

0:00:00 -> 0:00:02.49 Support for Yale Cancer Answers
0:00:02.49 -> 0:00:04.98 comes from AstraZeneca, dedicated
0:00:05.057 -> 0:00:07.432 to advancing options and providing
0:00:07.432 -> 0:00:10.42 hope for people living with cancer.
0:00:10.42 -> 0:00:14.08 More information at astrazeneca-us.com.
0:00:14.08 -> 0:00:16.27 Welcome to Yale Cancer Answers with
0:00:16.27 -> 0:00:18.669 your host doctor Anees Chagpar.
0:00:18.67 -> 0:00:20.65 Yale Cancer Answers features the
0:00:20.65 -> 0:00:23.084 latest information on cancer care by
0:00:23.084 -> 0:00:24.644 welcoming oncologists and specialists
0:00:24.644 -> 0:00:27.258 who are on the forefront of the
0:00:27.258 -> 0:00:29.058 battle to fight cancer. This week,
0:00:29.06 -> 0:00:31.281 it's a conversation about Hematologic
0:00:31.281 -> 0:00:33.136 malignancies with Doctor Francesca Montanari.
0:00:33.14 -> 0:00:35.06 Doctor Montanari is an assistant
0:00:35.06 -> 0:00:36.98 professor of clinical medicine and
0:00:37.041 -> 0:00:39.449 hematology at the Yale School of Medicine,
0:00:39.45 -> 0:00:41.676 where Doctor Chagpar is a
0:00:41.676 -> 0:00:43.16 professor of surgical oncology.
0:00:43.16 -> 0:00:43.53 Francesca, can we
0:00:43.9 -> 0:00:46.049 start off by you telling
0:00:46.049 -> 0:00:48.391 us a little bit about Hematologic
0:00:48.391 -> 0:00:50.626 malignancies, what they are,
0:00:50.63 -> 0:00:54.185 how common they are, and how people who have
0:00:54.185 -> 0:00:57.918 a hematological malignancy can present?
0:00:57.92 -> 0:00:59.483 Hematological malignancies
0:00:59.483 -> 0:01:02.609 include all types of blood cancers.
0:01:02.61 -> 0:01:06.738 So these are cancers that can affect the
0:01:06.738 -> 0:01:10.95 bone marrow where the blood cells are made,
0:01:10.95 -> 0:01:13.584 blood cells, lymph nodes and other
0:01:13.584 -> 0:01:16.626 parts of the lymphatic system and

0:01:16.626 -> 0:01:18.429 typical hematological malignancies
0:01:18.429 -> 0:01:21.434 or blood cancers are leukemias,
0:01:21.44 -> 0:01:22.424 lymphomas, Myelomas,
0:01:22.424 -> 0:01:26.369 and others that are rare, such as
0:01:26.369 -> 0:01:28.834 myelodysplastic and Myeloproliferative disorders,
0:01:28.84 -> 0:01:31.3 and these diseases represent less
0:01:31.3 -> 0:01:34.262 than 10% of all the cancers,
0:01:34.262 -> 0:01:36.727 and there are approximately 1.8
0:01:36.727 -> 0:01:39.773 million new cases of cancer per year
0:01:39.773 -> 0:01:42.67 in the United States and approximately
0:01:42.67 -> 0:01:45.6 180,000 cases of blood cancers.
0:01:45.6 -> 0:01:47.392 So every 3 minutes,
0:01:47.392 -> 0:01:50.773 one person in the US is diagnosed
0:01:50.773 -> 0:01:53.109 with one of these diseases.
0:01:53.11 -> 0:01:56.547 Approximately half of the blood
0:01:56.55 -> 0:01:58.975 cancers are lymphomas which account
0:01:58.975 -> 0:02:01.97 for 86,000 cases per year.
0:02:01.97 -> 0:02:04.425 They are further divided in Hodgkin
0:02:04.425 -> 0:02:05.898 and non Hodgkin,
0:02:05.9 -> 0:02:08.36 which are the most common
0:02:08.36 -> 0:02:10.328 and then Hodgkin is
0:02:10.33 -> 0:02:13.767 classified into over 60 distinct subtypes.
0:02:13.77 -> 0:02:16.23 So as you can imagine,
0:02:16.23 -> 0:02:19.8 numbers tend to become very very small
0:02:19.8 -> 0:02:23.737 for the most rare of these subtypes.
0:02:27.09 -> 0:02:29.55 Leukemia is approximately 60,000 cases
0:02:29.55 -> 0:02:33.302 per year and less than 10% are myelomas,
0:02:33.302 -> 0:02:35.226 so symptoms and manifestation
0:02:35.226 -> 0:02:37.6 of these diseases can vary.
0:02:37.6 -> 0:02:40.645 There is a very wide range of
0:02:40.645 -> 0:02:43.084 symptoms that can be associated

