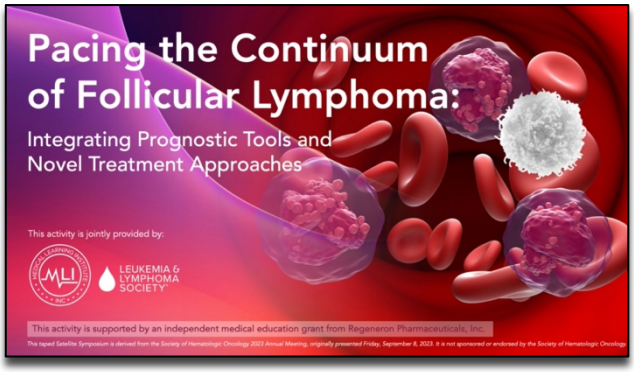
PACING THE CONTINUUM OF FOLLICULAR LYMPHOMA: INTEGRATING PROGNOSTIC TOOLS AND NOVEL TREATMENT APPROACHES

THIS IS INDEPENDENT SATELLITE SYMPOSIUM IS DERIVED FROM THE SOCIETY OF HEMATOLOGIC ONCOLOGY 2023 ANNUAL MEETING, ORIGINALLY HELD ON SEPTEMBER 8, 2023 IN HOUSTON, TEXAS



Adrienne Phillips, MD, MPH: I'd like to welcome you all to today's session, which is entitled, "Pacing the Continuum of Follicular Lymphoma: Integrating Prognostic Tools and Novel Treatment Approaches."

My name is Adrienne Phillips. I'm at RWJ Barnabas Health and the Rutgers Cancer Institute of New Jersey. And I'm joined by my esteemed colleagues who I will let introduce themselves.

Krish Patel, MD: I'm Krish Patel. I'm from the Swedish Cancer Institute in Seattle, Washington.

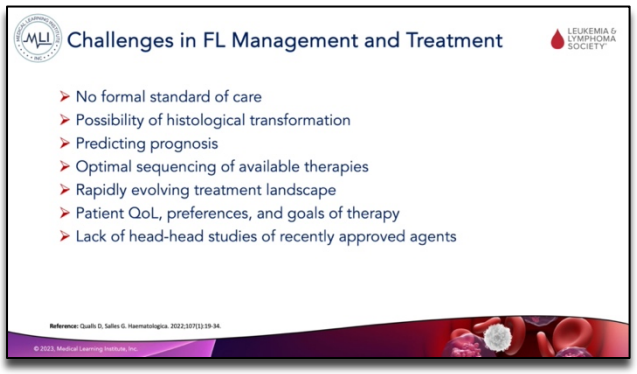
Tycel Phillips, MD: I'm Tycel Phillips, no relation, City of Hope, Duarte, California.

Dr. Adrienne Phillips: Yes, Tycel and I just met each other.

So today's session is probably going to be a little bit different, and we hope it will be fun and engaging. We will be using a gaming platform called Kahoot! and this will hopefully make this session engaging and interactive for us all.

ADVANCES IN THE TREATMENT OF R/R FOLLICULAR LYMPHOMA

Okay, so we're going to get started with our experts here, and I'll, I guess I'll turn it over to you, Dr. Patel. There's certainly been a lot of advances in the treatment of relapsed/refractory follicular lymphoma. But what do you find most challenging or tricky in this patient population?



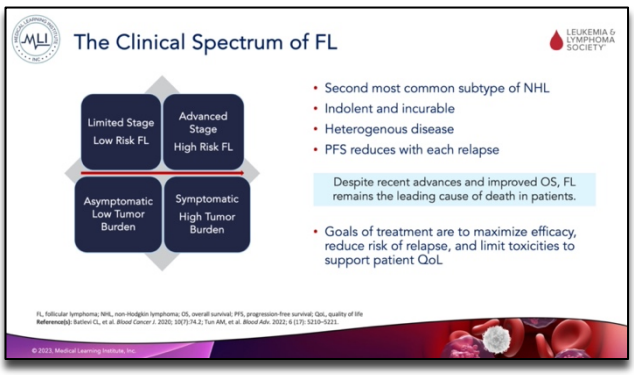
CHALLENGES IN FL MANAGEMENT AND TREATMENT

Dr. Patel: Yeah, yeah, that's a great question, Dr. Phillips. I mean I think we summarized here a couple of the kind of salient challenges. First, there, there really isn't a defined standard of care. There are lots of different treatment options that we have in follicular lymphoma, so that's a good thing for patients; but it can sometimes be challenging in thinking about how do we apply these different treatment paradigms to different patient types.

There's a lot of heterogeneity in follicular lymphoma, and so things like predicting prognosis or considering risk of transformation, which can, can be associated with poor outcomes is a challenge. And then sequencing these therapies. We have lots of different treatments available. What do we know about what order in which we

give these therapies to patients? How do we keep up with all the rapidly evolving new treatments that are available; and ultimately as we're juggling all these things, you know, how does this come back to the patient and center with their quality of life and their values?

So, these are, I think, really some of the challenges in follicular lymphoma is the heterogeneity of patient types, of treatments, and then really also I'd say that we're managing a disease over, you know, often two decades or more. And so, we really have to have a kind of long-term plan for some of our patients.



