Welcome to Yale Cancer Answers with your host doctor Anees Chagpar.

Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week it's a conversation about multiple myeloma and other hematologic conditions with Doctor Terri Parker. Dr Parker is an assistant professor of medicine in hematology at the Yale School of Medicine, where Doctor Chagpar is a professor of surgical oncology.

My specialty focuses on plasma cell neoplasms or plasma cell disorders. The most common of which is multiple myeloma, which is considered to be a haematological malignancy. So let’s back up a little bit. What exactly is a plasma cell? A plasma cell is a type of white blood cell that is found in the bone marrow.
It’s derived from a B lymphocyte, which is another type of white blood cell again found in the bone marrow. Tell us about multiple myeloma and what exactly it is. I mean when we think about cancers of white blood cells, oftentimes we’re thinking about leukemias, lymphomas, is multiple myeloma a type of that? Tell us more.

As stated, a multiple myeloma is considered to be a hematological malignancy and so that term encompasses leukemias, lymphomas, and plasma cell neoplasms, of which multiple myeloma is one. So in multiple myeloma the abnormal cell is a plasma cell and these plasma cells proliferate or increase in number in the bone marrow. It’s really not known what causes the plasma cells to proliferate in the majority of individuals, and it’s this proliferation that is defined as multiple myeloma.

In general, blood cancers are pretty rare, right? If you look at multiple myeloma, it’s currently the 14th most common cancer in the United States.
and it represents roughly 1.8% of all new cancers diagnosed so not as common as some of our solid tumors that we see. And where does it rank relative to leukemia and lymphoma? There’s some leukemias that are more common and some that are rare, so probably somewhere in the middle, not to be too specific. And who gets these blood cell cancers? These hematologic malignancies. Are there certain risk factors that put people at risk for developing them? As I stated previously for multiple myeloma, for most people we don’t really know why they developed the disease. However, there are some factors that may increase the risk of developing myeloma. One is age, so the majority of people are over the age of 50 at diagnosis. With the current median age of diagnosis here in the United States being 69, another risk factor is a precursor condition known as Monoclonal gammopathy of undetermined significance also known as MGUS. Tell us more about that. MGUS is considered to be a precursor condition.
and the individuals are asymptomatic and it’s usually discovered when blood work is done for another complaint, sometimes it can be that a primary care physician notices that there’s an increase in protein in a simple serum chemistry. So that’s a blood test that’s done for another reason. Sometimes this laboratory work is done for evaluation of other problems such as osteoporosis or neuropathies and then they get referred to a hematologist and have further evaluation that then reveals this precursor state. Those are pretty general risk factors in terms of age and MGUS for multiple myeloma. Are there risk factors for lymphoma and leukemia as well? In general, age again plays a factor as we do tend to see certain leukemias in older individuals. It again depends on the type of leukemia, as there are different types. Acute and chronic lymphoid versus myeloid. And other potential risks can include environmental exposures, so there have been studies looking at the link between radiation in addition to certain chemical exposures such as pesticides or Agent Orange.
And so those increase your risk of leukemias and lymphomas, but not multiple myeloma. Is that right? Multiple Myeloma as well, there have been studies specifically looking at Agent Orange and pesticides as well as radiation so you know pesticides is something that I think a lot of people kind of worry about. And you know, as we’re heading into the fall, people are still using pesticides as they’re trying to tend their lawn and do their gardening, get everything ready for the winter.