0:02:43.084 -> 0:02:46.204 with any of these blood cancers,
0:02:46.21 -> 0:02:48.595 which depends on the specific
0:02:48.595 -> 0:02:50.503 disease and the localization.
0:02:50.51 -> 0:02:51.378 For instance,
0:02:51.378 -> 0:02:53.982 lymphoma can present with the so-called
0:02:53.982 -> 0:02:56.72 constitutional symptoms,
0:02:56.72 -> 0:02:58.493 which are very
0:02:58.493 -> 0:03:00.857 specific, fever, chills,
0:03:00.86 -> 0:03:02.74 night sweats,
0:03:02.74 -> 0:03:05.56 unintentional weight loss.
0:03:05.56 -> 0:03:08.185 But there are a lot of other
0:03:08.185 -> 0:03:10.809 symptoms which depend on the specific
0:03:10.809 -> 0:03:12.697 localization of the disease.
0:03:12.7 -> 0:03:13.408 For instance,
0:03:13.408 -> 0:03:15.532 there are lymphomas that like to
0:03:15.532 -> 0:03:17.739 affect the gastrointestinal tract,
0:03:17.74 -> 0:03:19.84 and they cause gastrointestinal disturbances.
0:03:19.84 -> 0:03:21.905 Other lymphoma can involve the
0:03:21.905 -> 0:03:24.46 eye or the structures around the
0:03:24.46 -> 0:03:26.56 eye causing trouble with vision,
0:03:26.56 -> 0:03:29.08 or they can affect the skin.
0:03:29.08 -> 0:03:31.18 And as you can imagine,
0:03:31.18 -> 0:03:34.12 depending upon the organ that is involved,
0:03:34.12 -> 0:03:37.33 you can have very different symptoms.
0:03:37.33 -> 0:03:39.365 Leukemia tends to present with
0:03:39.365 -> 0:03:41.912 symptoms related to the bone marrow
0:03:41.912 -> 0:03:44.087 involvement and the cytopenias such
0:03:44.087 -> 0:03:46.66 as fatigue from the anemia,
0:03:46.66 -> 0:03:48.4 bleeding from low platelets,
0:03:48.4 -> 0:03:51.01 infection from low blood white cell
0:03:51.087 -> 0:03:53.493 count and multiple myeloma also

0:03:53.493 -> 0:03:55.989 can present with fatigue from anemia,
0:03:55.99 -> 0:03:57.542 infection and bone pain.
0:03:57.542 -> 0:04:01.069 But bone pain is a more distinct
0:04:01.07 -> 0:04:03.737 sign of a multiple myeloma as
0:04:03.737 -> 0:04:06.655 it involves the bone structure and
0:04:06.655 -> 0:04:08.919 can cause pathological fractures.
0:04:08.92 -> 0:04:11.536 Lethargy and other gastrointestinal
0:04:11.536 -> 0:04:13.871 symptoms related to the hypercalcemia
0:04:13.871 -> 0:04:16.937 also can be present at presentation.
0:04:17.42 -> 0:04:20.372 That seems like just an amazing
0:04:20.372 -> 0:04:23.421 potpourri of symptoms and
0:04:23.421 -> 0:04:26.373 sites that these blood cancers
0:04:26.373 -> 0:04:29.22 can harbor in so how
0:04:29.22 -> 0:04:32.993 do patients find out that they have
0:04:32.993 -> 0:04:35.348 one of these hematologic malignancies?
0:04:35.35 -> 0:04:39.27 It seems like they can be
0:04:39.27 -> 0:04:43.19 anywhere from your bone marrow to your eyes,
0:04:43.19 -> 0:04:44.99 to your gastrointestinal tract,
0:04:44.99 -> 0:04:47.69 and the symptoms can be completely
0:04:47.69 -> 0:04:50.63 nonspecific, like a little bit of
0:04:50.63 -> 0:04:53.4 fatigue to having visual loss
0:04:53.4 -> 0:04:55.928 or gastrointestinal problems.
0:04:55.93 -> 0:05:01.117 So how is the diagnosis actually made?
0:05:06.23 -> 0:05:09.527 It depends on the various scenarios.
0:05:11.036 -> 0:05:13.546 Some of these blood cancers
0:05:13.546 -> 0:05:16.138 tend to be
0:05:16.14 -> 0:05:19.916 very slow growing and might be picked up
0:05:19.92 -> 0:05:20.428 incidentally,
0:05:20.428 -> 0:05:22.968 just performing some routine blood
0:05:22.968 -> 0:05:25.924 work by the primary care physician
0:05:25.924 -> 0:05:28.885 on occasion of the well being visit.

0:05:28.89 -> 0:05:32.173 So finding a new presence of
0:05:32.173 -> 0:05:34.655 increased protein in the blood
0:05:34.655 -> 0:05:37.12 might raise the suspicion of myeloma
0:05:37.12 -> 0:05:41.008 and determine additional
0:05:41.008 -> 0:05:43.6 testing that eventually lead
0:05:43.701 -> 0:05:46.809 to the diagnosis and in other
0:05:46.809 -> 0:05:50.062 cases the symptoms can be more
0:05:50.062 -> 0:05:52.752 prominent and therefore as part
0:05:52.752 -> 0:05:56.016 of the initial investigation by
0:05:56.016 -> 0:05:59.308 the primary care physician,
0:05:59.31 -> 0:06:01.266 certain signs and symptoms
0:06:01.266 -> 0:06:04.2 might be detected that raise a
0:06:04.29 -> 0:06:06.35 flag for this condition,
0:06:06.35 -> 0:06:07.859 and further evaluation
0:06:07.859 -> 0:06:09.368 include imaging studies and
0:06:09.37 -> 0:06:12.97 more in depth blood work
0:06:12.97 -> 0:06:15.623 and eventually valuation by a blood
0:06:15.623 -> 0:06:18.929 cancer specialist and so once that
0:06:18.93 -> 0:06:22.038 happens, once they come to
0:06:22.038 -> 0:06:26.47 you as a blood cancer specialist,
0:06:26.47 -> 0:06:29.68 what's the next thing that happens?
0:06:29.68 -> 0:06:31.108 So typically we
0:06:31.11 -> 0:06:34.393 do really need to run a
0:06:34.393 -> 0:06:36.81 little bit more of a work up,
0:06:36.81 -> 0:06:39.18 and that includes imaging studies,
0:06:39.18 -> 0:06:43.455 which can be anything from MRI or CT scan,
0:06:43.46 -> 0:06:46.956 even a newer form of CAT scan
0:06:46.956 -> 0:06:50.479 that is called PET Scan where we
0:06:50.479 -> 0:06:54.046 use glucose to track down in the
0:06:54.046 -> 0:06:57.252 body where there is an increase in
0:06:57.252 -> 0:06:59.95 the metabolic activity that may

