --> 00:35:30.350 phase followed by those expansion phase.

00:35:30.350 --> 00:35:32.858 It did include.

00:35:32.860 --> 00:35:34.520 The various,
not subtypes that we discussed and.

So develop the cohort one included patient
develops if patients received develops.

If 25 milligram B ID and cohort two.

They received 75 milligram
vid as the starting dose.

The primary endpoint was overall
response rate with these two doses
and then the secondary endpoints
again looked at additional
safety and efficacy endpoints.

So here we are looking at cohort one and
go to each had 13 evaluable patients.
So the overall response rates.

Sorry so the overall response rates.

Seen here with the 25 milligram.
I was basically 35 to 40% by the investigator and the committee and compared with 75 it was a higher response rate.

Overall response rate of 54 to 62% and then similar trends being seen in CR rates. When they looked at looking here at the waterfall plot, it was seen that all the early dropouts based on you to progression were in the 25 milligram dose cohort, and therefore they did in those expansion phase they decided to go on with. Using a does starting with a dose of 75 milligrams vid for two cycles.
In those patients who had Disease Control, they would go on to receive 25 milligrams pob ID. And now with this combination of doses, an overall response rate of 50% was seen with the CR rate of 36% and so there for this was the overall those expansion phase, including included 25 patients and this is a swimmer plot showing the duration of response for these patients. Again, in terms of side effects, there were no unexpected side effects, and the combination of those 25 milligram was associated with...
better tolerability overall.

So again, this study highlights that develop is definitely an active agent in T cell lymphoma specific, especially in relapsed refractory PTCL.

This study provides data. For using this dual dose of 75 milligram, starting those with 25 milligram.

Having a. Efficacy while balancing the toxicity of this single agent.

So the last. See the last study in T cell lymphoma.

Later, like to highlight is that and this is I’m going to go over this very briefly,
but this looked at knew novel Interleukin antagonist. Starting the call going ambition of aisle 9 and I'll 15 by BNZ 1. And this was studied in a Phase 1 two study and it was presented by Doctor Klarfeld from City of Hope. Today study different dose levels and it was those level two of two milligram per kilogram was decided as the. Phase two day for phase two dose based on the PK PD data there was this drug was not associated with any major side effects and so therefore there was no MTD and based on the. So considering everything,
including the efficacy data
they discarded around to,
going ahead with the dose of
2 milligram per kilogram.
So this I want to highlight the fact
this is was a really highly refractory
population of CCL patients with medium
file median 5 prior lines of therapy
and without any major side effects of
an overall response rate of 52% was seen.
A subset of patients which is
definitely makes this a very promising
agent to go further in studies.
They do did highlight that you know
being targeted blocker of aise
to aisle 15 an aisle 9.

It has a 3 prong.

I can see where.

Including direct anti tumor effect.

Reduction of T regs and basically activation of anti tumor immune response and then also an anti inflammatory effect seen through I'll 15 blockade which is relevant for patients with PTCL who have a robust inflammatory reaction that leads to mobility in this disease.

A couple of CLL abstracts,
00:40:55.990 --> 00:40:59.230 so the first one is locked, so 305.

00:40:59.230 --> 00:41:01.255 This is the next generation,

00:41:01.260 --> 00:41:04.200 highly selective non covalent BTK inhibitor

00:41:04.200 --> 00:41:06.760 in previous previously treated CLL SLL.

00:41:06.760 --> 00:41:09.651 And this was a Phase 1 two

00:41:09.651 --> 00:41:12.180 study presented by Doctor Matot.

00:41:12.180 --> 00:41:14.778 So lock the three or five.

00:41:14.780 --> 00:41:16.864 It’s as previously mentioned,

00:41:16.864 --> 00:41:19.990 the highly selective non covalent BTK

00:41:20.075 --> 00:41:22.409 inhibitor in it inhibits both wild

00:41:22.409 --> 00:41:25.369 type as well as C481 mutated BTK.