Should people really be concerned about pesticides or are there particular pesticides that they should watch out for and others that might be safer? That’s a good question and I don’t have a specific answer for you and a lot of these are looked at and some of the common pesticides that people may use may have warnings on them most of the time people are usually safe because they’re using the regular household pesticides or chemicals if you will and ventilated outdoor space and really have minimal exposure.
I think that that’s kind of good information to get across. Just because people can sometimes worry about these things, but it may be that it’s really not as toxic as some people may think, unless you’re in contact with them in large quantities. So now that we’ve talked about the risk factors, how do people present with these hematologic malignancies? For a solid tumor, tumors we often can find a lump, or we’ll have some bleeding or will have some pain. Blood cells don’t generally cause those things, do they? If we walk through each thing individually, for patients who have leukemia a lot of times they will present with abnormal blood counts. By that I mean an abnormal white blood cell count, hemoglobin or red cells or platelets, which are the cell that helps prevent you from bleeding or blood clots. Sometimes an individual will be diagnosed when they have a blood count done.
for another reason and it’s picked up because there’s an abnormality.
Sometimes people present because these abnormalities lead to other symptoms.
For example, if there’s an alteration in a white blood cell count is specifically a lower white blood cell count,
someone may develop more frequent or recurrent infections if the red cells or hemoglobin is low.
That’s also known as anemia, and patients can become more tired or fatigued,
and if their platelet count is reduced they can present with bleeding or easy bruising,
so sometimes these people present because they have other symptoms and then it’s revealed that these symptoms are because of a low blood count.
For individuals who have lymphomas, sometimes they will present with a large lymph node and so in that case they may have a lump or bump if you will that causes them to present to medical attention and then for multiple myeloma, which is what I specifically focus in,
sometimes people will not have any symptoms and again it’s picked up because blood work is done.
for another reason, like an elevated total protein on a serum chemistry which is a type of blood test. Other symptoms that individuals could have could again be anemia. If the plasma cells increase in the bone marrow to the point where they start crowding out the normal cells, plasma cells also produce high amounts of protein that can be seen in the blood that are cleared through the kidneys and could lead to renal dysfunction or failure in severe cases if it has not been recognized, and plasma cells also accumulate in the bone, that can lead to weakness of the bone and hence pain or fractures. And so it sounds like a lot of these are really picked up on basic blood tests that you have when you go to your doctor. So how frequently should you be having routine blood tests done? Especially if these things don’t generally present with a lot of symptoms? There isn’t currently screening that’s recommended for multiple myeloma or MGUS which is the precursor condition. So typically we tell patients to follow the guidance from their primary care physician,
meaning their blood work really depends on other medical problems. For example, if someone has a heart condition, diabetes or another medical issue, they’re probably going to have blood work done more frequently because of monitoring of that condition and the medications that are needed. When you talk about these conditions being found in older patients, who are also the ones more likely to have other comorbidities that will require routine blood tests, I wonder how many people who are younger might be walking around completely asymptomatic but actually harboring one of these hematologic malignancies that have never been picked up simply because they’ve never had a blood test. Is that possible or do these things actually then progress to the point of being symptomatic? Again when you talk about hematologic malignancies that’s a very broad topic and so everyone is very individualized. And so if we look at multiple myeloma for individuals with the precursor condition MGUS, they can be asymptomatic for years.
and for many patients it never progresses. For individuals who have a low risk MGUS we tell them that the risk of progression is roughly 1% per year. So there’s a large majority of people who will never progress. If someone has multiple myeloma and it’s left untreated, it will progress to the point where they may develop symptoms, what was discussed being anemia leading to fatigue, potential kidney damage, or bone damage, so those patients will progress and become symptomatic at some point, it’s difficult to predict that rate of progression. And what about lymphomas and leukemias? Are those also ones that will progress to symptoms? Or is it possible for them to be pretty asymptomatic until they actually end up having a test that that diagnosis it? Yeah, so for your acute leukemias, and even the majority of your chronic leukemias, they will often progress again,
varying rates of progression to the point where people will become symptomatic. Similarly, if someone had an aggressive lymphoma or a high grade lymphoma, they would progress to the point of symptoms. It is possible for individuals who have a indolent or a slowly progressing lymphoma that they may have had it for several years before the point of progression. The other question that I had was you talk about one of the things that’s often a trigger to finding diagnosis of these conditions as being anemia. And for example, in multiple myeloma, where the plasma cells kind crowd out other cells, so the red blood cell count goes down. Two questions, first question is oftentimes anemia, especially in older people, can be associated with other things, right? GI bleeds, losing blood from other sources, iron deficiency anemia. How do you really tell that this is from something like multiple myeloma versus other things? Yeah, that’s a really good question, and as you mentioned,
people who are older and even younger individuals can have anemia for a variety of reasons. So typically we will work up and do a basic anemia evaluation, which includes looking at things like iron deficiency, other nutritional deficiencies, vitamin B12, and folic acid to make sure we exclude kind of the most common and treatable reasons for anemia first and then when we really don’t have a source, we kind of go on to kind of that next level of evaluation that does include hematological disorders. Well, we’re gonna need to take a short break for a medical minute, but when we get back we’ll learn more about how to diagnose and treat these hematologic conditions with my guest doctor Terri Parker. Funding for Yale Cancer Answers comes from AstraZeneca, dedicated to advancing options and providing hope for people living with cancer. More information at astrazeneca-us.com. There are many obstacles to As smoking involves the potent drug
Nicotine. Quitting smoking is a very important lifestyle change, especially for patients undergoing cancer treatment, as it’s been shown to positively impact response to treatments and decrease the likelihood that patients will develop second malignancies and increase rates of survival.

