Editorial: combination immunosuppressive therapy to treat Crohn’s disease – ready for all age groups?

Regardless of its origin, and whether it truly does sit in the Hippocratic Oath, one of the central tenets of medicine is to do no harm. It is no surprise then in medicine in general that clinicians have long been reticent to treat patients with drugs with potentially serious side effects, especially in cases where the disease is not thought to be life threatening. Although our understanding of treatment goals in the management of Crohn’s disease has evolved hugely, fear of harm is never far away, and for some patient groups there has always been a greater degree of caution. This is especially the case for the elderly patient. ¹

There are obvious reasons for this before we look at the data. Malignancy is more common as we age, the risk of infection is higher with immunomodulation, and ultimately the death rate is naturally higher. Paradoxically this however leads to clinicians either under-treating disease to avoid perceived side effects or overusing drugs and interventions that are wrongly considered to pose less of a risk, such as steroids. ²

Our knowledge of the safety of drug interventions in the elderly is hampered by the lack of available trial data, as this group is often excluded from studies. Instead, we have had to rely on post-marketing surveillance and more latterly a wealth of ‘real world’ experience. The REACT study, which compares conventional therapy and algorithmic early combined immunosuppression in multiple practices in Belgium and Canada, is interesting for a number of reasons, not least that it does not exclude older patients, in this paper defined as those over 60 years. ³

Singh et al present a post-hoc analysis from the REACT study and observed no difference in the efficacy and safety of early combined immunosuppression with an anti-TNF agent and immunomodulator, compared to conventional management, over a period of 2 years in older and younger patients. ⁴ The older age group represented 15.7% of the total, which is appropriate, since 15%-30% of the IBD population will consist of this age group.

Before adopting early combined immunosuppression in all of our older patients, we do need to consider a few things, as the authors have alluded to in their discussion. This study was not powered to definitively demonstrate the safety of these approaches in each of the two populations. It also relied on clinical endpoints, which as we now know do not necessarily correlate with mucosal disease, and importantly we therefore may expose some patients to unnecessary risk.

However, this study does add evidence that combination immunosuppressive therapy in some older patients may be safe and effective. It also reminds us that dogma and myth are increasingly unwelcome in medical practice. After all, we strive to treat the individual and we should be stratifying our patients using the tools and knowledge available rather than excluding populations under-represented in trial data.

Further studies in this patient group and with different immunosuppressive regimes are needed. If they give us the tools to personalise therapy further then we may demonstrate that rather than ‘doing no harm’, omission of therapy in all older patients may actually lead to the opposite.

ACKNOWLEDGEMENT

Declaration of personal interests: None.

LINKED CONTENT

This article is linked to Singh et al papers. To view these articles, visit https://doi.org/10.1111/apt.15214 and https://doi.org/10.1111/apt.15283.

Charles D. R. Murray  
Clinical Director GI Services, Royal Free London NHS Foundation Trust, London, UK  
Email: charliemurray1@me.com

ORCID

Charles D. R. Murray  https://orcid.org/0000-0001-6736-1546

REFERENCES

1. Ananthakrishnan AN, Shi HY, Tang W, et al. Systematic review and meta-analysis: phenotype and clinical outcomes of older-onset inflammatory bowel disease. J Crohns Colitis. 2016;10:1224-1236.
2. Benchimol EI, Cook SF, Erichsen R, et al. International variation in medication prescription rates among elderly patients with inflammatory bowel disease. J Crohns Colitis. 2013;7:878-889.
3. Khanna R, Breslser B, Levesque BG, et al. Early combined immunosuppression for the management of Crohn’s disease (REACT): a cluster randomised controlled trial. Lancet. 2015;386:1825-1834.
4. Singh S, Stitt LW, Zou G, et al. Early combined immunosuppression may be effective and safe in older patients with Crohn’s disease: post hoc analysis of REACT. Aliment Pharmacol Ther. 2019;49:1188-1194.