Slide 1: NEW AND EMERGING THERAPIES FOR BLOOD CANCERS

Operator:

Welcome to the telephone and web education program, *New and Emerging Therapies for Blood Cancers*. It is now my pleasure to introduce your moderator, Lizette Figueroa-Rivera. Thank you, Lizette. Please begin.

Slide 2: WELCOMING REMARKS

Lizette Figueroa-Rivera:

Hello, everyone. On behalf of The Leukemia & Lymphoma Society (LLS), I'd like to welcome all of you today. LLS is the largest nonprofit dedicated to creating a world without blood cancers. Since 1949, we've invested more than $1.8 billion in groundbreaking research, pioneering many of today's most innovative approaches. Our support of pioneering research worldwide is breaking new ground in the fight against cancer. We are in a period of building a transformational treatment. After a series of breakthroughs in recent years, including new precision medicines and immunotherapies, researchers are working hard to refine and expand their use so more patients can benefit.

Breakthroughs take years of research, and we owe it to patients to ensure we spend just as much time exploring every avenue after the breakthrough to make sure that these new drugs are used optimally. Thanks to targeted

therapies for so many types of cancers at all stages, more patients can avoid harsh chemotherapies. When chemotherapy is necessary, doctors can use updated versions of chemotherapy drugs, combine and deliver them in new ways, and they have better ways to reduce the serious side effects of chemotherapy that can limit or even prevent treatment in some patients, especially older patients.

Progress on all of these fronts will continue in 2025 and beyond with a wide range of research ongoing in each area. As the research continues, LLS continues to provide free information and support services as we are the voice for all blood cancer patients seeking access to quality, affordable, and coordinated care. Let us be here for you and your family, and please continue to tell us how we may assist you. Thank you so much for sharing your time with us.

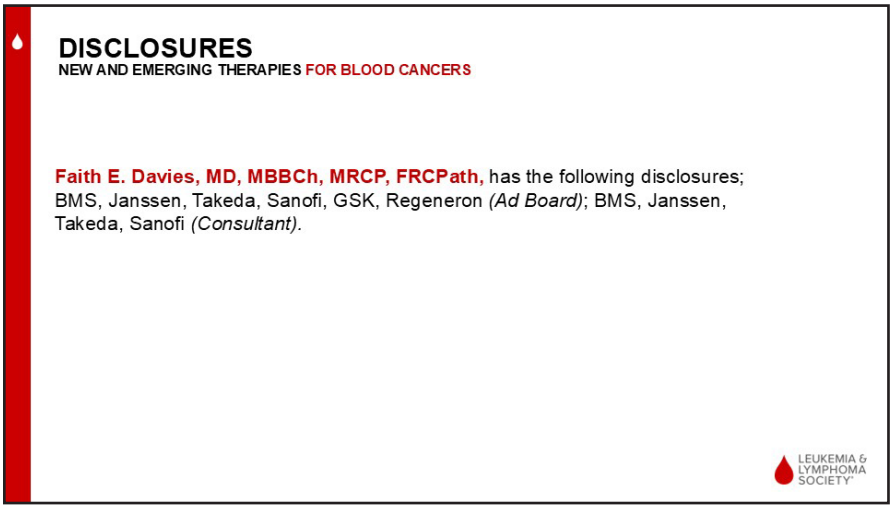
Support for this program is provided by Genmab US, Inc.

It is now my pleasure to introduce Dr. Faith Davies, Director of the Clinical Myeloma Program at NYU Langone Health and Professor of Medicine at NYU Grossman School of Medicine in New York, NY. Dr. Davies, I'm privileged to turn the program over to you.

Slide 3: FACULTY

Dr. Faith Davies:

Thank you so much, Lizette. It's a real privilege to be here today and to be chatting with you about some of the new things that are happening in blood cancers. It's actually a huge topic to squeeze into such a short time. I apologize if I missed some of the finer details about some of the blood cancers.

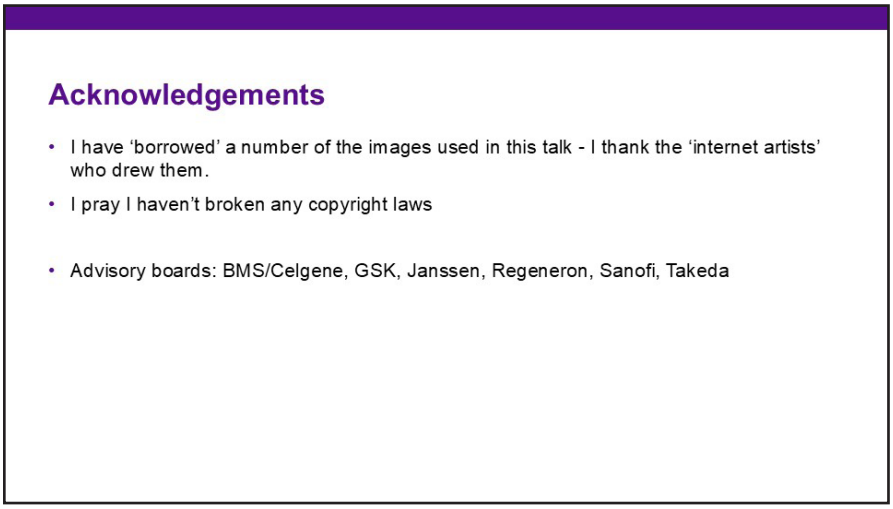


Slide 4: DISCLOSURES

As I think everybody's aware, blood cancers actually represent about 10% of all cancers, and you can imagine there's a lot of new and exciting things happening.

Slide 5: NEW AND EMERGING THERAPIES FOR BLOOD CANCERS

What I want to do over the next few moments is to talk about some of those things.



Slide 6: Acknowledgements

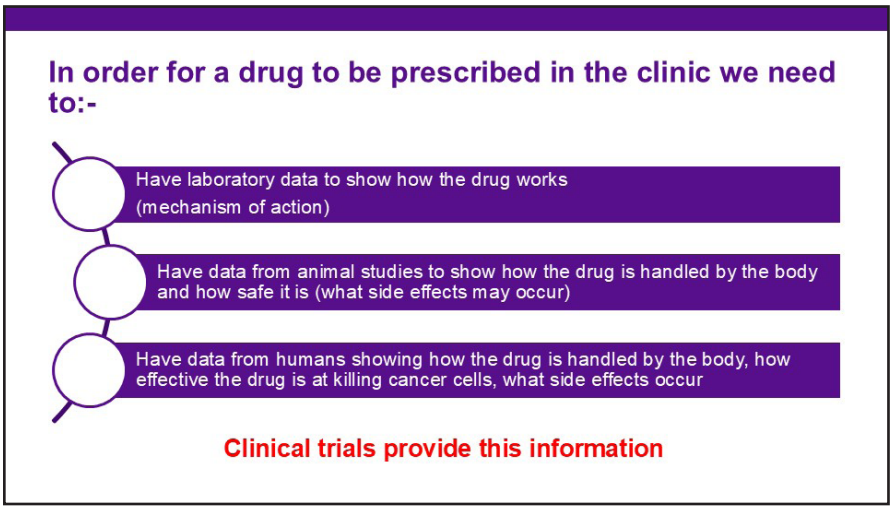
I think before I start, I have to say that I have borrowed some of my pictures from the internet. I have tried to check that I haven't broken any copyright laws. My drawing is absolutely awful, so I've taken some pictures that other people have drawn. Hopefully, we won't be causing any trouble and they will appreciate what we're trying to do with this. I also just need to tell you that I do work closely with a number of drug companies, really trying to ensure that new drugs get developed properly and get brought to patients as quickly and as efficiently as possible.

Slide 7: Talk Outline

What are we going to talk about today?

I want to start a little bit about clinical trials because I think that really sets the scene for us as to what we're trying to achieve and what regulatory framework we have to work in to make sure that our drugs are delivered to patients in an effective way and also in a safe way. Once we've chatted a little bit about that, I then want to talk about some of the new emerging therapies. As Lizette said, I want to talk a little bit to begin with about some of these targeted treatment approaches or precision medicine approaches, and then I'm going to move on to a little bit about immune therapies.

Hopefully, as we go through, we'll touch on some new treatments for leukemias, for myelomas, as well as for lymphomas.



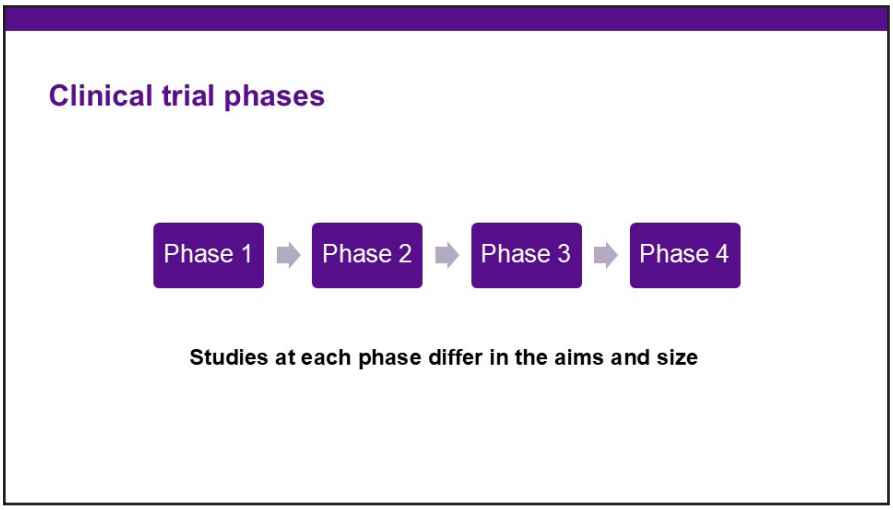
Slide 8: In order for a drug to be prescribed in the clinic we need to:

Let's start at the top. I'm sure many people who have unfortunately had blood cancer for a long time will already know many of these things, but just so that we get everybody on the same page before we get into the gory details. In order for us to prescribe a drug in the clinic, there is actually quite a strict process that a new drug needs to go through. The first things the drug needs to do is for researchers to really understand how that drug works and that work gets performed in a laboratory.

They're really ensuring how the drug will kill cancer cells but also how the drug might get metabolized in the body. The next stage, unfortunately, has to be performed on animals because that's going to give us some clues as to how the body handles the drug and also what side effects we might expect to occur. That's particularly around... does the drug get excreted by the kidneys, does it get broken down by the liver, what kind of things do we need to know about the drug so that we can give it to our patients safely?

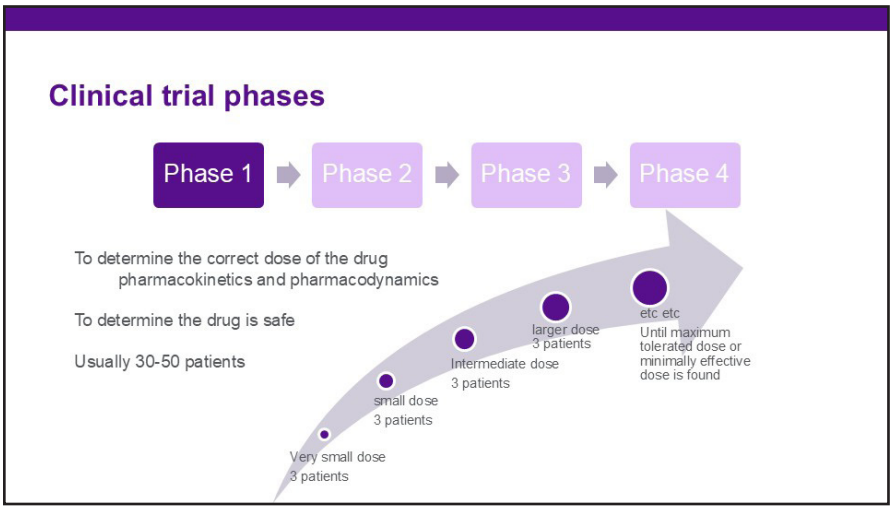
Then the final stage is actually showing in patients that the drug, number one, is handled well by the body but also is effective at killing cancer cells and then learning more about what side effects may occur. Once the drug has gone through all of those things, a large document is prepared for the regulatory authorities in the US (United States) that would be the FDA (Food and Drug Administration), and they review this and if they think that the data is strong enough and that the drug will help patients and not cause too many side effects, then that drug will get its license and we'll be able to use it for patients.

Now, clearly, there's that chunk of time between when the drug is initially made when we do those clinical trials on our patients to see a little bit more about the drug. This is really key to the development because no matter how much we do work in the lab, we never really know what's going to happen in patients.



Slide 9: Clinical trial phases

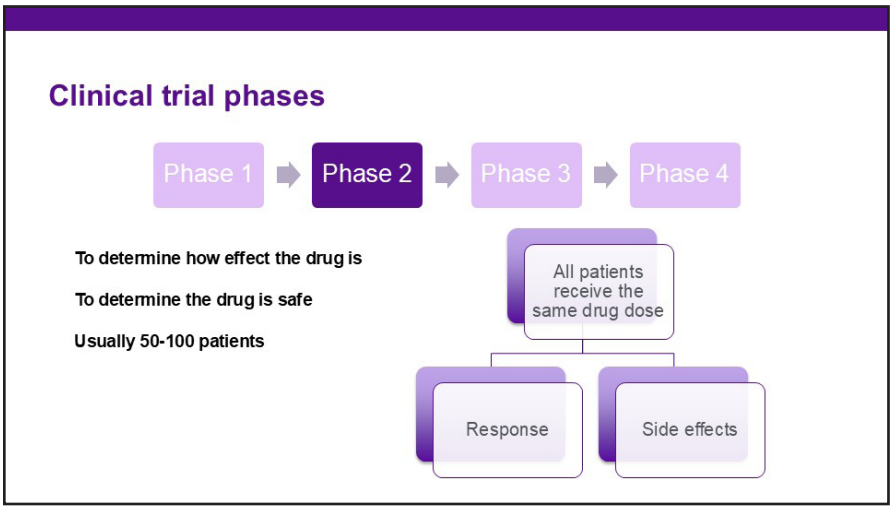
There are 4 different phases to the clinical trials that we can perform. I just want to talk a little bit about these because this lays the foundation for the next part of the study. Each of these different phases of a clinical trial has different aims of what it's trying to achieve and different numbers of patients who are actually included in the study.



