Pazopanib in the treatment of advanced solitary fibrous tumour

Pazopanib is the only tyrosine kinase inhibitor approved by the US Food and Drug Administration for the treatment of soft tissue sarcoma, with a broad spectrum targeting c-Kit, VEGFRs, PDGFR α/β, and FGFR. In *The Lancet Oncology*, Javier Martín-Broto and colleagues[1] reported the results of a prospective, single-arm, phase 2 trial that assessed the drug's activity in patients with advanced and previously progressing solitary fibrous tumour. 36 eligible patients were accrued to receive pazopanib 800 mg orally once daily, and 18 (51%) of 35 evaluable patients showed partial responses. The median decrease in tumour density of 28% (IQR 4–45), median progression-free survival of 5·57 months (95% CI 4·51–6·62), and 2-year overall survival of 73% (based on Choi criteria) indicate the substantial anti-tumour activity of pazopanib against advanced solitary fibrous tumour. However, we would like to address two concerns regarding this study.

First, the authors state that patients previously treated with antiangiogenic drugs would be excluded. However, two patients who received sunitinib, a VEGFR-targeted antiangiogeic agent, as previous systemic therapy were enrolled and showed a good response to pazopanib in the study, which is inconsistent with the exclusion criteria aforementioned.[1] Actually, cross-resistance to clinically used TKIs occurs frequently in patients with cancer,[2] and pazopanib has showed efficacy and is well tolerated in patients after failure of sunitinib.[3] Therefore, we believe it is feasible to modify the exclusion criteria to incorporate these patients in this trial.

Second, previous studies have shown that the efficacy of pazopanib in malignancies is strongly correlated with its pharmacokinetic exposure, as measured by plasma trough levels (C_{min}). Generally, pazopanib C_{min} higher than the efficacy threshold (>20 mg/L) is associated with significantly improved progression-free survival and tumour shrinkage, whereas lower C_{min} might render suboptimal treatment outcomes.[4,5] Solid fibrous tumour is a rare neoplasm with multiple subtypes, contributing to its high inter-patient heterogeneity. Moreover, pazopanib pharmacokinetics could be affected by numerous factors including food, interaction of concomitant medications, and even time of drug ingestion.[4] Despite the large variability in exposure, pazopanib was still administered at a fixed dose in the study by Martin-Broto and colleagues,[1] and dose reduction or re-escalation only occurred after severe toxicity.[1] Consequently, plasma exposure of pazopanib might vary markedly among patients and lead to the biased efficacy and toxicity in advanced solid fibrous tumour. We therefore suggest the necessary monitoring of pazopanib C_{min} to ensure adequate and more stable plasma concentrations, and believe that patients with cancer might benefit from increased efficacy and reduced toxicity through this pharmacokinetically guided treatment.

We declare no competing interests.

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