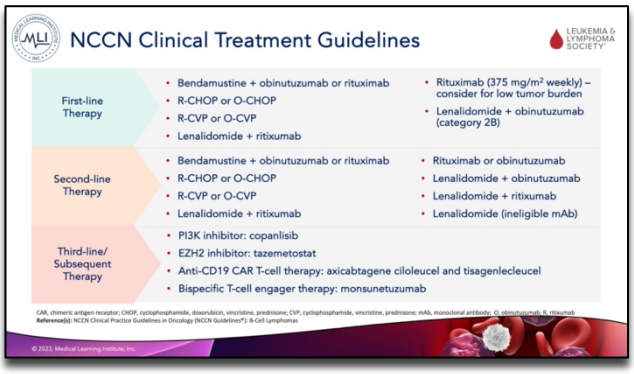
THE CLINICAL SPECTRUM OF FL

Dr. Adrienne Phillips: Dr. Patel, please start us off.

Dr. Patel: Yeah, so to kind of frame how we might approach a case like that, I think it helps us to think about how we clinically assess follicular lymphoma. And, you know, I think we can often bucket patient types into categories. I mean this is not certainly encompassing of all patients, but sometimes patients come to us with very limited stage disease. They maybe have a single lymph node in an area that was identified. They're relatively low-risk patients. We might have a specific or different treatment approach for those patients.

And sometimes we'll see patients who come to us with asymptomatic disease and a low treatment or, excuse me, a low burden of disease. And then sometimes we see the other end of the spectrum, patients that have, you know, really bulky disease and a lot of symptoms and need initial therapy.

So, we want our treatments really to be tailored to the patient's needs; and first and foremost, I'd say, you know, many patients can be observed, right? And we recognize that patients that are asymptomatic may not benefit in terms of long-term outcomes from treatment. But for some patients with low tumor burden, we might think about rituximab and the idea there really being to try to delay the time until patients receive first cytotoxic therapy.



NCCN CLINICAL TREATMENT GUIDELINES

For those patients who are more obviously symptomatic or have advanced stage disease, that sort of is reflected here in the NCCN Guidelines, we have a variety of different systemic therapy options; and these are largely antibody plus either chemotherapy-based or consideration of lenalidomide. Lenalidomide's not approved in the frontline setting, though we certainly have data that support its use.

And then as we move into subsequent therapy, we recognize that many of the treatment options that might not have been used before could be used, and then third line we'll talk about a little bit later on.

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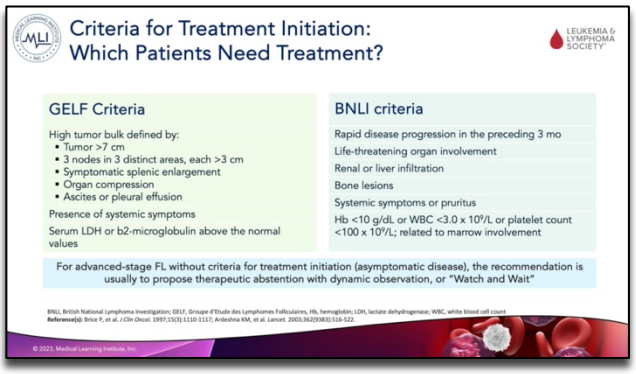
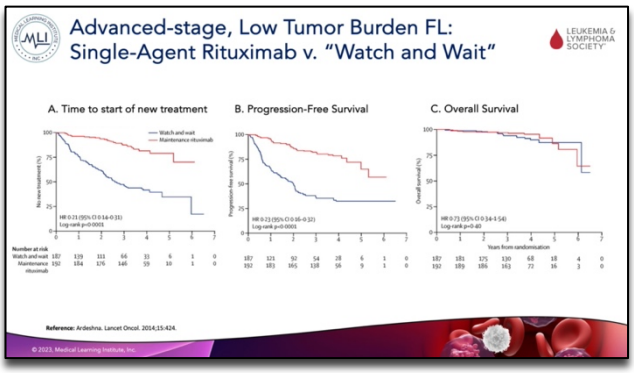


CRITERIA FOR TREATMENT INITIATION: WHICH PATIENTS NEED TREATMENT?

So, maybe it helps us to think about who are patients at diagnosis who need treatment, or how do we think about when to start treatment in follicular lymphoma? And I think, you know, you're all probably familiar with the GELF criteria. This is really a way to help define tumor bulk, and so patients that have large tumor bulk, defined here by either a single area of disease, more than 7 centimeters or more than three areas with nodes of at least 3 centimeters is commonly used. Certainly patients that have organ impairment or who have cytopenias or B symptoms are patients that we think about as being appropriate.

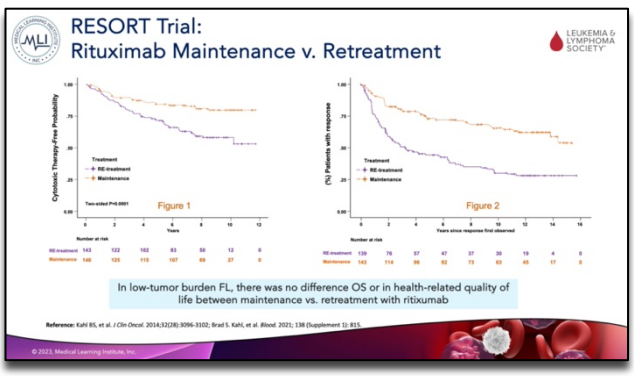
And so I think for patients with advanced stage disease, this is commonly what I use in my practice to help guide me. But ultimately, this is a conversation with the patient because patients have to feel comfortable with the plan for watch and wait. That's something for some people can be distressing. And it's also helpful to empower them to know what are the things we're looking for that are going to help us actually define when treatment might be beneficial to them.