Slide 10: Clinical trial phases

For our first phase, where we call this a Phase 1 study, the main aim of this approach is to try and ensure what the correct dose of the drug is. In this phase, we tend to treat a very small number of patients, it may only be 3 or 6 patients to begin with, with a small dose of the drug, and we watch to see how they respond to the drug and try and ensure that the drug is metabolized correctly by the body. Assuming those patients get on well with the drug, then we move forward with a slightly larger dose of the drug and treat another 3 to 6 patients with the drug.

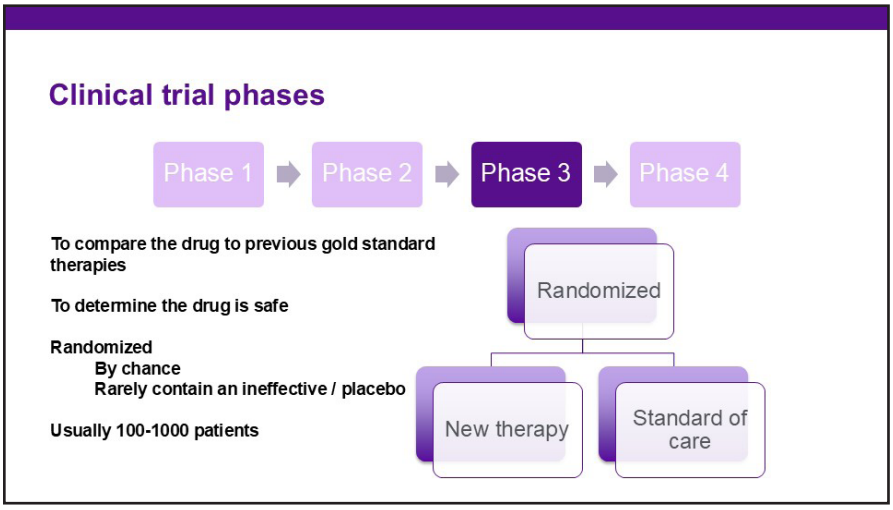
If they get on okay, we carry on doing that, treating more and more patients with the drug until we get up to what we call the maximum tolerated drug or MTD or the minimally effective dose or MED. Essentially, what those 2 things mean is that's what we think is going to be the best dose of the drug for patients, which ideally will kill the cancer cells and hopefully not have too many side effects. Usually, there's about 30 to 50 patients in total who would be included in those very early studies.



Slide 11: Clinical trial phases

The next phase of the study is what we call a Phase 2 study. In this particular phase of the study, we're actually going to determine how effective the drug is. That's key to know because a Phase 1 study is really aimed to look at safety, it's not aimed to look at how effective the drug is. In some studies, we do that as well, but usually, how effective a drug is in the Phase 2 portion. In this portion, it's usually maybe 50 or 100 patients.

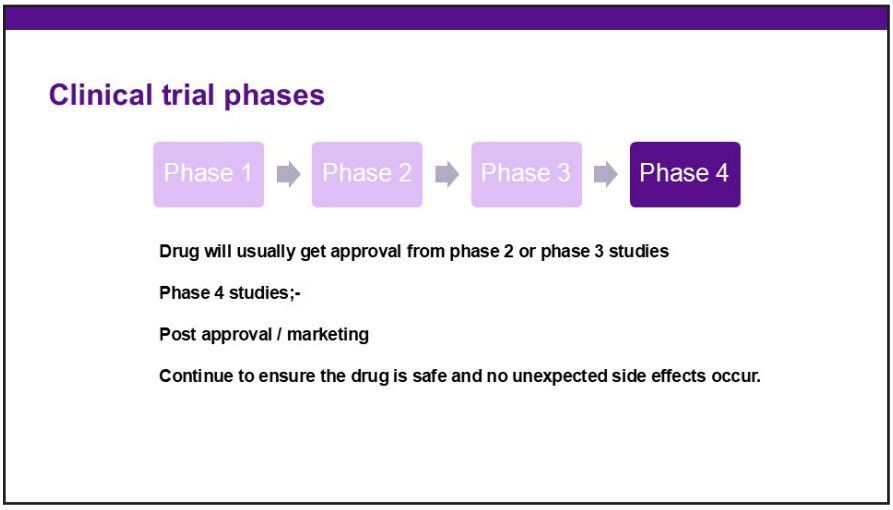
Those patients are looked at very closely, again, firstly to determine how they respond to the drug and how deep that response is and how long that response lasts, but then also to learn a little bit more about side effects and what side effects may occur and if they do occur, how we might manage them, but also when they may occur because as you know, some side effects can occur in a couple of days of having a new treatment, whereas other side effects may take a few weeks or indeed months before they occur.



Slide 12: Clinical trial phases

Once the drug has been demonstrated to be safe and effective, then the next phase is called a Phase 3 study. In the Phase 3 study, usually what happens is that the drug is compared to the previous standard of care for that disease area. Usually, in this study, patients are randomized. A computer determines by chance which treatment arm the patient should get. I have to say at this point, it's very rare that patients will get an ineffective treatment or a placebo, particularly in cancer studies. It usually is comparing one known effective treatment to the new treatment.

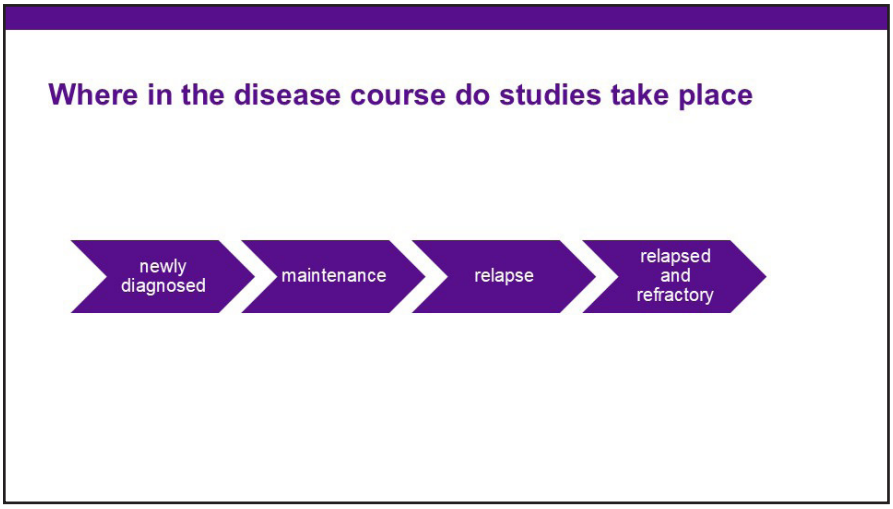
This area here, it can be anywhere between 100 and 1,000 patients really trying to determine which is the best approach and also learning a little bit more about side effects.



Slide 13: Clinical trial phases

Then finally, all of that data would be given to the regulatory authority, EMA or FDA, and the drug would get its license. After that, then clearly we still need to continue to monitor patients who have the drug. These are called Phase 4 studies or post-marketing studies. Essentially, this is that sometimes drugs can have very, very rare side effects or unexpected side effects that we may not have picked up in the previous studies.

It's important to ensure that we do pick these up. Patients will be continued to monitor just to make sure.

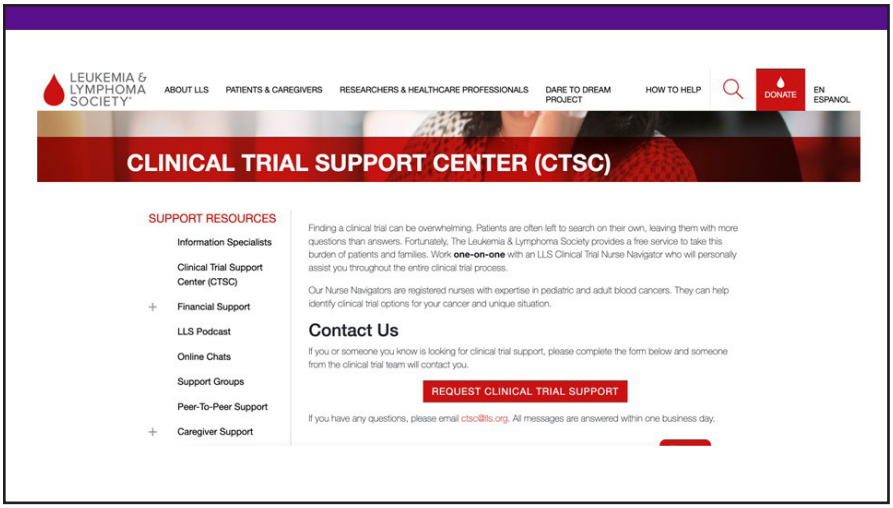


Slide 14: Where in the disease course do studies take place

Clinical trials can actually take place in any part of a patient's disease course. They are more common, I guess, for new drugs in the relapsed and refractory setting. Those are patients who have had all of the drugs that are available and unfortunately their disease comes back. Those patients will sometimes be offered the opportunity to try one of these new drugs. Once we learn a little bit more about those drugs, then the studies will often open up in the relapse setting, in the newly diagnosed setting, or indeed in the maintenance setting.

It does depend a little bit on what kind of drug is it and what side effects that can occur as to how quickly the drug may become widely available. Also, so for some drugs, let's say there's a new drug, it's exceptionally good, but it has quite a lot of side effects, it may be that actually you don't ever want to have that drug in the newly diagnosed setting because in that setting maybe you already have a drug which is very good and doesn't have quite as many side effects. There is a little bit of differences between drugs and where they end up getting placed in our treatments, but at each of these phases there are clinical trials.

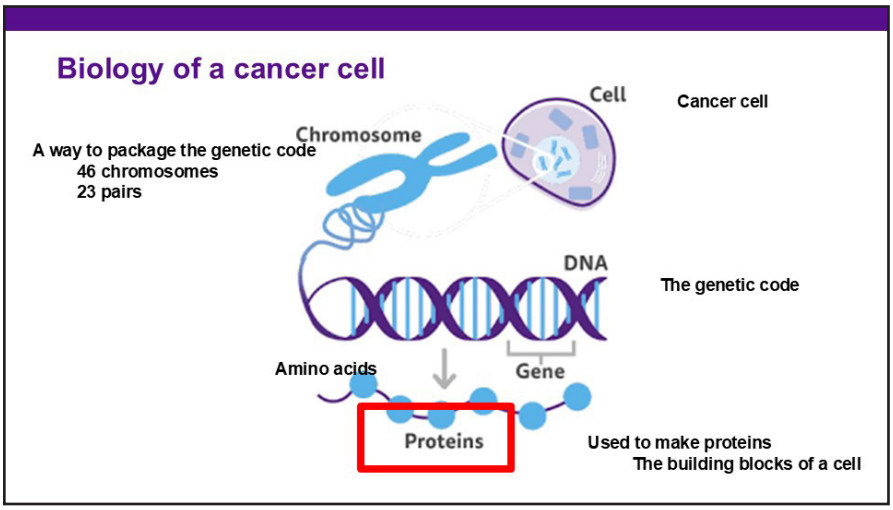
I would really encourage you that if you have the opportunity to take part in a clinical trial, either looking at a new drug completely or looking at a new way to give a new drug, that you at least consider it because that's the way that we make lots of progress.



Slide 15: LLS CLINICAL TRIAL SUPPORT CENTER (CTSC)

I just want to do a huge shout-out here for LLS because they do a really exceptional job of really working out which different hospitals have clinical studies ongoing. There is a government website that keeps hold of these as well, which is clinicaltrials.gov. The LLS have one that's specifically for blood cancers, and they would be more than happy to talk to anybody who's interested and to try and connect them up with a suitable clinical trial.

They have a tab on their website called the Clinical Trial Support Center. Please do feel free to go ahead and to have a look at that. That's my introduction. Let's get on and start talking about some of the new drugs. As I said, what I'm going to do is divide it into 2 parts. To begin with, I'm going to talk a little bit about some of these targeted drugs or precision medicine approaches.



Slide 16: Biology of a cancer cell

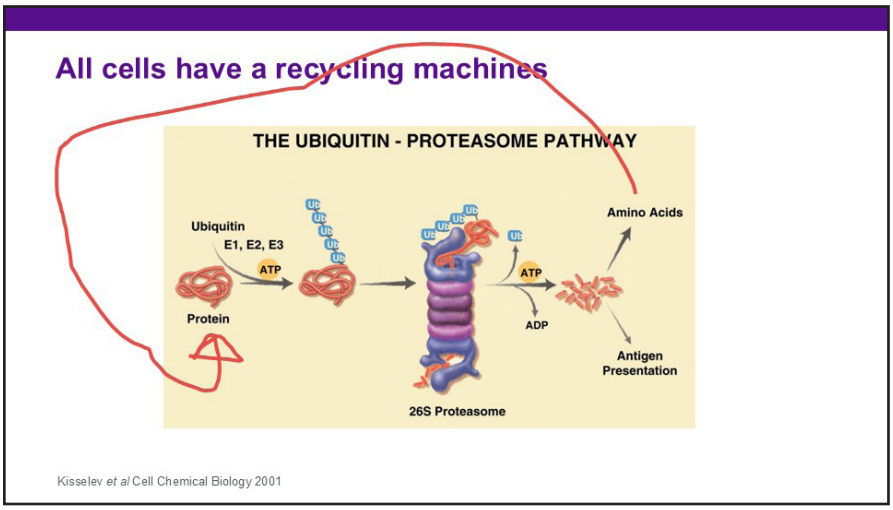
In order to do that, we need to do a bit of biology. Please bear with me for a few moments as I drag you back, kicking and screaming to your school days.

