

INTESTINAL RESEARCH

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# **Author's Reply**

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First of all, we very much thank the valuable comments  $^1$  to our paper "Efficacy of restarting anti-tumor necrosis factor  $\alpha$  agents after surgery in patients with Crohn's disease." We completely agree with their comments regarding the potential usefulness of therapeutic drug monitoring (TDM) for CD patients who had preoperative biologics treatment. As shown in our report,  $^2$  for the patients with preoperative anti-tumor necrosis factor (anti-TNF) therapy, the efficacy of the same biologics as used prior to surgery was limited, and was significantly lower than the efficacy for bio-naïve subjects.

Recent reports have shown that the loss of response of biologics could mainly be induced by 1 of the 2 reasons: low trough level of an anti-TNF-α antibody by the formation of the anti-drug antibodies, or unresponsiveness to an anti-TNF-α antibody despite enough trough levels because of predominant involvement of pro-inflammatory molecules other than TNF- $\alpha$ . In the meanwhile, previous reports also indicated that the presence of intestinal complications was known to be one of lower efficacy of anti-TNF agents.<sup>5,6</sup> The aim of our study was, therefore, to verify the effect of removal of intestinal complication by surgery on recovery of the efficacy of biologics. As the comment indicated, the recovery of efficacy may depend on the manner of loss of response of biologics, and could be estimated by TDM. Using TDM for the rationale for restarting the same biologics after surgery may be a new and promising approach, and should be validated for prospective studies in the future.

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In Japan, it is currently impossible to measure serum levels of anti-TNF- $\alpha$  agents and anti-drug antibodies in clinical practice due to the lack of the reimbursement of insurance. In view of not only clinical effectiveness but also economic burden, TDM for all CD patients with biologics, regardless of pre- or post-surgery, would be warranted.

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#### **CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

#### REFERENCES

- Kotze PG, Ma C, Regueiro M, Panaccione R. The old versus the new: which do you keep in postoperative Crohn's disease? Intest Res 2018;16:319-320.
- 2. Hiraoka S, Takashima S, Kondo Y, et al. Efficacy of restarting anti-tumor necrosis factor alpha agents after surgery in patients with Crohn's disease. Intest Res 2018;16:75-82.
- Nanda KS, Cheifetz AS, Moss AC. Impact of antibodies to infliximab on clinical outcomes and serum infliximab levels in patients with inflammatory bowel disease (IBD): a meta-analysis. Am J Gastroenterol 2013;108:40-47.
- 4. Gisbert JP, Marín AC, McNicholl AG, Chaparro M. Systematic review with meta-analysis: the efficacy of a second anti-TNF in patients with inflammatory bowel disease whose previous anti-TNF treatment has failed. Aliment Pharmacol Ther 2015;41:613-623.

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- 5. Zorzi F, Zuzzi S, Onali S, et al. Efficacy and safety of infliximab and adalimumab in Crohn's disease: a single centre study. Aliment Pharmacol Ther 2012;35:1397-1407.
- Campos C, Perrey A, Lambert C, et al. Medical therapies for stricturing Crohn's disease: efficacy and cross-sectional imaging predictors of therapeutic failure. Dig Dis Sci 2017;62:1628-1636.

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