ADVANCED-STAGE, LOW TUMOR BURDEN FL: SINGLE-AGENT RITUXIMAB V. "WATCH AND WAIT"

So these are some data that summarize sort of some of these approaches. So, for example, if we take the patient type that has advanced stage disease but has a relatively low tumor burden by definitions such as GELF, we know that one approach might be to watch these patients. And this was done in the Ardeshna trial. There's been long-term follow-up of this presented at last year's ASH. And what you see is in the blue curve, if we look at the number of patients with watch and wait, there's a fraction of patients out five years who have still never needed therapy. So for some patients, this can be reassuring. They don't want to initiate treatment. They recognize it could be some years before they needed therapy.

At the same time, we note that for some patients who did opt for initial therapy and maybe received rituximab followed by maintenance rituximab that this can actually delay the time to their next treatment. And so for some patients, that may be an important goal.



RESORT TRIAL: RITUXIMAB MAINTENANCE V. RETREATMENT

This is also supported by long-term follow-up from the RESORT trial. This was a US Intergroup study led by ECOG looking at a sort of similar question. The question was really more so is there a benefit to maintenance rituximab versus waiting until relapse and clinical need for retreatment in patients that had low tumor burden, follicular lymphoma?

And what we see in the long-term follow-up here is pretty similar, that for patients that receive maintenance therapy, we can delay the time to first cytotoxic therapy, so that might be an important goal for some patients. Alternatively, we can look at these data and recognize there's no overall survival benefit to maintenance rituximab. So for patients who are comfortable with the idea of retreatment at the time of need, then that may be an appropriate choice as well. So this is, I think, highlights just some of the heterogeneity of treatment approach in follicular lymphoma is that we can really actually tailor this to the patient's individual needs.

Dr. Adrienne Phillips: Great, thank you. So in what instances, you know, you mentioned sometimes it can be hard for patients to not get treatment. What are some strategies that you use to address their concerns and build their confidence in not getting treatment?

Dr. Patel: Yeah, I think one of the things I often tell, talk to patients about in that setting is to try to help them understand that there isn't a survival benefit associated with treatment of asymptomatic follicular lymphoma. So if we ask the question, do more people live at X, Y, or Z timepoint in the future, the answer is no. And I think helps them to take some time to really wrap your head around that and understand what that means.

And the other is sometimes to help people think, well, you know, if we're able to delay the start of treatment for four or five years, what we might have to offer as a first treatment may look very different than what we have today. And that may be advantageous to some patients. So these are some of the things I think help, but the most important part, I think, is helping them to understand that we aren't going to wait until they become really, really sick to start treatment. That we're going to follow this, that we have a plan for following this, and that we're really paying attention to changes that really impact their quality of life. And at the time the lymphoma starts to impact their quality of life, we want to intervene at the earliest moment that it's having an impact on their life.

Dr. Adrienne Phillips: Absolutely. How about you?

Dr. Tycel Phillips: No, I think I wholeheartedly agree with what Dr. Patel said.

I do think sometimes rephrasing "watch and wait." I know Dr. Zelenetz has advocated using the term "active surveillance" so that we are actively doing something, not sitting and just waiting for the disease to come. And I think the key point is, you know, treating early doesn't make patients live longer – at least we don't have any data to support that. And, you know, a little bit different from now, there's no free lunch when it comes to treatment. So there is always side effects; and, you know, so the argument of me treating you when you feel fine and then waiting for side effects to recover for you to get back to where you were clinically for disease I'm not going to cure, I mean that's sort of the argument.

If I'm not going to cure your disease, then there's no, there's no benefit at this point that we have data supporting of rushing into treatment other than allowing you to still enjoy your quality of life and sort of just thinking to try to move forward and know that, you know, this is free house money. I mean you're enjoying your life, you're not getting treated for a cancer that's not causing you any problems.

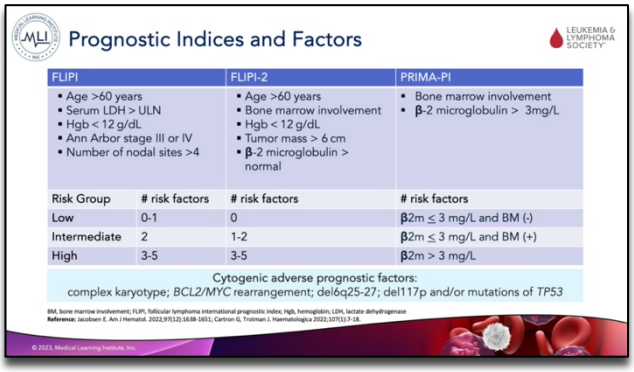
At some point, we may have to treat. At which point we fix the problem to get you back to where you are today so you can continue to enjoy your life because quality of life is really the key aspect that we're doing in these

incurable cancers because, again, we're not curing the cancers, though it'll be a lifelong problem and something we have to address as time goes along, so.

Dr. Adrienne Phillips: Yeah, I would also tell them even if we're not offering treatment, I'll see you back in three months. I'm going to get to understand your disease and the tempo and pace of how fast these nodes are growing. Maybe they're regressing a little bit.

Dr. Tycel Phillips: Yep.