If you think about it, we've got our normal cells. Our normal cells within them hold all of the genetic code to make sure that cell behaves itself and does its job properly. That genetic code gets packed, if that's the right expression, into what we call a chromosome. It's just the way the code is organized. Everybody has 46 chromosomes. Within that genetic code, which is also called DNA (deoxyribonucleic acid), we have a number of different genes. Everybody has slightly different genes, and these genes help to determine how tall you are, whether you have blue eyes, whether you have fair hair, etc, etc.

These genes then get read to make the proteins, which are the building block of our cells. Those proteins make sure that the cell grows well and interacts with other cells. When a cell becomes cancerous, it still looks a little bit like its normal counterpart, it's normal cell. But clearly something within that cell's programming, be it at the chromosome level, at the DNA level, or at the protein level, something has gone wrong, which makes that cell no longer behave properly. Instead, it is able to continue growing, to not die, and to not listen to any of the other cells that's around it.

What the targeted treatments are able to do is to pick out one of these abnormalities in the cancer cell and ideally try and either kill the cancer cell or stop it growing, but the abnormalities only in the cancer cell rather than in those normal cells, and so the normal cells don't get affected. That's very different from traditional chemotherapy, which for anybody who's had it, they'll realize that the traditional chemotherapy, yes it knocks off your cancer cell, but it also knocks off your normal cells as well. It's a bit of a, I'm going to say, bomb approach, whereas actually in an ideal world, we want a very specific approach.

What has happened is with the explosion of all of the different technologies we can use in the lab to understand cancer cell growth much better than this has resulted in us learning more about what's specific to a cancer cell and also what we can do to try and kill these cells off. I want to start off by talking a little bit about some of the new approaches to targeting specifically proteins in the cell.

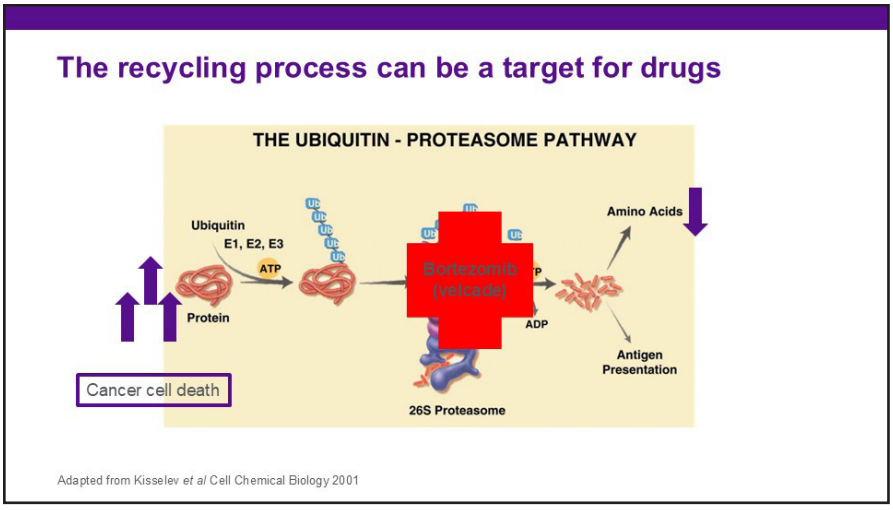


Slide 17: All cells have a recycling machines

I'm going to start off. There's going to be some long words, so please just bear with me. I'm going to start off talking about the ubiquitin-proteasome pathway.

Essentially, this is a process within the cell which really acts like a recycling machine. If you think about it, in order for a cell to behave properly, sometimes it needs to make some proteins, and other times it needs to stop making those proteins. Therefore, in order for it to continue to grow and survive, when it stops making that protein and no longer needs that protein, it puts a tag on it to say, "Hey, I don't need this protein anymore," and that protein gets thrown in the trash. The kind of trash machine is called a proteasome.

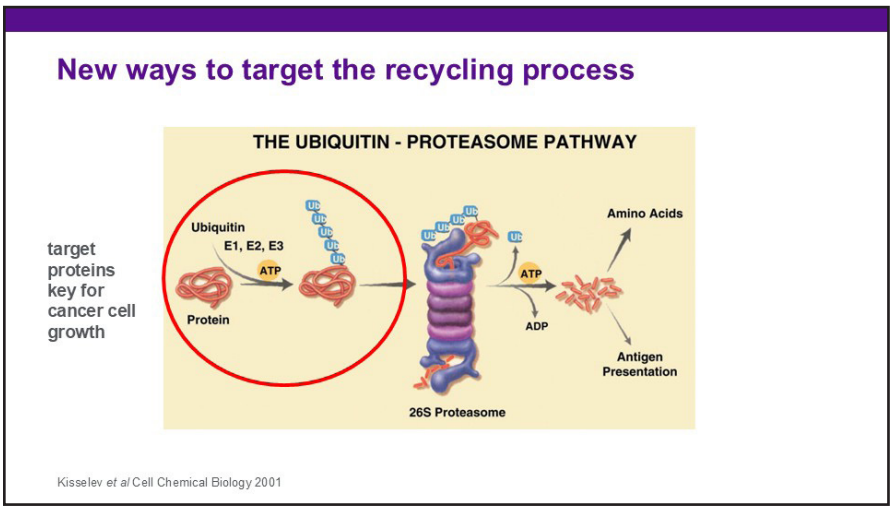
When that protein goes into the trash machine, into the proteasome, its components or its amino acids, its building blocks get spat out, and then those can be recycled to make new proteins for the cell. It's a recycling machine where you break down proteins you no longer need, and then you can reuse them to make proteins you do need.



Slide 18: The recycling process can be a target for drugs

Now we've known about this proteasome for many, many years. An actual fact, one of the drugs we use in myeloma is based on killing off this proteasome or inhibiting stopping this proteasome work. That drug is called bortezomib (VELCADE®). Essentially, what happens is bortezomib stops the proteasome working, and as a result of that, because the

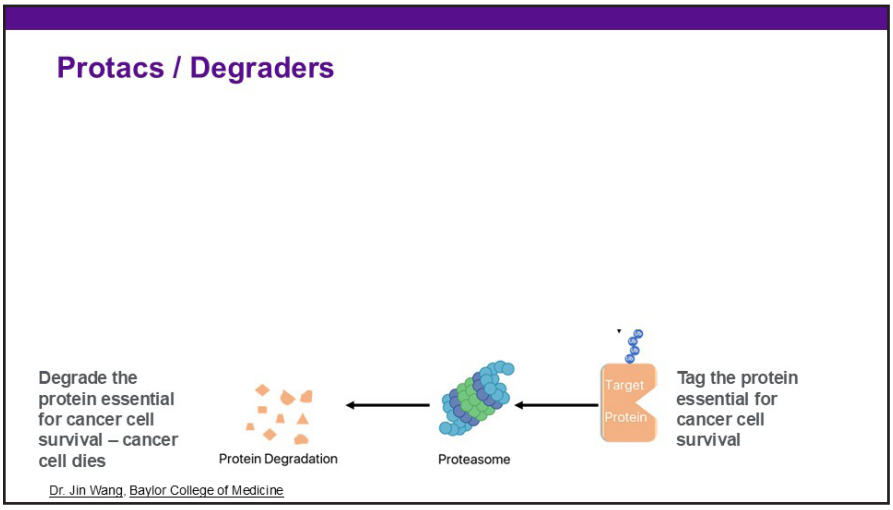
proteins don't get degraded, we don't get the amino acids, the small portions of the proteins, we don't get the recycling. Cells can no longer build new proteins, but also those old proteins that the cell wanted to get rid of hang around. When those cells are hanging around, then the cell gets very dirty, for want of a better expression, and that results in the cell dying. These drugs are now very effective. As I say, there's bortezomib, there's carfilzomib (KYPROLIS®), all used a lot in multiple myeloma. What the interesting thing is that actually now there's a number of drugs which are using a similar process, but are using it in different disease areas. Let me tell you a little bit about that.



Slide 19: New ways to target the recycling process

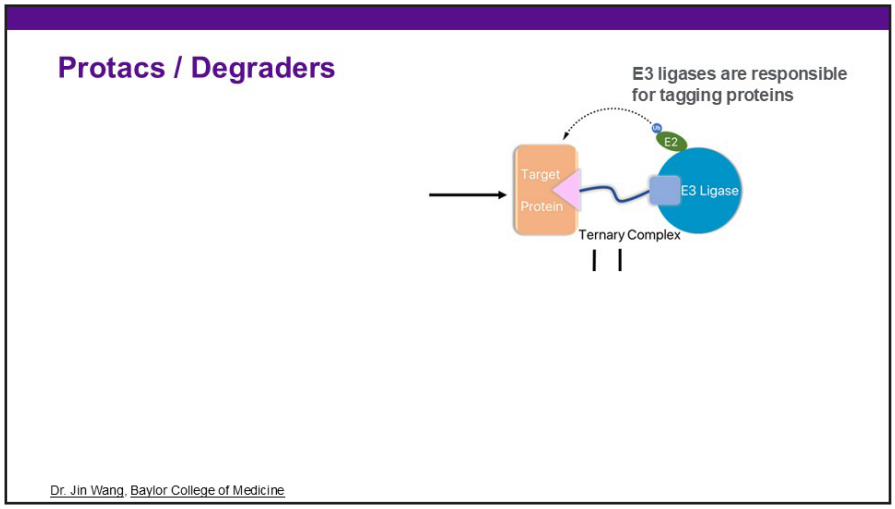
When we think about how a drug gets to the proteasome, so how the cell realizes that this protein is no longer needed and it needs to be killed off, it gets a tag put on it or a flag put on it to say, "Hey, get rid of me, throw me in the trash." What the scientists have been able to do is to hijack that process. That's the beginning bit of the process.

What they've been able to do is to say, what happens if we take a protein that is really key for our cancer cell growth, not for our normal cells, just for our cancer cells, and we confuse the cell and tag that protein and say, "Hey, this protein, which is important for our cancer cells, we want you to be destroyed and we want you to disappear." Therefore, the cancer cell no longer has that protein, and therefore the cancer cell dies.



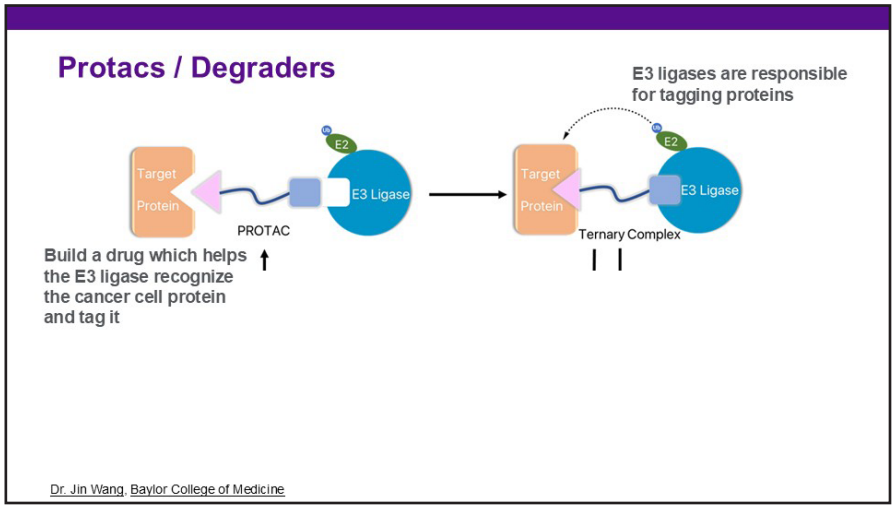
Slide 20: Protacs / Degraders

They've been able to do that with these new drugs, which are called PROTACs or degraders. Essentially, in my picture here, if we look on the right-hand side, we've got a protein, our target protein, which we stuck a tag on or a flag on. This protein's really key for our cancer cell. What we're doing is that we've put its flag on. We're saying, "Hey proteasome, degrade this for us." The proteasome gets rid of it and then the cancer cell dies because that key protein is no longer available.



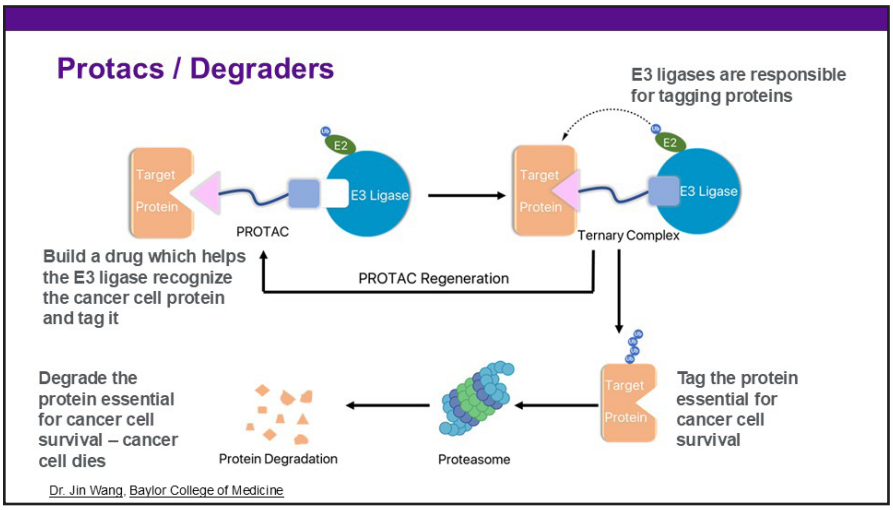
Slide 21: Protacs / Degraders

They've been able to design drugs which make the body recognize these target proteins and send the proteins to the proteasome.



