Pazopanib in the treatment of advanced solitary fibrous tumour

Authors' reply

We thank Chao Tu and colleagues for highlighting two concerns in relation to our Article. Their first point focuses on the two patients who had already received an antiangiogenic drug, sunitinib, before enrolment in the trial. We agree with Tu and colleagues, this was a protocol violation. However, this fact was permitted by the trial steering committee after considering that no reduction in benefit was expected. There were post-protocol treatment recommendations in this trial, so that patients with benefit from pazopanib (defined as stable disease or partial response, according to Choi, at least in the first assessment) would continue with 37·5 mg per day continuously of antiangiogenic sunitinib. The data on post-protocol treatment has not yet been formally analysed, but no apparent cross-resistance among anti-angiogenic drugs was observed in several patients. Furthermore, we are also convinced that the sequential use of anti-angiogenic drugs is recommended in advanced solitary fibrous tumour, at least when activity has been shown with the first anti-angiogenic drug.

Their second point addresses the fact that pazopanib has complex pharmacokinetic properties, with relevant inter-patient variability and low non-linear bioavailability. Therefore, the flat dose could have conditioned the activity of pazopanib in the trial, at least partly. Protocol guidelines attempted to minimise the interference of food and drugs with pazopanib in a reasonable way, and recommended the flat dose of 800 mg on a daily basis as the dose that showed significant benefit in the pivotal PALETTE trial in advanced soft tissue sarcoma.[1] In our study, there was no correlation between progression-free survival or overall survival and grade 3–4 hypertension in univariate analysis. Since studies have identified a relationship between pazopanib exposure and hypertension,[2] the real effect of having no personalised dose of pazopanib on progression-free survival or overall survival in this trial should be low.

JM-B reports research expenses from GlaxoSmithKline-Novartis, during the conduct of the study; grants and personal fees from Novartis and Pharmamar; grants from EISAI; and personal fees from Lilly, outside the submitted work. DSM reports grants and non-financial support from EISAI and Pharmamar, outside the submitted work. NH reports grants from Novartis, during the conduct of the study; grants and travel expenses from Pharmamar; and grants from Eisai, outside the submitted work.

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1 van der Graaf WT, Blay JY, Chawla SP, et al. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2012; **379:** 1879–86.

2 Suttle AB, Ball HA, Molimard M, et al. Relationships between pazopanib exposure and clinical safety and efficacy in patients with advanced renal cell carcinoma. *Br J Cancer* 2014; **111:** 1909–16.