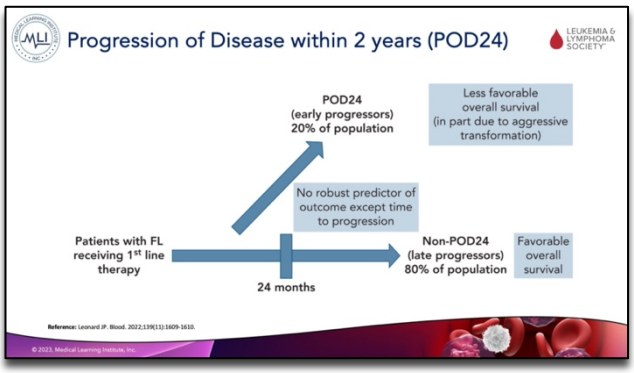
Dr. Adrienne Phillips: Great strategy, thanks.



PROGNOSTIC INDICES AND FACTORS

Dr. Tycel Phillips: So, I mean I think that case highlights a lot of the dilemma we run into with these patients who actually have, you know, follicular lymphoma and we actually treat as, you know, how to identify these higher-risk patients or the patients who may have bad outcomes. I think a lot of us, you know, advocate use of these prognostic scores; but I think for most practical purposes, the prognostic scores aren't really identifying a high-risk patient, even though we do include that data and it is very useful for, you know, retrospectively looking back and trying to see if we can, you know, help tee up some of these higher-risk patients.

But I think in routine clinical practice, I don't think a lot of us are using these prognostic scores. Well, there's FLIPI, FLIPI-2, you know, the PREMA-PI, or, you know, m7-FLIPI to sort of distinguish our high-risk, low-risk patients or making treatment decisions based off of these. But these scores are there and hopefully with continued improvement in our knowledgebase, we'll be able to utilize these scores to more so actually apply them as we would anticipate as when the patient is sitting in front of us in the clinic and helping determine which treatments will give best outcomes.



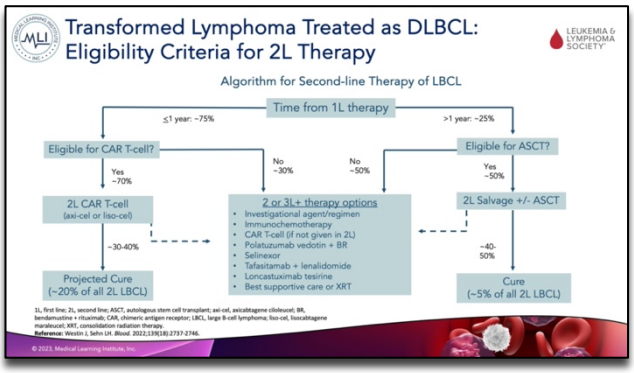
PROGRESSION OF DISEASE WITHIN 2 YEARS (POD24)

But, as of right now, you know, the biggest concern we have is POD24. I think it was a much bigger concern when these POD24 reports came out. When Dr. Casulo reported this, and, you know, we had 20% of follicular lymphoma patients who had really bad outcomes.

And the struggle we had was sort of how do we identify these patients. I wish I could sit here and say we've done a better job with identification prior to actually starting an initial therapy. But, you know, these are still patients that we are identifying on the back end.

I think one thing we have become smarter at is learning that the majority of these patients will probably have histologic transformation, you know, which highlights the needs of biopsies in these early relapsed and follicular

lymphoma patients to make sure that you are still dealing with follicular lymphoma or are you dealing with their transformed large cell lymphoma, at which point the whole treatment algorithm is quite different at that point.



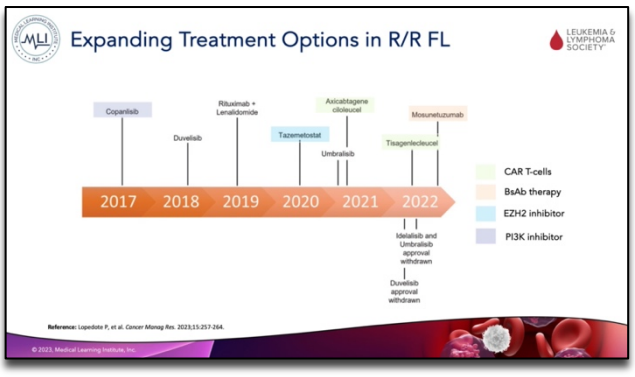
TRANSFORMED LYMPHOMA TREATED AS DLBCL: ELIGIBILITY CRITERIA FOR 2L THERAPY

So, if we can look at this algorithm here, time from frontline therapy, especially for large cell lymphoma, I mean again, if you have a transformative event that leads to large-cell lymphoma in these patients who do not respond to R-CHOP or maybe they got R-CHOP in the frontline setting for follicular lymphoma and then you left with a salvage therapy.

As you see, our NCCN Guidelines have changed quite a bit, whereas early relapsing patients are now designated to go to CAR T therapy, we have very solid data from two CAR T studies with axi-cel and liso-cel indicating that these CAR T therapies are better than what we had been previously doing with salvage chemo immunotherapy and autologous stem cell transplantation.

On the flip side, for those who relapsed or truly relapsed, and not these refractory patients, our typical algorithm of salvage treatment with chemoimmunotherapy or in patients who cannot tolerate chemoimmunotherapy, maybe even len-taf in this situation, can be applied in this situation. But I do think it's important that we emphasize the distinction between early and late relapses and how the outcomes are impacted in these patients and how patients with follicular lymphoma feed into this algorithm, especially if they have a transformative event which we need to necessarily pick up on biopsy. So biopsying these patients again is, I can't emphasize more the importance of making sure that you are treating follicular and not a large cell lymphoma.