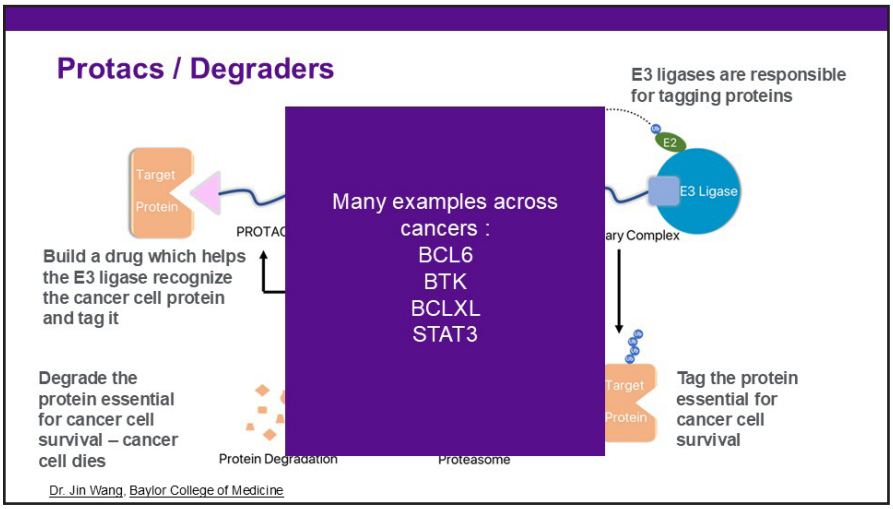
Slide 22: Protacs / Degraders

They're using the body's own system and tricking the body's own system into doing this. That's what we call a PROTAC.



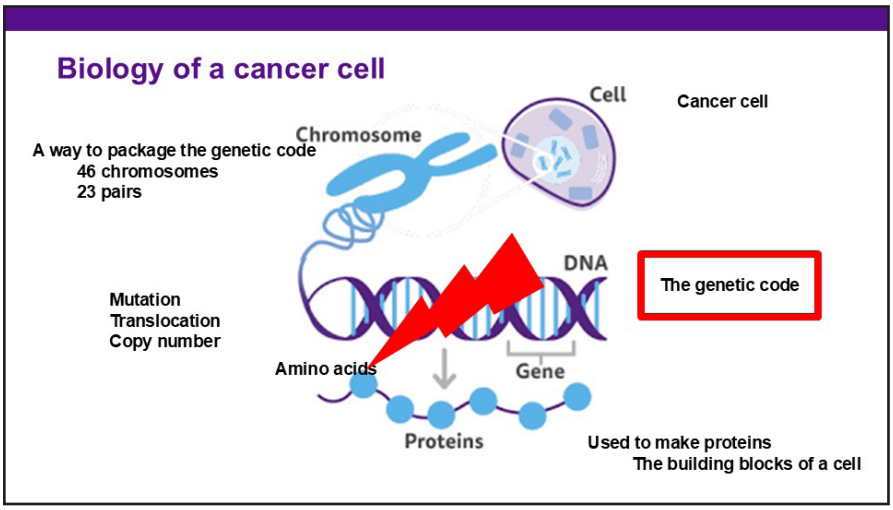
Slide 23: Protacs / Degraders

When that's in the system, this target protein will lead to cell death.



Slide 24: Protacs / Degraders

Now, there are actually lots of examples going through clinical trials now using this. None of them have actually made it to the approvals yet. They're still in these early phases of clinical trials. They seem to be very promising results. They're all targets for different cancers. For instance, for lymphoma, then BCL6 is known to be a protein which is really important for lymphoma cell growth. This is a way of getting at that protein and taking it out of the system. We know that BTK is an important protein for CLL (chronic lymphocytic leukemia) growth, and drugs like ibrutinib (IMBRUVICA®) or zanubrutinib (BRUKINSA®) have been used against this BTK. They act by binding to BTK and stopping it working. These new drugs would actually just take it out of the system. Then there's drugs which help cells to be killed off more easily or indeed help some of the signaling pathways. These are being looked at in leukemia. The actual process is important for all blood cancer cells, and the different types of these degraders are being used in different kinds of cancers. Something to look out for.

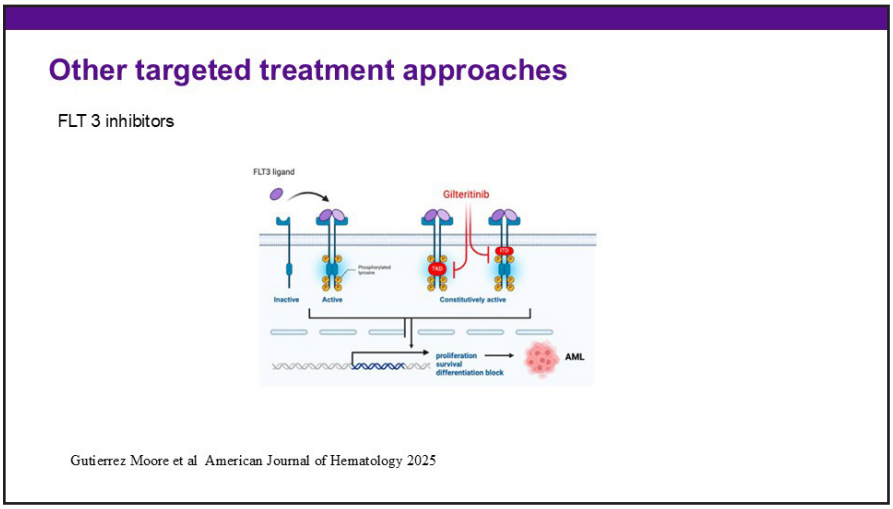


Slide 25: Biology of a cancer cell

We've talked a little bit about the proteins. What about going back to the genetic code, and what about drugs that are being developed that actually alter or help to interact with the genetic code?

This is incredibly important because we've learned an awful lot more about the genetic code and about which proteins go crazy within a cell to result in cancer. We've done a lot of this by what we call next-generation sequencing (NGS), where we learn what the cancer cell code is and what's gone wrong in it. I just want to give you a couple of examples.

This time, I'm going to use leukemia as my example. The way that the DNA can go wrong, it can either have just one spot on the genetic code that's changed, and that's called a mutation. It can be 2 spots where actually the genetic code has been broken apart and put together in a slightly wrong order, or it can be that you've got duplication or loss of the genetic code. The treatments I want to talk about that are coming through are ones that are particularly looking at the mutation.

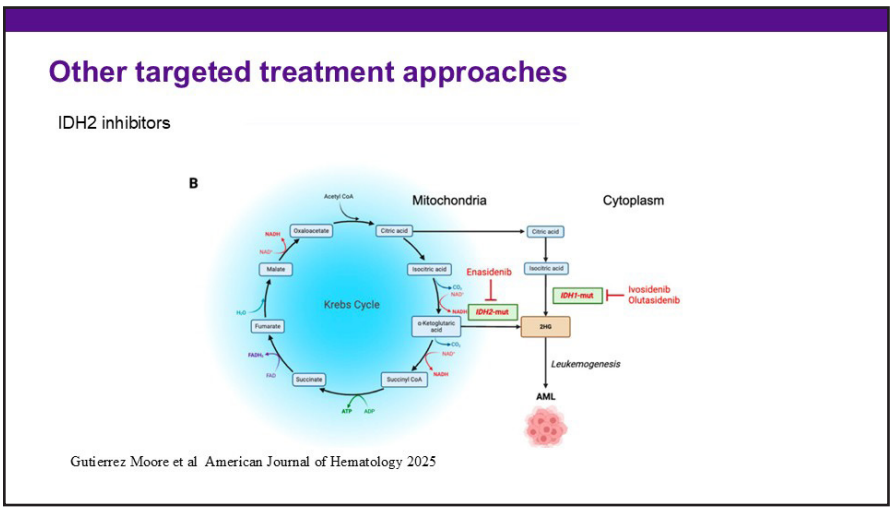


Slide 26: Other targeted treatment approaches

In AML (acute myeloid leukemia) we're going to talk a little bit about what we call FLT3 (fetal liver tyrosine kinase 3) inhibitors. These are a protein that's on the cell surface. Normally, this protein on the cell surface wouldn't do a lot until it was targeted or until it was activated by something, which would then result in it delivering a signal to the cell to say, "Hey, grow please."

What's happened in AML is that because of a change in the genetic code, these cells think that they should grow all the time. They're overactivated and over-busy. There have been a number of drugs, some of which now have approval, but others which are being developed, which are able to bind to this FLT3 and to be able to inhibit it and to stop it sending these signals to the cell and stop it making it continue to grow. There are actually 2 different parts in the FLT3 protein that can have an abnormality. It is very dependent on what kind of leukemia you have as to whether you may or may not have this abnormality.

There are now drugs which are able to target either one of the abnormalities or both of the abnormalities. These drugs initially were going through trials for relapse refractory patients, but they have now been shown to be very effective, and so they have been moved to the maintenance setting or the frontline setting to really try and take advantage of their potential in changing the disease course.

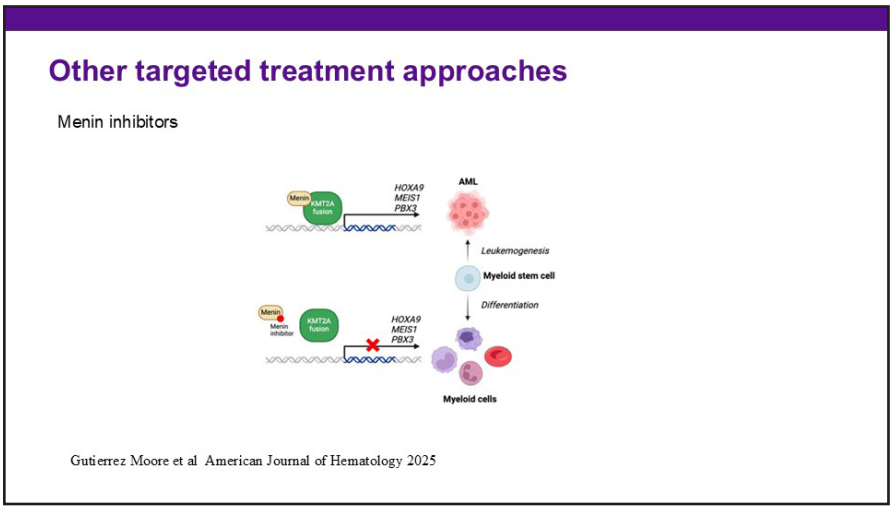


Slide 27: Other targeted treatment approaches

Another example in acute leukemia and MDS is targeting this thing called IDH2 (isocitrate dehydrogenase 2). IDH2 is another molecule, and what it does is it helps the cell to have enough nutrients to grow quickly.

The cancer cell is very clever. It's upregulated this protein. It's mutated it, so it's expressed a lot, and that means that it's continuing and sending a signal to the cell of, "Oh, eat, eat, continue to grow and eat." There are a number of different drugs, one of which has been approved, but a number of others which are going through the process which are able to target this specifically and actually convert the cell from being a leukemia cell and actually make it grow and differentiate as it should do into a normal cell.

These guys are being looked at in the relapse disease setting, but also in earlier disease settings. These are very targeted treatments, and so they have to do this genetic test first for patients to really make sure that this treatment's going to be specific and work for them.

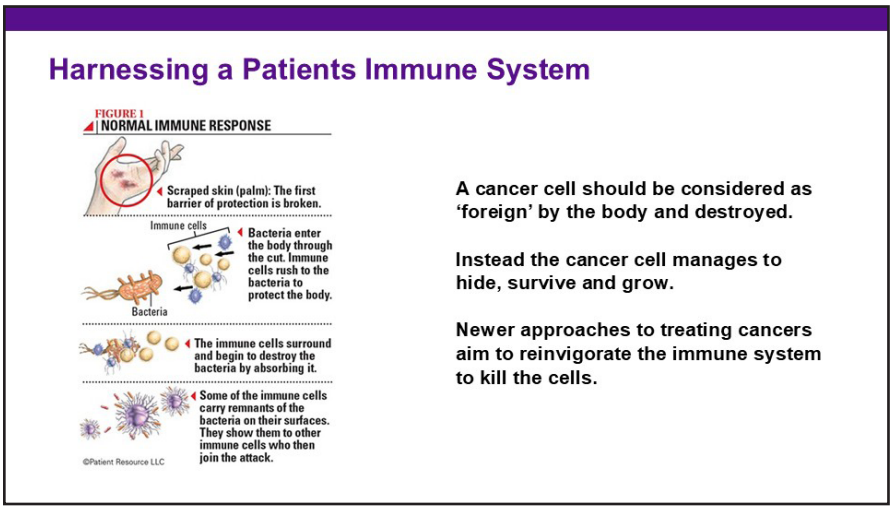


Slide 28: Other targeted treatment approaches

The final one in this kind of leukemia area I want to talk about are what we call the menin inhibitors. These are quite clever drugs. They fall into this whole area which is beginning to develop, which is called epigenetics. A methylation. This is quite a complicated way in which a cell learns whether it should be growing or not.

