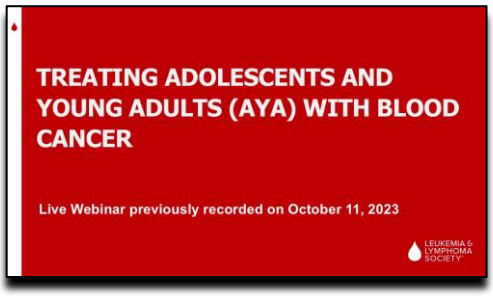


Slide 1: Treating Adolescents and Young Adults with Blood Cancer

Operator

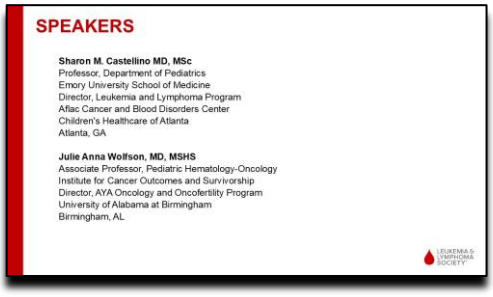
Greetings and welcome to Treating Adolescents and Young Adults with Blood Cancer, a web education program. It is now my pleasure to introduce your moderator, Ms. Lesley Hoerst. Thank you. You may begin.

Slide 2: Welcome and Introductions

Lesley Hoerst, BSN, RN

On behalf of The Leukemia and Lymphoma Society, thank you for joining us. Our organization is committed to improving patient's qualify of life through webinars such as this one, for healthcare providers and education and support resources for patients and caregivers. This webinar will focus on treating adolescents and young adults, including common cancers and AYAs, common symptoms of these cancers, and the diagnostic tools used to identify them, treatment options, management of short- and long-term effects and the unique considerations for the AYA population.

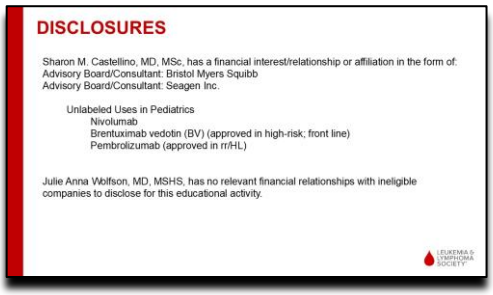
A review of resources you can provide to your patients, as well as additional education resources for you will also be provided.



Slide 3: Speakers

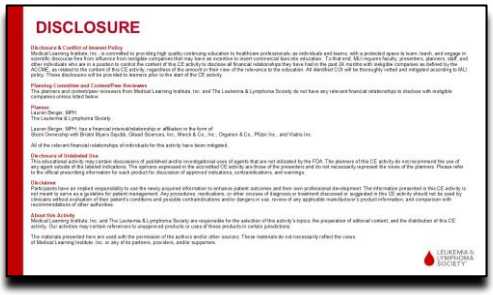
I am honored to introduce our presenters, Dr. Sharon Castellino, Director of the Leukemia and Lymphoma program at the Children's Healthcare of Atlanta, in Atlanta, Georgia; and Julie Wolfson, Director of the AYA Oncology and Oncofertility Program at the University of Alabama at Birmingham, in Birmingham, Alabama. Thank you for volunteering your time and expertise with us.

Following their presentations, we will share information about resources from The Leukemia and Lymphoma Society.



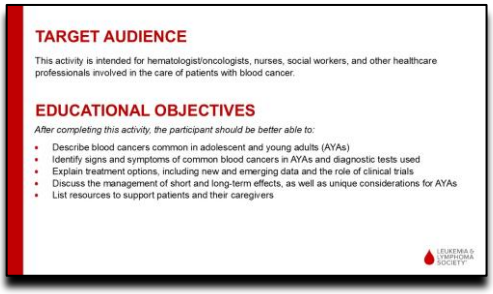
Slide 4: Disclosures

Faculty disclosures are listed here.



Slide 5: Disclosures

Planner disclosures are listed, also on this slide.



Slide 6:Target Audience/Educational Objectives

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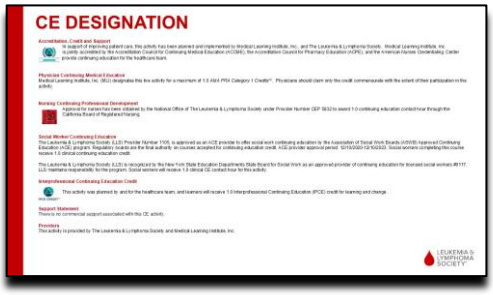
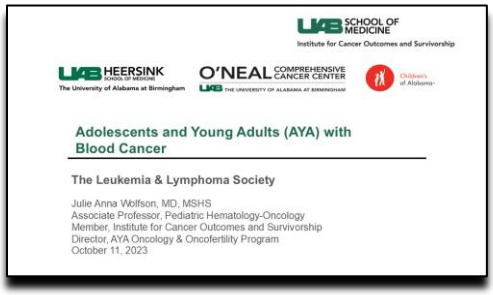


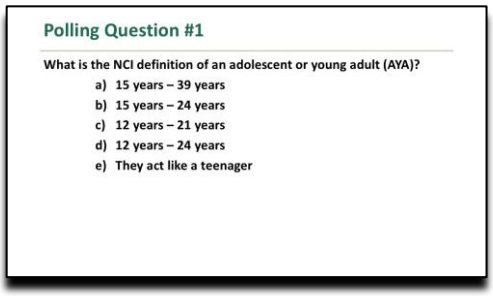
Slide 7: CE Designation

Continuing education information is listed here.



Slide 8: Adolescents and Young Adults with Blood Cancer

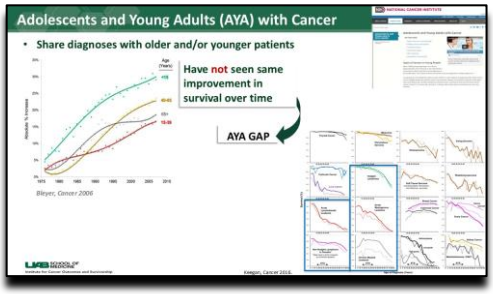
Julie Anna Wolfson, MD, MSHS: Thank you, so much for organizing this and I'm honored to be able to talk a little bit about something that is so important to us. I'll be starting off, talking about a general approach to adolescents and young adults, or AYAs, with blood cancers, and talking about leukemias, in specific. And then, I'll turn it over to Dr. Castellino to talk more about lymphomas and some other aspects of AYAs.



Slide 9: Polling Question 1

I wanted to start us off with a question. There'll be pulling questions throughout. So what the NCI definition of adolescent or young adult? Fifteen to 39 years, 15 to 24 years, 12 to 21, 12 to 24, or they act like a teenager?

Okay, so the majority of the of folks did answer the 15 to 39, which is the NCI definition. There is a lot of variability. There is a lot of institutional variability, in terms of what institutions feel is feasible and appropriate for their site. And they use anywhere from 12 or 15 to 21 or 24. But the NCI defines this as 15 to 39. And so, we'll talk about that a little bit more.

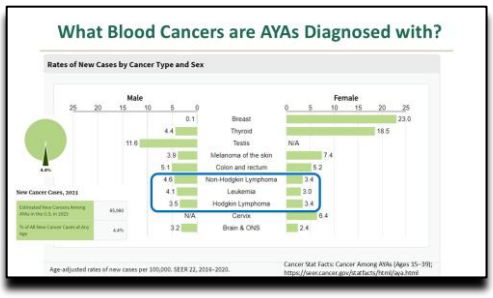


Slide 10: Adolescents and Young Adults (AYA) with Cancer Adolescents and Young Adults (AYA) with Cancer

Based on the NCI definition an AYA is this 15 to 39-year-old group.

And this is because patients share diagnoses with the older and the younger patients, but they simply have not seen the same improvement in survival over time.

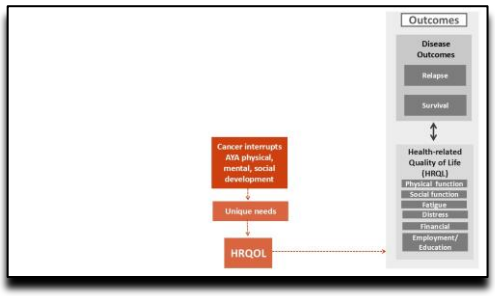
Now this basically coins the term AYA gap, and prompted the NCI to deem AYAs a vulnerable population. And here you see why there has been some improvement slightly in some venues.-There have been some persistent disparities. These blue boxes highlight the blood cancers we'll be talking about today.



Slide 11: What Blood Cancers are AYAs Diagnosed with?

And so, what blood cancers are AYAs diagnosed with? And so in general, there's over 85,000 new AYA cancers each year. And they account for about 4% of the total cancer diagnoses each year.

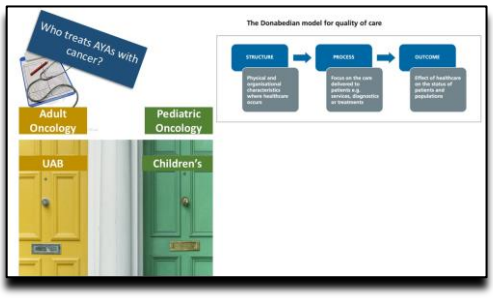
And here you see the non-Hodgkin lymphomas, the leukemias, and the Hodgkin lymphomas. And this is the cases per 100,000.



Slide 12: Image

So when we think about outcomes, in general, we think about disease outcomes. Right? We think about relapse and survival. And so I want to kind of walk through building a model together, looking at some boxes and arrows, so be patient with me. But we're going to talk through what leads to these differential outcomes that we just saw in those AYAs.

And we think about relapse and survival, but we also know that cancer interrupts AYA physical, mental, and social development, leading to them to have very unique needs. And this can impact health-related quality of life, based on the literature. And so, that is one of our additional outcomes. And these can be interrelated, as we all know, for those of us who take care of these patients.

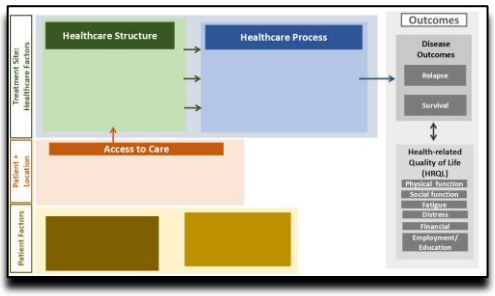


Slide 13: Image

Some of what influences this, is what door a patient walks in. So an AYA can walk through an adult oncology door or a pediatric oncology door. And at our site, this would be at UAB or at Children's. And there's differences in terms of how the patients are cared for. And a lot of that has to do with the healthcare system itself. And so, when we think about analyzing and getting to the heart of outcomes in health services research, we think about the structure or the physical and organizational characteristics, as well as the process -- how the care is actually delivered. And then, a number of different outcomes, in terms of how we look at these things.

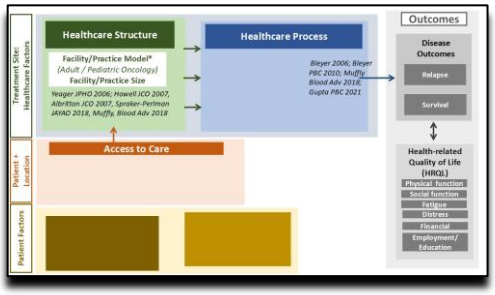
Slide 14: Image

So we can think about treatment site in those healthcare factors, the patient and the location, and then patient factors, in general.