And sometimes actually using chemical context when you can't biopsy. If a patient has a rapid progression, symptomatic and high LDH, if you can't get a tumor biopsy, it's best just to assume you're dealing with a transformative event and still treat as a follicular lymphoma in that situation because, again, my personal opinion and others can chime in, it's best to, in that situation, overtreat because you may overtreat some versus undertreat in the large cell lymphoma because, again, the more you treat large cell lymphoma and the more it relapses and, or stays present, the harder it is to cure these patients. And unlike follicular, you can't live with large cell lymphoma.



EXPANDING TREATMENT OPTIONS IN R/R FL

Dr. Patel: So as Dr. Phillips mentioned, over the years we've had more and more therapies available in relapsed/refractory follicular lymphoma. So this is just a timeline. So putting in broad categories, we have cellular therapy is like CAR T. We have bispecific antibodies recently approved. And we have epigenetic modifier which is tazemetostat, an EZH2 inhibitor, and PI3 kinase inhibitors, although a few of these have been withdrawn from the market. Copanlisib remains available.

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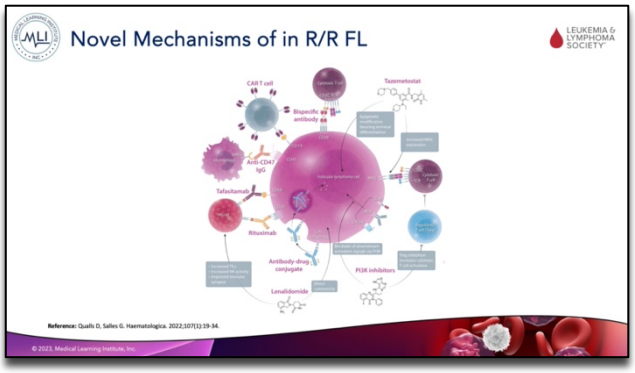
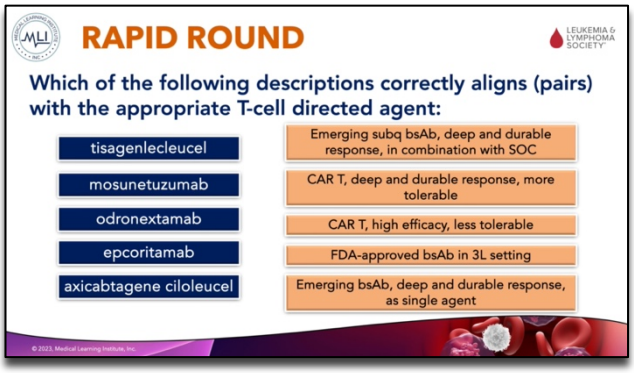


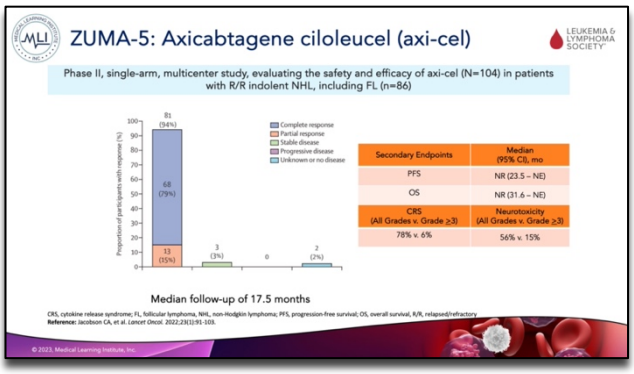
NOVEL MECHANISMS OF R/R FL

So, when we think about follicular lymphoma, again with a diversity of biology and now we also have a diversity of mechanisms by which our therapy works, they're kind of summarized here. There's a lot for us to really kind of take in. You know, therapy's like tazemetostat may work more globally in epigenetic modification and lead to changes in gene expression. That can also potentially lead to improvement in the immune system's ability to kill follicular lymphoma through increased expression of MHC. And then we have bispecific antibodies and CAR T-cells, which are T-cell engaging or T-cell mediated anti-tumor killing therapies. And we have several different monoclonal antibodies targeting a variety of different cell surface antigens; and so there really is a lot of potential for different approaches in follicular lymphoma and potentially in combination strategies as well.



RAPID ROUND

Okay, we're going to change it up. We're going to do a round of rapid fire questions, and essentially we've listed, let's see, five T-cell-directed agents here in the blue. And I'm going to give you 10 seconds to match or pair them with their description on the right in the orange. So, if we're ready, let's see the first one.

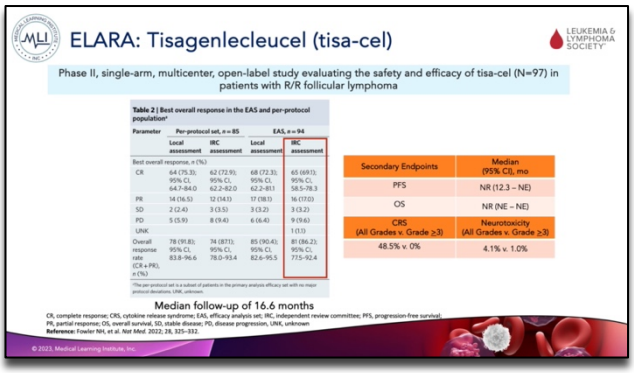


ZUMA-5: AXICABTAGENE CILOLEUCEL (AXI-CEL)

Dr. Patel: All right, so to take you through some of the data that describes these T-cell-engaging therapies, the first we have is axi-cel which is a CD19-targeting CAR T-cell therapy with a CD28 co-stim domain.

