

Targeted heat therapy offers new standard treatment option for soft tissue sarcoma

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Patients with soft-tissue sarcomas at high risk of spreading were 30% more likely to be alive and cancer free almost three years after starting treatment if their tumours were heated at the time they received chemotherapy, according to new research. The finding bolsters the case for intensifying exploration of the strategy in other types of cancer.

The study, which found that the addition of the innovative heat technique more than doubled the proportion of patients whose tumours responded to chemotherapy without increasing toxicity, is also the first to show that any treatment other than surgery followed by radiation can prolong survival of this type of patient.

"These findings provide a new standard treatment option and we believe they are likely to change the way many specialists treat these tumours," said the study's leader, Professor Rolf Issels, a professor of medical oncology at Klinikum Grosshadern Medical Center at the University of Munich in Germany, who presented the results today (Tuesday 22 September) in Berlin at Europe's largest [cancer](#) congress, ECCO 15 - ESMO 34.

"But the implications of these findings are more far-reaching," Prof Issels said. "This is also the first clear evidence that targeted heat therapy adds to chemotherapy. We expect our findings will encourage other researchers to test the approach in other locally advanced cancers. Targeted heat therapy has already shown promise in recurrent breast and locally advanced cervical cancer in combination with radiation and

studies combining it with chemotherapy in other localised tumours such as those in the pancreas and rectum are ongoing."

Soft tissue sarcomas involve cancer that starts in the soft, supporting tissues of the body, such as muscle, fat, [blood vessels](#), nerves, tendons, tissue around the joints and deep layers of the skin. They are relatively rare, accounting for about three percent of all cancers, but are more common in children and young adults. Surgery is the primary treatment, but sometimes these tumours are difficult to remove completely, so they are often also treated with radiotherapy and sometimes chemotherapy. However, in cases where the disease is localised, the benefits of chemotherapy have been shown to be limited. In high-risk patients, any relapse usually occurs within two or three years. Survival varies widely depending on the location and severity of the tumour, with abdominal sarcomas being the most deadly.

The phase III study involved 341 patients being treated at several centres in Europe and the United States between July 1997 and November 2006 for locally advanced soft tissue sarcomas that were at high risk of recurrence and spread. More than half of the tumours were located in the abdomen, while the rest were in the arms and legs. All patients were given chemotherapy before and after surgery and radiotherapy.

Half were randomly given targeted heat treatment along with the chemotherapy. The technique, known as regional hyperthermia, uses focused electromagnetic energy to warm the tissue in and around the tumour to between 40 and 43 degrees Celsius (104 - 109.4 degrees Fahrenheit). The heat not only kills cancer cells, but it also seems to make chemotherapy work better by making cancer cells more sensitive. It also improves blood flow, which allows chemotherapy to be more effective.

After an average follow-up of 34 months, only 153 patients (44.9%) in

total had died. The improvement in overall survival was not statistically meaningful when all patients were analysed, but an analysis of the 269 who completed the full treatment of either four cycles of initial chemotherapy alone or four chemotherapy cycles and eight heat treatments found that those who got the heat therapy were 44% less likely to die during the follow-up period than those who got chemotherapy alone.

"The patients receiving the targeted heat therapy fared better on all outcome measurements," Prof Issels said. "Almost three years after starting treatment, they were 42% less likely to experience a recurrence of their cancer at the same site or to die than those who were getting chemotherapy alone, surviving an estimated 120 months before local progression of their disease, compared with an estimated 75 months. Similarly, the average length of time that patients remained disease free was 32 months in the group that got both treatments, compared with 18 months in the group that got chemotherapy alone - an improvement of 30%."

At two years, 76 percent of the patients in the heat therapy group were still alive without local progression of their cancer, compared with 61 percent in the chemotherapy alone group. The proportion of patients who experienced tumour shrinkage rose from 12.7% in the chemotherapy alone group to 28.8%, while the proportion of patients who saw their tumour grow was 6.8% in the heat therapy group, compared with 20% in the chemotherapy alone group.

The most frequent side effect of the heat therapy was mild to moderate discomfort, reported in 45% of patients. The most serious side effect was severe burns, seen in one patient (0.6%). Blisters occurred in 17.8%.

"This strategy has been in development for about 20 years, with about 150 leading groups studying it, but the clear results of this trial show that

the field has now matured to the point where we must step up efforts to explore its potential to offer an entirely new way of treating locally advanced disease in several major cancers," Prof Issels said. "That will take investment from public funders to underwrite trials that investigate, for instance, whether it will be possible to reduce the dose of [chemotherapy](#) drugs by boosting their effectiveness with targeted heat therapy and whether the technique can enhance the effectiveness of newer targeted drugs."

Other questions remaining include whether targeted heat therapy can play a role in stimulating the immune system to more effectively attack cancer, Prof Issels said, adding that studies of heat shock protein therapy indicate that they may activate the immune system against the disease.

Source: ECCO-the European CanCer Organisation

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