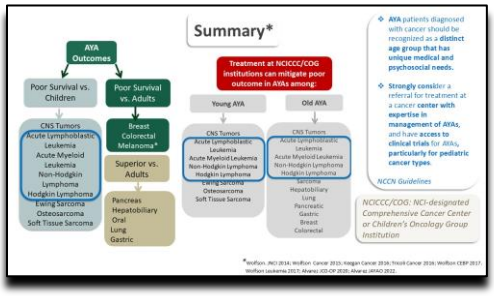
Slide 15: Image

And so first, we'll think about the structure and process. We're building our boxes and access to care and some of those patient factors.



Slide 16: Image

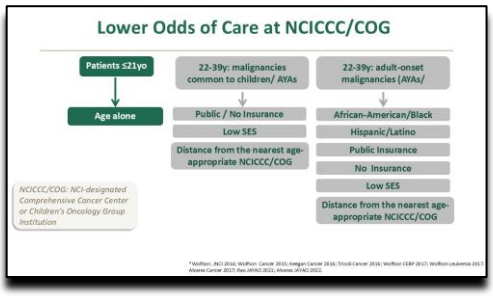
So facility and practice model, whether patients are taken care of in an adult or pediatric oncology site, and then, the facility and practice sides have all been shown in a number of different investigations to influence outcomes.



Slide 17: Summary

In summary, in terms of looking at where a patient is treated, we know that AYA outcomes -- that AYAs have poor survival, as compared to children, in a number of cancers, including these blood cancers here, and poor survival versus superior survival as compared to adults, are mostly in these solid tumors. What -- there's been work in our group, and others, to look at treatment at an NCI-designated, comprehensive cancer center, or COG site, showing that treatment at one of these institutions can mitigate the poor outcome of AYAs, among a number of cancers in young an old AYAs, and specifically in these blood cancers.

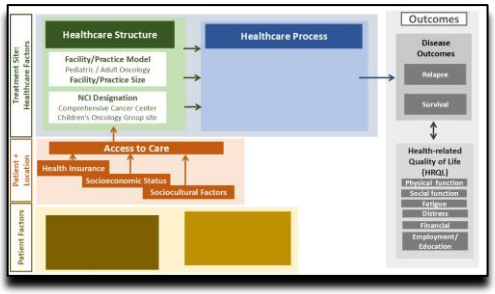
And this leads us to say, not necessarily that that means that every AYA should be seen at one of these centers, but that we need to understand what is being done at those centers and those investigations that led to those -- just those -- the mitigation of those outcomes, and thinking about this, in the framework of the NCCN guidelines. They recommend that AYA patients diagnosed with cancer should be recognized as a distinct age group that has unique medical and psychosocial needs, and to strongly consider a referral for treatment at a cancer center with expertise in management of AYAs, and have access to clinical trial for AYAs, particularly for pediatric cancer types.



Slide 18: Lower Odds of Care at NCICCC/COG

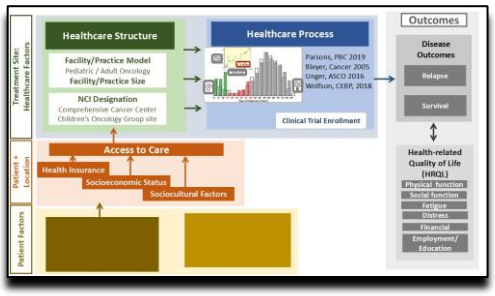
But unfortunately, not everybody gets to one of these centers, as we all know. And so, when we looked at who was getting to these specialized sites, we found that in patients 21 or under, it was really age alone that determined whether they were treated at a specialized site or elsewhere. But in the patients that were 22 to 39, with malignancies common to children in AYAs, patients with public or no insurance, low SES, and living further from the nearest, age-appropriate center, all had a much lower likelihood of reaching those centers.

And at 22 to 39-year-old patients with adult-onset malignancies common to AYAs and adults, we found that race and ethnicity, as well as public or no insurance, the low SES, and living further from that nearest, age-appropriate center all impacted.



Slide 19: Image

Whether or not they were treated at those sites. And we can put this in our access to care box, in terms of this influencing where a patient is treated and what they have access to, beyond that, including access to clinical trial enrollment.



Slide 20: Image

So let's think about how clinical trial enrollment impacts outcomes. This is Archie Bleyer's, work that has become the hallmark reference, in terms of us thinking about clinical trial enrollment impacts outcomes in AYAs. And what you see here is boxes that are not shaded in, that represent clinical trial approval. And then, the annual percent change in five-year, overall survival is the shaded boxes.

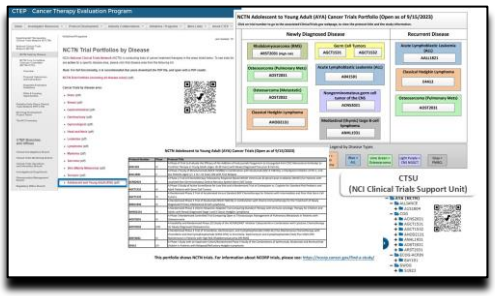
The green shows improvement in these children. And the gray shows improvement in these adults over 40. But the red is the AYAs, where there was not improvement. And so, this actually shows, then, our squared coefficient of 0.85, which shows very strong correlation between enrollment in clinical trials and survival. But unfortunately, we also know from these other citations that I'm showing you here, that the` minority of AYAs are enrolled on clinical trials.

Slide 21: Image

As well as less than 5%, in some studies. And so, what's been being done about this?

So from a national level, in the early 2000s, the AYA progress review group convened, as many of you know. This was led by the NCI with the Lance Armstrong Foundation. They published this landmark publication, which led to the NCI founding, in 2010, and then launching in 2014, the National Clinical Trials Network. One of their goals, which will focus on increasing awareness of trials for AYAs. And so, this led to combining four medical oncology groups, one pediatric oncology, and one international group, into this NCTN clinical trials network.

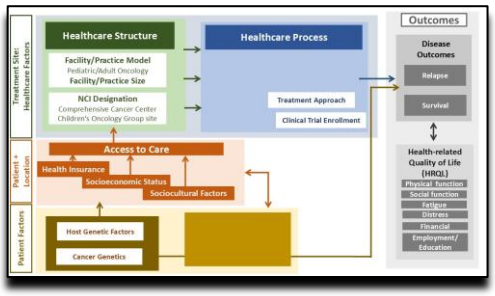
When they looked at the proportion of treatment trials that were represented by AYAs, before and after creation of the NCTN recently, it was 9.5% versus 14%. And this was statistically significant, with the mean difference in proportions being 4.4%. And so, we know that AYA discipline committees have been evolving in the cooperative groups, both pediatric and adult. And most recently, our sarcoma colleagues have formed a joint adult and pediatric sarcoma clinical trials working group that was recently published and is, hopefully, leading the way for more and more collaboration, as a working group.



Slide 22: CTEP Cancer Therapy Evaluation Program

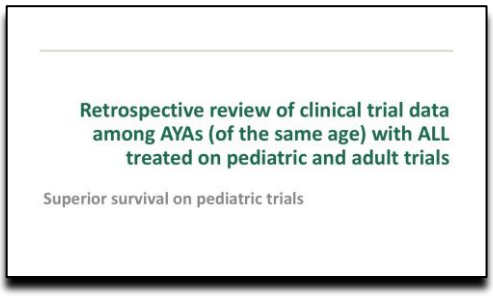
Dr. Castellino will talk more of the collaborative trials that have been developed within this framework. But the CTSU, the NCI clinical trials support unit, is basically a place where we can find these trials that have been jointly developed and are jointly eligible for patients to enroll, from either a pediatric cooperative group or an adult cooperative group. And so, this is what the folder looks like, if you haven't been on here before. There's an AYA folder specifically.

And then, it has the lead group as the folder name. And basically, these trials, you can enroll on, whether you're coming from COG or Alliance or ECOG-ACRIN, or SWOG, etc. The other place to find a list of these is on the CTEP site, where you look at the NCTN trial portfolios by disease. And I have the QR codes to link to both these sites here. There's an AYA portfolio, specifically. And when you click on that, you come up with the current list of clinical trials. And this was the one, as of September 15th, it was most recently updated. And it provides these. And then, you can go find the protocol right here.



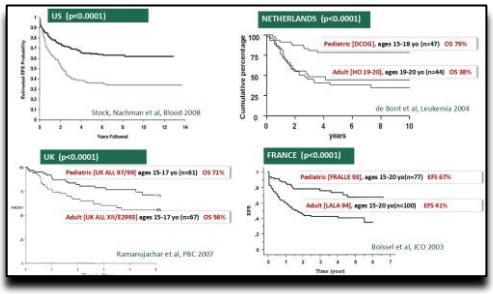
Slide 23: Image

And so, we can't ignore the fact that there's biology at play. There's the biology of the patient and the biology of the cancer, of course. And that influences outcomes, as well, as does the treatment that a patient received.



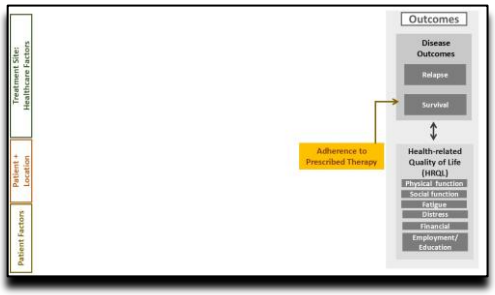
Slide 24: Retrospective Review of Clinical Trial Data Among AYAs (of the same age) with ALL Treated on Pediatric and Adult Trials

So we know, from retrospect of review of clinical data among AYAs of the same age, with ALL, treated on pediatric and adult trials, that there was superior survival in pediatric trials.



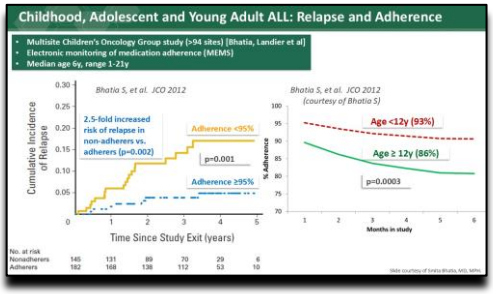
Slide 25: Image

So, this shows us, when we stop in Jim Nachman's work, looking at the pediatric CCG patients and comparing them to the adult CALGB patients, both of them in the 16 to 20-year age group, with superior EFS for patients treated on the CCG trials. And then, this was replicated, worldwide.



Slide 26: Image

So any of us that treat AYAs can also discuss, probably for a long time, how important adherence to the prescribed therapy is, in this population.



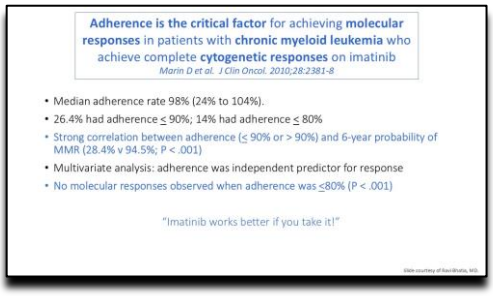
Slide 27: Childhood, Adolescent and Young Adult ALL: Relapse and Adherence

And the fact that this has an influence on survival.

