Correspondence

Response letter on *Micromanagement of drug-resistant advanced gastrointestinal stromal tumors: regorafenib—new ammunition in battling exon 17 mutations*

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Provenance: This is an invited Correspondence commissioned by Editor-in-Chief Jia-Fu Ji, MD, FACS (Department of Gastrointestinal Surgery, Peking University School of Oncology & Beijing Cancer Hospital, Beijing, China).

Response to: Eckardt AJ, Klein O. Micromanagement of drug-resistant advanced gastrointestinal stromal tumors: regorafenib—new ammunition in battling exon 17 mutations. Transl Gastroenterol Hepatol 2018;3:12.

Received: 27 May 2018; Accepted: 11 June 2018; Published: 19 June 2018.

doi: 10.21037/tgh.2018.06.03

View this article at: http://dx.doi.org/10.21037/tgh.2018.06.03

We thank Eckardt and Klein for their interest in our phase II trial delineating the treatment efficacy of regorafenib in patients with metastatic and/or an unresectable gastrointestinal stromal tumor harboring secondary mutations of exon 17 (1). Several issues emerged (2).

Regarding the historical cohort, although there are many additional factors that may have affected the outcome, including tumor biology, number of surgical procedures, ablative therapies and the previous use of tyrosine kinase inhibitor (TKI), the fact is that all the aforementioned treatment modality cannot overcome drug resistance raised by secondary mutations of exon 17. So the treatment outcome of regorafenib is more promising. Of course, randomized trial is still mandatory.

For 6 out of 18 (33.3%) patients had stable disease (SD) upon study inclusion under treatment with another TKI because the patients should be resistant to available first- or second-line TKIs. So we use multi-modality treatment to keep the patient is SD. According to our recent analysis, the overall survival may be improved by regorafenib with exon 17 mutation failed to imatinib and sunitinib (unsubmitted data). So the trail shows that the primary endpoint of disease control was reached in 93.3% of patients, which compares favorably to the 52.6% of patients in the GRID-trial, who were not pre-selected by their mutational status, suggesting that regorafenib holds some promise in this setting (3).

As shown in our trial, 8 patients who were refractory to imatinib, but did not receive previous second-line treatment with sunitinib, which suggests that regorafenib should be evaluated as second-line (or even first-line) treatment for patients with exon 17 mutations. So we totally agree that a clinical trial regarding evaluation of regorafenib as primary or secondary treatment, especially in patients with exon 17 is warranted.

Regarding grade 3 toxicity from hand-foot skin reaction (HFSR) was 55.6% in the study as compared with 19.7% in the GRID-trial (3). It is interesting and unclear the impact of exon 17 mutations on the high incidence of keratinocyte toxicity. HFSR was still the most frequently observed adverse event and the most common reason for dose reduction. Although HFSRs are not life-threatening, these adverse reactions are related to substantial tenderness that affects daily functioning and the quality of life, often resulting in dose modifications or discontinuation of treatment (1). In this and other previous studies, Asian patients exhibited increased susceptibility to regorafenib-induced HFSRs (1,4,5). Nonetheless, mechanistic studies are urgently warranted to elucidate potential solutions for these adverse events.

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

References

1. Yeh CN, Chen MH, Chen YY, et al. A phase II trial of regorafenib in patients with metastatic and/or a unresectable gastrointestinal stromal tumor harboring secondary mutations of exon 17. Oncotarget 2017;8:44121-30.
2. Eckardt AJ, Klein O. Micromanagement of drug-resistant advanced gastrointestinal stromal tumors: regorafenib—new ammunition in battling exon 17 mutations. Transl Gastroenterol Hepatol 2018;3:12.
3. Demetri GD, Reichardt P, Kang YK, et al. Efficacy and safety of regorafenib for advanced gastrointestinal stromal tumours after failure of imatinib and sunitinib (GRID): an international, multicentre, randomised, placebo-controlled, phase 3 trial. Lancet 2013;381:295-302.
4. Son MK, Ryu MH, Park JO, et al. Efficacy and Safety of Regorafenib in Korean Patients with Advanced Gastrointestinal Stromal Tumor after Failure of Imatinib and Sunitinib: A Multicenter Study Based on the Management Access Program. Cancer Res Treat 2017;49:350-7.
5. Saito Y, Takahashi T, Tanaka K, et al. Treatment of Regorafenib in Patients with Metastatic or Unresectable Gastrointestinal Stromal Tumor after Failure of Imatinib and Sunitinib. Gan To Kagaku Ryoho 2018;45:121-3.

doi: 10.21037/tgh.2018.06.03
Cite this article as: Yeh CN. Response letter on *Micromanagement of drug-resistant advanced gastrointestinal stromal tumors: regorafenib—new ammunition in battling exon 17 mutations*. Transl Gastroenterol Hepatol 2018;3:33.

