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Article type : Invited Edi

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Editorial: histologic normalisation in ulcerative colitis - authors' reply

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We thank Drs Pai, Jairath, and Feagan for their insights regarding our work and for a robust discussion on the role of histologic activity in ulcerative colitis<sup>1,2</sup>. We agree there is now a growing burden of literature demonstrating persistent histologic activity to be associated with a worse disease course including risk of relapses, hospitalization, surgery, and colorectal neoplasia<sup>3-5</sup>. However, there are mostly retrospective and few rigorous studies examining the utility of histologic remission as a therapy target once the two more commonly recommended endpoints – clinical remission and endoscopic remission – have been achieved<sup>6</sup>. In distinction from our study, most of the prior studies on histologic remission also included patients with This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/APT.15621

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endoscopically active disease or those with mild persistent inflammation (Mayo 1). Given the correlation between endoscopic severity and histology, and the recognition that those with Mayo 1 endoscopic activity may have worse outcomes than those with Mayo 0<sup>7</sup>, such studies may be biased towards showing a higher predictive value of neutrophilic infiltration. As pointed out by Drs Pai and colleagues, the likelihood of histologic normalization (scored blinded in our study) is much greater in our cohort that was restricted to those with complete endoscopic remission (Mayo 0). While we acknowledge their concerns about sample size, ours remains one of the largest to examine the value of blinded scoring of histologic activity in those with complete endoscopic remission. As the field moves towards assessing both the clinical utility and cost-effectiveness of histologic healing, trials such as proposed by Pai et al. examining the incremental value of histology in those who have already achieved endoscopic and clinical remission are essential to establish the relevant features that lead to improved outcomes for all our patients.

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Disclosures: The authors' declarations of personal and financial interests are unchanged from those in the original article<sup>2</sup>.

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