So there was elegant work done by my colleagues, Dr. Bhatia and Dr. Lindeer doing a multi-site, children's oncology group study at more than 94 sites, using electronic monitoring of medication adherence. This included AYAs, although there was a lower median age range, because it

was done in a pediatric world. But they did find that, if patients took less than 95% of their prescribed dose of 6 NP, they had a much higher cumulative incidence of relapse than the patients who took at least 95% of their doses.

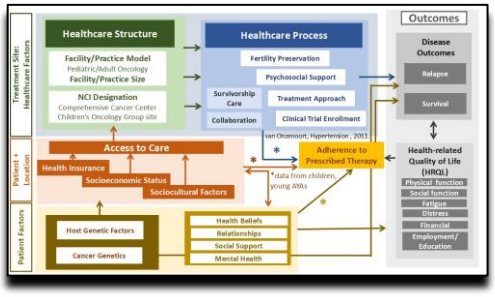
So in multi-variable analysis this revealed a 2.5-fold increased risk of relapse in the non-adherent patients. When they drilled down and looked at age, they found -- which would not surprise us, unfortunately -- that patients under 12 had a much higher adherence than those over 12. And they've now developed an intervention for these patients that are in the pediatric world, that are AYAs.



Slide 28: Adherence is the critical factor for achieving molecular responses in patients with chronic myeloid leukemia who achieve complete cytogenetic responses on imatinib

And so, in thinking about CML - adherence is the critical factor for achieving molecular responses in patients with chronic myeloid leukemia, or CML, who achieve complete cytogenetic responses on imatinib.

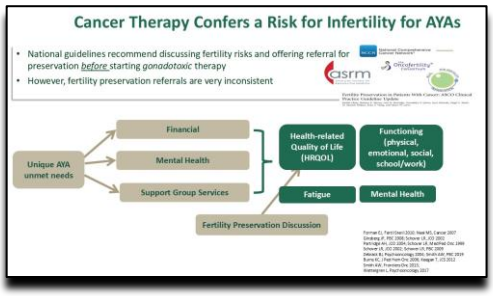
And so, there is a strong correlation between adherence in the CML world -- the cut-off point was 90% -- and then six-year probability of a major, molecular response. And this was 28% versus almost 95%. No molecular responses were observed when adherence was less than 80%. And so, Dr. Bhatia was very kind to share this slide with me. And his quote was, "imatinib works better if you take it."



Slide 29: Image

And so, what we know, from the literature, is that there are a number of process points that influence adherence -- as do some of these access points. And there are patient level factors, as well, that we'll talk about. But that -- this helped a lot of these elements and, hopefully, quality of life, can influence it, as well. And these are those patient-level factors that can influence adherence to prescribed therapy. And a lot of these data are from children, young AYAs, or AYAs in other disciplines.

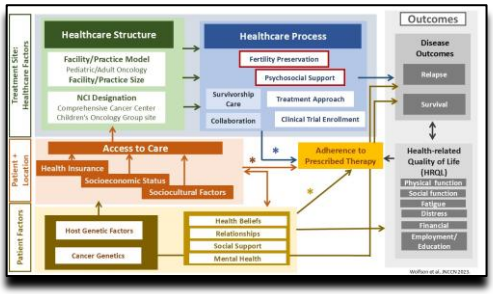
So Dr. Castellino will talk more about survivorship care. But this is an important concept, as well. And then, collaboration between pediatric and adult faculty and staff has been shown to be important, as well.



Slide 30: Cancer Therapy Confers a Risk for Infertility for AYAs

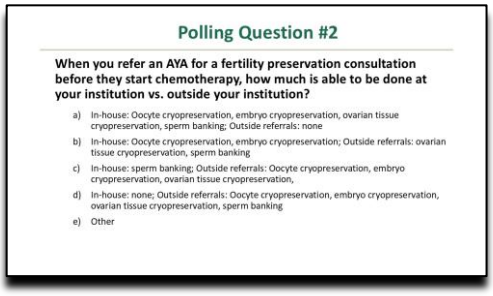
So fertility preservation and psychosocial support is so crucial in this population. What we know is that cancer therapy itself confers a risk for infertility in the AYAs, and that national guidelines recommend discussing fertility risks and offering referral for preservation before starting gonadotoxic therapy.

But fertility preservation referrals are very inconsistent, unfortunately. So we do know that these discussions influence health-related quality of life, but that there are a number of additional, unique needs that are unmet among AYAs. And in the AYAs hope study, which was a large, national study, the largest of its kind, they were able to identify that AYAs themselves identify financial needs, mental health needs, and support group services as unmet needs, and that these influence health-related quality of life, as well.



Slide 31: Image

And so these are incredibly important to keep in mind as we think about treatment among AYAs.



Slide 32: Polling Question 2

So, our second polling question -- when you refer an AYA for fertility preservation, consultation before they start chemotherapy, how much is able to be done at your institution versus outside your institution? And so, each of these looks a little different.

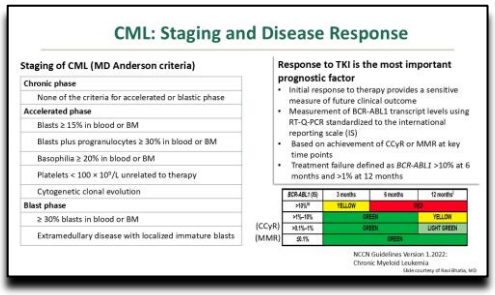
The first one -- in-house, we can do egg freezing, oocyte cryo-preservation, embryo freezing, ovarian tissue cryo-preservation, sperm making, and we don't refer anyone outside. The second one -- we can do eggs and embryos, but then, for ovarian tissue cryo-preservation or sperm banking, we refer outside. For C, in-house, we do sperm banking, but outside is everybody for oocytes, embryo, cryo, and ovarian tissue cryo. And for D, in-house, we don't do anything, we refer everybody outside. And E would be other.

So as you can see, it really does look like the majority of the sites are not able to do any of this, in-house, and do need to refer everyone outside. But about 15% are able to do everything in-house, with smaller proportions in the B and C, where it's a little bit mixed.

And I imagine E is just a different mixed bag between the B and C. But we could only put so many answers. It's not easy. It's definitely not easy, but I think we all appreciate effort that's being made out there.

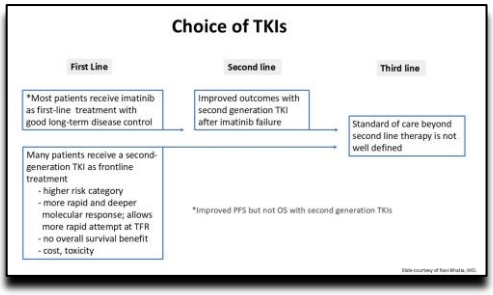
Slide 33: Treatment Options and New Emerging Data: Leukemias

So I'm now going to talk about some of the treatment options and new, emerging data in leukemias, CML, ALL, and AML. And I'm going to give advanced thanks right now to some clinical colleagues that I work closely with, that were able to provide me some very nice slides. I do take care of leukemias and lymphomas, clinically. But I have some colleagues who chipped in and were really able to help with this, as well.



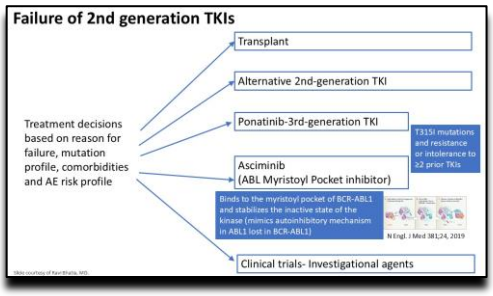
Slide 34: CML: Staging and Disease Response

So Dr. Robbie Bhatia provided some CML help, and really just a review of the fact that we all know that these CML patients, based on MD Anderson criteria, can present in chronic, accelerated, or blast phase, and that response to TKIs is the most important prognostic factor. And that initial response really provides that sensitive measure of future outcomes, but really, the optimal way to monitor this, is using RTQPCR measurement of BCR-ABL1 transcript levels, standardized to the international reporting scale. And so, based on either a cytogenic response or major, molecular response at key time points, is predictive of their future outcomes. And the treatment failure as defined as a level of over 10% at six months or over 1% at 12 months.



Slide 35: Choice of TKIs

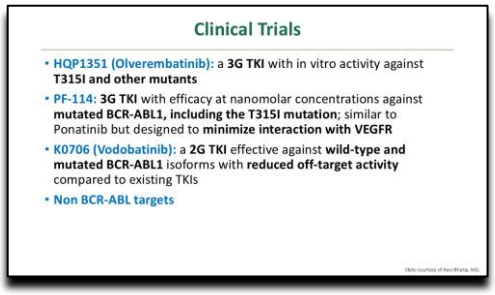
And so, in terms of choosing TKIs, there was improved progression for survival, but not overall survival, shown with second-generation TKIs. So most patients receive imatinib as first-line treatment with good, long-term disease control. But many patients receive a second-generation TKI as front-line treatment, whether they're in a higher-risk category ~~or they~~ -- but do need to keep in mind that there's a rapid and deeper molecular spots that can allow for more rapid attempt at a treatment-free remission, meaning stopping the TKIs. But there's definitely no overall survival benefit. And cost and toxicity are definitely important to keep in mind. There are improved outcomes with second-generation TKIs, after imatinib failure.



Slide 36: Failure of 2nd generation TKIs

But there's no standard of care beyond second-line therapy that's well defined at this point. Treatment decisions, are really based on the reason for failure, the mutation profile, the co-morbidities, and the adverse events risk profile. So one considers transplant an alternative, second-generation TKI.

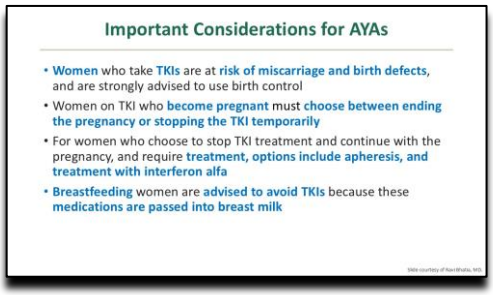
Ponatinib, which is a third-generation TKI, and asciminib, which is a non-TKI, binds to the myristoyl pocket of BCR-ABL1 and stabilizes the inactive state of the kinase -- and then, the clinical trials and investigational agents.



Slide 37: Clinical Trials

So current trials are a third-generation TKI, which has activity against T315I and other mutations.

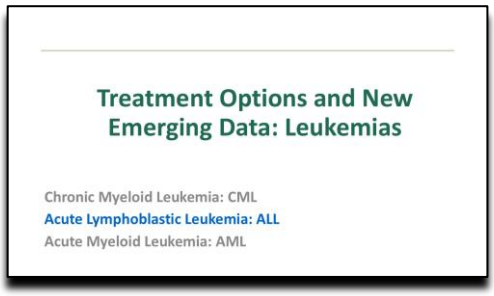
And then, this third generation TKI that has efficacy right now, as well, against mutated BCR-ABL1, including a cy-mutation. And it's similar to ponatinib but designed to minimize interaction with VEGFR. And then, this second-generation TKI, which has been shown so far effective against wild-type and mutated isoforms, with reduced off-target activity, so few less toxicities, and then non-BCR-ABL targets, as well.