0:06:59.95 -> 0:07:03.31 reveal the presence of a cancer.
0:07:03.31 -> 0:07:05.582 And ultimately the diagnosis
0:07:05.582 -> 0:07:08.422 is made through a pathology,
0:07:08.43 -> 0:07:13.334 so we would need a tissue sample either
0:07:13.334 -> 0:07:19.357 from a lymph node or from the bone marrow.
0:07:19.36 -> 0:07:23.217 Or sometimes a blood sample is
0:07:23.217 -> 0:07:26.599 sufficient where we do run specific
0:07:26.599 -> 0:07:30.386 tests to detect these diseases and
0:07:30.493 -> 0:07:34.213 once we have a pathological confirmation
0:07:34.213 -> 0:07:37.752 then other tests might be warranted
0:07:37.752 -> 0:07:41.434 depending on the nature of the disease
0:07:41.434 -> 0:07:45.777 and typically this test helps us with
0:07:45.777 -> 0:07:48.257 prognostication and with staging.
0:07:49.22 -> 0:07:51.746 Let's talk about that.
0:07:51.75 -> 0:07:53.85 How do we determine prognosis?
0:07:53.85 -> 0:07:55.89 And in general, what is the
0:07:55.89 -> 0:07:57.25 prognosis of these hematological
0:07:57.315 -> 0:07:58.899 malignancies, understanding,
0:07:58.9 -> 0:08:01.372 however, that this is a
0:08:01.372 -> 0:08:03.525 varied group of diseases that
0:08:03.525 -> 0:08:06.057 are lumped into this basket term.
0:08:07.45 -> 0:08:11.522 Right, so there is a lot of variability
0:08:11.522 -> 0:08:15.65 in the behavior of these diseases,
0:08:15.65 -> 0:08:19.857 and as we have improved our knowledge
0:08:19.857 -> 0:08:23.366 in the biology and mechanism
0:08:23.366 -> 0:08:26.53 that drives these diseases,
0:08:26.53 -> 0:08:31.549 we have a very complex way to
0:08:31.549 -> 0:08:35.28 assess prognosis and prognosis
0:08:35.28 -> 0:08:40.67 typically depends on very general
0:08:40.67 -> 0:08:42.176 information
0:08:42.176 -> 0:08:45.188 such as the burden of

0:08:45.188 -> 0:08:47.22 disease at presentation, and
0:08:47.22 -> 0:08:49.8 the performance status of the
0:08:49.8 -> 0:08:53.586 patient plays a big role and
0:08:53.586 -> 0:08:56.356 the presence of comorbidities or
0:08:56.356 -> 0:08:59.778 end organ damage from the disease,
0:08:59.78 -> 0:09:05.716 and then there are other markers that we
0:09:05.72 -> 0:09:09.17 gather from the pathology evaluation
0:09:09.17 -> 0:09:12.735 and from the genetic makeup through
0:09:12.735 -> 0:09:16.239 molecular studies and based on each
0:09:16.239 -> 0:09:19.536 disease as a specific list of
0:09:19.536 -> 0:09:22.572 features that we pay attention to
0:09:22.58 -> 0:09:25.31 when we determine the risk
0:09:25.31 -> 0:09:26.948 stratification and ultimately
0:09:26.948 -> 0:09:29.89 based on all this information,
0:09:29.89 -> 0:09:32.695 we determine what is the
0:09:32.695 -> 0:09:34.378 best treatment approach.
0:09:35.67 -> 0:09:39.065 What is the treatment
0:09:39.065 -> 0:09:41.29 approach for these cancers
0:09:41.29 -> 0:09:42.826 in general?
0:09:42.826 -> 0:09:46.4 The type of approach is very variable.
0:09:46.4 -> 0:09:51.026 So first of all, the most important
0:09:51.026 -> 0:09:55.593 point that I'd like to make is that,
0:09:55.6 -> 0:09:58.426 as I mentioned, the behavior of
0:09:58.426 -> 0:10:01.22 blood cancer is very variable.
0:10:01.22 -> 0:10:04.148 There are blood cancers that are
0:10:04.148 -> 0:10:06.9 very indolent and slow growing.
0:10:06.9 -> 0:10:09.89 And we don't necessarily start
0:10:09.89 -> 0:10:11.684 treatment upon diagnosis.
0:10:11.69 -> 0:10:14.09 These diseases are considered
0:10:14.09 -> 0:10:17.088 generally not curable, but very,
0:10:17.088 -> 0:10:19.484 very manageable and treatable