Now, what the menin inhibitor does is it doesn't actually target the leukemia protein directly, it targets a step beforehand and stops that leukemia protein being made in the first place. It's able to target this KMT2A (lysine methyltransferase 2A) protein and take it out of the system. What that then means is that those signals for the acute leukemia cell to grow are no longer there, so that acute leukemia cell will grow normally. Now, as you can imagine, all of these treatments do have some side effects, and that's what these early studies are showing us. The 3 I've just spoken about for acute leukemia, they're actually all tablets, which is always good news.

As with many tablets, they do have some issues with a little bit of nausea and vomiting and digestion. Interestingly, their main side effect is actually what we call this thing called differentiation syndrome, which is where the acute leukemia cells actually grow out to be slightly more normal cells, and this can cause a few problems just in those first few days. We have to be very careful about that. It's now well recognized, and doctors know how to deal with it. These are becoming... number one, there's more of them coming into the market, but number two, they're also moving to a little earlier in the disease course.

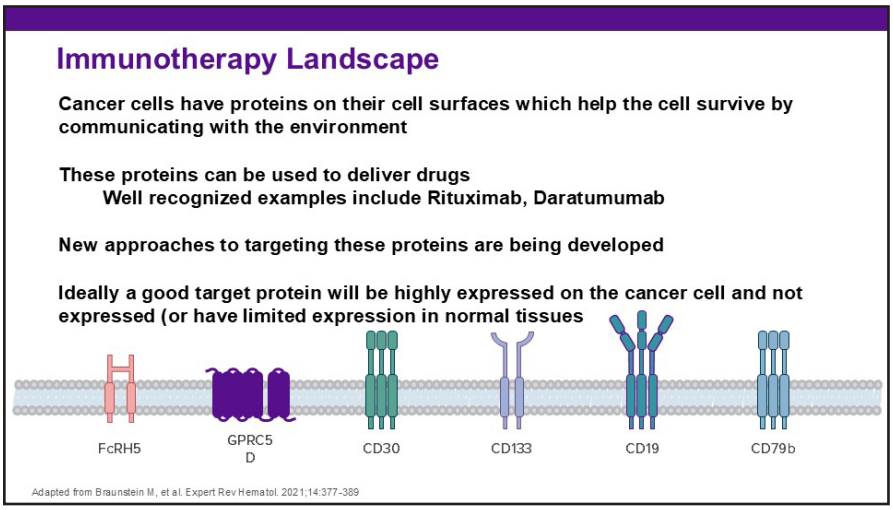


Slide 29: Harnessing a Patient's Immune System

Let's move on a little bit now to our immune therapy side of things. A little step to get us all on the same page. We all have or used to have good immune systems. If you think about the role of an immune system, let's say we scratch our hand, the role of the immune system is that your immune cells charge to that area where you've scratched your hand and really make sure that any bacteria or bugs are not able to get into that wound. If they do get into that wound, what they do is that they get signaled and they kill off those bugs. That's often like when we cut ourselves or something like that and we get that ring of redness around, that's those immune cells coming to the site and helping to kill off any bugs.

Sometimes, obviously, we can get pus, and those pus cells are those immune cells trying to kill off our bugs. Immune cells are really looking for anything foreign in the body. You could think of a cancer cell as being something foreign in the body. If you think of it like that, the idea would be that your immune system ought to recognize it and to kill it off. Clearly as we've mentioned before, cancer cells are really clever. They have actually managed to find ways of hiding, growing, and surviving within a human. They've managed to hide away from the patient's own immune system.

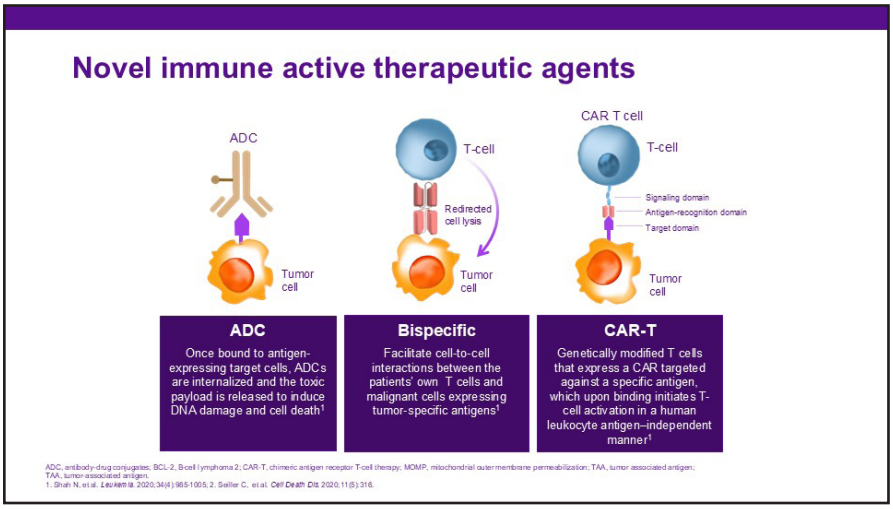
What our new immune treatments are trying to do is trying to overcome this. This can be done in a couple of different ways. It can either be a way of reeducating the patient's immune system and reinvigorating it to kill the cancer cells, or it can be trying to take the cloak of invisibility off the cancer cell so that the patient's immune system can now see it and do its job.



Slide 30: Immunotherapy Landscape

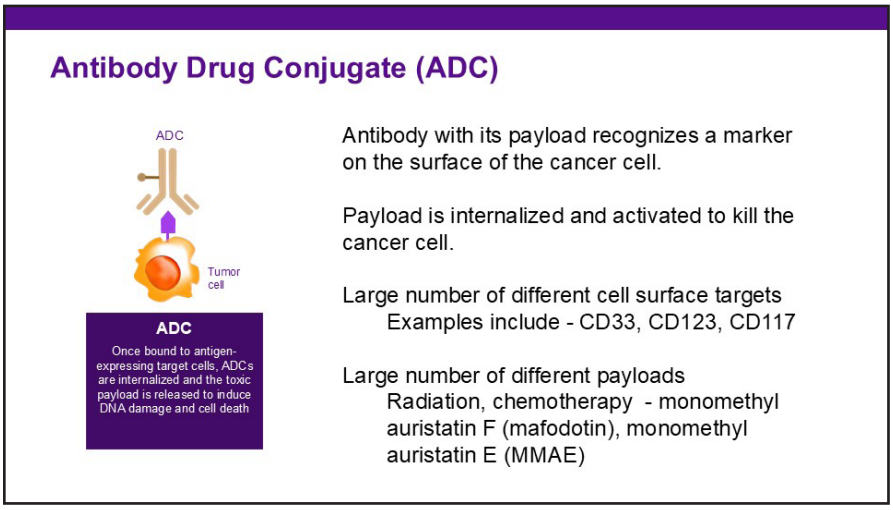
There's lots of different ways of doing this. All of the ways have one thing that's very much in common, which is that they target the surface of the cancer cell. On each cancer cell and on every normal cell as well, there are a series of proteins which help that cell interact with its environment, interact with other cells, and learn how to grow and divide. Now, usually on a cancer cell, those proteins are either much more numerous or they're slightly abnormal. We can use those as a specific way of trying to target them. There's some good examples of this that have been around for many, many years. For instance, one of the drugs we use in many lymphomas and CLL, rituximab (RITUXAN®). that's been around for many, many years and that targets CD20 on the cancer cell surface. It is able to kill off the cancer cell. Importantly, we know it does target CD20 on the normal B cells surface, and so you do actually lose some of your normal B cells, which is why patients who've had the treatment before may be a little more prone to infections or indeed can have a dormant response to a vaccine.

In myeloma, another good example is daratumumab (DARZALEX®), which targets CD38 on the myeloma cell but also does the same thing on a normal regular plasma cell. Nearly all of our cancers have examples of these, but what's happened recently is that these ways of using the immune system have actually gotten much more sophisticated.



Slide 31: Novel immune active therapeutic agents

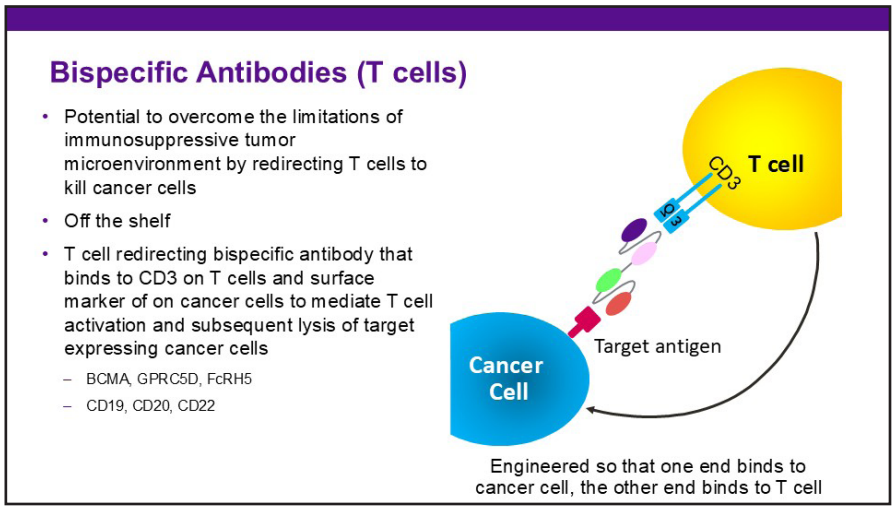
I want to talk about 3 different approaches, what we call antibody drug conjugates, bispecific and trispecific antibodies, and then lastly CAR T.



Slide 32: Antibody Drug Conjugate (ADC)

What's an antibody drug conjugate (ADC)? That is where we make a molecule that recognizes one of these specific proteins on the cell surface of the cancer cell. The molecule is able to charge to the cancer cell, recognize it, but then what the clever thing is that, that molecule actually has what we call a payload or a toxin or something on it, like a secret bomb on the end of it, and so when it gets seen by the cancer cell and taken up by the cancer cell, it's actually able to kill the cell.

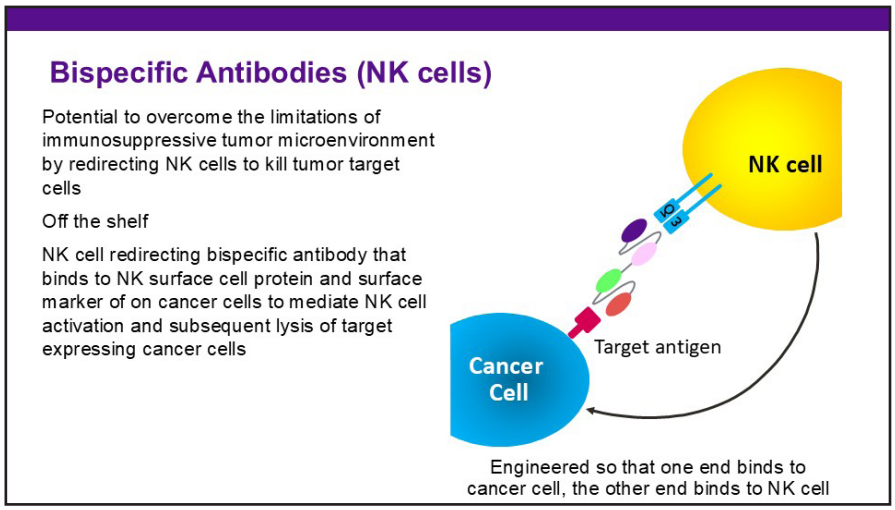
There's many different kinds of examples of this, some of which are already in the clinic. For lymphoma, an example would be polatuzumab (POLIVY®). For AML, an example would be name's forgotten me but the shortened version's called GO for AML. Then for myeloma, more recently there's been belantamab (BENLYSTA). There's many more of these which are coming through, some of which the payload or the toxin is actually something we might use for radiotherapy, whereas others can have a kind of chemotherapy which is attached to them. I guess a little bit like the RITUXANS or the DAZALEXANS are available now but with this extra toxin load.



Slide 33: Bispecific Antibodies (T cells)

The second area is really quite a clever area of using the immune system. This is where we have bispecific antibodies. What happens with this is, we know that a patient's immune system is usually present but for some reason the cancer cells are able to evade it. What these antibodies do is that with one hand, they grab the cancer cell and then with the other hand they grab the T-cell and force the 2 cells to come together. Then when that happens, the T-cell is able to kill the cancer cell. Many different examples that are out there and available in multiple myeloma, we can have ones against BCMA (B-cell maturation antigen) or against GPRC5D (G protein-coupled receptor class C group 5 member D). Again, proteins on the cell surface.

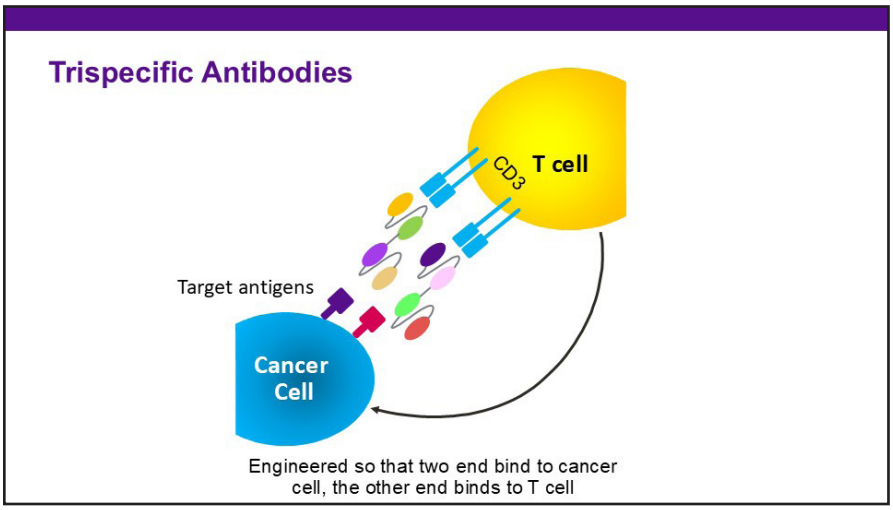
There's also other targets which are being developed like FcRH5 (Fc receptor homolog 5). Then in lymphoma Waldenström's CLL, they're looking at CD19, CD20, CD22, all proteins on the cell surface. In AML, they're also looking at things like CD117. It's not just the T-cell you can do that with, there's also other cells in the immune system.



