Author/s:
Loft, M;Wong, HL;Gibbs, P

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# Author Reply

**Matthew Loft[1,2], Hui-Li Wong[1-3], Peter Gibbs[1,2,4]**
1. Division of Personalised Oncology, Walter and Eliza Hall, Parkville VIC
2. Department of Medical Biology, University of Melbourne, Parkville VIC
3. Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne VIC
4. Department of Medical Oncology, Western Health, Footscray VIC

**Corresponding Author:** Matthew Loft, Division of Personalised Oncology, Walter and Eliza Hall, 1G Royal Parade, Parkville, Victoria, 3050, Australia. P: +61403971016. E: matthewjloft@gmail.com
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We thank Guven et al for their interest in our work and for their analysis and comments (1). They highlight that variable outcomes may be observed across different populations of patients with locally advanced rectal cancer and that potential drivers of this include differences in cancer biology and variable compliance.

Our key observation was of a significantly lower rate of pCR with capecitabine versus infusional 5-fluorouracil when either was combined with neoadjuvant radiation therapy (2), largely reproducing the results of another Australian series (3). In contrast, Guven et al in their analysis of data from the Far East found a hazard ratio favouring capecitabine. One potential explanation would be differences in biology, but unlike for gastric cancer in Asian versus non-Asian populations (4, 5) where differences appear driven by differing epidemiology, there are no reported differences in colorectal cancer therapy response. While it has been reported that Asian patients experience fewer toxicities with fluoropyrimidines (6, 7), and hence may have better outcomes versus non-Asian patients due to the decreased need for dose reductions, differences in efficacy for capecitabine versus 5-fluorouracil have not previously been reported.

Capecitabine is substantially cheaper than 5-fluorouracil (8) from a health systems perspective, adding to the attraction of the convenience of an oral therapy approach. Whilst from an Australian patient perspective there is a modest out-of-pocket cost for capecitabine ($41.30 per prescription for general and $6.60 for health card holders) this is for only 5-6 weeks, and seems a modest imposition that is in part offset by cost and time savings in not having to attend for intravenous chemotherapy. Anecdotally there is no evidence that patients fail to fill prescriptions in the Australian context, unlike in the US where the cost of medication is a far more significant impost (9) with resultant impact on patient behaviour.

The key takeaway message we believe is the importance of capturing real world data for any medication to ensure that the results produced in the carefully controlled environment of clinical trials, with a fit and motivated study population, can be reproduced across a diverse range of real world settings. This is particularly so for any new oral therapy, given the added issue of compliance, something we still struggle to measure. Clinicians also have a role to play by routinely emphasising the importance of taking medication as prescribed and regularly reviewing with patients any compliance issues.

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