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**Fluorescently labelled vedolizumab to visualise drug distribution and mucosal target cells in inflammatory bowel disease (IBD)**

Gabriëls R, van der Waaij A, Linssen M, et al. [Fluorescently labelled vedolizumab to visualise drug distribution and mucosal target cells in inflammatory bowel disease](https://gut.bmj.com/content/73/9/1454). Gut 2024; 73:1454-1463. doi: 10.1136/gutjnl-2023-331696.

Vedolizumab is a biologic therapy for IBD consisting of a monoclonal antibody inhibitor α4β7 (alpha 4 beta 7) integrin which is specific to gut-homing T-cells found in intestinal Peyer’s patches. This study utilised fluorescent labelled Vedolizumab (vedo-800CW) to analyse the distribution of the drug both endoscopically by fluorescence molecular imaging and subsequently by fluorescence microscopy of histological samples. In phase A of the study patients were given 0mg, 4.5mg and 15mg of labelled vedolizumab. Gabriëls et al., found the 4.5mg dose provided insufficient fluorescence for analysis so subsequent patients in phase B were administered 15mg.

Phase B entailed 18 patients being administered vedo-800CW one hour after unlabelled IV vedolizumab infusion with endoscopy 2-4 days later. Five vedolizumab naïve patients were given a preceding subtherapeutic 75mg vedolizumab dose, 13 patients were tested after a therapeutic dose with three of them being tested after their first therapeutic dose. Gabriëls et al., utilised a fibre optic bundle through the instrument channel to take fluorescence signals from the mucosa in vivo of both inflamed and non-inflamed segments. All anatomical sites studied had at least two biopsies taken with subsequent macroscopic and microscopic fluorescence testing.

The authors found significantly higher endoscopic fluorescence in inflamed gut compared to healthy mucosa with similarly elevated fluorescence from biopsies of inflamed compared to healthy mucosa. Gabriëls et al., found increasing doses and duration of prior unlabelled vedolizumab reduced uptake in the inflamed mucosa, proposing that target saturation by unlabelled drug prevented vedo-800CW binding. Immunohistological analysis showed that vedo-800CW was bound to plasma cells, intracellular in eosinophils and macrophages and abundant CD3+ (cluster of differentiation 3) and CD8+ (cluster of differentiation 8) in high uptake regions.

This approach of using fluorescent labelled biologic therapy shows potential promise for gaining further understanding of the complexities of therapeutic mechanisms as well as which patients may respond to therapy. Identifying early on in patient treatment whether therapeutic drug concentrations are reaching their target may allow prompt stratification of response to treatment. The additional immune cells outside of gut homing T-cells that show significant vedolizumab avidity in vivo demonstrates the potential multifarious mechanism of action. This single centre feasibility trial shows the safety and potential utility for fluorescent labelled biologic treatment for better understanding IBD biologic pharmacokinetics and pharmacodynamics on both macroscopic and cellular scales.