0:10:19.484 -> 0:10:21.88 with certain drugs.
0:10:21.88 -> 0:10:26.092 And the most important thing upon
0:10:26.092 -> 0:10:30.909 diagnosis is determining if a patient
0:10:30.909 -> 0:10:34.683 requires treatment or can be watched.
0:10:34.69 -> 0:10:36.87 We call that
0:10:36.87 -> 0:10:38.505 watchful monitoring,
0:10:38.51 -> 0:10:41.78 and once there is an indication
0:10:41.78 -> 0:10:43.96 when therapy is warranted,
0:10:43.96 -> 0:10:48.88 then the decision of which kind of therapy
0:10:48.88 -> 0:10:53.597 depends on the specific type of disease,
0:10:53.6 -> 0:10:55.825 the staging of the disease,
0:10:55.825 -> 0:10:57.605 and the predicted behavior,
0:10:57.61 -> 0:11:00.396 which is usually based on the genetic
0:11:00.396 -> 0:11:03.388 makeup of the specific blood cancer.
0:11:03.39 -> 0:11:05.17 Another important factor that
0:11:05.17 -> 0:11:07.84 helps the decision about the best
0:11:07.911 -> 0:11:10.096 strategy is based on patients
0:11:10.096 -> 0:11:12.281 characteristics such as the age,
0:11:12.29 -> 0:11:13.625 the performance status,
0:11:13.625 -> 0:11:15.85 the presence of medical conditions
0:11:15.85 -> 0:11:17.86 which might have an impact
0:11:17.86 -> 0:11:19.87 on the tolerability of the
0:11:19.953 -> 0:11:22.077 treatment and if transplant,
0:11:22.08 -> 0:11:25.428 if bone marrow transplant can be
0:11:25.43 -> 0:11:26.693 used for that
0:11:26.693 -> 0:11:27.956 specific patient,
0:11:27.96 -> 0:11:30.48 as part of the treatment strategy.
0:11:30.48 -> 0:11:33.006 Another factor that is very important is
0:11:33.01 -> 0:11:35.3 a patients preference now that
0:11:35.3 -> 0:11:37.59 we have multiple therapy options
0:11:37.66 -> 0:11:39.6 which offer similar results

0:11:39.6 -> 0:11:42.821 in the long term but differ in
0:11:42.821 -> 0:11:44.831 terms of administration
0:11:44.831 -> 0:11:47.071 modality and side effects profile.
0:11:47.071 -> 0:11:49.456 Patient preference might play a
0:11:49.456 -> 0:11:52.217 big role in the final decision.
0:11:55.26 -> 0:11:58.49 During the past year there is another
0:11:58.49 -> 0:12:01.806 factor that has played
0:12:01.806 -> 0:12:05.026 a big role in our decision making,
0:12:05.03 -> 0:12:07.82 which has been the COVID pandemic.
0:12:07.82 -> 0:12:10.898 So having an aggressive blood cancer
0:12:10.898 -> 0:12:13.857 that requires treatment and has not
0:12:13.857 -> 0:12:16.72 had any variation.
0:12:16.72 -> 0:12:18.978 But because of the presence of the COVID pandemic,
0:12:18.98 -> 0:12:21.35 for those diseases that are
0:12:21.35 -> 0:12:23.728 more indolent and not immediately
0:12:23.728 -> 0:12:25.17 life threatening,
0:12:25.17 -> 0:12:28.182 we have been shifted away from
0:12:28.182 -> 0:12:30.913 using certain drugs or certain
0:12:30.913 -> 0:12:34.663 strategies to maintain the disease in
0:12:34.663 -> 0:12:38.06 remission for longer period of time.
0:12:38.06 -> 0:12:40.508 Unless there was an overall survival
0:12:40.508 -> 0:12:43.148 benefit in order to minimize the
0:12:43.148 -> 0:12:45.944 risks of increasing the severity and
0:12:45.944 -> 0:12:48.338 mortality from the infection.
0:12:50.605 -> 0:12:53.79 There's a few points there that you
0:12:53.882 -> 0:12:56.514 mentioned that I want to pick up
0:12:56.514 -> 0:12:59.79 on and the first is that some of
0:12:59.79 -> 0:13:01.84 these diseases are fairly indolent
0:13:01.92 -> 0:13:04.12 and may not require treatment.
0:13:04.12 -> 0:13:05.816 This kind of expectant
0:13:05.816 -> 0:13:07.088 watchful waiting approach.

0:13:07.09 -> 0:13:09.215 How do you determine whether
0:13:09.215 -> 0:13:11.34 that's the case for patients,
0:13:11.34 -> 0:13:13.61 particularly when you mentioned that
0:13:13.61 -> 0:13:16.84 many of these cancers are not quote
0:13:16.84 -> 0:13:19.04 curable but they are manageable?
0:13:19.04 -> 0:13:22.67 And do patients get some anxiety over
0:13:22.67 -> 0:13:26.66 the idea that they may have a cancer
0:13:26.66 -> 0:13:29.708 that were simply watching?
0:13:29.71 -> 0:13:32.77 It's very important to have that
0:13:32.77 -> 0:13:35.405 clear communication with the patient
0:13:35.405 -> 0:13:37.445 that initiating treatment earlier
0:13:37.445 -> 0:13:41.053 for this kind of cancer does not
0:13:41.053 -> 0:13:43.488 necessarily translate in a prolongation
0:13:43.488 -> 0:13:46.492 of their life expectancy and the
0:13:46.492 -> 0:13:50.09 goal of the treatment in their case
0:13:50.09 -> 0:13:52.826 is to minimize the toxicity related
0:13:52.826 -> 0:13:56.445 to the use of certain agents and
0:13:56.445 -> 0:13:59.847 maximizing the effect in terms of
0:13:59.847 -> 0:14:03.526 allowing them to live their normal life
0:14:03.526 -> 0:14:06.57 without having any side effects from
0:14:06.57 -> 0:14:09.66 either the treatment or the disease.
0:14:10.62 -> 0:14:12.61 So important to
0:14:12.61 -> 0:14:13.804 have good communication.
0:14:13.81 -> 0:14:16.216 We're going to learn a
0:14:16.216 -> 0:14:17.82 lot more about hematological
0:14:17.889 -> 0:14:20.043 malignancies right after we take a
0:14:20.043 -> 0:14:22.589 short break for a medical minute.
0:14:22.59 -> 0:14:25.376 Please stay tuned to learn more with
0:14:25.38 -> 0:14:26.706 my guest Doctor
0:14:26.706 -> 0:14:28.474 Francesca Montanari.
0:14:28.474 -> 0:14:30.6 Support for Yale Cancer Answers comes from

