COVID-19 and implications for thiopurine use

Thomas M Goodsall
Gastroenterologist
The Queen Elizabeth Hospital
Department of Gastroenterology
Woodville South, South Australia
Australia

Clinical Lecturer
The University of Adelaide
Faculty of Health Sciences
Adelaide, South Australia
Australia

Sam Costello
Consultant Gastroenterologist
Queen Elizabeth Hospital
Department of Gastroenterology
Woodville South, South Australia
Australia

Clinical Lecturer
The University of Adelaide
Department of Medicine
Adelaide, South Australia
Australia

Robert V Bryant
Head of IBD Services
The Queen Elizabeth Hospital
Department of Gastroenterology
Woodville South, South Australia
Australia

Clinical Lecturer
The University of Adelaide
Faculty of Health Sciences
Adelaide, South Australia 5000
Australia
Thiopurines are used in oncology, immunology and inflammatory bowel disease (IBD). In the COVID-19 pandemic, patients taking thiopurines face uncertainty as to the risk of serious complications or death if infected.

Traditionally, thiopurine use has been associated with an increased risk of opportunistic viral infections.\textsuperscript{1,2,3} A large IBD registry study found that thiopurines and active disease were associated risk of serious viral infection.\textsuperscript{3} However, all identified causative agents were species of the \textit{Herpesviridae} genus.\textsuperscript{1,2,3} The risk associated with thiopurine use can therefore not yet be generalised to other virus genera and indeed only corticosteroid use is associated with risk of contracting influenza in IBD.\textsuperscript{4}

COVID-19 is a novel coronavirus and there are no available data from previous coronavirus strains such as SARS-CoV or MERS-CoV to allow for estimation of risk in patients on thiopurines.\textsuperscript{3,5} Although intuitively immunosuppression with thiopurines may increase the risk from COVID-19, there are in vitro and in silico data to suggest that thiopurines constrain maturation of MERS-CoV via inhibition of a viral protease.\textsuperscript{5} Although this study has not been replicated for COVID-19 or progressed into animal models, it does raise the possibility that thiopurines use may not necessarily increase COVID-19 risk.

Thiopurine withdrawal is associated with a 12 month relapse rate of 17-53% in Crohn’s disease and 11-77% in ulcerative colitis.\textsuperscript{6} This is an important consideration during COVID-19 as disease relapse requiring steroid use has previously been associated with increased risk of viral complications.\textsuperscript{3,4} The consequences of thiopurine withdrawal due to COVID-19 are not yet clear and this information is eagerly awaited as many centres collect prospective data.

Preliminary data from SECURE-IBD, a COVID-19 database for IBD, report 67 cases to date in patients on thiopurines, 39 of whom were managed as outpatients and 28 of whom were hospitalised, with one reported death.\textsuperscript{7} These evolving data provide cautious support for the relative safety of thiopurines but cannot be interpreted conclusively in the setting of the rapidly evolving situation.

Perhaps the best advice we can currently offer patients is that effective control of disease may carry less risk than poorly considered withdrawal of therapy. The Gastroenterological Society of Australia has issued recommendations that the minimum level of immunosuppression should be continued to control disease although a drug holiday may be considered in some patients with long term stable disease.\textsuperscript{8} This dilemma highlights the importance of online registries to gather vital data as we work together as a profession to provide evidence based advice for our patients during this pandemic.
References