NEW TREATMENTS IN IBD: VEDOLIZUMAB AND GOLIMUMAB IN UC

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Ulcerative colitis (UC)[1] results from pathological immune responses to endogenous microbial antigens.[2] Genetic susceptibility is a major determinant of this immune dysregulation. Recently, multiple susceptibility genes[3] have been identified which, for the most part, code for proteins that are relevant to innate or adaptive immunity. Although recognition of genetic susceptibility loci holds out the promise of highly selective therapy, conventional management of inflammatory bowel disease (IBD) is based upon the use of broad-spectrum anti-inflammatory drugs such as corticosteroids and thiopurines, with an aim to both relieve symptoms and prevent long-term complications. However, broad-spectrum immunosuppression comes at a cost, since it frequently causes "off- target" side effects, notably serious infection.[4] Over the past decade, development of more specific drugs, namely the tumour necrosis factor (TNF) antagonists, has led to greater efficacy with less morbidity.[5] Infliximab, adalimumab and golimumab have been shown to be effective for induction and maintenance of remission in UC and provide options for patients who fail treatment with purine antimetabolites and/or corticosteroids. However, infectious complications remain an important limitation to the use of these agents since TNF is a vital mediator of systemic immune responses to microbial pathogens.

Based on these considerations the development of selective therapies that differentially target gut inflammation while preserving systemic immune responses has become a priority.[6] Recognition that leukocyte trafficking to the bowel is regulated through highly specific molecular interactions has led to the concept of gut–specific immunosuppression based on blocking these key processes.

Vedolizumab (Millennium Pharmaceuticals Inc.; Takeda, Cambridge, Massachusetts), previously known as MLN-02, LDP-02, MLN0002, is a humanized IgG-1 monoclonal antibody directed to the integrin α4β7. Following promising results obtained in the cotton-top tamarin model of UC, human studies of this antibody were initiated, based on the notion that selective inhibition of gut leukocyte trafficking would likely prove to be a safe and effective strategy to treat IBD. The efficacy and safety data for vedolizumab as a treatment for ulcerative colitis will be reviewed.

References

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