00:41:25.370 --> 00:41:27.351 So when we see look at patients

00:41:27.351 --> 00:41:29.279 who have a BTK resistance,

00:41:29.280 --> 00:41:31.716 the most common cause of that is

00:41:31.716 --> 00:41:34.099 because of the mutations in BTK.
And this drug does target that population of patients. But this was a these patients were heavily pretreated, including patients who had failed or discontinued, became a better for due to toxicity and also had this is a high risk population of patients with 17 P deletion and TP 53 mutation present in a total of over 50% of patients. So the Phase one study, so the date data presented is from the Phase one study which included patients with CLL and SLL. And.
This loss of three or five safety profile was unique, as in the most common grade three side effect was actually fatigue and the typical. Side effects associated with other BTK innovators like atrial fibrillation. The side effects were not very prominent with locks or two or five. Since there was no DLT’s, the maximum tolerated dose was not reached, and. Based on the PK data and the efficacy data dose of 200 milligrams was decided as the recommended phase two dose. Again, here it was in a heavily
pretreated well population.

Locks or three or five was found to be.

Continue to have.

Made up a very good efficacy in this.

Beta in this patient population and looking at the overall response rate of 63%.

So it was.

Good basically good response in this without a lot of toxicity in this patient population.

So lots of three or five was active at all those levels, and typical became a bitter or related toxicities were not seen.

These responses were independent,
BTK mutation and even patients who had received BCL two inhibitor. When I took LAX as well as three kinase inhibitors, did respond to this drug. So there’s a safety and efficacy signal in CLL. Yeliz will be passed participating in the phase two portion of this study. Um? And then finally I just want to mention this particular study that was open at Yale in the past and that is umbrella civs and you’ve lytic seemab you two study which
00:44:22.968 --> 00:44:25.344 used a novel dual inhibitor,
NOTE Confidence: 0.725289520333333
00:44:25.350 --> 00:44:27.320 three kinase and casein kind
NOTE Confidence: 0.725289520333333
00:44:27.320 --> 00:44:29.700 is money in a better and.
NOTE Confidence: 0.8235949
00:44:31.770 --> 00:44:34.269 The only issues with this study was
NOTE Confidence: 0.8235949
00:44:34.269 --> 00:44:36.527 that you know the comparator arm
NOTE Confidence: 0.8235949
00:44:36.527 --> 00:44:39.124 was a bit as a map chlorambucil,
NOTE Confidence: 0.8235949
00:44:39.130 --> 00:44:41.356 which is not really a very
NOTE Confidence: 0.8235949
00:44:41.356 --> 00:44:43.549 relevant in this day and age,
NOTE Confidence: 0.8235949
00:44:43.550 --> 00:44:45.746 at least for treatment naive patients.
NOTE Confidence: 0.8235949
00:44:45.750 --> 00:44:47.622 But this is being studied further
NOTE Confidence: 0.8235949
00:44:47.622 --> 00:44:49.396 in combination both in frontline
NOTE Confidence: 0.8235949
00:44:49.396 --> 00:44:51.268 and relapsed refractory setting.
NOTE Confidence: 0.8955445
00:44:53.740 --> 00:44:54.560 That’s all I have.
NOTE Confidence: 0.82034147
00:45:15.680 --> 00:45:16.550 Tell everybody.
NOTE Confidence: 0.76212716
00:45:27.840 --> 00:45:32.224 Hello everybody, I’m going to go over the.
NOTE Confidence: 0.76212716
00:45:32.230 --> 00:45:34.556 Abstract relevant to heart killing
form for the sake of time I'll try to be brief and uncover only heart killing form at this time.

So since the introduction of Brentuximab and Odin and checkpoint inhibitors in general, the paradigm of treatment for this disease is changed substantially, and. And this agent, that now you been used earlier and earlier in the course of the disease. So I will review the knew updates and the new data relevant the uses regarding the using of these agents in first line in the relapsed refractory setting and maintenance.
Adding after transplant and in the elderly population.

Let’s start with that.

The five year update of action on one, as we all know, this is a very large open label, multicenter randomized phase. Three study that was initially presented at three years ago at the Ash meeting with a 2 year follow up over 1300 patients were randomized either to get brentuximab avd for six cycles or abvd, which is the standard treatment at city was performed after two cycles, but this was not a pet adapted approach.