So ZUMA-5 is a trial that led to accelerated approval of axi-cel in follicular lymphoma. What you see here is overall very high response rates. The majority of patients, 79% achieving complete responses. These can be quite durable as is noted. Note haven't yet reached median PFS or overall survival, but axi-cel can cause substantial toxicities.

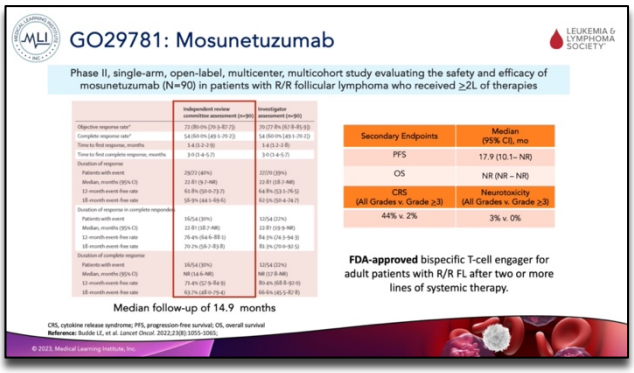
So we think about, for all CAR T-cells, cytokine release syndrome, high-grade cytokine release syndrome was uncommon, but in Grade 1 and Grade 2 was quite common. And the neurotoxicity, which can have a number of different manifestations, high-grade neurotoxicity occurring in 15% of patients and All Grade 0 Toxicity in 56% of patients.



ELARA: TISAGENLECLEUCEL (TISA-CEL)

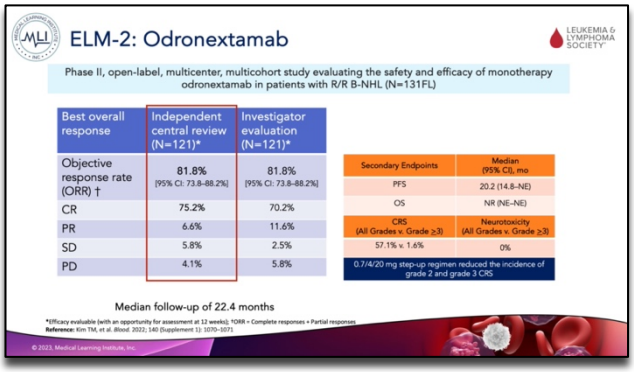
Kind of shifting gears, different CAR T-cells, tisa-cel, which is a 4-1BB co-stim CAR T-cell, also targets CD19. What we see is also high response rates here, CR rate of about 69%. Also durable responses with a little bit shorter follow-up shown here.

And what we see primarily is a difference in toxicity profile. So with a 4-1BB CAR, we see that there was no high-grade CRS in this trial. And then in terms of neurotoxicity, I think pretty remarkably we see very low all-grade neurotox and extremely low, high-grade neurologic toxicity. So this is maybe the main distinction between tisa-cel and axi-cel is the safety profile.



GO29781: MOSUNETUZUMAB

Dr. Tycel Phillips: And on the flip side, if we look at the bispecific antibodies, we have mosunetuzumab, which is the currently only approved bispecific antibody in follicular lymphoma. So for the single-arm Phase II study, we had about 90 patients. We do see in this patient population a very high overall response rate and complete response rate. I'll bet the difference being in this patient population whereas the CAR T agents are single treatments, the bispecifics in this case, mosunetuzumab after step-up dosing was given every three weeks for a total of either 8 cycles or 17 cycles of therapy based on achievement of a complete response. So there is some continuation of therapy, but it is a finite therapy in this patient population.

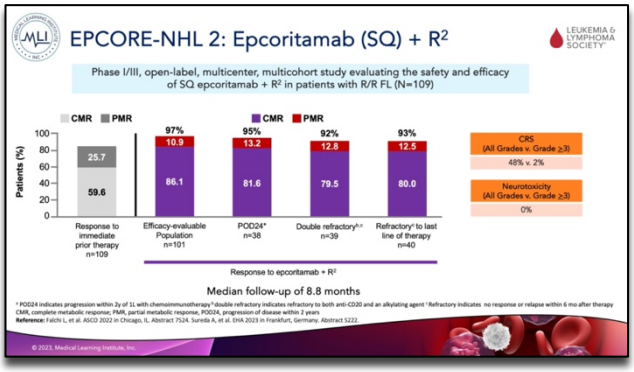


ELM-2: ODRONEXTAMAB

Progression-free survival we see as the median was 17.9 months. Now, if we look more recently, there is a second bispecific antibody that has some data, odronextamab, which was presented at the most recent ASH meeting. This has a little bit more complicated infusion schedules as compared to mosunetuzumab. So it's a split dose during the step-up dosing and given more frequently versus weekly and then every other week versus every three for mosunetuzumab. But you see a little bit higher objective overall response rate, even though, obviously, we should do cross-trial comparisons, but a slightly higher CR rate.

The PFS in this patient population all appeared to be a bit longer also than what we saw in mosunetuzumab. And we will see if this will become an option as we move along.