Slide 38: Important Considerations for AYAs

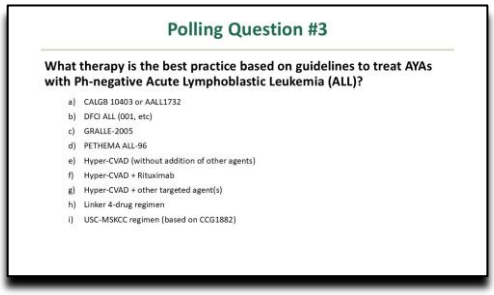
Important consideration for AYAs is really the thought that women who take TKIs are at risk of miscarriage and birth defects and are strongly advised to use birth control. But if they do become pregnant, it's an unfortunate choice between ending the pregnancy or stopping the TKI, temporarily. So women who do choose to stop TKI treatment and continue with the pregnancy, and require treatment, options include apheresis and treatment with interferon alpha.

And then, breastfeeding women are advised to avoid TKIs, because these medications are passed into breastmilk. Dr. Bhatia and I actually co-managed a patient, just in this very situation.



Slide 39: Treatment Options and New Emerging Data: Leukemias

In thinking about ALL…

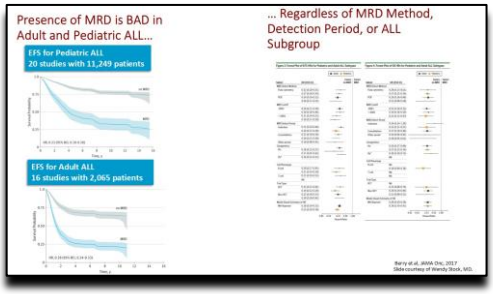


Slide 40: Polling Question 3

We'll do our next polling question. So what therapy is the best practice, based on guidelines, to treat AYAs with PH-negative ALL?

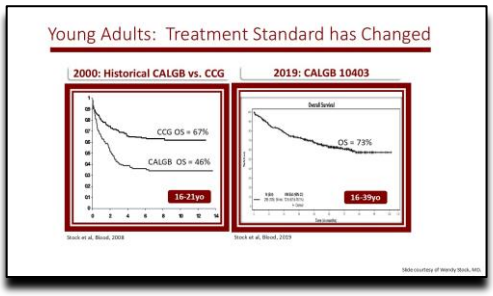
A, is CALGB 10403, or AALL1732; B, would be the DFCI ALL protocols; C, the GRALLE 2005 protocols; D, PETHEMA ALL 96; E, hyper-CVAD, without the addition of another agent; F, hyper-CVAD with rituximab; G, hyper-CVAD with another targeted agent; H, linker 4-drug regimen; or I, the USC Memorial Regimen, based on CCG1882?

So it does look like the majority of us are split between A, the CALGB10403 or 1732, or F, which is hyper-CVAD, or rituximab. When we think -- look at the NCCN guidelines, it is technically A, CALGB10403 or the 1732 type regimen, that are preferred, with additional regimens that -- listed below, including the hyper-CVAD with rituximab as options. But they're lower on the list. So you're not incorrect, by any means. All of these are listed. But A is listed at the top. And we can talk about that a little bit more.



Slide 41: Presence of MRD is BAD in Adult and Pediatric ALL…

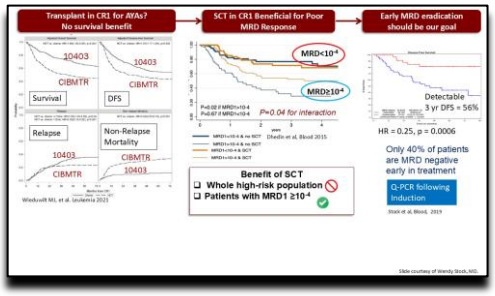
And so, big picture, the presence of MRD is bad, in both pediatric and adult ALL. And so, when we look at event free survival, this is 20 studies with over 11,000 patients in pediatric ALL and 16 studies with over 2,000 patients in adult ALL. And in both of them, the patients without MRD had significantly superior survival as opposed to those -- as compared to those with MRD.



Slide 42: Young Adults: Treatment Standard has Changed

And this was regardless of the MRD method, the detection period, or the ALL sub-group.

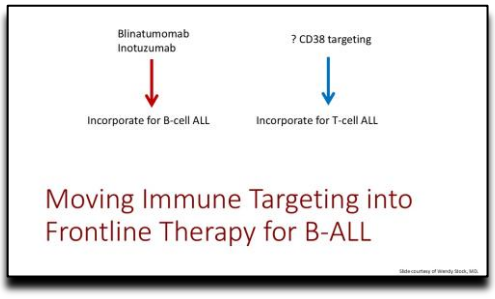
The treatment standard has changed, in general. And we looked at this before this was this CCG versus the CALGB data, in terms of the historical data. And this was the 2019 study with CALBGB10403 showing 73% survival in the 16 to 39-year-olds.



Slide 43: Image

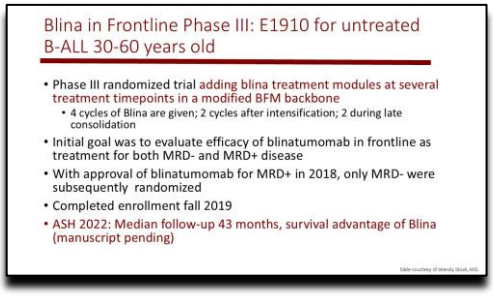
Then, when we think about transplant in CR1 for AYAs, in first, clinical remission, there has not been shown to be survival benefit, when treated with this approach to therapy. And so, when looking at survival and disease free survival, there are superior outcomes, with 10403 as compared to those that were transplanted. This is CIBMTR patients. And in terms of relapse, there's a higher relapse with 10403, but a higher non-relapse mortality, as well, with those patients that were transplanted. So transplant on CR-1 was beneficial, specifically for those with a poor MRD response. So not for the whole, high-risk population, but for those with positive MRD.

And so thus, early MRD eradication should be our goal. Right? And specifically, Dr. Stock would recommend QPCR, following induction.



Slide 44: Moving Immune Targeting into Frontline Therapy for B-ALL

Moving front immune therapy into immune targeting into front-line therapy for B-ALL, we think about blinatumomab and inotuzumab for B-cell ALL and CD38 targeting for T-cell ALL.

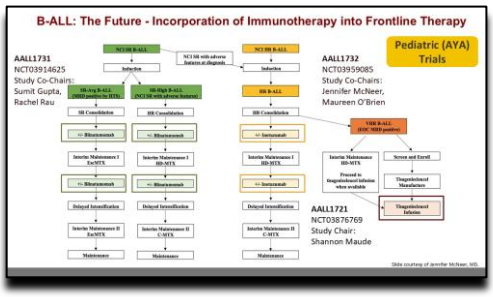


Slide 45: Blina in Frontline Phase III: E1910 for untreated B-ALL 30-60 years old

So in terms of blinatumomab, E1910 for untreated B-ALL -- this study was for patients 30 to 60, so only a small portion of them were AYAs.

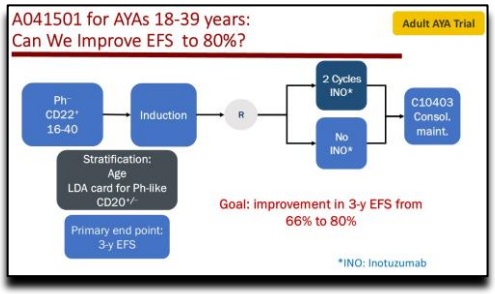
But in the adult world, this has been a really hot conversation, in terms of working blinatumomab into

front-line therapy, because with the medium follow-up of 43 months, there was shown to be a survival advantage of blinatumomab. This was presented at ASH in 2022. The manuscript is still pending,



Slide 46: B-ALL: The Future - Incorporation of Immunotherapy into Frontline Therapy

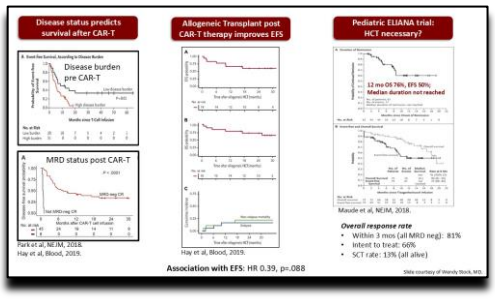
But was defiantly significant. When we look at this in the pediatric trials, the pediatric world is doing the same thing, in terms of integrating blinatumomab into up-front therapy, with standard-risk patients. None of these patients are AYAs, by definition. The AYAs are in the high risk group. But there is this investigation of blinatumomab here, as well. And then, in the high-risk study, the investigation is adding inotuzumab into up-front therapy, and the very high-risk, adding CAR T cell into MRD positive patients.



Slide 47: A041501 for AYAs 18-39 years: Can We Improve EFS to 80%?

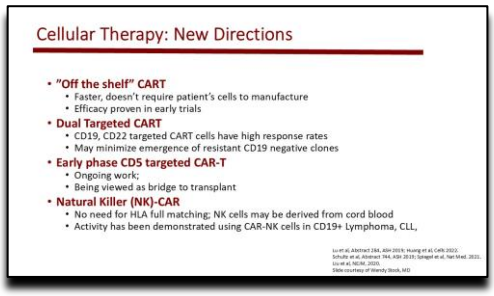
And AO41501, for AYAs that are 18 to 39, this is an active trial, as well. It's being run in parallel to that pediatric inotuzumab study. So the goal is to improve the FS in negative patients 16 of 40, who are CD22 positive.

And so, once they're in remission, they're randomized to two cycles of inotuzumab or no inotuzumab, stratified by age, at a LDA card for Ph-like ALL, as well as their CD20 status. And this the goal is to improve the three-year EFS.



Slide 48: Image

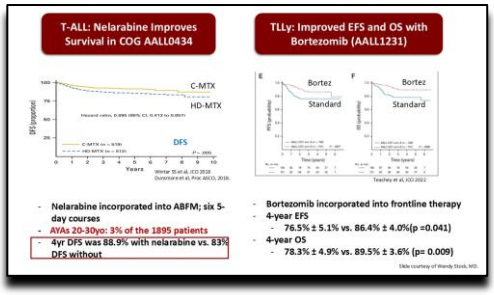
I won't really delve into the CAR T cell concept. But in the big findings, more recently, have been that disease statuses predict survival after CAR T. So disease burdened, pre-CAR T and MRD status post CAR-T, and that allogenic transplant post-CAR T does improve the EFS, and that the question, then, though, in the pediatric trial, is whether the transplant is necessary, because we there's persistence on survival, without relapse, of event-free survival without transplant. Within three months, all MRG negative. The overall response rate was 81%, with an intention to treat analysis was 66%, 13% were transplanted.



Slide 49: Cellular Therapy: New Directions

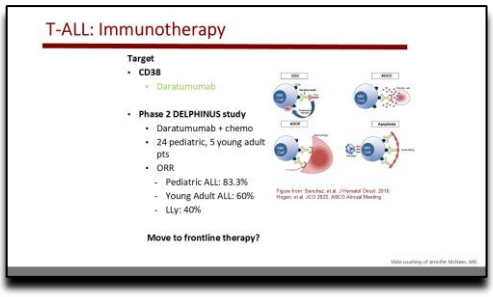
So in thinking of new directions, though, for CAR T. The benefits of the off-the-shelf CAR T are that it's faster, doesn't require the patient's cells to manufacture efficacy is proven in early trials. The dual target, CAR T, CD19 and CD22 have higher response rates. And it may minimize the emergence of resistance CD19-negative clones.