The primary endpoint of the
00:46:55.030 --> 00:46:57.630 study was a modified PFS.
NOTE Confidence: 0.8009456
00:46:57.630 --> 00:47:00.045 Which is which included time to progression
NOTE Confidence: 0.8009456
00:47:00.045 --> 00:47:02.110 that and not completely response
NOTE Confidence: 0.8009456
00:47:02.110 --> 00:47:04.530 and use of subsequent chemotherapy.
NOTE Confidence: 0.8009456
00:47:04.530 --> 00:47:07.050 This modified PFS was meant to capture
NOTE Confidence: 0.8009456
00:47:07.050 --> 00:47:09.974 all the events that reflected the failure
NOTE Confidence: 0.8009456
00:47:09.974 --> 00:47:12.184 of frontline treatment and patient
NOTE Confidence: 0.8009456
00:47:12.184 --> 00:47:15.485 and were followed up with the serial imaging.
NOTE Confidence: 0.8009456
00:47:15.490 --> 00:47:18.584 The first data set that was presented
NOTE Confidence: 0.8009456
00:47:18.584 --> 00:47:21.697 from this dialogue after a follow up
NOTE Confidence: 0.8009456
00:47:21.697 --> 00:47:24.253 Papa to essentially two years showed
NOTE Confidence: 0.8009456
00:47:24.338 --> 00:47:27.335 a benefit in using a plus abvd A plus.
NOTE Confidence: 0.8009456
00:47:27.340 --> 00:47:30.854 Abd compared to a DVD with an
NOTE Confidence: 0.8009456
00:47:30.854 --> 00:47:33.079 absolute in benefit of 5%.
NOTE Confidence: 0.8009456
00:47:33.080 --> 00:47:34.988 this modified progression free
NOTE Confidence: 0.8009456
survival was 82 versus 77.

This came at the cost of significant increase in side effects.

Neutropenia 58% versus 45 from Europe.

But there was a big big one with a 67% incidents.

An informercial city was the one that was reduced due to the omission of the.

Bleomycin.

So why this is the five year update is important.

