

Targeted therapy with pazopanib prolongs progression-free survival in advanced soft-tissue sarcoma

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For patients with metastatic soft-tissue sarcoma whose disease has progressed following standard chemotherapy, treatment with pazopanib (a drug that targets the growth of new cancer-related blood vessels) nearly tripled progression-free survival (PFS) compared with placebo, according to results of the PALETTE trial, published Online First in *The Lancet*. This is the first time a randomised phase 3 trial in metastatic soft-tissue sarcoma has shown improvement in PFS.

Soft-tissue sarcomas are relatively rare and account for just 1% of all adult cancers, with the annual number of new cases in the USA estimated at 11 000. In the last 30 years there has been little progress in developing effective new treatments. In advanced stages of the disease, median overall survival is about 12 months. Recent research has shown that [pazopanib](#) has promising activity in patients with soft-tissue sarcomas.

Pazopanib is a drug that targets platelet-derived [growth factor receptors](#) (PDGF) and all three [vascular endothelial growth factor](#) (VEGF) receptors involved in angiogenesis (the growth of new blood vessels) and has been approved to treat [kidney cancer](#).

In the PALETTE study, Winette van der Graaf from Radboud University Nijmegen Medical Centre, Netherlands and colleagues from the European Organisation for Research and Treatment of Cancer Soft

Tissue and Bone Sarcoma Group, and other cancer centres worldwide, enrolled 369 patients with metastatic soft-tissue [sarcoma](#) whose disease had progressed after chemotherapy. Patients with gastro-intestinal stromal tumors (GIST) and liposarcomas were not included. In total, 72 institutions across 13 countries participated in the study. Patients were randomly assigned to oral pazopanib (246 patients) or placebo (123).

Results showed that the time it took for a patient's disease to progress was improved by 3 months for those receiving pazopanib (4.6 months) compared with those given placebo (1.6 months) at a median follow-up of 15 months.

However, there was no significant gain in overall survival (12.5 months vs 10.7 months) in patients receiving pazopanib.

Common side effects of pazopanib included fatigue, diarrhoea, hypertension, nausea, and weight loss. Newly reported side effects were venous thromboembolic events, pneumothorax, and cardiotoxicity.

Pazopanib was discontinued in 34 (14%) patients because of toxic effects related to the drug. Of eight fatal adverse events in the pazopanib group, one was multi-organ failure that might have been related to the study drug. Overall, self-reported quality of life did not differ significantly between the placebo and pazopanib groups, but individual components such as diarrhoea, nausea, and fatigue were significantly worse on pazopanib.

The authors conclude: "Progression-free survival improved in patients of all ages and for most histological subgroups. Pazopanib is the first active oral agent for patients with soft-tissue sarcomas, excluding liposarcomas and GIST, and is a new treatment option for patients with this rare group of tumours."

In an accompanying Comment, Vivien Bramwell from the Tom Baker Cancer Centre, Calgary, Canada says: "This was a well-designed and conducted study, that showed a 3 month improvement in the primary outcome of progression-free survival. [But] the desired effect of palliative chemotherapy is that tumour shrinkage or delay of progression will improve patients' activity or well-being, but this effect was not definitively shown."

She adds: "The investigators conclude that pazopanib provides a new treatment option, and there will be demand for it, but will funding agencies be willing to, or able to, pay?"

More information: Study online: [www.thelancet.com/journals/lan... \(12\)60651-5/abstract](http://www.thelancet.com/journals/lan... (12)60651-5/abstract)

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