DOI: 10.1111/apt.14166

Editorial: gut selective immunosuppression—is it a double edged sword? Authors' reply

The Editorial on the safety of vedolizumab by Sheridan and Doherty[1] in response to our safety review[2] is thoughtful and well balanced, but there are post-marketing data on malignancy after >25 000 patient-years of experience with vedolizumab that they do not mention.[3]

Post-marketing surveillance data should be interpreted with caution. Nevertheless, the tendency to under-report malignancy in patients exposed to novel therapy is likely to be lower than for other adverse events. The study on 25 831 patient-years of post-marketing exposure to vedolizumab reported 25 malignancies.[3] Half (12/25) were gastrointestinal and seven colorectal (including one adenoma), which is about what one would expect in such a large cohort.[4,5] Where reported, vedolizumab exposure was of short duration (≤6 months' treatment, or after ≤7 infusions at the time of malignancy diagnosis). Confounding factors included prior use of immunosupressants including anti-tumour necrosis factor therapy, smoking history, and previous malignancy prior to initiating treatment with vedolizumab.

Although α4β7 inhibition may affect intestinal NK cell activity, the authors have not elaborated on what pro-malignant 'theoretical concerns' that they vaguely intimate are at play. There is no biologically plausible carcinogenic pathway that would be specifically activated by α4β7 inhibition. Thus, vedolizumab is unlikely to have any greater effect on the development of dysplasia than other immune modulators. The frequencies of dysplasia in the trials and post-marketing data are within the bounds of what one would expect in long-standing IBD. It is conceivable that there is a minimum exposure time per patient to identify any risk. Only time will tell. Meanwhile, watchfulness rather than concern about the potential for vedolizumab to increase the risk of gastrointestinal malignancy is appropriate.

ACKNOWLEDGEMENTS

Thanks to Professor Simon Leedham, Wellcome Trust Centre for Human Genetics and Translational Gastroenterology Unit, Oxford, for informal discussion.

The authors' declarations of personal and financial interests are unchanged from those in the original article.[2]

LINKED CONTENT

This article is linked to Bye et al, and Sheridan and Doherty papers. To view these articles visit https://doi.org/10.1111/apt.14075 and https://doi.org/10.1111/apt.14149.

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DOI: 10.1111/apt.14155

Editorial: the risk of cancer in patients with gastric intestinal metaplasia

Gastric cancer is the fifth most common cancer worldwide, only preceded by malignancies of the breast, colorectum, lung and prostate. Gastric cancer makes up for close to 7% of all human cancers.[1] The global annual incidence is 951,000 cases, 73% of which are noncardia cancers.[2] We have for long come to understand the most common pathway of these cancers, via gland loss or atrophic gastritis, intestinal metaplasia (IM), dysplasia to invasive cancer. Large cohort studies with longer follow-up have confirmed these pathways.[3-5] There is a marked

association between disease stage at diagnosis and treatment outcome. These factors together make gastric neoplasia theoretically suitable for screening as well as for surveillance of early lesions. There are, however, a number of hurdles to conquer for optimal benefit of screening and surveillance. These include improved diagnosis. In Western countries, there has been a lot of emphasis on endoscopic recognition of early lesions of the oesophagus and colon, but we continue to miss approximately 12% of early cancers of the stomach despite use of the same equipment.[6] This requires more appropriate training and quality measures. Furthermore, as atrophic gastritis and intestinal metaplasia are common conditions, we need appropriate tools to select those subjects who may benefit most from surveillance and early intervention. The international guidelines on management of premalignant gastric lesions recommend using the OLGA or OLGIM classification for that purpose.[7]

We need further studies to identify the actual progression rates of different degrees of atrophy and metaplasia in various populations. A recent study in this journal provided such information. It was a retrospective study from Thailand on 91 patients with gastric intestinal metaplasia.[8] One of 81 patients with complete IM progressed to high-grade dysplasia; 5 of 10 with incomplete IM progressed to dysplasia or cancer. The main factors associated with progression were male sex and incomplete IM, but not OLGA/OLGIM stage.[8] This important observation is in line with a recent study from Spain that followed 649 patients with premalignant gastric lesions for a mean of 12 years.[9] In total, 24 (3.7%) patients developed gastric cancer, a rate similar to other studies.[3] In comparison with complete IM, incomplete IM was associated with a hazard ratio of 2.75 (95% confidence interval: 1.06-6.26) for progression to cancer.[9] These studies provide valuable additions to the existing literature, and ask for expansion with data from other countries. Together, these will allow us in the near future to update guidelines and improve the management of patients at risk of an invasive cancer with poor prognosis.

ACKNOWLEDGEMENT

Declaration of personal interest: None.

FUNDING INFORMATION

None.

LINKED CONTENT

This article is linked to Pittayanon et al, and Pittayanon and Barkun papers. To view these articles visit https://doi.org/10.1111/apt.14082 and https://doi.org/10.1111/apt.14160.

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DOI: 10.1111/apt.14160

Editorial: the risk of cancer in patients with gastric intestinal metaplasia—Authors' reply

We thank Professor Kuipers for his valuable editorial[1] on our retrospective cohort study[2] and accentuation of the burden of gastric cancer, not only in high prevalence countries but all over the world.

We agree that gastric cancer can be prevented by a strategy of early diagnosis, especially in patients with precancerous lesions, because of the well-known Correa pathway of gastric cancer.[3] There exists a 12% miss rate in diagnosing early gastric cancer in Western