We nearly all recurrences of Hodgkin lymphoma happen usually within five years,

so we think that PFS of five year

is a good surrogate for for cure

and here the five year data we
NOTE Confidence: 0.8009456
00:48:19.433 --> 00:48:22.369 do see the PFS for the A plus.
NOTE Confidence: 0.8009456
00:48:22.370 --> 00:48:25.636 A vd is the red curve 82% of five
NOTE Confidence: 0.8009456
00:48:25.636 --> 00:48:28.150 years compared to 75% in the
NOTE Confidence: 0.8009456
00:48:28.150 --> 00:48:30.350 ABVD Ann and these disadvantage.
NOTE Confidence: 0.8009456
00:48:30.350 --> 00:48:32.320 And that was observed initially
NOTE Confidence: 0.8009456
00:48:32.320 --> 00:48:33.896 persisted overtime maybe depend.
NOTE Confidence: 0.8009456
00:48:33.900 --> 00:48:36.518 And this was how they threw in
NOTE Confidence: 0.8009456
00:48:36.518 --> 00:48:38.535 in patients achieving the path
NOTE Confidence: 0.8009456
00:48:38.535 --> 00:48:40.590 to negativity after two cycles.
NOTE Confidence: 0.8009456
00:48:40.590 --> 00:48:43.958 This hopper curb is 2 cars here compared
NOTE Confidence: 0.8009456
00:48:43.958 --> 00:48:46.788 to those that were at negative.
NOTE Confidence: 0.8009456
00:48:46.790 --> 00:48:49.838 So this was not a fat adapted approach.
NOTE Confidence: 0.8009456
00:48:49.840 --> 00:48:50.196 Again,
NOTE Confidence: 0.8009456
00:48:50.196 --> 00:48:52.688 the rates of if you remember the
NOTE Confidence: 0.8009456
00:48:52.688 --> 00:48:54.788 data from this work started.
NOTE Confidence: 0.8009456
Yes, after two cycles received ended up receiving escalated Beacopp for six cycles. This PFS compared favorably to patients that received and much more aggressive course of treatment with a very high rate of secondary malignancies, and based on the profile and different risk characteristics. Applications are in the trial. Or the essentially all the group favored the use of brentuximab plus avd. So I think that was a highlighted and I think it’s very important to note is
NOTE Confidence: 0.8391127
00:49:28.938 --> 00:49:30.746 that the peripheral neuropathy,
NOTE Confidence: 0.8391127
00:49:30.750 --> 00:49:33.494 which was one of the concern major concern
NOTE Confidence: 0.8391127
00:49:33.494 --> 00:49:36.270 when the initial results were released,
NOTE Confidence: 0.8391127
00:49:36.270 --> 00:49:38.240 has really improved or complete.
NOTE Confidence: 0.8391127
00:49:38.240 --> 00:49:41.691 Completely resolved in the vast majority of
NOTE Confidence: 0.8391127
00:49:41.691 --> 00:49:45.347 the patient and with an improvement that.
NOTE Confidence: 0.8391127
00:49:45.350 --> 00:49:46.726 Happened progressively over the
NOTE Confidence: 0.8391127
00:49:46.726 --> 00:49:48.790 course of the years and currently
NOTE Confidence: 0.8391127
00:49:48.844 --> 00:49:50.220 patients will receive one.
NOTE Confidence: 0.8391127
00:49:50.220 --> 00:49:52.308 Prefer neuropathy, have a really low
NOTE Confidence: 0.8391127
00:49:52.308 --> 00:49:54.338 grade of peripheral neuropathy, if any.
NOTE Confidence: 0.8391127
00:49:54.338 --> 00:49:56.252 Another thing that was noted in
NOTE Confidence: 0.8391127
00:49:56.252 --> 00:49:58.498 this five year update is that
NOTE Confidence: 0.8391127
00:49:58.498 --> 00:50:00.418 the rate of secondary malignancy.
NOTE Confidence: 0.8391127
00:50:00.420 --> 00:50:02.555 And the rate of successful
NOTE Confidence: 0.8391127
pregnancies compared well to the ABVD. Um, so I think that with this five year update of the action and one, we have more compelling. Data now to support the use of this. Judgment and more widely in the upfront setting in hybrids. in untreated stage, 4, three and four patients. Um, I just want to briefly mention this. This trial, which was presented as a post office there is more that concept that was presented because this is an ongoing trial and we're part of it at Yale. He said as we just reviewed the
addition of brentuximab window tint

to avd improves PFS in advanced age,

but still 15 to 20% patients are relapse,

relapse or refractory and BV

addition increases toxicity and

require growth factors.

So this is the largest.

North American Cooperative group

trials in Advanced Hodgkin study that

is being conducted in collaboration

with Canada and even with the

collaboration of the children.

The theology.

Patrick Oncology group for Hodgkin is

a study that is planning to enroll
987 patients and two randomized

NOTE Confidence: 0.8391127

them either to nivolumab avd versus

NOTE Confidence: 0.8391127

Brentuximab and Odin and Avd for six cycles.

NOTE Confidence: 0.8391127

The patients are going to be satisfied

NOTE Confidence: 0.8391127

based on the age Ipsy and intended

NOTE Confidence: 0.8391127

use of radiation and the primary

NOTE Confidence: 0.8391127

endpoint is progression free survival,

NOTE Confidence: 0.8391127

but a lot of other data are planned

NOTE Confidence: 0.8391127

to be gathered.

NOTE Confidence: 0.8391127

And in particular,

NOTE Confidence: 0.8391127

patient reported outcomes including fatigue,

NOTE Confidence: 0.8391127

neuropathy, scoring and quality of life.

NOTE Confidence: 0.8391127

So despite covid,

NOTE Confidence: 0.8391127

it looks like the TARDIS.

NOTE Confidence: 0.8391127

This trial is at the target of the

NOTE Confidence: 0.8391127

expected accrual and the results
00:52:02.697 --> 00:52:05.115 of this trial are eagerly awaited.

00:52:05.120 --> 00:52:08.240 So let’s move them to the salvage treatment.