And there's early-phase CD5 targeted CAR Ts that are being worked on and being as abridge to transplant. And K-cell CAR T wouldn't require HLA full matching and may be derived from cord blood. There has been some demonstration of activity in CD19-positive lymphoma, in CLL, etc.



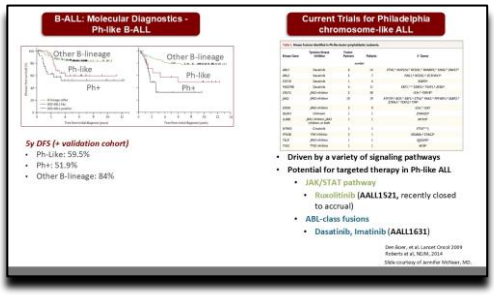
Slide 50: Image

For T-cell, quickly, the T-ALL pediatric trial, COG AALL0434, showed a benefit of adding nelarabine into up-front therapy, so disease-free survival at four years, of 89% versus 83%. And in T lymphoblastic lymphoma and the pediatric trial, ALL1231, there was a benefit of adding bortezomib into up-front therapy for four-year EFSs of 77% versus 86% and 78 versus 89.



Slide 51: T-ALL: Immunotherapy

In terms of future targets for immunotherapy, both groups are working on adding datarumumab, potentially, into up-front therapy, based on the benefit of using this in the relapse setting.



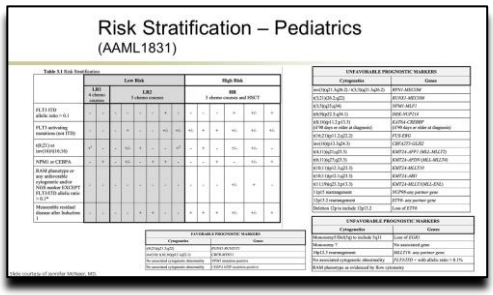
Slide 52: Image

In terms of Ph-like ALL, we know that the Ph-like patients have poor survival, as compared to other B lineage ALLs, and that these are driven by a variety of signaling pathways. Potential for targets -- the JAK-STAT pathway, the Ruxolitinib 1521 study just recently, post-accrual in the pediatric world. But there's ABL-class fusions being targeted with dasatinib and imatinib, currently in ALL1631.

Slide 53: Treatment Options and New Emerging Data: Leukemias

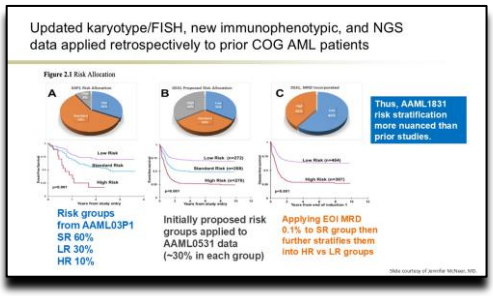
Slide 54: 2022 ELN AML Risk-Stratification (Adult)

In terms of AML -- without delving into exceeding detail, this is the risk stratifications of the adult world, where there's favorable, intermediate, and adverse risk groups, where some are transplanted in CR1, some not until CR2, if they're favorable. But then, CR1, for the majority of patients in the intermediate group.



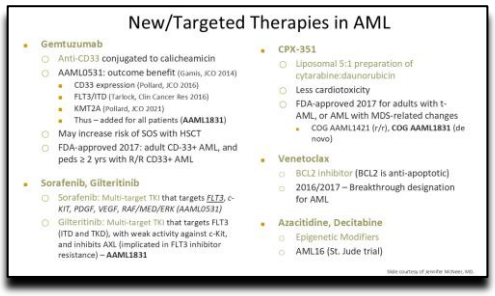
Slide 55: Risk Stratification – Pediatrics

Whereas this is the pediatric risk stratification, which is a little bit different. And this is based on unfavorable and favorable prognostic markers, along with FLT3 ITD.



Slide 56: Updated karyotype/FISH, new immunophenotypic, and NGS data applied retrospectively to prior COG AML patients

This is based on taking the patients from the previous study and looking at the risk group. This is the risk groups from O3P1, and then applying the proposed risk groups that they were thinking of instituting, to then the O531 data. And about 30% per group. But then, applying end-of-induction MRD of only at 0.1% to the standard risk group. And then, further stratifying and, then to a true low- and high-risk group. Thus, the AML1831, where stratification is a little bit more nuanced than the prior studies.

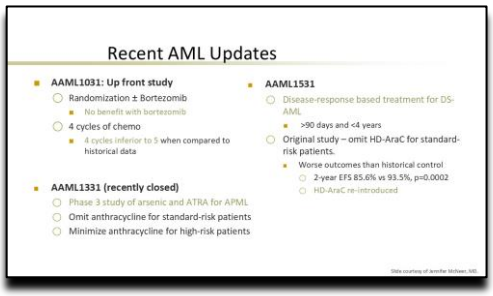


Slide 57: New/Targeted Therapies in AML

In terms of new and targeted therapies, gemtuzumab isn't necessarily new, but this is the anti-CD33 conjugated to calicheamicin, and we know that -- from the 0531, there was outcome benefit in patients with CD33 expression, as well as split-3 ITD and KMT2A, thus it's been added for all patients in 1831.

And then, sorafenib is a multi-target TKI, as is gilteritinib, with a little bit different targeting. And gilteritinib has been added into 1831 for the FLT3 positive patients. CTX351 is a liposomal preparation of cytarabine and daunorubicin but offers less cardio toxicity. And this has been integrated into 1831, as a study question, as well. And then venetoclax is a BCL2 inhibitor, which is anti-apoptotic. And this was a breakthrough designation for AML in 2016 and '17.

Azocitadine and decitabine are epigenetic modifiers that are being investigated, in terms of epigenetic priming in AML16, which is the same true trial.



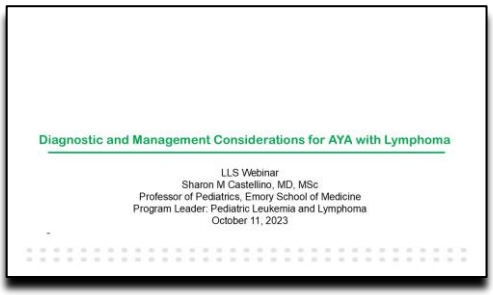
Slide 58: Recent AML Updates

There was, in terms of the recent AML study findings in PEDs, there was no benefit of adding bortezomib. Then, we tried to cut down to four cycles of chemotherapy rather than five, but that was inferior. So, went back to five for certain groups.

The APML study was the phase III of arsenic and ATRA, omitting anthracycline for standard-risk patients and minimizing anthracycline for high-risk patients. And then, 1531 is the disease-response based treatment for Down syndrome AML and initially tried to omit HD-AraC for the standard-risk patients that have worse -- their outcomes and their historical controls. And so, it was reintroduced.

Slide 59: Thank You

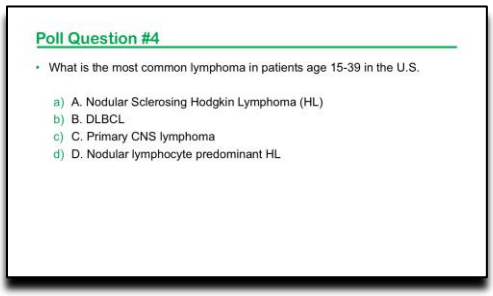
Thank you. I'm going to turn this over, now to Dr. Castellino.



Slide 60: Title Slide

Sharon Castellino, MD, MSc

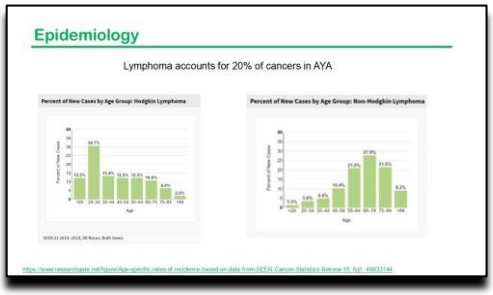
Thank you, Julie. I'm Sharon Castellino. And I'm at Emory University in Children's Healthcare of Atlanta. And I'm going to go through diagnostic considerations and treatment for AYA with lymphoma.



Slide 61: Polling Question

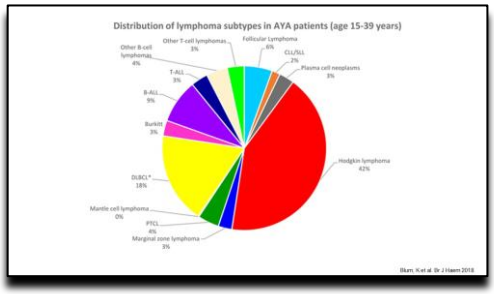
So my first poll question is, what is the most common lymphoma seen in patients age 15 to 39, in the U.S.?

So the majority of people stated that it's Hodgkin lymphoma. And yes, the nodular sclerosing sub-type is most common.



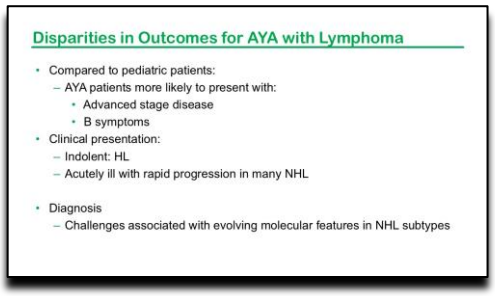
Slide 62: Epidemiology

So lymphoma accounts for 20% of cancers in adolescents and young adults, as defined by the 15 to 39 age group, and by the NCI. Hodgkin's, as you see here, has its first incident peak in the AYA years. And pediatric, non-Hodgkin lymphoma is rare. And the peak really comes outside of the AYA years. But there are considerations for treatment.



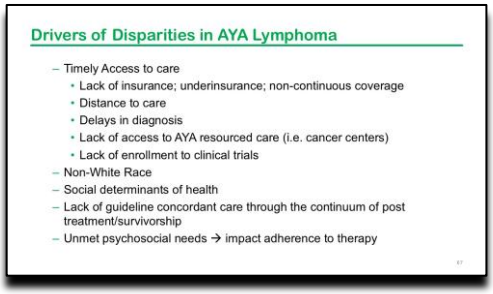
Slide 63: Distribution of lymphoma subtypes in AYA patients (ages 15-39 years)

So, SEER data has confirmed that Hodgkin's accounts for about 42% of the AYA lymphoma. And non-Hodgkin's includes about 800 cases in pediatrics a year, and many more in adults, overall. And large distribution, as you see, of histologies and sub-types sometimes within those histologies.



Slide 64: Disparities in Outcomes for AYA with Lymphoma

So the disparities and outcomes for AYA with lymphoma is that most patients who are of AYA age are more likely to present with advanced-stage disease and with these symptoms, especially in Hodgkin lymphoma. And, as you know, the clinical presentations can really vary, from being indolent to acutely ill, with rapid progression in many non-Hodgkin lymphoma sub-types. In non-Hodgkin lymphoma, there are also challenges that are associated with evolving, molecular features that define the various sub-types -- within histology.