Tobacco treatment programs are currently being offered at federally designated Comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital. All treatment components are evidence based and patients are treated with FDA approved first line medications as well as smoking cessation counseling that stresses appropriate coping skills.

More information is available at Yale Cancer Center dot org. You’re listening to Connecticut Public Radio.

Welcome back to Yale Cancer Answers. This is doctor Anees Chagpar and I’m joined tonight by my guest doctor Terri Parker. We’re talking about hematologic malignancies, and particularly Doctor Parker’s specialty of multiple myeloma.
Now, right before the break, Terri, you were saying that a lot of people are diagnosed with multiple myeloma when anemia is found on a routine blood test. And that the first step is oftentimes to rule out the things that are common, rule out iron deficiency, anemia and B12, and folic acid. And all of those good things. But ultimately, if all of those things are ruled out, how then does the diagnosis proceed for people actually to be found to have multiple myeloma? And so the first step is actually additional blood in urine studies, so we will do a battery of tests, specifically tests that are called a serum protein electrophoresis, which is a blood test that looks to see if there’s an increase in abnormal or monoclonal protein in the blood. We do a similar test in the urine. We will test other specific things called an immunofixation electrophoresis, quantitative immunoglobulins, and serum free light chains. And we put together all of these blood test and urine studies to determine if there is a monoclonal protein present.
which is a protein that’s being secreted by an abnormal plasma cell. And so if you find that, then that means that people have multiple myeloma? Not necessarily, as I mentioned earlier, we can see a monoclonal protein precursor conditions, and so we take a look at the whole picture. So we look at the amount of monoclonal protein. If the patient has any other systemic symptoms, such as anemia, renal kidney insufficiency, or bone pain, this is more consistent with what we would call a monoclonal gammopathy of undetermined significance, that would be considered low risk that we would just have to observe, or if there were a significant amount of protein or other symptoms that would make us go one step further, which would be a bone marrow biopsy, which is the definitive way to diagnose multiple myeloma. And so when somebody has a bone marrow biopsy what exactly does that tell you? The bone marrow biopsy itself tells us what is the actual
percentage of abnormal plasma cells.

So we're looking for these abnormal or monoclonal plasma cells.

So kind of one type of plasma cell, and they need to be over 10% in the bone marrow.

So that's what we're looking for, and that is diagnostic of multiple myeloma.

And then if you find that,

what's the next step?

Is there staging or do you go straight to treatment?

Then we have to make another determination so we have what we call smoldering Multiple myeloma, which are asymptomatic.

so individuals who have smoldering multiple myeloma meet that strict cutoff of 10%

involvement of bone marrow but are really otherwise asymptomatic,

meaning they don’t have anemia,

they have preserved kidney function,

their calcium levels are within normal range,

don’t have any bone pains or what we call lytic lesions or holes in their bones,

and so these people we would really observe.