00:52:08.240 --> 00:52:10.580 What’s new in the salvage treatment?

00:52:10.580 --> 00:52:13.112 So usually provision that are relapsed

00:52:13.112 --> 00:52:15.589 refractory after the first line of

00:52:15.589 --> 00:52:17.731 treatment of the general approach is

00:52:17.731 --> 00:52:20.078 to proceed to salvage chemotherapy.

00:52:20.080 --> 00:52:22.355 Usually platinum based or genocide

00:52:22.355 --> 00:52:24.630 happen based with an expected

00:52:24.709 --> 00:52:27.392 response rate in the 50-60% range with

00:52:27.392 --> 00:52:29.056 introduction of brentuximab concurrently

00:52:29.056 --> 00:52:31.739 or sequentially in the salvage regiment,

00:52:31.740 --> 00:52:34.332 we now expect responses in the

00:52:34.332 --> 00:52:35.984 60 and 70% range,

00:52:35.984 --> 00:52:39.170 but the use of a print aksamit now is

NOTE Confidence: 0.8391127

00:52:02.697 --> 00:52:05.115 of this trial are eagerly awaited.

NOTE Confidence: 0.8391127

00:52:05.120 --> 00:52:08.240 So let’s move them to the salvage treatment.

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NOTE Confidence: 0.8391127

00:52:13.112 --> 00:52:15.589 refractory after the first line of

NOTE Confidence: 0.8391127

00:52:15.589 --> 00:52:17.731 treatment of the general approach is

NOTE Confidence: 0.8391127

00:52:17.731 --> 00:52:20.078 to proceed to salvage chemotherapy.

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00:52:22.355 --> 00:52:24.630 happen based with an expected

NOTE Confidence: 0.8391127

00:52:24.709 --> 00:52:27.392 response rate in the 50-60% range with

NOTE Confidence: 0.8391127

00:52:27.392 --> 00:52:29.056 introduction of brentuximab concurrently

NOTE Confidence: 0.8391127

00:52:29.056 --> 00:52:31.739 or sequentially in the salvage regiment,

NOTE Confidence: 0.8391127

00:52:31.740 --> 00:52:34.332 we now expect responses in the

NOTE Confidence: 0.8391127

00:52:34.332 --> 00:52:35.984 60 and 70% range,

NOTE Confidence: 0.8391127

00:52:35.984 --> 00:52:39.170 but the use of a print aksamit now is

NOTE Confidence: 0.8391127
getting limited by the fact that is
used more widely in the first line
and therefore alternative strategies
that are being explored in this study.
Specifically,
is a face to study using bumper
lizama in addition to our regular
which is one of the historically
used salvage treatment as
a second line for relapsed refractory
article informal and eligibility
dissipation that our love story factory.
The first line of treatment.
Primary endpoint is the PCR rate
because that’s the most important
factor that we have to achieve after salvage treatment. With Adima to pursue to transplant. So patients received the regular GBD combination and they want and they ate with addition of populism on day one. After two cycles of patients but positive patient back, negative were allowed to pursue directly to transplant. Otherwise everybody received 4 cycle and then that was evaluated at the end and then that was evaluated at the end of treatment before the transplant. So let’s see what happened. There were 939 patients enrolled in this
study, with a median age of 38 years. Importantly, most of the patients were advanced age of the initial diagnosis and the time of enrollment. When they relapsed, many patients had extranodal site, 1/3 of them extranodal sites of disease involvement, and the symptoms was present in 15% of the patient. Almost like 40% were refractory or either they relapsed in first year so very high risk patient. received up front was primarily ABVD,
but some patients reserved receive the
print axiom an and or Veeco approaches.
So after the first 2 cycles
of pembrolizumab T 92% of the
patients were found to be in a CR,
and that’s unprecedented data
for a salvage attachment.
And after an additional 2 cycles and
there was an additional CR rate,
so the total see CR rate for this
group of patients was 95 percent,
proceeding to transplant and a
good amount about a third of them
preceded to maintenance with the
print accent windowed in for a year.
Based on the accurate trial study, none of the patient with limited follow up that we have now for this study at progression of disease. After the transplant. So why this this? This regiment works so well. It even outperformed what checkpoint plus chemotherapy does in first line. Sony Vollmer Avd does not have the same efficacy and one of the reasons that the others are looking into is if there is anything specific in this may be the synergy between the chemotherapy agent that is unique to checkpoint inhibitor in particular.
the ability of selectively eliminate.