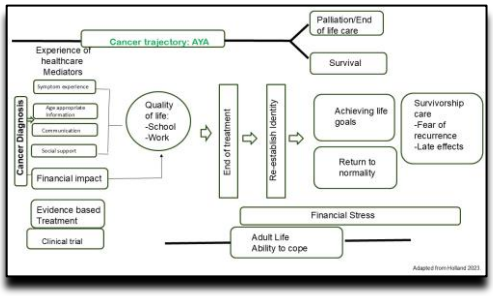


Slide 65: Drivers of Disparities in AYA Lymphoma

Drivers of disparities in lymphoma have been addressed earlier, by Dr. Wolfson. But as a reminder, it can be timely access to care, due to lack of insurance, under-insurance, or non-continuous coverage, which we're realizing more is a problem in the AYA group. It certainly delays in diagnosis, especially when it presents in an indolent way, lack of access to resource care and some of our knowledge gaps are due, as you know, to lack of enrollment of this age group to clinical trial.

I'll also show some data that indicates that non-White races -- overlaps and intersects with AYA demographics, in terms of leading to disparities and outcomes, and then, social determinants of health are variable, in terms of some of the things that have been addressed earlier. Lack of guideline-concordant care, through the continuum of post treatment and survivorship is important, although relapse is rare in many of these diseases, as currently stands, the trade-off is between late effects and the care that can impair overall survival, at that point.

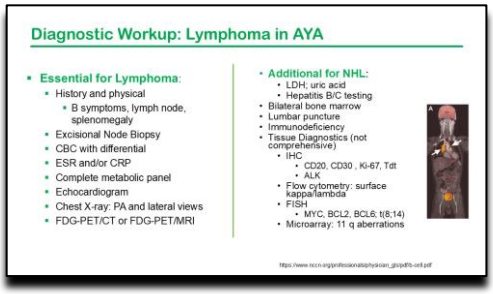
And this group has unmet psychosocial needs that can impact their adherence to therapy.



Slide 66: Image

So this was just a schema that was a reminder that, between the cancer diagnosis and survivorship. But this group has developmental considerations that effect their treatment and access and -- to not only initial therapy, but to retrieval therapy, and then to survivorship. And financial stressors are an important

part of that, especially if patients are suffering relapse.



Slide 67: Diagnostic Workup: Lymphoma in AYA

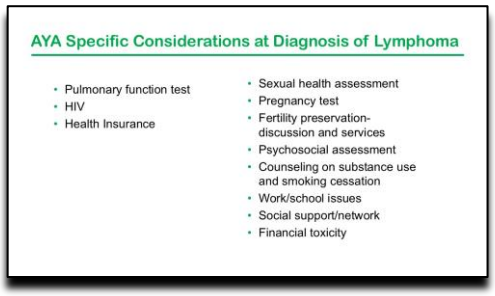
The diagnostic work-up, largely based here on the NCCN guidelines. And it's not inclusive, but I would really encourage people to look at the guidelines and remember that there are things that are essential for a lymphoma diagnosis, including lymph node group presentations, the presence or absence of splenomegaly, the presence or absence of these symptoms. But all of that has to be done in the context of knowing the histology, including tissue diagnosis for molecular features.

So excisional biopsy is really the preferred route for both Hodgkin's and non-Hodgkin's, to confirm the diagnosis. In addition, systemic disease and prognostic scores are influenced by features found on the CBC, on the SED rate, and on the metabolic panel. And most therapies will likely involve some degree of anthracycline in their inclusion, and so baseline echocardiogram, and considering that anthracycline burden is advised.

Chest x-rays, and then now FDG PET and CT or FDG PET and MRI, with attention to getting anatomical definition of disease by the CT contrasted component, is important for baseline evaluation of tumor burden. Separate from Hodgkin lymphoma, additional considerations for non-Hodgkin's include looking at the tumor burden with LDH being a stratifier of disease in management in pediatric patients. And that may be applicable to young adults being treated, as in pediatrics and with Burkitt lymphoma.

The tumor lysis burden can come high and fast a diagnosis. Checking for hepatitis is important, as we include NTCD20 antibody based therapies, because they can lead to a re-activation of hepatitadies. Bone marrow biopsy and lumbar puncture are not required, always, in Hodgkin lymphoma, but are essential to staging in non-Hodgkin's. And immunodeficiency should be considered in AYA age groups, based on a family history. And that includes not just primary congenital immunodeficiencies, but acquired immunodeficiencies, such as HIV, as well.

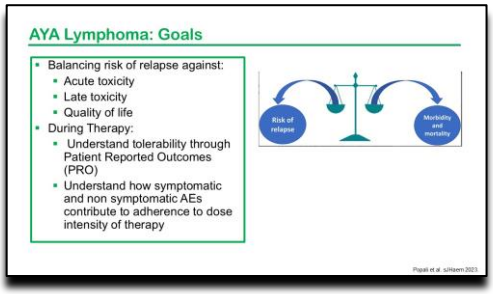
Tissue diagnostics specific for determining sub-types and classification in non-Hodgkin's are listed here. And, as I said earlier, this is not comprehensive, but distinguishing CD20 positive disease and CD30 positive disease, aggressiveness of disease, by Ki-67 in that, and ALK expression is important for distinguishing things like A-LCL for some of the other types of lymphomas. Flow cytometry is important for distinguishing Burkitt's type sub-groups, and then make BCL2 and BCL6 are parts of what can be found on FISH, in order to ascertain some of the sub-groups.



Slide 68: AYA Specific Considerations at Diagnosis of Lymphoma

So, the NCCN guidelines, as I mentioned before, have now specific guidelines separated for Hodgkin's in pediatrics and adults, but non-Hodgkin's, because of the heterogeneity of the disease, does not have different sub-sets of guidelines, until you get within the guidelines themselves, like in Burkitt's. There are some difference in factors. And then AYA-specific guidelines right now are limited to supportive care and survivorship issues and -- with a nice publication in GNCCN this past year, summarizing the updated AYA specific considerations.

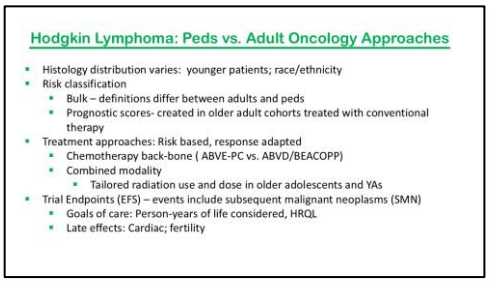
And some of those include the things we've been talking about, like attention to health insurance, attention, at baseline, to do doing a sexual health assessment, fertility preservation, and psychosocial assessments. In addition, counseling on substance use and smoking cessation is an important part of ascertaining risk for toxicity with various regimens, and, in terms of knowing which patients may have more trouble with adherence, if substance abuse is intersecting with decision making.



Slide 69: AYA Lymphoma: Goals

So the goals in treatment and current therapies for lymphoma, are to balance the risk of relapse against acute toxicity. And then, really, against late toxicity and quality of life, which we know that, with diseases like Hodgkin's and some of the non-Hodgkin's, you get very intense, high-dose chemotherapy. But late effects are a continued risk. And so the goals of current trials have been to substitute out, where possible, some of these more toxic agents, without compromising efficacy.

During therapy, more and more patients are getting assessed for their own assessment of tolerability as opposed to just the clinician adverse events grading. And these are now also reports coming out of the clinical trials to look at patient experience. And this is, I think, especially true, in AYAs who have different regard for symptom burden. And this will be important to understand how symptomatic and non-symptomatic AEs, adverse events, contribute to adherence to dose intensity of therapy, which is often more rigorously able to be delivered in younger patients.



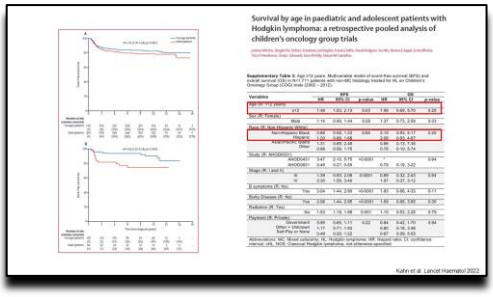
Slide 70: Hodgkin Lymphoma: Peds vs. Adult Oncology Approaches

So in Hodgkin's, as an example, the peds and adult oncology approaches are different, in several regards. The histology distribution, while nodular sclerosing histology is more prevalent in North America, in young patients, very young patients, and more in the pediatric and younger adolescent age group also have higher prevalence of mixed cellularity disease. But right now, that is all treated similarly, in the form of classic, Hodgkin lymphoma.

This is also influenced by race and ethnicity, where younger children, boys who are of Black race or Hispanic ethnicity, may be more likely to have an ex-cellularity disease. Mixed classifications have different, in terms of the measurements, bulk, between adult and pediatric standard care approaches. Prognostic scores that have been utilized by the adult lymphoma community have not always been evaluated in pediatrics and younger patients and just even the prognostic score -- one of the indicators, is age greater than 45, which doesn't apply the AYA patients.

Pediatric patient -- more recent trials, have been risk-based and response adapted. And the chemotherapy backbones have been very different. And I'll speak to that a little bit more. Pediatric regimens have maintained somewhat higher efficacy than adult regimens, historically, because the tailored addition of radiation use. But we know that those can have downstream risks associated. And then, it's been hard to compare trials, because trial end points have differed, in terms of progression-free survival being one of the markers in adult trials, and EFS of -- including subsequent malignancy with seeing the end point in pediatric trials.

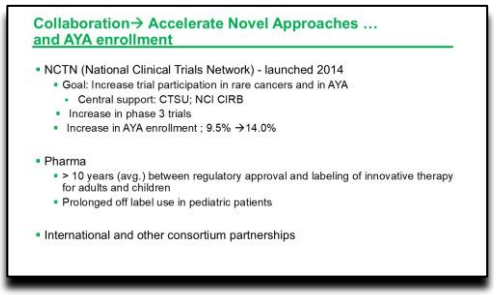
But overall, for both pediatrics and adults, the goal is to preserve first, person years of life, health-related quality of life, and to minimize cardiac events and late fertility and second malignancies.



Slide 71: Image

So, a pooled analysis, done by the Children's Oncology Group study, found that patients greater than 12 years of age had a 1.48 hazard of an event, with comparable, overall survival, when treated, and in comparison to younger patients. However, data that you don't see here, is that patients greater than 15 years of age had worse EFS and overall survival, and specifically, patients of Black and Hispanic race and ethnicity had, on-trial, comparable eventually survival, but poorer, late-post-relapse survival.

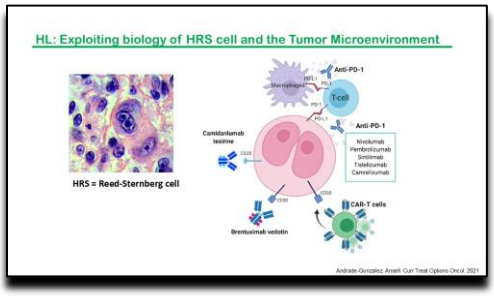
And so, all of those points I make to introduce the fact that they highlight that new approaches were needed for adolescents and young adults.