0:14:30.6 -> 0:14:32.42 AstraZeneca, working to eliminate
0:14:32.42 -> 0:14:34.558 cancer as a cause of death.
0:14:34.56 -> 0:14:37.948 Learn more at astrazeneca-us.com.
0:14:37.95 -> 0:14:39.805 This is a medical minute
0:14:39.805 -> 0:14:41.66 about head and neck cancers,
0:14:41.66 -> 0:14:43.575 although the percentage of oral
0:14:43.575 -> 0:14:45.91 and head and neck cancer patients
0:14:45.91 -> 0:14:48.353 in the United States is only about
0:14:48.353 -> 0:14:50.302 5% of all diagnosed cancers,
0:14:50.302 -> 0:14:52.292 there are challenging side effects
0:14:52.292 -> 0:14:53.739 associated with these types
0:14:53.739 -> 0:14:55.384 of cancer and their treatment.
0:14:55.39 -> 0:14:57.006 Clinical trials are currently
0:14:57.006 -> 0:14:59.026 underway to test innovative new
0:14:59.026 -> 0:15:00.95 treatments for head and neck cancers,
0:15:00.95 -> 0:15:02.96 and in many cases less radical
0:15:02.96 -> 0:15:05.4 surgeries are able to preserve nerves,
0:15:05.4 -> 0:15:07.626 arteries and muscles in the neck,
0:15:07.63 -> 0:15:09.6 enabling patients to move, speak,
0:15:09.6 -> 0:15:12.576 breathe and eat normally after surgery.
0:15:12.58 -> 0:15:14.564 More information is available
0:15:14.564 -> 0:15:15.556 at yalecancercenter.org.
0:15:15.56 -> 0:15:18.548 You're listening to Connecticut Public Radio.
0:15:19.53 -> 0:15:21.888 Welcome back to Yale Cancer Answers.
0:15:21.89 -> 0:15:24.256 This is doctor Anees Chagpar
0:15:24.256 -> 0:15:26.622 and I'm joined tonight by my
0:15:26.622 -> 0:15:28.194 guest doctor Francesca Montanari.
0:15:28.2 -> 0:15:31.161 We're talking about the care of patients
0:15:31.161 -> 0:15:32.84 with hematologic malignancies and
0:15:32.84 -> 0:15:34.94 Francesca right before the break we
0:15:34.94 -> 0:15:37.639 were talking about the fact that these

0:15:37.639 -> 0:15:39.619 hematologic malignancies are so varied,
0:15:39.62 -> 0:15:42.78 varied in terms of where they present,
0:15:42.78 -> 0:15:45.924 some being in the bone marrow,
0:15:45.93 -> 0:15:47.9 some being in the lymph nodes,
0:15:47.9 -> 0:15:50.648 some being organs like
0:15:50.65 -> 0:15:53.586 eyes and GI track and bone and other
0:15:53.586 -> 0:15:56.288 places, they are varied in terms of
0:15:56.288 -> 0:15:58.648 their clinical presentation and the
0:15:58.648 -> 0:16:01.3 symptoms that they cause
0:16:01.3 -> 0:16:03.777 in terms of their clinical course.
0:16:03.777 -> 0:16:06.039 Some being very indolent and slow
0:16:06.039 -> 0:16:08.565 growing such that they wouldn't even
0:16:08.565 -> 0:16:10.329 warrant necessarily treatment and
0:16:10.329 -> 0:16:12.749 others being far more aggressive.
0:16:12.75 -> 0:16:15.459 Can you tell us a little bit
0:16:15.459 -> 0:16:17.43 more about the cancers,
0:16:17.43 -> 0:16:18.854 specifically what you treat?
0:16:18.854 -> 0:16:20.99 Is there a certain type of
0:16:21.063 -> 0:16:23.01 these hematologic malignancies
0:16:23.01 -> 0:16:24.23 that you specialize in?
0:16:25.43 -> 0:16:29.83 Yes, so in terms of blood cancer
0:16:29.83 -> 0:16:32.83 my research interest has
0:16:32.83 -> 0:16:36.43 always been on the lymphoma side.
0:16:36.43 -> 0:16:39.2 So lymphomas by themselves
0:16:39.2 -> 0:16:41.97 constitute the
0:16:42.073 -> 0:16:45.229 biggest part of the blood cancer.
0:16:45.23 -> 0:16:46.88 They are approximately half
0:16:46.88 -> 0:16:49.63 of all the blood cancers,
0:16:49.63 -> 0:16:52.708 but they are very diverse themselves
0:16:52.708 -> 0:16:56.499 and we do typically
0:16:56.5 -> 0:17:00.308 divide them into big categories,