But they have a higher risk of progression to symptomatic multiple myeloma that would need treatment.

Wait a minute, wait a minute.

So how do these people with

16
smoldering multiple myeloma

present if they don’t have anemia?

They don’t have any

abnormal kidney function.

How do you see them?

Yeah, so a lot of times these individuals

are referred because they had a blood

test done and that was what we call

a comprehensive metabolic panel that

included a total protein and they

were noted to have a total protein

that was elevated and so their primary

care physician picked up that the

total protein was high and then sent

them for further evaluation for an

issue such as a monoclonal protein.

So that’s one way we often will see

these individuals, another is that monoclonal

gammopathy’s and multiple myeloma can

be associated with other medical problems,

for example as serum protein electrophoresis,

which is the blood tests that we do

as part of the evaluation for myeloma

often done an evaluation for

secondary causes for osteoporosis,

so sometimes patients will have it done as

a work up if they are have osteoporosis at

a younger age.

We also can see neuropathy,

so that’s kind of numbness and tingling

in the extremities in patients who
have come up with these as well and so sometimes a neurologist as part of a work up for other reasons for a patient to have a peripheral neuropathy will send these studies, so that’s how a lot of these patients present to us if they don’t have any other organ damage. So these people with smoldering multiple myeloma still could have symptoms, right? They could still have this peripheral neuropathy, or they could still have osteoporosis, but they just can’t have the other things that you mentioned, right? The anemia, the kidney function, the lytic lesions of the bone? Do I have that right? Yeah, that’s right. So they can’t really have what we call this end organ damage. You know our classification between smoldering myeloma and myeloma has changed over the years, and we now also have a set of criteria that I call my myeloma defining events which don’t have to be organ damage but just a kind of a significant amount of disease burden, and we will treat those individuals as myeloma,
0:21:22.24 -> 0:21:24.607 even if they don’t have any of the other
0:21:26.46 -> 0:21:28.945 So really, we’re looking for a significant
0:21:28.945 -> 0:21:30.769 involvement of the bone marrow,
0:21:30.77 -> 0:21:32.989 and we classify that as over 60%
0:21:32.99 -> 0:21:35.55 involvement or a very significant
0:21:35.55 -> 0:21:38.11 serum free light chain burden.
0:21:38.11 -> 0:21:40.558 And for those individuals we will treat them
0:21:40.56 -> 0:21:41.571 as multiple myeloma,
0:21:41.571 -> 0:21:43.93 even if they don’t have those classic
0:21:43.989 -> 0:21:45.987 end organ damage that we mentioned.
0:21:46.49 -> 0:21:49.388 What does treatment entail?
0:21:49.39 -> 0:21:51.03 Yeah, so treatment for a
0:21:51.04 -> 0:21:54.024 newly diagnosed patient is
0:21:54.024 -> 0:21:57.008 a combination of drugs.
0:21:57.01 -> 0:21:57.798 Typically what you would
0:21:57.8 -> 0:21:58.664 consider chemotherapy.
0:21:58.664 -> 0:22:02.12 So we often refer to it as frontline
0:22:02.195 -> 0:22:04.1 or induction chemotherapy,
0:22:04.1 -> 0:22:07.775 as we’re trying to induce a response.
0:22:07.78 -> 0:22:09.328 The treatment typically consists
0:22:09.328 -> 0:22:11.263 of a combination of three
0:22:11.27 -> 0:22:13.556 or four drugs and the determination
0:22:13.556 -> 0:22:16.234 of how many drugs and which drugs
0:22:16.234 -> 0:22:18.747 are often based on a few different
0:22:23.59 -> 0:22:25.32 And so when we talk
0:22:25.32 -> 0:22:26.434 about patient specific factors,
0:22:26.434 -> 0:22:29.49 we really look at a patient and ask
0:22:30.201 -> 0:22:32.296 the question, how well do we think
this individual could tolerate the treatment?
What is their fitness?
We don’t necessarily look at age but kind of the overall person.
What are their other medical problems, their comorbidities?
What medications are they taking?
Do they have heart dysfunction at baseline?
Do they already have a neuropathy that’s pretty severe?
And then we look at the myeloma itself,
meaning for every bone marrow biopsy that we do,
we also send a study called cytogenetics and that is the study of chromosomes within that plasma cell.
So we’re really looking to see if there is any rearrangements.
Additions, deletions, breaks and by utilizing these cytogenetic testing, we determine if someone is considered high risk or standard risk and that influences which treatment we give.
And so what is the difference between a high risk and a standard risk patient in terms of treatment?
I mean is it more drugs?
Is it more duration?
Is it more toxic?
Yeah, so it’s not necessarily more drugs. Fortunately, in multiple myeloma most of our drugs are very targeted to the plasma cell, but it may just be a different type of drug. So it may consist of four drugs versus a 3 drug regimen. You know there’s still a lot of research being done to see what is truly the best regimen for high risk individuals, and there’s a lot of different opinions out there, but it’s usually going to be a four or three drug regimen with potentially one difference in one of the medications. And as we think about multiple myeloma and how you treat it, it seems to me that part of this has to do with how advanced the myeloma is in terms of how much of the bone marrow is actually involved, whether there’s end organ damage, health, how fit the patient is, and so on. All of which makes me wonder about how important it is to get to a doctor as soon as you have those symptoms, how important it is to come to get diagnosed early versus late?
I mean certainly that’s something we talk about in a lot of cancers, but it sounds like in multiple myeloma there’s really no real screening tests. No recommendations for annual blood work, for example.