Slide 72: Collaboration→ Accelerate Novel Approaches … and AYA enrollment

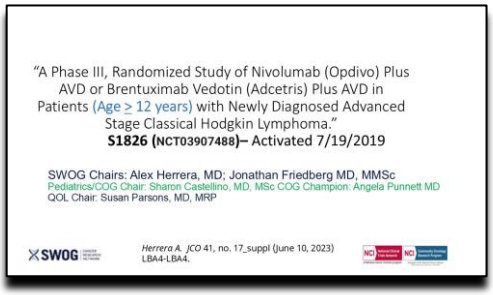
And the point that, in the young adults, each threshold in Hodgkin's may in fact be 12 and not 15. So NCTN was introduced to you by Dr. Wolfson's talk. But the goal here has been an increase in phase III trials and an increase in harmonization of enrollment of AYAs. And, as we saw, that that this went from 9.5% of trial enrollment, being in the AYA age group, to 14%.

And it's important to remember the context that, in pharma, it takes greater than 10 years, on average, between regulatory approval and labeling of innovative therapies for adults and for children. And prolonged, off-label use in pediatric patients is known. So it's important that we continue to garner international and consortium partnerships to harmonize our approaches.



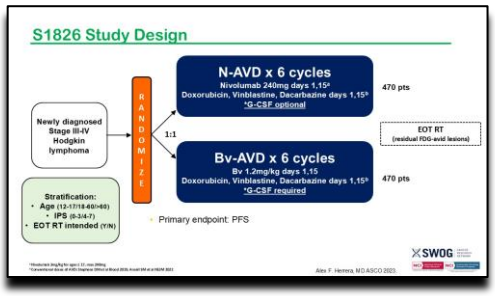
Slide 73: HL: Exploiting biology of HRS cell and the Tumor Microenvironment

In Hodgkin's, we've been able to exploit the biology of the Reed-Sternberg cell and the tumor microenvironment, specifically utilizing antibody drug conjugates, such as brentuximab vedotine against a CD30 epitope, which is ubiquitous of Reed-Sternberg. So -- and in the Hodgkin's micro environment and anti-PD1 approaches, due to the recognition of the importance of that pathway in lymphoma biology and in the micro-environment.



Slide 74: SWOG

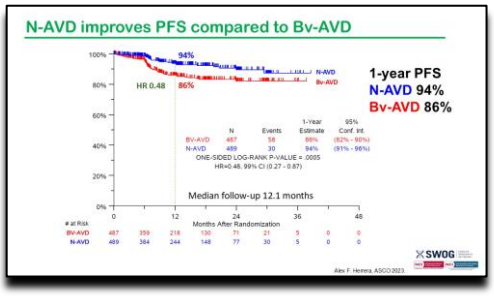
So alluding to what I discussed earlier, recently we had initiated and enrolled and completed a phase III trial, which went from age 12 up to -- all the way through the adult spectrum of age. And it was a randomized trial of incorp -- looking at nivolumab and AVD versus brentuximab AVD. And that's adriamycin, vinblastine, and dacarbizine in patients in AYAs with newly-diagnosed, advanced-stage Hodgkin's.



Slide 75: S1826 Study Design

The study design is noted here -- stage III and IV, entry was stratified by age and by intent to radiate for the pediatric population, since that had previous episode in the standard of care in advanced stage disease.

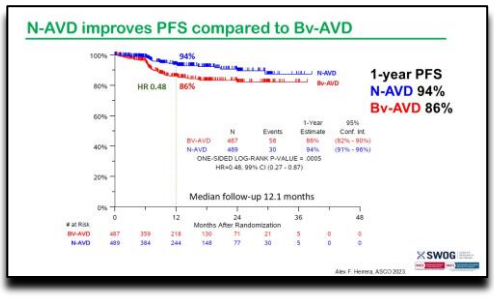
Nivolumab AVD for six cycles was compared to brentuximab AVD for six cycles and radiation, based on end of therapy results.



Slide 76: N-AVD improves PFS compared to Bv-AVD

At ASCO this year in June, Dr. Alex Herrera, who is the chair of this study, presented the data for the overall cohort. And, a median follow-up of 12.1 months, the curve had separated enough that the data safety monitoring committee recommended release of the results of this study, as nivolumab AVD had a progression-free survival of 94% at one year, versus 86% in the brentuximab AVD group.

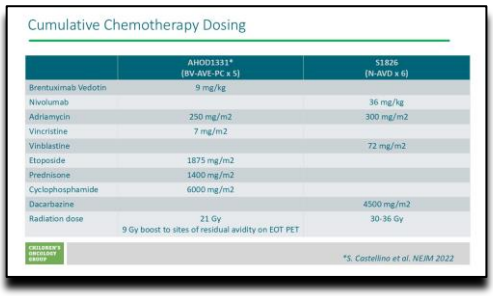
And sub-group analyses are pending and will need to be evaluated for the AYA population, over time, as this study matures.



Slide 77: Successful Collaboration with the Adult NCTN

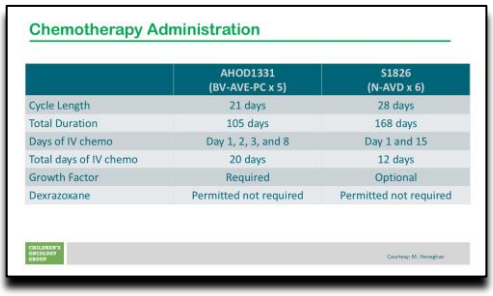
But the point that we know, at this point in the study, is that this collaboration allowed us to give earlier access to novel agents, in this case nivolumab for adolescents, and then to try and harmonize the approach of -- between adults and pediatric providers. And we'll have some parallel comparisons to the echelon one data, BVAVD, and the 1331 data that we had reported in the New England Journal in 2022, from COG.

We also have the ability to evaluate the role of RT in the setting of the new agents. And what I didn't show you on the prior slide, was that, in the overall cohort, the use of RT was under 2%. So that is a big change for the pediatric population, where we had most recently reported a reduction of RT, from 76% to still 53% of patients needing consolidated radiation. Patient reported outcomes will facilitate measurement and tolerability of these new agents and capture the new and related adverse events as a potential late effect.



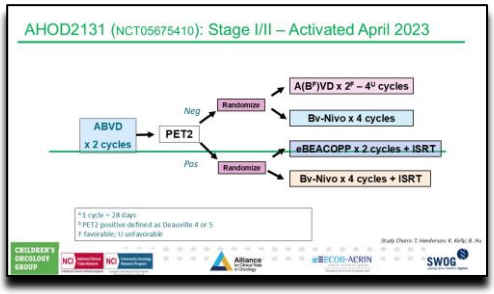
Slide 78: Cumulative Chemotherapy Dosing

And I show that just to indicate that the 1331 trial, which had a 92% event-free survival for pediatric patients up to 21 years of age, was this – dose stand regimen of brentuximab with AVE-PC, is compared to S1826, which I just described. And we'll fix this on the slide, where this is 36 mg/kilo, cumulative dose. But I wanted you to see that the cumulative doses are different and radiation dosing was different between the two trials. And so that needs to be regarded when picking a regimen for your patient.



Slide 79: Chemotherapy Administration

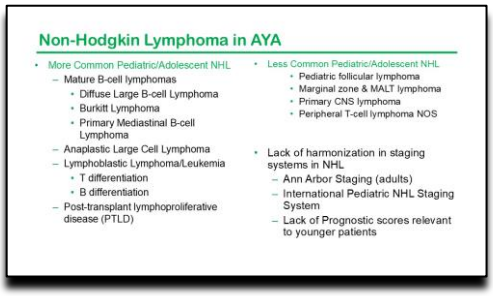
Chemotherapy administration, in terms of cycle length, duration, and days of IV chemo, for which you need to be in the clinic, also differ between the pediatric and adult regimen. And so, needs to be a consideration for AYA patients, especially those who will be in the workforce already and not have assistance with coming to clinic.



Slide 80: AHOD2131: Stage I/II – Activated April 2023

Similarly, we have an ongoing trial now, the AHOD2131 trial for early stage disease, stage I and II disease. This was activated in April of this year and uses the ABVD backbone more familiar to adult oncology practitioners and evaluates and randomizes to combinations of standard chemotherapy versus chemotherapy with immunotherapy of BV and nivolumab, based on initial response and unfavorable and favorable features, at the beginning.

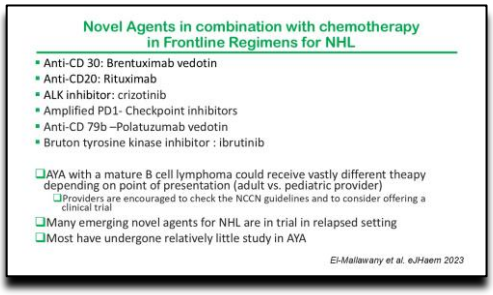
This, also, we hope will prove to be a nice collaboration and give us added information, in a standard way, in terms of the AYA sub-group that will be enrolled on these trials.



Slide 81: Non-Hodgkin Lymphoma in AYA

Non-Hodgkin lymphoma is a little bit difficult to talk about, in a succinct way, because there is so much heterogeneity in sub-types of histologies. What I will say is that there are over 30 histologic sub-types of NHL. And the majority in children and the younger, young adults are high-grade B-cell lymphomas, which have shared epidemiological and clinical patterns.

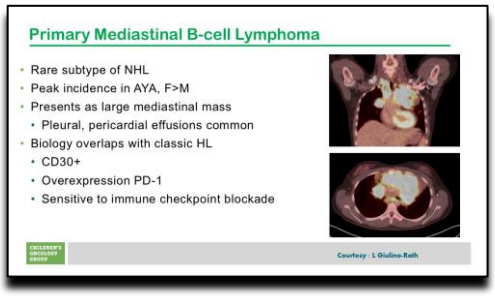
And mostly, those are Burkitt lymphoma and diffuse, large, B-cell lymphoma. Once again, the lack of harmonization in staging systems in NHL and the lack of prognostic scores, have made it difficult to always know which approach to use in your AYA patient. But I would refer you, again, to the NCCN guidelines.



Slide 82: Novel Agents in NHL

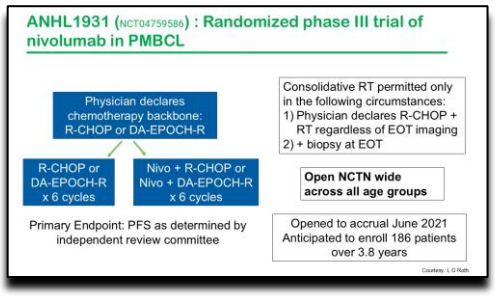
The novel agents in NHL -- and this is not inclusive and deliberately restricted, because this is what is in practice right now, with the fact that 95% of patients with aggressive, B-cell lymphomas can be pushed into remission, the new agents are mostly being explored in relapse settings.

But in terms of front-line agents, it's important to note that, in the era of rituximab, curative outcomes for high-grade, B-cell lymphomas approach 95%. And in DLBCL, adult trials generally separate their approach of DLBCL from Burkitt's, whereas pediatric regimens have, until now, treated the two very similarly. In adult oncology, R-CHOP tends to be the standard, with the newer addition of polatuzumab showing success last year in trial. But not that clear that its success extends to the adolescent and young adult group. So the standard regimens now are going to include some degree of NTCD30 therapy for diseases like anaplastic large-cell lymphoma combined with chemotherapy, rituximab based regimens in the aggressive, B-cell lymphomas. Crizotinib is an alk inhibitor, which may be of benefit in ALCL, but has a toxicity profile, including thrombo-embolic events that have to be considered, with caution, in applying this. And then, more and more, the checkpoint inhibitors are also coming into trials, as we address the micro-environment.