Toxicity wise, CRS, again, is something we see with bispecific antibodies in follicular lymphoma. But ICANs and neurological toxicity are things that are pretty much nonexistent with the bispecific antibodies in these patient populations.

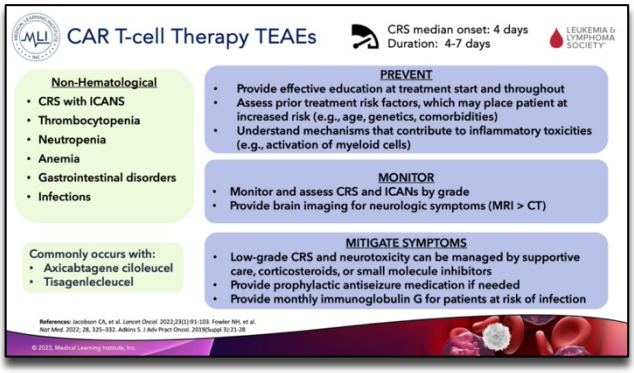


EPCORE-NHL 2: EPCORITAMAB (SQ) + R2

And I think next we'll finish off with looking at epcoritamab, which is approved for diffuse large B-cell lymphoma. And so far we have more data with epcoritamab in follicular lymphoma as a combination with R2, even frontline and even in the relapsed/refractory setting. As you can see, very high overall response rate and complete response rate in combination with R2, suggesting that the combinability of bispecifics with other agents is there without any significant changes in toxicity profile with either agent. You don't see more CRS, more ICANs, or you don't necessarily see more adverse events that you note with the lenalidomide alone except you may see slightly more neutropenia.

But I think moving forward, obviously, without the risk of higher CRS and ICANs, the other issues are more manageable, especially for those in the community. And again, if these high overall response rates translate into improvement compared to R2, we could see a paradigm shift in the second-line setting with patients with follicular lymphoma of using a combination of a bispecific plus R2 versus single-agent bispecific, so R2 alone.

Dr. Adrienne Phillips: Great. Thank you for reviewing those differences.

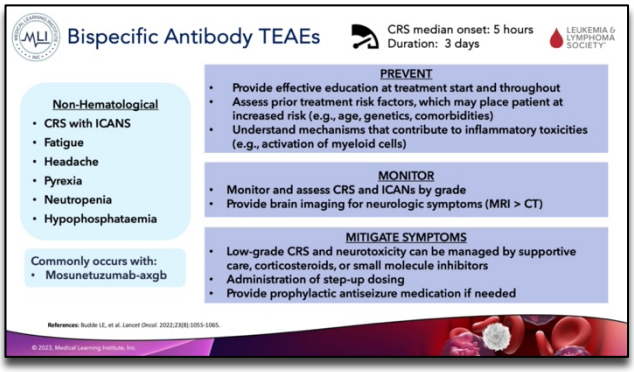


CAR T-CELL THERAPY TEAEs

Dr. Patel: All right, so to talk through some of this, so we can see cytokine release syndrome with bispecifics and CAR T-cells, but there are some distinctions. So remember with a CAR T-cell, we have a living drug; that, that CAR T-cell is going to proliferate; and that's going to sort of lead to immune activation and then, subsequently, we may see cytokine release syndrome.

So median onset in CAR T-cell therapy tends to be different by different product. But, you know, around four days or so is what was seen in ZUMA-5. The duration can be four to seven days. That maybe reflects, again, the fact that these are proliferating cells.

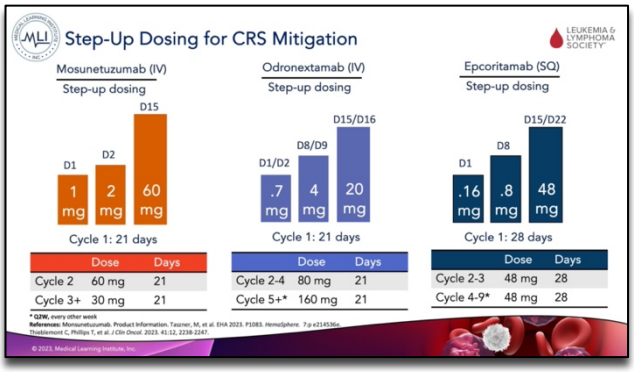
The manifestations are common, whether we're using CAR T-cells or bispecifics. We typically think about fever, hypotension, hypoxia. We can see other adverse events as well. And then in particular when we're managing CAR T-cell-related CRS, our friends are dexamethasone and tocilizumab. And in some settings we may even be able to give prophylactic dexamethasone to help reduce the risk of CRS.



BISPECIFIC ANTIBODY TEAEs

And then, remember, because the CAR T-cell is really a perpetual living therapy, some of our patients can develop long-term B-cell aplasia and may have a need for gamma globulin replacement.

