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Pazopanib or methotrexate-vinblastine combination chemotherapy in adult patients with progressive desmoid tumours (DESMOPAZ): a non-comparative, randomised, open-label, multicentre, phase 2 study

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Abstract

Background: Desmoid tumours are locally aggressive tumours associated with substantial morbidity. No systemic treatments are approved for this disease, with methotrexate-vinblastine the only chemotherapy regimen assessed in a clinical trial setting to date. VEGF overexpression is a common feature in aggressive desmoid tumours. Pazopanib is an oral antiangiogenic agent targeting VEGF receptors 1, 2, and 3, platelet-derived growth factor receptor-like protein (PDGFR) α and β, and c-KIT tyrosine kinases. We aimed to assess antitumour activity and safety of targeted therapy or combination chemotherapy in progressive desmoid tumours.

Methods: DESMOPAZ was a non-comparative, randomised, open-label, phase 2 trial conducted at 12 centres from the French Sarcoma Group. We enrolled adults (≥18 years) with progressive desmoid tumours, normal organ function and centrally documented progressive disease according to Response Evaluation Criteria in Solid Tumors version 1.1 based on two imaging assessments obtained within less than a 6-month interval. Participants were randomly assigned (2:1) to oral pazopanib 800 mg per day for up to 1 year or to an intravenous regimen combining vinblastine (5 mg/m^2 per dose) and methotrexate (30 mg/m^2 per dose), administered weekly for 6 months and then every other week for 6 months. Randomisation was stratified according to inclusion centre and tumour location. The primary endpoint was the proportion of patients who had not progressed at 6 months in the first 43 patients who had received one complete or two incomplete cycles of pazopanib. This endpoint was also assessed as a prespecified exploratory endpoint in all patients who had received one complete or two incomplete cycles of methotrexate-vinblastane. Safety analyses were done for all patients who received at least one dose of allocated treatment. This trial was registered with ClinicalTrials.gov, number NCT01876082.

Findings: From Dec 4, 2012, to Aug 18, 2017, 72 patients were enrolled and randomly assigned (n=48 in the pazopanib group; n=24 in the methotrexate-vinblastine group). Median follow-up was 23·4 months (IQR 17·1-25·5). 46 patients in the pazopanib group and 20 patients in the methotrexate-vinblastine group were assessable for activity. In the first 43 patients assessable for the primary endpoint in the pazopanib group, the proportion of patients who had not progressed at 6 months was 83·7% (95% CI 69·3-93·2). The proportion of patients treated with methotrexate-vinblastine who had not progressed at 6 months was 45·0% (95% CI 23·1-68·5). The most

common grade 3 or 4 adverse events in the pazopanib group were hypertension (n=10, 21%) and diarrhoea (n=7, 15%) and in the methotrexate-vinblastine group were neutropenia (n=10, 45%) and liver transaminitis (n=4, 18%). 11 patients (23%) had at least one serious adverse event related to study treatment in the pazopanib group, as did and six patients (27%) in the methotrexate-vinblastine group.

Interpretation: Pazopanib has clinical activity in patients with progressive desmoid tumours and could be a valid treatment option in this rare and disabling disease.

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Comment in

The necessity for rigour in rare disease study design.
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