Letter to the Editor

The Importance of Molecular Immune Investigation in Therapeutic Clinical Development for Biomarker Assessment

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We thank Roosenboom et al. for their interest in our paper exploring the relative expression of \(\alpha E\) integrin in the colon and ileum in inflammatory bowel disease (IBD) patients and in healthy subjects. The \(\alpha E\) integrin [CD103] is a cell surface molecule that forms a heterodimer with \(\beta 7\) integrin and, through interactions with E-cadherin, serves to retain \(\alpha E\beta 7\)-expressing cells at mucosal surfaces.\textsuperscript{1} Therapeutic treatment with etrolizumab, which binds to \(\beta 7\) integrin and blocks both \(\alpha 4\beta 7\):MAdCAM-1 as well as \(\alpha E\beta 7\):E-cadherin interactions, led to a reduction in crypt-associated \(\alpha E\) cell numbers in a phase 2 clinical trial.\textsuperscript{2} Baseline levels of colonic \(\alpha E\) expression were also associated with remission in a post-hoc analysis of the same study.\textsuperscript{2} Our present study was designed to evaluate the prevalence and localization of \(\alpha E\) cells in the colon and ileum and the potential impact of inflammation and concomitant medication on \(\alpha E\) expression.\textsuperscript{3} We found \(\alpha E\) expression to be stable and not dependent on either concomitant medications or degree of inflammation. These findings are of importance given the future potential of biopsy-based predictive biomarker assessment for etrolizumab treatment.

Roosenboom et al. suggest that the role of \(\alpha E\) cells in IBD pathology is not currently understood.\textsuperscript{4} While studies are on-going, previous work from our labs and others using enzymatic digestion of intestinal biopsies has shown that \(\alpha E\) integrin is expressed on approximately 90% of intraepithelial lymphocytes in the intestine, 40% of T cells in the lamina propria, and <3% of circulating lymphocytes.\textsuperscript{5} Therapeutic treatment with etrolizumab, which binds to \(\beta 7\) integrin and blocks both \(\alpha 4\beta 7\):MAdCAM-1 as well as \(\alpha E\beta 7\):E-cadherin interactions, led to a reduction in crypt-associated \(\alpha E\) cell numbers in a phase 2 clinical trial.\textsuperscript{2} Baseline levels of colonic \(\alpha E\) expression were also associated with remission in a post-hoc analysis of the same study.\textsuperscript{2} Our present study was designed to evaluate the prevalence and localization of \(\alpha E\) cells in the colon and ileum and the potential impact of inflammation and concomitant medication on \(\alpha E\) expression.\textsuperscript{3} We found \(\alpha E\) expression to be stable and not dependent on either concomitant medications or degree of inflammation. These findings are of importance given the future potential of biopsy-based predictive biomarker assessment for etrolizumab treatment.

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Personalized medicine has been identified as a major unmet research need of importance to patients and clinicians in IBD,\textsuperscript{11} and has the potential to direct the right treatment to the right patient at the right time, thereby maximizing the likelihood of a positive clinical outcome whilst aiming to minimize risk of side effects and cost. The potential utility of \(\alpha E\) or other genes\textsuperscript{12} as predictive biomarkers for etrolizumab is being tested prospectively in on-going phase 3 clinical trials. To reach the goal of personalized medicine for IBD patients, predictive biomarkers such as \(\alpha E\) for etrolizumab must be prospectively tested as well as evaluated in patient datasets to move the field forward.

References