0:17:00.31 -> 0:17:02.81 Hodgkin and non Hodgkin,
0:17:02.81 -> 0:17:05.31 and then furthermore into
0:17:05.31 -> 0:17:08.322 aggressive and indolent in the
0:17:08.322 -> 0:17:11.087 non Hodgkin lymphoma type and
0:17:11.09 -> 0:17:14.394 so the focus of my research
0:17:14.394 -> 0:17:17.817 has been in trying to better
0:17:17.817 -> 0:17:21.597 understand the biology of the more
0:17:21.597 -> 0:17:25.04 rare of these lymphoma types.
0:17:25.04 -> 0:17:28.864 And based on the insights in the
0:17:28.864 -> 0:17:32.452 biology to develop new treatment
0:17:32.452 -> 0:17:34.976 strategies that are targeted
0:17:34.976 -> 0:17:38.38 for these less known subtypes.
0:17:38.38 -> 0:17:39.328 In particular,
0:17:39.328 -> 0:17:42.172 the focus of my research over
0:17:42.172 -> 0:17:47.334 the past decade or so has been on
0:17:47.334 -> 0:17:49.392 posttransplant lymphoproliferative disorders,
0:17:49.4 -> 0:17:52.837 which are a rare lymphomas that arise
0:17:52.837 -> 0:17:56.55 as potentially life threatening complication
0:17:56.55 -> 0:17:58.582 of solid organ transplant.
0:17:58.582 -> 0:18:02.315 These are lymphomas that arise in the
0:18:02.315 -> 0:18:05.285 setting of reactivation of infection
0:18:05.285 -> 0:18:08.263 due to the immunosuppressive treatment
0:18:08.263 -> 0:18:11.311 or due to the chronic dysregulation
0:18:11.311 -> 0:18:15.008 of the immune system in the setting
0:18:15.008 -> 0:18:16.634 of chronic immunosuppression,
0:18:16.64 -> 0:18:17.75 and historically,
0:18:17.75 -> 0:18:21.08 the prognosis of these lymphomas have
0:18:21.08 -> 0:18:24.449 been very poor because of inability
0:18:24.449 -> 0:18:27.154 to deliver full dose treatment.
0:18:27.16 -> 0:18:29.904 And due to the frailty and
0:18:29.904 -> 0:18:32.032 risk of infectious complication

0:18:32.032 -> 0:18:36.1 that this patients experience with a
0:18:36.1 -> 0:18:38.63 regular conventional chemotherapy,
0:18:38.63 -> 0:18:41.6 the risk of dying of infection
0:18:41.6 -> 0:18:44.285 during treatment in this population
0:18:44.285 -> 0:18:47.36 has been estimated around 30%,
0:18:47.36 -> 0:18:49.675 which is extraordinarily high and
0:18:49.675 -> 0:18:53.423 in order to try to minimize the
0:18:53.423 -> 0:18:56.095 complication from the treatment,
0:18:56.1 -> 0:18:58.734 I developed the
0:18:58.734 -> 0:19:02.246 risk stratified treatment adapted
0:19:02.246 -> 0:19:07.609 strategies which are based essentially on
0:19:07.61 -> 0:19:08.108 induction phase
0:19:08.108 -> 0:19:11.096 where we do
0:19:11.096 -> 0:19:13.91 not use cytotoxic chemotherapy but
0:19:13.91 -> 0:19:16.985 more a targeted antibody approach.
0:19:16.99 -> 0:19:20.23 And then we do reserve escalation
0:19:20.23 -> 0:19:22.96 to chemotherapy only to patients
0:19:22.96 -> 0:19:26.271 that do not achieve a full response
0:19:26.271 -> 0:19:29.688 on the least invasive treatment.
0:19:29.69 -> 0:19:33.38 And with these strategies we have
0:19:33.38 -> 0:19:35.225 been able to
0:19:35.23 -> 0:19:37.996 limit the use of cytotoxic agent
0:19:37.996 -> 0:19:41.406 to less than half of the patient
0:19:41.406 -> 0:19:43.358 population that we do treat.
0:19:43.36 -> 0:19:46.228 Another area
0:19:46.228 -> 0:19:48.14 where I've been conducting
0:19:48.14 -> 0:19:50.996 research is in T cell lymphoma.
0:19:51 -> 0:19:53.868 Those are also very rare lymphomas.
0:19:53.87 -> 0:19:57.198 They are much rarer than the B cell
0:19:57.198 -> 0:19:59.921 lymphoma which are the most common
0:19:59.921 -> 0:20:02.171 non Hodgkin lymphoma out there

0:20:02.171 -> 0:20:04.623 and unfortunately historically we
0:20:04.623 -> 0:20:06.54 have been using
0:20:06.54 -> 0:20:08.376 a treatment
0:20:08.376 -> 0:20:10.671 that has been extrapolated from
0:20:10.671 -> 0:20:12.639 the B cell counterparts,
0:20:12.64 -> 0:20:16.042 so not really specific to these
0:20:16.042 -> 0:20:19.303 subtypes of lymphomas and the
0:20:19.303 -> 0:20:22.418 results are not as optimal as in
0:20:22.418 -> 0:20:24.966 the B cell counterpart's.
0:20:24.966 -> 0:20:27.626 Over the past few years,
0:20:27.63 -> 0:20:30.262 4 new drugs have been approved in
0:20:30.262 -> 0:20:32.302 the space for this, specifically
0:20:32.302 -> 0:20:35.214 for T cell lymphoma and one of
0:20:35.214 -> 0:20:38.02 the challenges that we have now
0:20:38.02 -> 0:20:39.868 are trying to identify
0:20:39.87 -> 0:20:42.481 what is the best sequencing of this
0:20:42.481 -> 0:20:45.391 agent and what is the best way to
0:20:45.391 -> 0:20:47.792 combine them to improve the outcome
0:20:47.792 -> 0:20:50.837 of patients with additional malignancies.
0:20:51.69 -> 0:20:54.45 It sounds like in both of those
0:20:54.45 -> 0:20:56.66 scenarios the overarching theme
0:20:56.66 -> 0:20:58.584 is really personalizing treatment
0:20:58.584 -> 0:21:01.389 to the patients individual disease,
0:21:01.39 -> 0:21:05.313 so I wanted to just take a step back
0:21:05.313 -> 0:21:08.457 and talk a little bit more about
0:21:08.457 -> 0:21:11.536 the intricacies of each of these.
0:21:11.54 -> 0:21:14.361 So with regards to the post transplant
0:21:14.361 -> 0:21:16.616 lymphoma, help us to understand
0:21:16.616 -> 0:21:19.026 again how these lymphomas occur,
0:21:19.03 -> 0:21:21.72 'cause certainly there are listeners
0:21:21.72 -> 0:21:25.216 who may have gone through a solid organ