Slide 34: Bispecific Antibodies (NK cells)

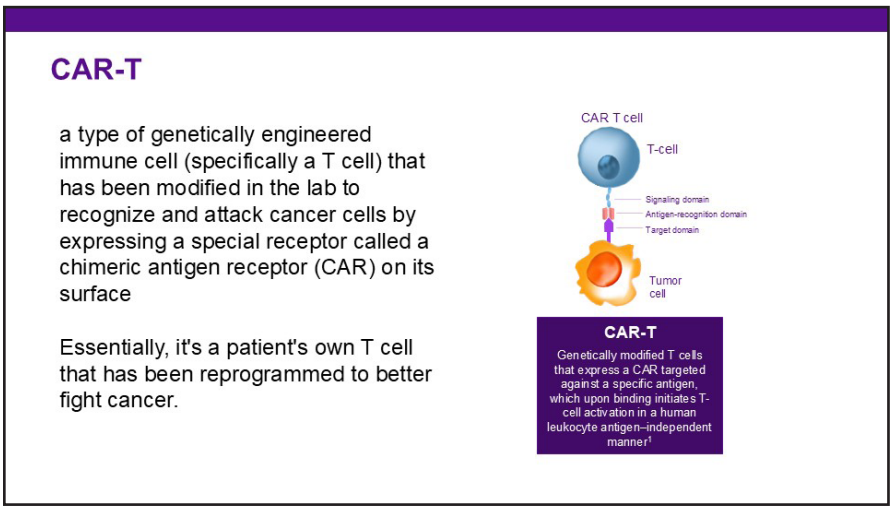
Other cells which help to fight our foreign antibodies, our bugs, are cells called NK cells. They're called natural killer cells. You can tell by their name that what they're supposed to do is to kill things.

They can now use these similar approaches where you redesign these cells, or you use this antibody to grab an NK cell and grab a cancer cell and force the 2 together.



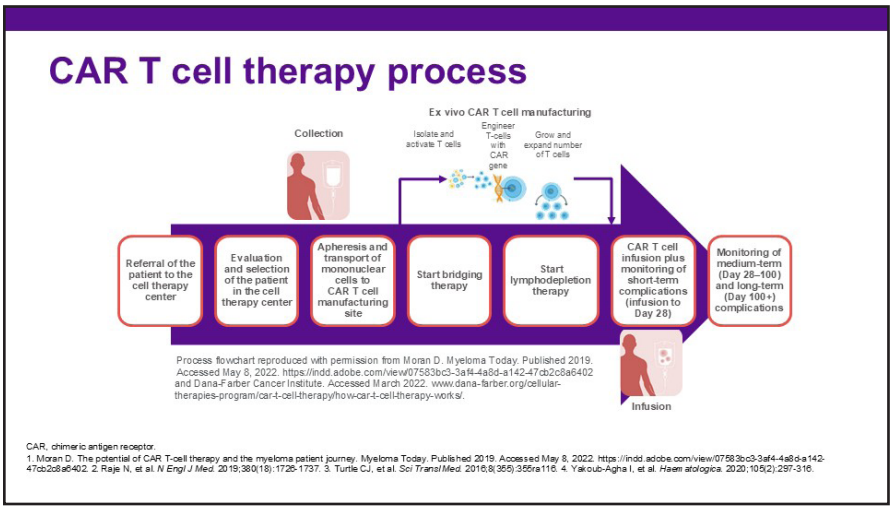
Slide 35: Trispecific Antibodies

Because these have been so effective, it will come as no surprise they're actually starting to do trispecific. Now they're saying, "Okay, let's have the T-cell and rather than it just being able to grab one molecule on the cancer cell, let's get it to grab 2 molecules on the cancer cell so that it's really specific for the cancer cell but also so that if the cancer cell decides to change its spots and get rid of one of those targets, the antibody can still work." These are being used in relapse patients, but they also have been really quite effective and are now becoming to be used in newly diagnosed patients too.



Slide 36: CAR-T

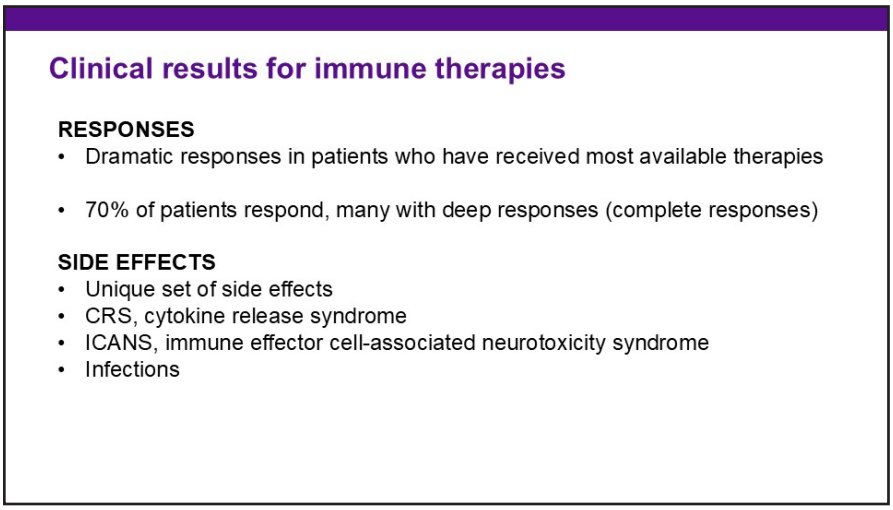
The final drug I want to talk about is a CAR T cell. I'm sure you've probably heard a little bit about these before. This is where you take a T-cell, be it either the patient's own T-cell or a T-cell from a normal donor. You take those to the lab, and you alter their code by putting in a virus to re-express and to make them see the tumor cell much better.



Slide 37: CAR T cell therapy process

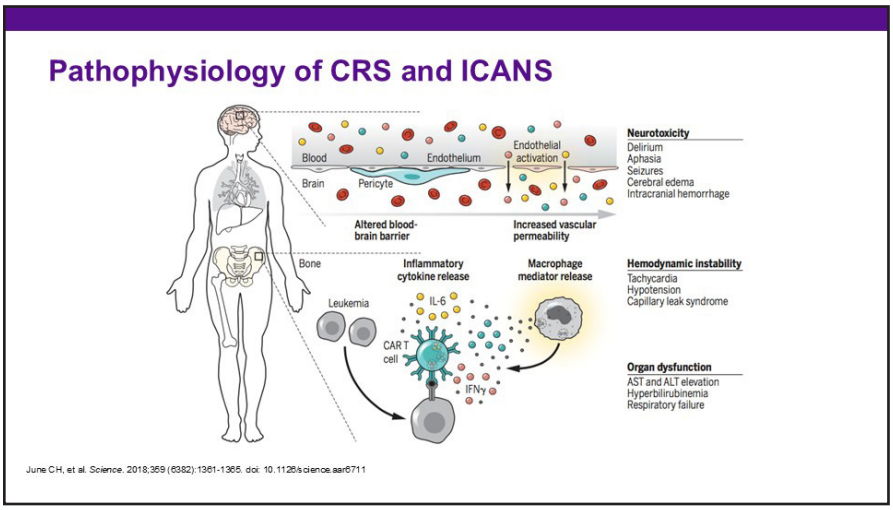
The actual process is quite involved. Whereas the bispecific is a treatment that you store in your pharmacy, this is a treatment that has to be manufactured off-site. There's usually quite a process involved in the fact that you have to first see the patient at a specialized site, usually the bone marrow transplant center, and that when the patient goes there they have their T cells collected for them. Those cells go off to a specialized lab to be altered. Then they get given back to the patient. Now that gap between taking them and giving them back can be somewhere around 4 to 6 weeks. Often the patient may need some more treatment in that gap just to keep their lymphoma or their leukemia quiet.

You then give those cells back and then watch the patient because hopefully, those cells will take effect and have a good effect.



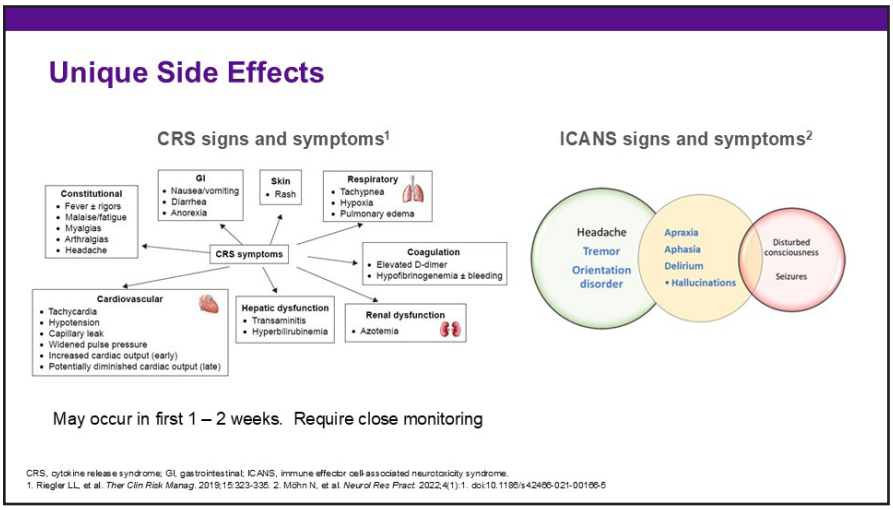
Slide 38: Clinical results for immune therapies

All of these immune therapies have been having some very dramatic responses and usually around the 70% mark, which is very good for patients who have had all other treatments before. We have learned that they have some very unique set of side effects. Just as traditional chemotherapy has those side effects of the hair falling out, feeling nauseous, losing weight, vomiting, etc, these have this whole new group of side effects. That's really because they activate the immune system and sometimes they can over-activate the immune system.



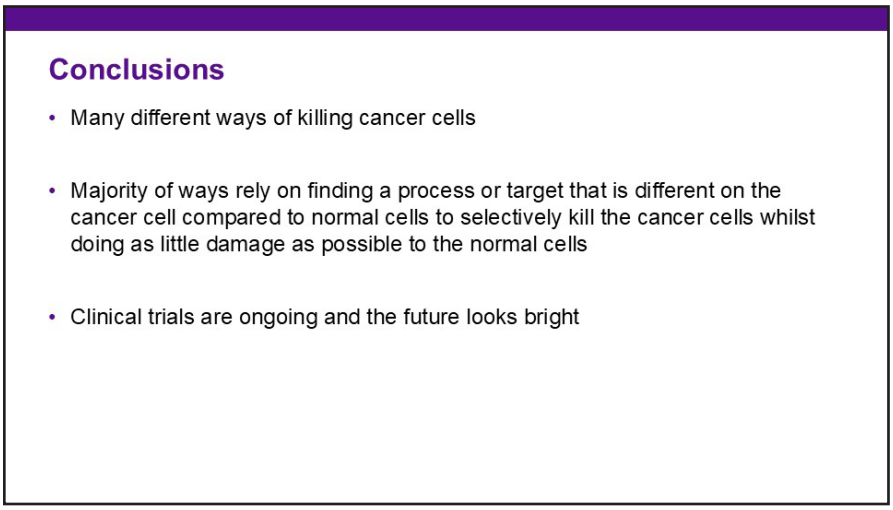
Slide 39: Pathophysiology of CRS and ICANS

It will be a little bit like when a patient has an infection or the flu or something and you know you get those shakes and those shivers, you get body aches, the temperature goes up, etc, etc, that's all the immune system being over-activated. That can actually happen in a patient as well.



Slide 40: Unique Side Effects

We can get those things like the fever, the muscle aches, and so on, but it can also then go on to a slightly more worrisome stage where the patient can drop their blood pressure or have problems with bleeding or indeed getting a little confused. Now, this usually, if it's going to happen—doesn't happen in everybody—if it's going to happen, it's usually just the fevers and the shakes and the shivers. That can be relatively easily managed. Because it can happen, if it's going to happen, it's usually in the first week or two, patients tend to stay close to the transplant center at that time so that they can receive the treatment. Once they're over that initial hurdle, then patients will go back to their local doctor and be followed up closely there.



Slide 41: Conclusions

Hopefully, what I've talked a little bit about is that there are actually a whole host of different ways of killing cancer cells. We're very much moving away from the let's kill everything, both the cancer cell and the normal cell approach, and trying to be much more sophisticated. They can be this targeted precision medicine approach where we try and either take out specific proteins or change the genes a little bit, or they can be this way of altering the patient's own immune response to make the patient's cells recognize the cancer cell much, much better.

Really, all of these trials are going on, there are thousands and thousands of them. I really do think that treatment looks very, very bright.

Slide 42: THANK YOU

I thank you for listening. If you do get the opportunity to take part in a trial, then please do consider it. I really look forward to taking your questions as we move forward. Thank you so much.

