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5-FU, Irinotecan, Nab-Paclitaxel in Gastrointestinal Cancers-Response

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We would like to thank Maeda and colleagues for their letter regarding our manuscript. They suggest that the dose of irinotecan should be escalated above 180 mg/m² in patients with the *UGT1A1* *1/*1 and *1/*28 genotypes. To support their view, they cite two studies that explored the safety and tolerability of dose escalated irinotecan in the FOLFIRI regimen. We are certainly aware of these studies, as one of us (Sharma) was a co-investigator on a genotype-guided dosing study of irinotecan in FOLFIRI plus bevacizumab, also published in *Clinical Cancer Research*.¹ In that study, the maximum tolerated dose of irinotecan was 310 mg/m² in *1/*1 patients and 260 mg/m² in *1/*28 patients. However, we contend that FOLFIRINOX (rather than FOLFIRI) is the most analogous regimen to FOLFIRABRAX, as both are regimens with a third cytotoxic chemotherapy drug (oxaliplatin or nab-paclitaxel) in addition to 5-fluorouracil/leucovorin and irinotecan. In our previous study of genotype-guided modified FOLFIRINOX, we used the same doses of irinotecan as in the current study, and the percentage of dose limiting toxicities observed led us to conclude that dose escalation of irinotecan above 180 mg/m² in the *1/*1 and *1/*28 patients would be very unlikely to be tolerable.²

Maeda and colleagues contend that the irinotecan dose should be escalated “to enhance the therapeutic efficacy in wild-type and heterozygous patients”. However, it should be noted that escalated doses of irinotecan in the FOLFIRI regimen have never been demonstrated to result in superior efficacy compared to standard doses in a randomized study. It would not be fair to assume that escalated doses of irinotecan in FOLFIRABRAX would result in higher response rates than those reported in the current study.

References

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