0:21:25.216 -> 0:21:28.765 transplant or may know someone who has and
0:21:28.765 -> 0:21:32.64 these patients are on immunosuppressives.
0:21:32.64 -> 0:21:34.746 So does that immunosuppressive
0:21:34.746 -> 0:21:36.328 therapy automatically increase
0:21:36.328 -> 0:21:38.44 their risk of lymphoma?
0:21:38.44 -> 0:21:42.598 And is there anything that they can do to
0:21:42.598 -> 0:21:46.336 reduce their risk of developing lymphoma
0:21:46.34 -> 0:21:47.918 in that setting?
0:21:47.918 -> 0:21:50.56 That's a really good question,
0:21:50.56 -> 0:21:54.592 so we do after the transplant patient
0:21:54.592 -> 0:21:56.32 received different immunosuppressive
0:21:56.401 -> 0:21:59.943 treatment which are related to the different
0:21:59.943 -> 0:22:03.409 kind of transplant that they have received.
0:22:03.41 -> 0:22:04.546 For transplant,
0:22:04.546 -> 0:22:06.818 such as intestinal transplant,
0:22:06.82 -> 0:22:08.593 multi visceral transplant,
0:22:08.593 -> 0:22:11.548 immunosuppressive treatment is much tougher
0:22:11.548 -> 0:22:15.358 and much deeper than a patient that
0:22:15.36 -> 0:22:19.128 for instance receives renal transplant where
0:22:19.128 -> 0:22:21.012 immunosuppressant treatment required
0:22:21.012 -> 0:22:24.458 for the recipient to accept the graft is much less.
0:22:33.46 -> 0:22:35.852 And the reason we do see as a
0:22:35.852 -> 0:22:38.153 consequence of the immune suppression
0:22:38.153 -> 0:22:40.329 reactivation of common infection,
0:22:40.33 -> 0:22:41.539 and most important,
0:22:41.539 -> 0:22:43.957 is the Epstein Barr virus,
0:22:43.96 -> 0:22:46.788 which is the virus that causes mononucleosis.
0:22:46.79 -> 0:22:49.653 Most of the adult population has been
0:22:49.653 -> 0:22:52.846 exposed by adulthood to the virus,
0:22:52.85 -> 0:22:55.699 and the virus is dormant in
0:22:55.699 -> 0:22:58.1 a silent state in our body,

0:22:58.1 -> 0:23:01.736 and is kept at bay by our immune system.
0:23:01.74 -> 0:23:03.86 So conditions such as immunosuppression where
0:23:04.71 -> 0:23:07.585 our immune system defenses are lowered
0:23:07.585 -> 0:23:11.058 allow the virus to thrive again
0:23:11.058 -> 0:23:14.076 and replicate and
0:23:14.08 -> 0:23:16.83 this particular kind of virus,
0:23:16.83 -> 0:23:20.876 in the absence of an immune system
0:23:20.876 -> 0:23:25.097 that fights it and keeps it at bay,
0:23:25.1 -> 0:23:29.33 is able to transform the blood
0:23:29.33 -> 0:23:32.66 cells into lymphoma cells so
0:23:32.66 -> 0:23:34.673 typically in the first year
0:23:34.673 -> 0:23:35.876 after the transplant,
0:23:35.88 -> 0:23:39.485 most of the lymphoma that we do
0:23:39.485 -> 0:23:42.9 see are related to Epstein Barr
0:23:42.9 -> 0:23:44.756 reactivation in the
0:23:44.756 -> 0:23:47.076 setting of the immune suppression,
0:23:47.08 -> 0:23:49.852 the lymphoma that arise after one
0:23:49.852 -> 0:23:53.158 year still can be
0:23:53.158 -> 0:23:55.882 linked to the Epstein Barr virus,
0:23:55.89 -> 0:23:58.584 but approximately half of them happen
0:23:58.584 -> 0:24:01.46 without a reactivation of Epstein virus,
0:24:01.46 -> 0:24:04.505 and they do not hardwire the genetic
0:24:04.505 -> 0:24:07.105 material of the virus and are
0:24:07.105 -> 0:24:09.517 thought to arise in the setting
0:24:09.517 -> 0:24:12.599 of a chronic immune dysregulation
0:24:12.6 -> 0:24:16.11 due to the longstanding immunosuppression.
0:24:16.56 -> 0:24:18.53 Is there anything that
0:24:18.53 -> 0:24:21.125 people can do to limit that
0:24:21.125 -> 0:24:23.81 reactivation of Epstein Barr virus?
0:24:23.81 -> 0:24:26.516 You mentioned that most adults have
0:24:26.516 -> 0:24:28.79 already experienced Epstein Barr virus,