Lizette:

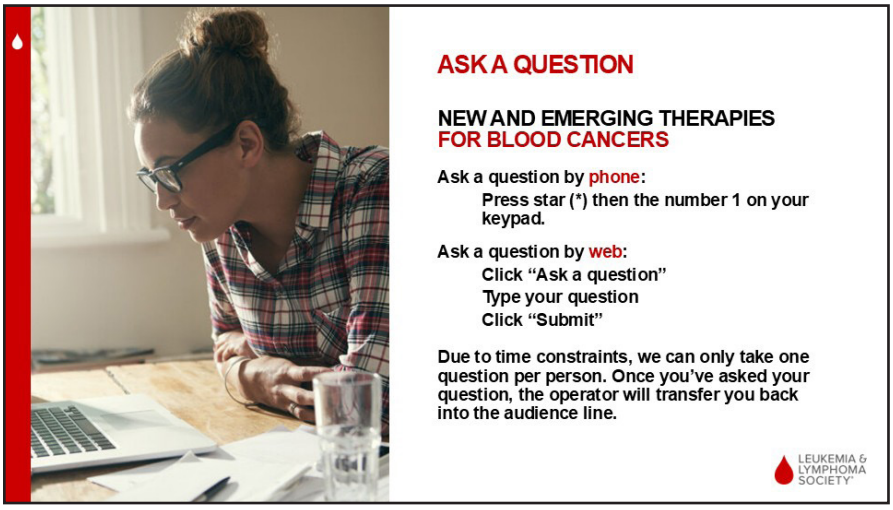
Thank you so much for such great information, Dr. Davies. I know that there are many people on this program, and we have many different types of diagnoses, blood cancer diagnoses. I see CMML (chronic myelomonocytic leukemia),

Waldenström's macroglobulinemia, cutaneous T-cell leukemia, plasma cell leukemia. These are more rare diagnoses. With these more rare diagnoses, are there clinical trials for them?

Dr. Davies:

Yes, definitely. You're right. Some of these rare diagnoses. Often, patients may get lumped into their bigger clinical studies. Nowadays we're often doing these trials where we say that actually the underlying cancer is not the key criteria, it's actually what the target is. What I mean by that is, let's say many lymphomas can have a problem with BCL6 (B-cell lymphoma 6). Previously, we would always just do a clinical trial in diffuse large B-cell lymphoma (DLBCL), or a clinical trial in Waldenström's, or a clinical trial in follicular lymphoma (FL). Whereas now, the way that many of these studies are saying is let's just do our clinical trial in cancers that have an abnormality of BCL6 and see if all the patients can benefit from that. They're called basket studies, so that's one study.

Then you are right, for some of the rarer cancers, there are now networks of doctors that have got together to try and bring forward these clinical trials. Some of these networks are physical networks and others of them are more of virtual networks. A good example would be I guess work done by LLS, is that CMML is a very rare cancer. The LLS have a big initiative about trying to make sure that people can have access to CMML studies around the country. Yes, clinical trials are definitely going on in all of the different disease areas.



Slide 43: ASK A QUESTION

Lizette:

Thank you so much, Dr. Davies.

As you mentioned, it is now time for our question-and-answer portion of our program.

Our first question comes from our web audience, Dr. Davies. With all of these new innovative therapies, do we have any curative therapies for any of our blood cancers?

Dr. Davies:

Yes, definitely. It's interesting, we were very, very hopeful, for instance, the CAR T-cells would cure all kinds of blood cancers, but it actually turns out that they are able to cure some blood cancers, but maybe not all blood cancers. For instance, a number of patients who have diffuse large B-cell lymphoma if they have a CAR T-cell, many of them are cured. Whereas, for multiple myeloma, for instance if you have a CAR T-cell, yes, some patients will be cured but not all patients will be cured.

It's really teaching us a lot about these different diseases, and importantly, that not every patient is the same, which I think we've probably known for many many years. There is definitely the ability to cure patients, but it does depend on the specific kind of blood cancer that you have.

Lizette:

We'll take the next question from our telephone audience, please.

Operator:

Our next question comes from Ellen from Florida. Go ahead, Ellen.

Ellen:

Hi. I have been diagnosed with both Waldenström's and marginal zone lymphoma, and I'm wondering is there a treatment that could work together for both of these diagnoses.

Dr. Davies:

Yes, it's not uncommon sadly for people to be diagnosed with 2 different kinds of blood cancers. Often it depends how similar the blood cancers are. The way we decide how similar the blood cancers are, is that we know that acute leukemias tend to come from one kind of blood cell, whereas lymphomas tend to come from another kind, and myeloma from another kind.

If you have 2 cancers that are coming from the same kind of cell, then that makes it much easier to treat. Waldenström's and marginal zone are actually quite similar. They both are what we call a B-cell lymphoma. Fortunately for you, if you need to have treatment, interestingly not all of Waldenström's and marginal zone patients actually need any treatment. If you do need treatment, there would be quite a few different drugs that would be available to treat both of your conditions at the same time.

Lizette:

Our next question comes from Fred. Fred is asking: When is the best time to choose a new therapy? How do you measure the effectiveness of these new therapies?

Dr. Davies:

For any clinical trial and also for patients generally, for each of the different diseases, we have a very standard way of defining how a treatment works. Dare I say it, some of this very much depends on the dreaded bone marrow test. For myeloma and lymphoma, we will often use a combination of blood markers, a bone marrow test, and some form of scan. Whereas, for acute leukemias and chronic leukemias, we will usually use a combination of blood markers and the bone marrow.

The actual criteria we have are very strict, and they are worldwide what we call response criteria. As far as when is the best time to start treatment, as well as having response criteria, we also have criteria for when to start treatment. Again, they differ depending on the kind of blood cancer, and also on what kind of symptoms the patient is having, and potentially how quickly the disease is coming back. For instance, some patients with lymphoma, it may be that their disease comes back with a new lymph node or a small lymph node and that it's maybe under the arm and is not giving them any trouble.

It may be for that patient that actually we don't jump into a new treatment at that stage, and that we just keep an eye on things, and see what's going to happen? Is that lump going to stay the same size? Is it going to grow? Whereas in other instances, it could be let's say it's an acute leukemia, we know they grow very quickly, and so if we were to see a few of those cells, we would be much more worried and would want to jump in quickly before the patient becomes unwell.

Lizette:

We'll take the next question from our telephone audience, please.

Operator:

We do have a question from Arlene from New York. Go ahead, Arlene.

Arlene:

My husband has multiple myeloma and he had 5 treatments then it stopped because he had a bad reaction and he hasn't had any treatments now for 7 months. Do I continue when he is able to go to another treatment or what? I'm confused.

Dr. Davies:

That's actually quite a common question. As in, clearly when we're giving treatment, ideally we want to give treatment to make the patient feel better not to make the patient feel worse. As you mentioned, sometimes when we're doing that, patients can have a reaction to the drugs and that results in those requiring a break from therapy. Now, the question really is: How long can a patient have a break from therapy? That is very, very patient-specific.

I don't know, it may well have been that when your husband had his initial treatment that his myeloma actually responded very well. It may well be that the doctors moving forward can just keep a close eye on that and monitor it very closely. If it's staying very, very quiet, he can stay off treatment and wait till he gets much stronger if he needs to start treatment.

The alternative is that maybe, yes he had a reaction, but maybe the myeloma didn't respond quite as well as the doctors may have wanted, in which case it may be that the doctors want to swap treatment a little bit. They probably wouldn't want to go back on the same treatment because it caused a bad reaction, but might want to swap treatment to something else, ideally with less side effects or different side effects so that they can continue to get the myeloma into response but not cause any issues.

I guess what I would encourage is that, if patients do have side effects that they let their doctors know and that if they are coming off treatment because of side effects, that they have a chat with the doctor and or the nurse and really make sure that their disease is going to be monitored whilst they're off the treatment, whilst they recover from the side effects. Then have that conversation as to whether it's okay to carry on with that drug holiday, as we sometimes call it, or whether you need to go back on the treatment.

Lizette:

Our next question comes from Donna. Donna is asking: Is it wise to watch-and-wait and not treat the cancer immediately? Very confused on why to wait. I feel like I'm just waiting for it to take over my body.

Dr. Davies:

The old watch-and-wait trauma. It's very difficult and there's lots of discussion about this ongoing. Just so everybody knows what we're talking about, some of the blood cancers actually grow very, very slowly. Examples can be things like smoldering myeloma, MDS (myelodysplastic syndrome), follicular lymphoma (FL), and sometimes chronic lymphocytic leukemia (CLL).

Because they grow very, very slowly, and when I say that, it may be that patients don't need treatment for 5 years or for 10 years. It's important to try and judge and to get as much information from the patient as possible so that we can try and make sure that as we're monitoring that patient, no harm is being done, and that actually the disease isn't going rampant, but we're actually doing benefits.

Now, to some extent, this watch-and-wait policy really was around many years ago when we had absolutely awful

treatments and the treatments actually caused side effects and having the side effects was worse than not having any treatment. Whereas now there's lots of new treatments that are available that people are now wondering whether it's worth trying to start and treat some of these cases.

Examples including the smoldering myeloma field working out as much as we can, whether patients may or may not relapse, and then deciding that if we think that they may get active disease in 6 months, offering those patients treatments. What we really don't want to do is to be offering patients treatment now if we know they're not going to need it for 5 years or 10 years and giving them side effects that they may not need.

I agree, it's very tough. I think there's a really interesting study going on at the moment in Iceland. Again, it's a myeloma study, but it's actually looking-- because Iceland has a small patient population, what they're doing is looking at the psychological impact of people being on this watch-and-wait policy and really what does that do to your general wellbeing.

Lizette:

We'll take the next question from the telephone audience please.

Operator:

The next question is from Ismail from New York. Go ahead.

Ismail:

I've been diagnosed with polycythemia vera (PV) and that was after I had a central thrombocythemia. What I'm scared about is that my disease, it's getting worse and I'm not sure what's going on inside my body. I was taking JAKAFI® and then I stopped the JAKAFI because I took it for 18 months, but then I went back on it because my doctor said that my blood count was out of order. I'm just worried. Can this polycythemia really get worse?

Dr. Davies:

It brings about a number of different kinds of things and rolls into some of the questions that people have been asking on the internet as well, is that many of these new treatments that specifically target the abnormal cell, particularly the tablets, so let's say JAKAFi or in CML there is ibrutinib in CLL, CLL it's ibrutinib, sorry in CML it's GLEEVEC®.

There's a whole host of these ones which you take daily and you actually have to continue taking them daily forever because they stop that cancer cell growing. As you found, if you stop the treatment then what can happen is that the cancer cell will begin to grow again. I think it is important exactly as you've said, to have that chat with your doctor and to say, "Hey, is this something I need to be on long-term or is it something that I can potentially have drug holidays from?"

Certainly, for some of the diseases it is possible to come off the drug for a certain length of time and then to go back on it without any problems. The polycythemia vera and the essential thrombocythemia, the ET, they're both kinds of disorders that we call myeloid neoplasia. They're both due to problems with the way that you make your blood.

There is a very, very small chance that they can go on and cause acute leukemia. Your doctor will be keeping a very close eye on you to try and ensure that that doesn't happen. One of the ways to help ensure that doesn't happen is to be on those drugs, such as JAKAFI. I think it sounds as if yours is now well controlled, which is great. I'd encourage you to chat with your doctor a little bit more about it.

Lizette:

Getting back to your mentioning monitoring, there's a follow-up question on the watch-and-wait, does that mean monitoring consistently, repetitive blood work, and tests during that time?

Dr. Davies:

Usually the monitoring for some of these watch-and-wait is usually blood tests rather than bone marrows I can say, but we do sometimes have to do bone marrow, but ideally, we try to make sure that we do it with a test which is the most user-friendly we can do. Yes, it can sometimes be a series of blood tests.

Then depending on the kind of thing that we're monitoring for, then it can be anywhere between 2 months and 6 months as our monitoring frequency. Also as well, if it's something like a lymphoma, then clearly we don't want to be putting you through the CT scanner all the time as well so we'll often do it manually, look for lumps and bumps as well.

Lizette:

The next question comes from Lavelle. Lavelle's asking: How can doctors incorporate more natural means to health? It's very difficult finding options that don't harm an already compromised body.

Dr. Davies:

This is absolutely great and it's really important as well. I think with all doctors you will find that some doctors are very pro exploring these areas and other doctors are very anti. For me, personally, I'm very comfortable and happy for patients to be looking at natural approaches. I do think it's important that we let doctors know if you are using natural products because just because something is natural doesn't necessarily mean that it won't interfere with some of our medications and counteract one way or the other.

I think it's important that we ensure that patients do know which drugs patients are taking and that there are no interactions. There's a particularly great study that I'm really excited about that's happening at MSK (Memorial Sloan Kettering Cancer Center) at the moment and they're actually looking at diets and are looking to see whether having a plant-based diet may actually be a good thing for treating different kinds of blood cancers. That's really because there's a lot of work now going on about what we call our microbiome. Those are the good bacteria that hide out in our mouth and in our colons and how those good bacteria may actually alter how we respond to our treatments and so on. There's a lot of work now going on about what our diet may do to these things and also can we improve our microbiome to make our treatments more effective.

Lizette:

Along the same lines, Gary's asking: He's being monitored by a cancer hospital for his MDS and his MDS is classified as stable, but is really asking: Are there any preventative treatments, lifestyle, or diet change that can hold back the advancement of the MDS? He's also noticed that during periods of stress, his white blood count has actually gone up. Is that something that's typical?

Dr. Davies:

This is where we 100% at the moment don't know if there's any kind of dietary or lifestyle changes that will hold back these things. Again, it's another area of active intervention on research. I think probably what is important is, I think as the patient mentioned, making sure that you know your body and that you recognize if something is wrong.

