

## GAS agents limit pazopanib activity in soft-tissue sarcoma



The concomitant administration of pazopanib—a tyrosine kinase inhibitor (TKI) with absorption that is PH-dependent—and gastric acid-suppressive (GAS) agents, such as proton pump inhibitors (PPIs), might limit the absorption and therapeutic benefits of pazopanib in soft-tissue sarcoma, according to a recent study.

In a retrospective review of the single-arm, phase 2, EORTC 62043 trial and the placebo-controlled, phase 3, EORTC 62072 PALETTE trial, Olivier Mir (Gustave Roussy, Villejuif, France) and colleagues analysed data from 333 patients with soft-tissue sarcoma treated with pazopanib, of whom 59 (18%) had received GAS therapy concomitantly for at least 80% of pazopanib treatment duration, while 117 (35%) did so at least once during pazopanib treatment. The study investigated whether GAS therapy affected clinical

outcomes in these patients using multivariate analyses; progression-free survival was the primary endpoint and overall survival was a secondary endpoint.

At a median follow-up of 27.6 months (IQR 22.9–35.4), median progression-free survival was significantly worse in patients who received concomitant GAS therapy than in those who received pazopanib alone, at 2.8 months versus 4.6 months, respectively (hazard ratio [HR] 1.49, 95% CI 1.11–1.99;  $p=0.008$ ). Concomitant administration of GAS therapy and pazopanib was also associated with worse median overall survival, 8.0 months versus 12.6 months (1.81, 1.31–2.49;  $p<0.001$ ).

“[This study] represents a serious warning in clinical practice, not only for prescribers of GAS (oncologists and GPs), but also pharmacists and soft-tissue sarcoma patients

themselves (especially in countries where GAS is available over the counter)”, explained Mir. “Whether these findings are extrapolable to patients with other cancers treated with pazopanib (such as renal cancer) is likely, but remains to be confirmed by further studies.”

“Although PPIs are commonly prescribed during TKI therapy, there is still a lot of controversy about whether or not the resulting drug interaction is clinically relevant”, commented Roelof van Leeuwen (Erasmus University Medical Center, Rotterdam, Netherlands). “The current study by Mir and colleagues clearly shows that concomitant use of PPIs can have major impact on TKI efficacy. Therefore, structured screening for drug interactions should take place before the start of TKI therapy.”

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For more on the **study by Olivier Mir and colleagues** see *Clin Cancer Res* 2019; published online February 14.  
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