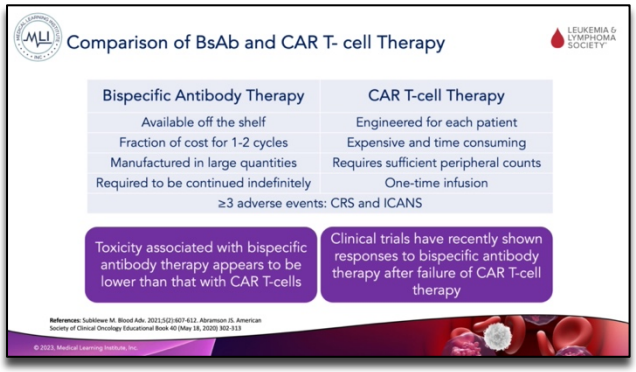
With bispecifics, similar clinical manifestation; but the median onset tends to be, first and foremost, dependent on where we are in step-up dosing. So this varies a little bit by bispecific, but it tends to happen pretty quickly, usually within the first 24 hours after an active dose is given. The duration is, perhaps, a little bit shorter. And then in terms of management, this is where we tend to see across trials less use of tocilizumab is needed in bispecific antibodies, although it may be used. And dexamethasone, also a useful tool here. And so the rate of CRS varies across the different bispecific products like it does across different CAR T-cells as well.



STEP-UP DOSING FOR CRS MITIGATION

So I mentioned step-up dosing. So, this is a strategy that's been used in all bispecific antibody development to try to reduce the risk of CRS. And the idea here is to really kind of step into the full dose of therapy so that we're not getting very high levels of T-cell activation and cytokine release with the very first dose. And so that's been used across these three bispecifics that we've described – mosunetuzumab, odronextamab, and epcoritamab.

You'll see the step up is a little bit different, and so for odronextamab, it's more of an intermediate dose for that second dose. With mosunetuzumab and epco, you see there's a big jump from second dose to, to full dose. And so this is something we want to be aware of, and then the dosing schedules are a little bit different across these different agents. With mosunetuzumab, it's primarily study. There's a fixed duration therapy.



COMPARISON OF BsAb AND CAR T-CELL THERAPY

Dr. Tycel Phillips: So, I think some of the points we summarized, if we look at the differences between bispecifics and CAR T, I mean I think both are, obviously, trying to utilize T-cells to elicit response.

But Dr. Patel said CAR T is a living treatment where the bispecific off the shelf is utilizing the patient's own T-cells.

And so CAR T, obviously, is a one-time treatment. The CRS onset is a little bit later. CS duration may be a little bit longer. The risk of ICANs and neurotoxicity is there with CAR T, even though low rates, depending on which agent you're using, ideally, is not something you specifically will see with bispecifics.

Obviously, one-time treatment, cytopenias, you know, count recovery can sometimes be an issue. Infection is probably an issue with both agents, especially in our new era of, you know, perpetual COVID-19. I mean, but it does give us options for our patients, depending on the patient's preference, the patient's needs, if they don't have caregivers, they live in an area where they're not near CAR T centers. Obviously, you do have the bispecific antibodies that you can use off the shelf.

If you, obviously, live near a CAR center, you don't want to necessarily go through a treatment that you may be on for a year, then, obviously, you know, CAR T is an option in that patient population.

So I think options are there. Sequencing is also a consideration. You know, one before the other is also something that we can consider. So, I think given our patients options, having these discussions, and sort of tailoring the treatment to what best fits the patient's needs and lifestyle at that point is a benefit for all of us and things that we can take into account when we make these treatment decisions and something that will, obviously, benefit our patients all moving forward.

Dr. Adrienne Phillips: Right, so, yeah. I think, you know, there's no right answer; and frequently with follicular lymphoma, you follow these patients for years. You get to know their values, their goals, what's going on in their life. And this question is just asking how do you involve your patients in shared decision-making and tackle these barriers that present themselves?

Dr. Tycel Phillips: Yeah, honestly, as I mentioned before, obviously, you know the patients. You discuss the pros and cons of the treatments, and I think you sort of get a feel for what your patients would necessarily prefer at that period of time. Then in a situation like this, where it's a little bit different from what we deal with diffuse large B-cell lymphoma, I mean again both of these treatments and some of the other drugs that we have available are all appropriate options that we can consider because, again, it's the incurable nature of follicular lymphoma that allows us to know that in a person's lifetime, they may receive all these treatments. So, you can continue to discuss and sort of pick and choose how each treatment may fit where the person is in their time, in their life and what's going on in their life. Maybe they don't have a caregiver at that point in time, or maybe they just don't prefer to come to the clinic every three months. Maybe they want an oral treatment for the time being. So, you can have these discussions and sort of address things appropriately, knowing again, like I said, that these other things are there; and one does not exclude the other.

Dr. Patel: Yeah, I think similarly, I try to explain all the options that are available to the patient and try to fit that into what I know about that patient and what they preference; and sometimes it takes time, right? This is a lot of information to download.

And so one of the things about follicular lymphoma is we generally are not pressed to make a decision right away. And so I think introducing these ideas of treatment, giving the patient materials, time to think about it, ask questions, bring them back, and then as Dr. Phillips mentioned, recognizing that for some patients, you may actually get all of these different therapies; and maybe the order might make a difference to you based on where you are in life, what's going on right now.

And so I think this is something that really takes a lot of time and effort; and, you know, fortunately, in follicular lymphoma, we usually have that time to be able to engage the patient and their family and talk about this. And I think that's super important.

Dr. Adrienne Phillips: Yeah, and I would just add in terms of tackling barriers, being a transplanter and cell therapist, I think referring patients to a transplanter and cell therapist sooner than later because we didn't talk about the logistics of manufacturing these CAR T products, but it can take time. And you want to begin those discussions, so I would, you know, if you have the option, get those specialists involved sooner than later.

Congratulations. I want to thank everyone for participating. I hope you've learned a lot.

I'd like to thank our colleagues as well, and we're going to finish up.