So does that really play a role? Or does it not matter as much? Yeah, so in multiple myeloma as in a lot of the hematological malignancies we don’t stage it as we do our solid tumors and so really the amount of bone marrow involvement doesn’t play a role in what we decide to do for upfront treatments. So our staging is really based on blood work and we will often treat someone who is a stage one versus stage three very similarly because we have very effective drugs in the first line setting. But obviously we would want to seek medical attention if you had any symptoms, because say you present with kidney dysfunction, renal failure that does limit some of the treatments that we could give up front. And obviously if you start to have bone pain,
you want to seek medical attention because you wouldn’t want to end up with a pathological fracture. So we do encourage people if they have any symptoms to really seek medical attention. And the sooner you are diagnosed, the potentially more treatment options you have and the better shape you will be in to tolerate treatment. The other thing that you mentioned, which I think is something that it’s important that we pick up on, is that you said that the treatments now are very effective. So tell us a little bit about prognosis of patients who are treated with multiple myeloma. Fortunately we have keep moving our overall survival and the percent surviving at five years each year thanks to the development of newer treatments. And so it used to be, several years ago, say in 2005, if we were giving this talk, we would talk about an overall survival of two to five years and so more recently we say five to 10 years and we’re now talking about potentially
moving that to 10 to 15 years.
If you look at the most recent data in the United States regarding the percentage of patients that are alive at five years, it's about just over 55%. So, very encouraging.
That's really great, and I guess that leads me to my next question, which is what are the exciting advances that are going on in terms of multiple myeloma research. How are you and others trying to move the ball even further down the field? That's a great question.
There is so much exciting research being done here at Yale and within the field of multiple myeloma. And really at all stages.
Right now we often will refer to multiple myeloma as a cancer that is treatable but not curable. So we're currently looking at ways to improve that frontline therapy maintenance therapy, in individuals who have relapsed refractory.
The most exciting things are probably the development of CAR T which recently gained FDA approval and in addition to looking at the biospecific antibodies which are
Doctor Terri Parker is an assistant professor of medicine and hematology at the Yale School of Medicine. If you have questions, the address is cancer answers at yale dot edu and past editions of the program are available in audio and written form at yalecancercenter.org.

We hope you’ll join us next week to learn more about the fight against cancer here on Connecticut Public radio. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital and AstraZeneca.