Then also, as much as possible, trying to be as fit and as in tune with your body as you can. Really working on the theory that should you need any treatment in the future then you're in a good shape to actually receive and have that treatment. There are studies going on but nobody really knows the correct answer at the moment.

Lizette:

Bruce is asking to address current and/or potential future developments for MRD, so minimal or measurable residual disease assessment for a stratifying disease level status. He has MALT NHL.

Dr. Davies:

That's a great question and a really hot topic. I don't know if LLS has done one of these videos on that as of yet, but if they haven't, I'd point that one forward because I think that's really important. As the patient mentioned, there are a number of different ways of measuring disease and sometimes we can use either a very sensitive test on the bone marrow or a very sensitive test in the blood to pick up tiny amounts of disease.

These sensitive tests can pick up maybe one cancer cell in a million. What we've been able to, we in the bigger worldwide speaking of the web, been able to show is that if you can detect one cancer cell in a million or one cancer cell in 100,000, that those patients probably or may need some extra monitoring or some extra treatment to stop their cancer coming back.

Now the FDA are very keen on having this moving forward. They've just approved it actually for myeloma and it's used quite a lot in acute leukemia now. The idea being that potentially if you can catch patients early and start patients on treatment before the disease has gone haywire, then actually you may get a really good response and do better with your therapy.

The key kind of things that everybody is struggling with at the moment, or is certainly researching maybe rather than struggling, is I think exactly what the question implied is, what's the best way of testing for this? It seems that the FDA don't mind as long as the test is a good robust test. If you do the test in New York and you do the test in Seattle, you get the same answer.

It's not that you're doing a test in 2 different sites, therefore getting 2 different answers and are altering the treatment for patients not based on a good test. That's one key area that is being looked at. Then the other key area that's being looked at is making sure again that we don't treat patients too early, that we use the test as a kind of warning sign. At the moment, it may be that just because the test becomes positive, it may be that you don't want to treat at that point, but that you just need to follow them for a little bit longer.

Lizette:

We'll take the next question from the telephone audience, please.

Operator:

The next question comes from Taryn from Alabama. Go ahead, Taryn.

Taryn:

I have MDS and I was on VIDAZA for 2 years and now I'm on INQOVI®. Should I expect to be on INQOVI for quite a long time or is there another treatment that's coming along? The other thing is, it seems like all I do is sleep anymore. I get so tired. I'm just asking, is INQOVI probably where I'll stay for a while?

Dr. Davies:

That would be the hope. That would definitely be the hope. This is MDS is another good example of one of these blood cancers where we try and give continuous treatment. Sometimes we can do a treatment for just 6 months and then stop. Other times we would like recheck all of our bone marrow and blood tests. If we need to carry on and carry on doing treatment, then we would do that. I think it's really important to chat with your doctor or your nurse about some of those side effects.

Side effects can occur for all sorts of things. Certainly for patients with MDS, it could be you get a little bit tired because of anemia, because the blood counts are a little bit low. It could also be because of the treatment itself, as you say. Also if you're on other medications as well, sometimes they can make you tired. Good examples of beta blockers and blood pressure tablets and so on and so forth.

I think it's really important if you're having a side effect that's really-- whether it's affecting your quality of life or just

a niggly side effect. Either way, it's really important to chat with your doctor so that they can then discuss things with you and see if between you, you can come up with a solution.

Lizette:

Speaking of anemia, doctor, Stephen's asking: How do you address anemia caused by cancer treatments? Can infrared therapy address anemia treatments? Stephen does have CML. Just are there ways to treat anemia?

Dr. Davies:

Yes, there are definitely ways to treat anemia. Some of them, it depends. There's many different causes of anemia, and so some of the ways of treating anemia are surrounding diet. Making sure that you have a good intake of vitamin B12, folates, and iron. There's the dietary side of anemia. We do know that the cancers itself can cause anemia because there's cancer cells in the bone marrow. Usually if that's the case, it's a matter of killing the cancer cells off in the bone marrow so there's enough room for the normal red blood cells to grow.

Then another thing that can sometimes happen is that for some reason, red blood cells will sometimes not grow very effectively, and that can either be because the signals for growth are not quite correct or that the kidney itself isn't giving the right signals. In those cases, we can actually sometimes give a hormone called erythropoietin to get those signals much better and to stimulate red blood cell health. You're right, sometimes, occasionally we will need to use a blood transfusion if it's urgent.

Then I think as the listener was suggesting, there are a number of alternative therapies which have been tried. I personally don't know the data about infrared lights, but again, I would suggest it's something that you chatted with your doctor about.

Lizette:

Thank you. Continuing this conversation about side effects. Liz is asking: How long will side effects, particularly memory loss or any form of memory loss or any other neurological brain dysfunction last? Will it take weeks, months, years? Is there anything that could be done?

Dr. Davies:

I'm working on the theory that question is around chemo brain. Which is one of those terms that we throw out there because it's a non-specific, we can't often get to the bottom of it, but we know when patients are having treatment that sometimes for instance, it gets more difficult to do the crossword or things that you have usually been in the brains that are very easy to think about disappear. I think I'm going to address that one. If it's anything more severe than that, then that really does need to be discussed with the doctor. The way of managing that would be very different.

Examples I would be thinking of there is, let's say that you are getting pins and needles or numbness in your fingers or your toes because of your medication. Or you would want to talk to the doctor about that to change the medication.

Often this kind of chemo brain is a combination of the toxic effects of the treatment, as well as the general tiredness on the body. It can also be a little bit dependent on the treatment itself. Certainly in lymphomas and myelomas and acute leukemia, we use a lot of steroids and they really mess with the brain.

I think a little bit, usually it's during active treatment and then once the treatment gets less intensive, that chemo brain begins to settle and so on. Certainly when you're on active treatment, I would really encourage you to take people up on their offers. People always want to help you when your friends and family when you're unwell and we're often worried and scared about asking for help, but sometimes little things like, hey could you do this kind of job for me, take this to the post office or cook this or whatever, just takes a little bit of pressure off yourself and just gives the brain a chance to relax a little bit.

Lizette: Barbara is asking: Has CRISPR been used yet in patients with blood cancers?

Dr. Davies:

CRISPR (clustered regularly interspaced short palindromic repeats) is a technology where you can specifically alter some of the DNA code. Specifically go in and alter that DNA code and put it back to normal. There's kind of 2 ways that we potentially can look at CRISPR. One would be to alter a patient's immune cells and get them to target the cancer cell better. The other alternative would be to try and change the actual cancer cell and convert it not from being a cancer cell into being a normal cell.

At the moment, the CRISPR technologies are still very much under development. They have been shown to be effective for a number of genetic blood problems, such as thalassemia and sickle cell disease. The clinical trials are ongoing looking at cancer therapies. Now, most of the cancer therapies at the moment are around this immune side of things, so altering CAR T-cells. A bit like the CAR T-cells, but the CRISPR approach potentially would be much more specific, much quicker, and have much less potential side effects and what we call off target effects, but they're coming down the line.

Lizette:

Jessica is asking: What are your thoughts on sequencing for therapies and do you see CAR T-cell therapy or bispecific therapies moving closer to an initial or first-line therapy?

Dr. Davies:

Just about every meeting of doctors I go to there's always a discussion and a debate now about which treatment should we be using first. These CAR Ts and bispecifics seem to have been so very good in the relapse setting, they have been moving up to second-line treatment and in some instances first-line treatment.

The 2 questions that are being asked are: Do you have a CAR T-cell before a bispecific or do you have a bispecific before a CAR T? I don't think anybody truly knows the answer. There is a suggestion that if both are available, then it may be better to have the CAR T before the bispecific. That hasn't been from clinical trial data. That's been much more looking at patients and following patients. What we really need is truthfully, a clinical trial looking to see which is the best way to do these treatments. I think one thing for certain is that trying to get one or the other, if you need it, is really key.

Now, are they going to be in first-line? I think it really depends how the side-effect profile of these falls out, and whether the side-effect profile is better than the side-effect profile for those patients that we are currently treating with other approaches as their first therapy. What may happen is that we don't use these for all patients, that we potentially just use these therapies first-line for maybe some of the more problematic patients where we're not sure that the current first-line treatment will be used. That's all kind of coming out in the wash over the next couple of years.

Lizette:

Our last question today Dr. Davies. Is there anything that you're particularly excited about with these new therapies for our blood cancers?

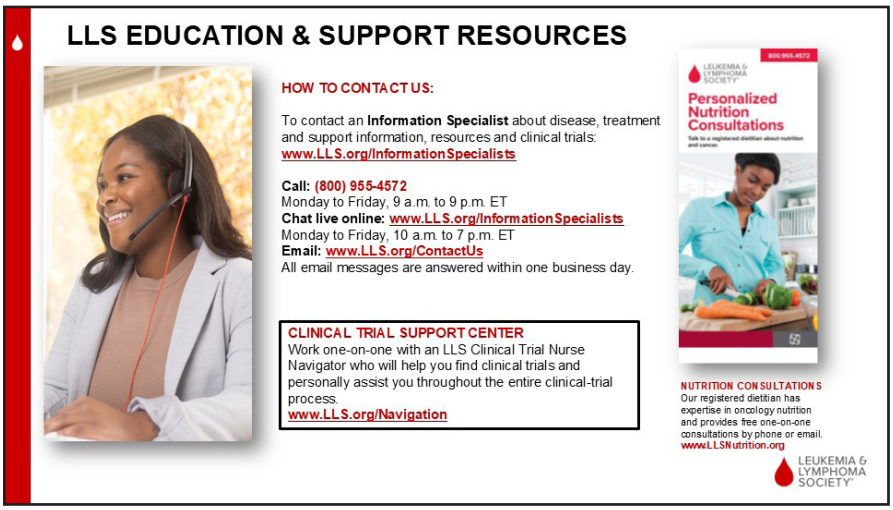
Dr. Davies:

I think I'm most excited about the fact that there's so much activity. Actually people, be it the researchers, the clinicians, and the pharmaceutical companies are all actually very now actively engaged in this area looking for new approaches and dare I say, talking to each other. 20 or 30 years ago, nobody really spoke to each other or shared their experiences, whereas now actually everybody talks to each other and it's no longer them and us, it's actually a team approach.

I'm really excited about the change in people's thought process moving forward, but also the very clever ways that we're now being able to use the science we've learned about the cancer cells to actually target them. Actually, to go after the cancer cell very specifically, rather than just taking this bomb approach to it.

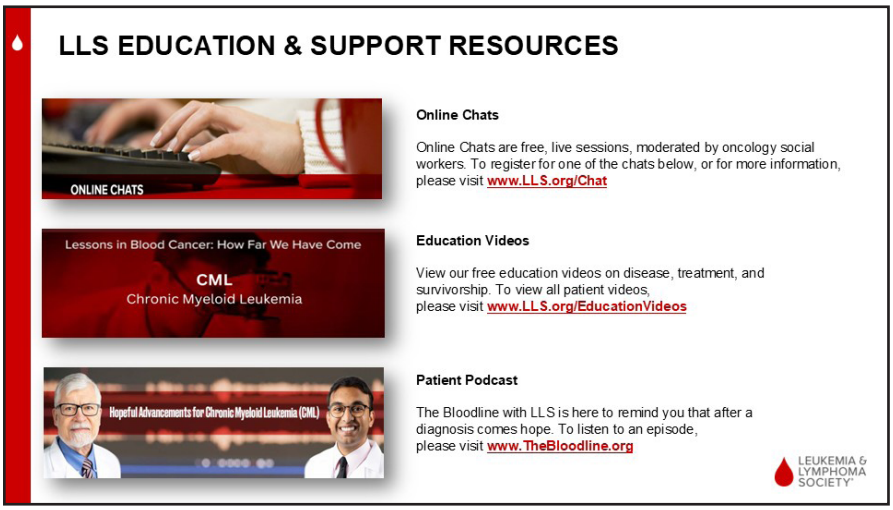
Lizette:

Thank you so much, Dr. Davies. Thank you so much for volunteering your time and your expertise with us today.



Slide 44: LLS EDUCATION & SUPPORT RESOURCES

If you want more information or resources, you may speak to an LLS Information Specialist at 1-800-955-4572 from 9:00 AM to 9:00 PM Eastern Time or reach us by email at LLS.org/ContactUs. You may also reach out to one of our Clinical Trial Nurse Navigators in our Clinical Trial Support Center as Dr. Davies mentioned by visiting LLS.org/Navigation, or contacting an Information Specialist. Our Nurse Navigators are able to identify clinical trial options for your cancer and your unique situation.



Slide 45: LLS EDUCATION & SUPPORT RESOURCES

If you haven't already done so, please make an appointment with one of our Nutrition Educators. They are registered dietitians that can answer questions for patients and caregivers with any type of cancer. They are free consults and you may contact them by visiting LLSNutrition.org, or you may call toll free, 877-467-1936.

Slide 46: LLS EDUCATION & SUPPORT RESOURCES

The Leukemia Lymphoma Society offers financial assistance to help individuals with blood cancer. For more information, you can visit LLS.org/Finances. We have also started a medical debt case management program that provides one-to-one in-depth personalized support to empower patients to address their medical debt. They may be reached at LLS.org/MedicalDebt, or by calling 833-507-8036 and that's 8:30 AM to 5:00 PM Eastern Time, Monday through Friday.

Slide 47: THANK YOU

Again, thank you for the support from Genmab US, Inc.

On behalf of The Leukemia Lymphoma Society, thank you all for joining us for this program. Dr. Davies, again, thank you for volunteering your time with us today, and on behalf of The Leukemia Lymphoma Society, goodbye and we wish you well.