0:24:28.79 -> 0:24:31.49 and so should have some degree
0:24:31.49 -> 0:24:34.23 of natural immunity to the virus,
0:24:34.23 -> 0:24:35.99 although they're on immunosuppressants.
0:24:35.99 -> 0:24:39.154 So has anybody looked at ways that
0:24:39.154 -> 0:24:41.449 people who are on immunosuppressants
0:24:41.449 -> 0:24:43.74 can prevent that reactivation?
0:24:43.74 -> 0:24:46.59 That is a really good question, and
0:24:46.59 -> 0:24:48.91 indeed,
0:24:48.91 -> 0:24:52.256 a part of these
0:24:52.256 -> 0:24:56.078 strategies in the period after transplant
0:24:56.08 -> 0:24:58.8 include close monitoring of the
0:24:58.8 -> 0:25:02.16 EBV presence in the blood.
0:25:02.16 -> 0:25:05.466 So after a solid organ transplant,
0:25:05.47 -> 0:25:09.646 depending on the kind of solid
0:25:09.646 -> 0:25:12.43 organ transplant there are
0:25:12.43 -> 0:25:14.266 algorithms
0:25:14.266 -> 0:25:18.55 and there is a monitoring of the
0:25:18.665 -> 0:25:22.788 EBV which is done
0:25:22.788 -> 0:25:26.26 in certain cases twice a month.
0:25:26.26 -> 0:25:28.92 Other cases once a month,
0:25:28.92 -> 0:25:32.136 depending on the nature of the
0:25:32.136 -> 0:25:33.744 immunosuppression and preemptive
0:25:33.744 -> 0:25:35.299 strategies to intervene.
0:25:37.79 -> 0:25:40.742 Treating the EBV before the lymphoma
0:25:40.742 -> 0:25:43.148 appears has been attempted,
0:25:43.148 -> 0:25:46.66 but the results are not optimal
0:25:46.66 -> 0:25:50.108 because there is a lot of variation in
0:25:50.108 -> 0:25:54.02 the levels of EBV that is noted
0:25:54.02 -> 0:25:57.154 in patients post transplant and not
0:25:57.154 -> 0:25:59.839 everybody that experience a reactivation
0:25:59.839 -> 0:26:04.04 of the virus end up developing a

0:26:04.04 -> 0:26:07.1 lymphoma and therefore there is not
0:26:07.1 -> 0:26:10.01 good guidance out there regarding
0:26:10.01 -> 0:26:12.92 who to treat preemptively
0:26:12.92 -> 0:26:15.332 and who to observe.
0:26:15.332 -> 0:26:19.61 When I was at Columbia University prior
0:26:19.61 -> 0:26:23.978 to joining the group here at Yale
0:26:23.98 -> 0:26:28.372 I was leading the effort to come up with
0:26:28.372 -> 0:26:33.078 with guidelines to help clinician in the
0:26:33.078 -> 0:26:37.659 solid organ transplant team to troubleshoot
0:26:37.66 -> 0:26:39.499 these problems,
0:26:39.499 -> 0:26:43.177 meaning want to check the EBV
0:26:43.177 -> 0:26:46.585 at what intervals and what
0:26:46.585 -> 0:26:50.738 is the threshold of the
0:26:50.738 -> 0:26:54.118 virus to consider potentially
0:26:54.12 -> 0:26:57.963 leading to a lymphoma and when
0:26:57.963 -> 0:27:00.61 to utilize treatment to reduce
0:27:00.61 -> 0:27:04.186 that virus level and it is still a
0:27:04.294 -> 0:27:08.158 discussion and a work in progress.
0:27:09.02 -> 0:27:11.48 And do we know what factors
0:27:11.48 -> 0:27:14.113 kind of trigger that EBV
0:27:14.113 -> 0:27:16.807 to turn into a lymphoma?
0:27:16.81 -> 0:27:18.542 Because potentially that's another
0:27:18.542 -> 0:27:21.14 place to intervene in thinking about
0:27:21.14 -> 0:27:24.06 is there a way to
0:27:24.06 -> 0:27:28.128 potentially mitigate that transformation.
0:27:28.13 -> 0:27:30.07 That is an excellent
0:27:30.07 -> 0:27:32.6 question, and unfortunately the reason
0:27:32.6 -> 0:27:37.07 why EBV can turn in vitro
0:27:37.07 -> 0:27:39.39 into malignant cells is because
0:27:39.39 -> 0:27:42.728 one side triggers
0:27:42.728 -> 0:27:45.616 the proliferation of these cells and

0:27:45.616 -> 0:27:48.694 the other side blocks an important
0:27:48.694 -> 0:27:51.849 mechanism that is called apoptosis,
0:27:51.85 -> 0:27:55.458 by which the cells die but alone is
0:27:55.458 -> 0:27:59.308 not able to induce lymphoma in vivo.
0:27:59.31 -> 0:28:03.23 And the thought is that there are,
0:28:03.23 -> 0:28:08.147 like in all the other kinds of cancer,
0:28:08.15 -> 0:28:11.832 a multi step process where the
0:28:11.832 -> 0:28:14.22 cells progressively gain additional
0:28:14.22 -> 0:28:16.389 mutation and overtime
0:28:16.39 -> 0:28:19.45 the addition of this mutation together
0:28:19.45 -> 0:28:24.048 sort of cause the transformation into cancer,
0:28:27.2 -> 0:28:30.735 but we are not able in 2021 to predict
0:28:30.735 -> 0:28:33.689 which mutation and when these
0:28:33.689 -> 0:28:35.69 mutations are acquired.
0:28:36.35 -> 0:28:38.395 Doctor Francesca Montanari is assistant
0:28:38.395 -> 0:28:40.44 professor of clinical medicine and
0:28:40.504 -> 0:28:42.828 hematology at the Yale School of Medicine.
0:28:42.83 -> 0:28:44.358 If you have questions,
0:28:44.358 -> 0:28:45.886 the address is canceranswers@yale.edu
0:28:45.886 -> 0:28:47.995 and past editions of the program
0:28:47.995 -> 0:28:49.921 are available in audio and written
0:28:49.982 -> 0:28:51.59 form at yalecancercenter.org.
0:28:51.59 -> 0:28:54.398 We hope you'll join us next week to
0:28:54.398 -> 0:28:57.137 learn more about the fight against
0:28:57.137 -> 0:29:00.071 cancer here on Connecticut Public Radio.