That my little derived suppressor cells,

so these exciting results poised base

for the next court on this study,

were actually the aim is to treat

everybody with Pembridge EBD for four cycles,

and then skip the Trump’s transplant

altogether and have the patient instead.

Being on maintenance with 13 cycles

So this is going to be very exciting to

see what the outcome of this patient is.

Moving forward,

let’s talk about consolidation after

transplant. What’s new in that?
We know that patients at high risk of relapse after the transplant based on the characteristic primary refractory disease. As general involvement with symptoms of relapse order requiring more than one line of salvage treatment, not in CR, the time of transplant, they are higher risk of relapsing after transplant. So now there have been strategies that have been explored that to improve their PFS and. We all know about the if their trial where baby consolidation was utilized after at least himself transplant.
00:56:52.778 --> 00:56:55.330 with an improvement of the PFS, although with a significant there
00:56:57.320 --> 00:57:00.104 was a 33% and drop off patients that could not complete the study
00:57:00.104 --> 00:57:02.480 due to neuropathy and another study that has been done used that embolism up in this setting.
00:57:02.557 --> 00:57:04.502 It was much smaller study only with 30 patient and patient population and better risk factors.
00:57:04.502 --> 00:57:07.303 So the apotheosis behind this study is to use the these two agents in combination Vivian Evil as consolidation and utilizing only eight cycles instead of the 16 cycles.
that was used in the fair trial,

and again, patients that were enrolled,

59 patients were enrolled in this trail and they were started on that.

These are the combination between evil about them,

between 30 and 6075 days after a transplant.

And I just want to point out that there was a lot of patients that could not complete the eight cycles that were planned.

59% could not complete the treatment plan and only 76% completed 8 cycles of either brentuximab or nivolumab.

So the take home message from this, that is that the treatment the maintenance after transplant is a much.
It is very difficult.
Treatment too, for the patients to undergo as the side effects associated with the utilization of these agents in this setting. Is associated with an increased side effects, in particular immune related adverse event that we’re seeing up to 27% of the patients enrolled in this study. But nevertheless, it’s very encouraging that there is a 92% progression free survival in this high risk patients for relapse even despite their prior exposure either to BB and anti PD one.
And since I want to leave sometimes for question. I'm just going to mention briefly that this study think the merit of this study has been literally to enroll older patients which are under representative in most of the Hodgkin lymphoma trial. They have less prognosis and unfortunately it's not a randomized trial, so patients were received either BV chemotherapy and just to be very, very quick. The take home messages that DV monotherapy has been with.
Very, very active, but as shown, the employer in prior studies, the PFS, was not very long, whereas when we've is combined with chemotherapy, the risks are outside effects increases, but it is associated with that much longer PFS. The only thing that they want I like is that the brand tax amount window 10 plus bendamustine armor was closed due to an excess of toxicity is not a good treatment in this elderly population.
And with this I left panel open for question.

Thank you all for presenting.

It was really quite comprehensive.

We're going to go over our allotted hour and folks can stay in.

Will have a little question answer period.

While we're on the topic of Hodgkin, that was really nice.

Presentation documents tomorrow.

How do you interpret and how do you take together? that was really nice.

Presentation documents tomorrow.

How do you interpret and how do you take together?

You know the five year data

on the TV

and first line.

Incredible salvage options for patients you know.
How do you put that together when you have someone that has advanced stage first line has come before you are you? You know the five year data compelling you to give more BVD or you still doing adaptive kind of raffle approach? This is a very good question. Interesting isn’t it? It’s very I mean, one of the argument against intensifying Firstline treatment is that is so well tolerated and that we have so many, I mean salvage therapy works in our chicken. So in order to improve. A small percentage of the outcome of all the patients you end up
like exposing a lot of patients to a more aggressive treatment.

