

Combination Chemo Helps People with Leiomyosarcoma Live Longer

Leiomyosarcoma is a malignant tumor of smooth muscle cells; it's most common in the uterus, abdomen or pelvis.

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By Sharon Reynolds

For decades, the chemotherapy drug doxorubicin has been the mainstay of treatment for people with many types of advanced sarcoma, cancers that begin in the bone or the soft tissues of the body. Previously tested combinations of doxorubicin with other chemotherapy drugs helped some people live longer. But, compared with doxorubicin alone, the side effects of such combinations were severe, leading many doctors to consider them to be too risky to use in everyday patient care.

But that may soon change, based on the results of a [clinical trial](#) conducted in France. The trial showed that adding [trabectedin \(Yondelis\)](#) to doxorubicin as an initial treatment for people with a type of sarcoma called [leiomyosarcoma helped them live longer than people initially treated with doxorubicin alone](#): a median of 33 months versus 24 months.

The findings were published September 5 in the New England Journal of Medicine.

Giving the drugs at the same time also appeared to be more effective than giving one for a period followed by the other (sequentially). Although almost 60% of people in the trial initially treated with doxorubicin alone later received trabectedin, they still didn't live as long as those who got both drugs together from the beginning of their treatment.

People initially treated with the combination, which was given for about four and a half months, could continue taking trabectedin by itself for up to almost a year, a strategy called [maintenance therapy](#).

This makes it hard to tease out the effects of the combination from the effects of longer treatment overall, explained Margaret von Mehren, MD, a sarcoma expert from Fox Chase Cancer Center, who was not involved with the study.

But people in the trabectedin plus doxorubicin group lived almost a year longer, she continued, "which argues that the initial response to combination treatment and maintenance was helpful in a

way that sequential therapy is not” she said.

The combination treatment did come with a spike in side effects, including serious issues that can substantially impact [quality of life](#). But many patients may accept that risk if it can potentially help them live longer, said Robert Benjamin, MD, of the University of Texas MD Anderson Cancer Center, another sarcoma expert who was not involved with the study.

Rare tumors, difficult studies

Sarcomas are rare, making up less than 2% of all cancer diagnoses. This already small number includes around 70 different subtypes. Because of their rarity, clinical trials of new treatments have often included people with many different types of sarcomas in order to have enough participants to produce meaningful results.

But research has indicated that different subtypes of sarcoma may be sensitive to different drugs, suggesting that treatment strategies need to be tailored to each subtype.

The combination of doxorubicin and trabectedin had shown promise in small studies of leiomyosarcoma, a tumor that develops in smooth muscle cells. Although it can arise almost anywhere in the body, it’s most common in the uterus, abdomen, and pelvis.

It took the French Sarcoma Group several years to enroll 150 people into their trial. Participants had been diagnosed with leiomyosarcoma that couldn’t be removed surgically or had spread (metastasized) and hadn’t yet received any treatment.

The researchers randomly assigned about half of the participants to receive up to six cycles of doxorubicin given once every 3 weeks, and the other half to six cycles of doxorubicin plus trabectedin given over the same time frame. Participants in both groups received medications to prevent the number of blood cells in the body from dropping dangerously low.

People in the combination chemotherapy group could continue to receive trabectedin as maintenance therapy for almost a year, as long as the drug appeared to be keeping their cancer in check.

More treatment, longer survival

After a median of more than 4.5 years of follow-up, people who received the combination therapy lived twice as long without their cancer getting worse as those who only got doxorubicin at the start of treatment: 12 months versus 6 months. Two years after starting treatment, 30% of people in the combination chemotherapy group were alive without their cancer getting worse, compared with only 3% who received doxorubicin alone.

Of the people who initially got doxorubicin alone, about 38% eventually received trabectedin after

their cancer had come back, or [relapsed](#), and 23% received it after a third or later relapse.

The six cycles of planned chemotherapy shrank the original or metastatic tumors enough to allow for complete surgical removal in 20% of people who received both doxorubicin and trabectedin, compared with only 8% of those who initially received only doxorubicin.

Historically, patients who are able to have their cancer completely removed with surgery “have the same potential for long-term survival” as those whose cancer is completely eradicated by chemotherapy alone, Dr. Benjamin explained.

With more side effects come decisions about best treatment choice

The addition of trabectedin to doxorubicin did substantially increase the number of serious side effects among participants in the combination chemotherapy group.

Almost everyone (97%) in this group had at least one major treatment side effect, including drops in the number of red or [white blood cells](#) and temporary liver damage. By comparison, just under 60% of people in the doxorubicin-alone group had serious side effects during treatment.

Despite the higher rate of side effects, 81% of people in the combination chemotherapy group finished all six initial cycles of chemotherapy, compared with 71% of people in the doxorubicin group. One death related to treatment—from heart failure—occurred in the doxorubicin group.

Some people with other health conditions, such as heart problems, liver disease, or problems with their [bone marrow](#), may not be able to receive both drugs together, explained Dr. Benjamin.

“But I think for most patients with leiomyosarcomas, if you need to use chemotherapy, this [combination] is what you would want to use,” he said.

There are other strategies that could be explored to let more patients try combination chemotherapy up front, including the use of drugs that protect the heart, such as dexrazoxane, Dr. Benjamin added.

But some people with advanced sarcomas may still prioritize fewer side effects over a chance at living longer, said Dr. von Mehren. “You have to take into account the patient’s preference on the impact of treatment on their ability to [live] their life day to day,” she said.

Others may want to join a clinical trial testing newer treatments, such as immunotherapies, she added. And people shouldn’t be discouraged from joining studies that include people with different sarcoma subtypes if that gives them the opportunity to try other treatment options, she said.

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