Slide 83: Primary Mediastinal B-cell Lymphoma

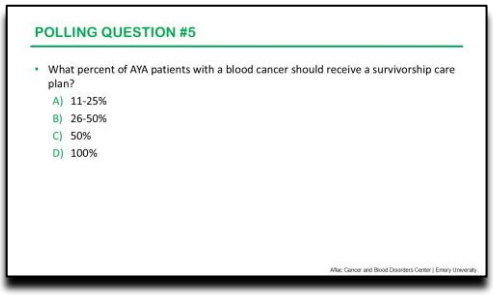
I included in here, a disease, another disease, where we have more AYA type considerations. primary mediastinal B-cell lymphoma was previously thought to be a sub-group of DLBCL, but recently been noted to have some overlapping biology with classic, Hodgkin lymphoma, including the fact that there is over-expression of PD1. And so that -- this disease entity may be sensitive to immune checkpoint blockade. So this trial, led by Lisa Giuliano-Roth, is being undertaken, as we speak.



Slide 84: ANHL1931: Randomized phase III trial of nivolumab in PMBCL

And will be looking at a combination of comparison of R-CHOP versus dose-escalated EPIC, with or without nivolumab, for six cycles, and with the primary end point being progression-free survival.

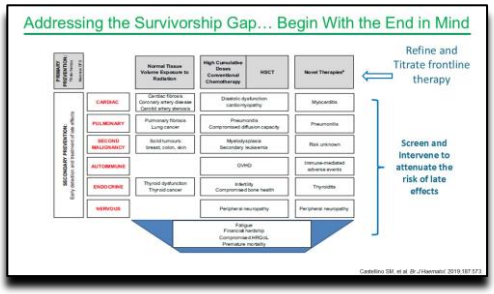
And this is a joint collaboration between the COG and Alliance, with all the cooperative groups in the NCTN enrolling. So consolidated radiation is permitted in some circumstances, but again, the goal is to reduce the need for radiation to the mediastinum, based on end of therapy imaging.



Slide 85: Polling Slide

So what percent of AYA patients with a blood cancer should receive a survivorship care plan? This is polling question number five.

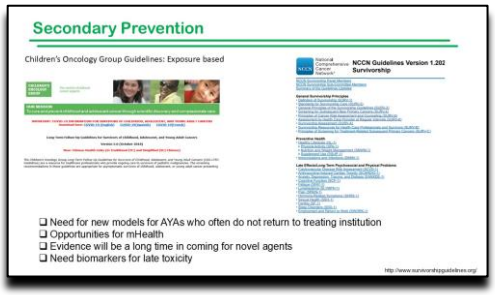
Okay, so great. So all of you agree that 100% of patients should receive a survivorship care plan.



Slide 86: Addressing the Survivorship Gap… Begin With the End in Mind

And here, I wanted to remind you that we have been discussing the beginning of treatment, but we are always, right now, in lymphoma, having our goal post eye on survivorship gap. As we have taken a primary prevention approach of refining and titrating front-line therapy, we continue to need to -- especially in our AYA patients, to screen and intervene to attenuate the risk of late effects.

And here on the left, I have the organ system based late effects that are of concern. And all of them can culminate in fatigue and in financial toxicity.

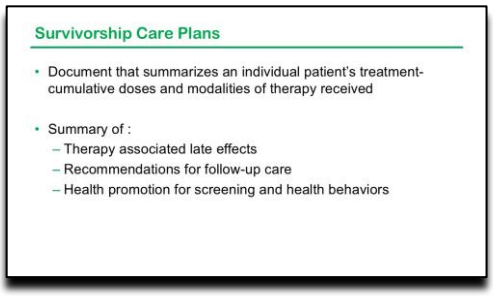


Slide 87: Secondary Prevention

And so, secondary prevention includes get -- giving patients a survivorship care plan and following screening for the risk of late effects. The Children's Oncology Group has done this, based on exposure to certain chemotherapies and based on cumulative chemotherapy dosing. And in contrast, the NCCN

guidelines for survivorship, including some of the AYA guidelines, go more by disease and by specific organ toxicity at risk.

So we need to continue to develop new models for AYAs who often don't return to their treating institutions. I think we have opportunities to utilize mobile health in applications in cancer survivors that have not been evaluated yet, but are specifically needed for the AYA population.



Slide 88: Survivorship Care Plans

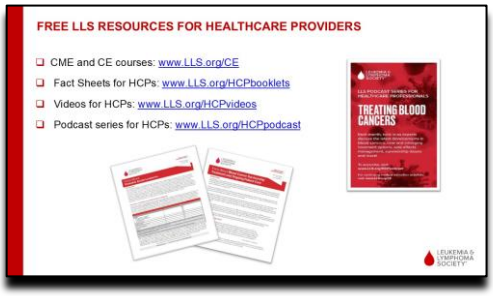
And then, just a reminder here, that survivorship care plans should include documentation of patient's treatment, cumulative doses, and modalities of therapy, at a very minimum.

And then, for the patient, helping them to be an advocate for their own health by discussing therapy associated late effects and the recommendations for follow-up, specific to health promotion for screening and health behaviors. And so, I'll turn this back over to Lesley.

Slide 89: Thank You

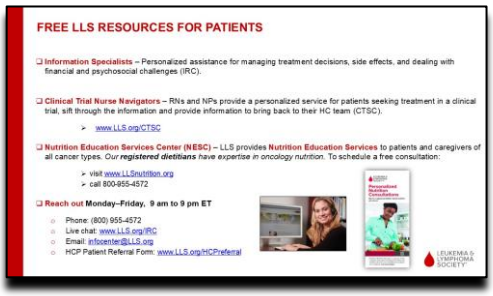
And thank you for the opportunity to present.

Lesley Hoerst, BSN, RN: Thank you, Dr. Castellino and Dr. Wolfson, for your very informative and comprehensive presentations.



Slide 90: Free LLS Resources for Healthcare Providers

I am now pleased to share free resources from The Leukemia and Lymphoma Society, for you and your patients. The Leukemia and Lymphoma Society offers free CE and CME online courses, as well as a podcast channel, where you can listen to healthcare professionals discuss treatment, side effect management, and strategies to support your patients. New and interesting topics are added every few weeks. To access these, as well as our videos and fact sheets on a variety of different topics, please visit lls.org/ce.



Slide 91: Free LLS Resources for Patients

The Leukemia and Lymphoma Society Information Specialists are highly trained oncology social workers and nurses, who provide accurate, up-to-date disease treatment and support information, including financial information. Patients can contact them directly, or you can complete a referral form. Information Specialists can also help you access or order multiple, free copies of booklets to give to your patients.

Our Clinical Trial Support Center Nurse Navigators are registered nurses and nurse practitioners, with expertise in blood cancers. They work one-on-one with patients, via telephone, to provide user-friendly information, help find appropriate clinical trials, personally assist them throughout the clinical trial process, and provide information for the patient to bring back to their healthcare provider. This is a unique services from LLS.

For information or to refer and connect a patient with an Information Specialist or a Nurse Navigator, please use the URL listed on the slide. Referring your patients for free, one-on-one nutrition consultations with one of our registered dietitians through The Leukemia and Lymphoma Society's nutrition education services sector -- consultations are by phone, available for patients of all cancer types and all ages, and are available in many languages, using our interpretation services.
I hope you will consider all of these specialists as an extension of your healthcare team.

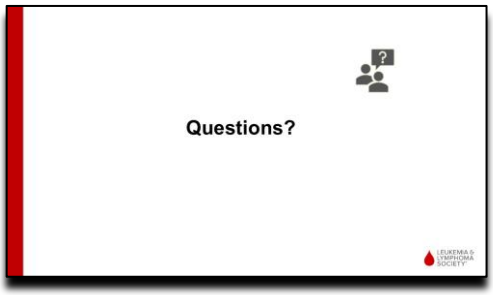
Slide 92: Free LLS Resources for Patients and Caregivers

LLS offers blood cancer, disease-specific information and support resources for patients and caregivers, including telephone and web education programs, videos, podcasts, and booklets. You may know about LLS's financial assistance program, and I encourage you to stay up to date on the availability of funds, as well as additional support resources using the links on the slide.

Slide 93: Free LLS Resources for Your Patients

Here are examples of booklets and informational cards you can order from LLS, at no charge, to give to your patients. Or, they can access them on the LLS website. Also available, are LLS's survivorship workbook for children and adolescents and survivorship workbooks for young adults, as well as our new team cancer magazine, which you can see

listed on this slide. If you have any questions on any of the LLS resources, please contact an Information Specialist.



Slide 94: Q&A
It is now time for the question and answer portion of the program.

Before beginning, there was a question that was submitted prior to the program, about what resources and grants have you found for AYA for fertility preservation expenses? And I wanted to just mention that we do have a list of scholarships and other helpful organization on the LLS website. And you can also call our information resource center that can give you that information, as well.

So we will take our first question. Can you speak to how we can make clinical trials more accessible for the AYA population?

Sharon Castellino, MD, MSc
I'm happy to take that, Julie. I think that with these collaborative NCTM trials, that having them open at more centers, including community centers, the NCORE centers, is going to be important to reach this population, in terms of them being able to access the resource. And then, I think, just remembering, for providers, to include a discussion with these patients and to not assume that they won't want to go on trial.

And sometimes that might take a little bit more effort, in terms of their understanding, their needs, maybe even though their adult "age" they may need to look toward caregivers and be able to have some support. And so, it's -- it may just take a little bit more time. But I think that the goal of the NCTN is to be able to make these trials accessible in more places, and so that you don't just have to be a COG site and ~~you don't --~~ that there's going to be so many ways to access.

Lesley Hoerst, BSN, RN
Okay. And we'll just take one, final question. How does your clinic engage and retain follow-up for AYA patients, in the long-term follow-up setting?

Julie Wolfson, MD, MSHS
I know we have a childhood cancer survivorship program that will see patients all the way through -- there's no end date. So we encourage patients to try to come see us if they were diagnosed in the age range for that. I think it's a little bit harder on the adult side, because they're so transient and they move a lot, right? So, I don't know if you have any wisdom to share on that, too?

Sharon Castellino, MD, MSc
Yeah, I think just remembering that the NCI says senior survivorship starts at the day of diagnosis. And my points earlier with that, if you can get a treatment -- a survivorship care plan to them, even as early as the end of the treatment, in diseases that we know have a high survival and not wait until two years or five years, when they disappear and don't come back. I think they are captive in that first year after leukemia and lymphoma therapy, because of the anxiety -- are bound relapse and scans and blood work.

And I think the longer I've gone on, I realize, the earlier you do it and teach them to be their advocate before they leave for college, before they finish whatever they're going to do and enter the workforce, you have a better chance of keeping them in the fold, whether it's at your own center or referring them to another survivorship care elsewhere.

At our institution, because we're a children's hospital, we can't see patients past age 23. So we have a transition program to the adult side. But I think that just getting them in early is what our approach has been, so that they understand what their long-term goals and needs are going to be.

Slide 95: Thank You!
Lesley Hoerst, BSN, RN
Thank you so much. And thank you to the audience for those questions. Again, thank you Dr. Castellino and Dr. Wolfson for your continued dedication to patients and fellow healthcare professionals. This concludes our program.

Thank you, all, for participating. We hope the information presented will be useful in your work with patients and families. We look forward to your participation on future LLS programs.