While you could have served salvage only to those that do not respond to a DVD.

So, but I think that this five year update I really like to see that the peripheral neuropathy was not getting better progressively year after year and there were not major sequelae regarding that approach and.

I really like the fact that there was no not an increase of secondary malignancy or of. The.

Any bad outcome on pregnancies,

but what I really think is the value of this approach as compared to PET adopted
one is that you don’t need to adopt it.

The PFS of patients that have a pet positive after 2 cycle is very good and is as good as the one that you get using escalated beacopp and especially population.

That’s a really nice summary and I have very similar feelings of that, so it’s a complicated conversation that certainly patients should be presented both. Kind of adaptive Anet DVD and tailored to patient preferences and kind of a profile.
Not surprisingly, there are a number of questions about CNS prophylaxis of Doctor Kothari can step up to the plate, but you know how? How do you interpret the two abstracts that were presented oral session? I know there was a lot of kind of discussion during that meeting. Has that informed how you approach patients that are high risk for sinas that relapse? I think both abstracts kind of confused us further. To be honest. I mean it’s great set of data, especially the second set of data that I presented which is a multi institutional US.
You know study where there are more than a thousand patients so you know the end was pretty good to have meaningful interpretation, but I think. Overall, I think my summary of, I think both abstracts would be that we need better, stronger frontline regiments to eradicate the real high risk DCL from the get go because that eventually leads to a CNS relapse and that was shown through the Alberta, Canada study where patients who got intensive chemo immunotherapy. The trend was towards better.
CNS relapse rates. And I guess the same could be told even you know the fact that autologous stem cell transplant was helpful. So overall, I would say that this these abstracts don’t change my practice of using high dose methotrexate with R CHOP or most likely into fecal methotrexate with those adjusted epoch in high risk blpi atients. What I would say I think, which was interesting to note, is the liver involvement and testicular involvement, which we traditionally don’t.
Think of it that way, although there are some scattered papers about it, I think this is just to highlight that you know liver and testicle involvement also portends higher CNS relapse rate. Thank you for that and then Doctor Safi. Really, I think lots of exciting early phase studies in T cell. But certainly I think we need kind of larger randomized prospective data and basically everyone with T cell lymphoma should be on.
protocol, right? If we’re going to really start improving the outcomes, can you talk about some of the trials that we have open in T cell lymphoma either currently or in the future? We hope to kind of increase our accruals for.

Yes, absolutely. Actually we have. We do have a few exciting things coming down the Pike so we do use those adjusted epoch quite a bit for aggressive T cell lymphoma here at Yale. And so we have an IIT that is in the works which is funded and
basically the protocol is being developed. And that’s with those suggested epoch with mogamulizumab as frontline therapy in these patients and. So epoch does have overall, you know, looking at the chop response rates of like 35-40% CR rates, epoch does tend to have a better overall response rate in CR rates in the 60% think you know 60% range. So the idea is really to try to get this. These patients and the deepest remission that you can and you know then then take them to transplants and. It’s really an excited study.
It is a phase two single arm study, but I think it’s a novel combination that we’re excited about. As far as the and one additional study would be in CD 30 positive patients looking at the combination of rituximab and pembrolizumab and that’s kind of an idea that I wrote at Vanderbilt and that we’re hoping to open. In the coming months as well. As far as the present studies are concerned, the ones that we are still enrolling on, we have a couple of oral agents, including the DIETY study, which is basically an IDH one, IDH, two inhibitor.
And it has to be.

It has, you know, single agent activity in relapsed refractory T cell lymphoma, and definitely something that we’ve seen responses with, and sometimes it’s just the right treatment to try to get these patients in remission, take them to transplant.

Thank you so much and this was great. Amazing talks and thanks God for this the moderation. The questions as you heard a lot of exciting developments.
going on in the informal work.

We have a lot of actually active clinical trials,

so feel free to reach out to any further Informa experts or any questions about your patience or any referrals for clinical trials.

Reminder that a recording of this session will be available next week and along with the slides and should be an enduring material.

For your future reference,

next week will have the by Lloyd updates and thank you so much everyone and have a great weekend.

Thank you.