Combination therapy with Leukocytoapheresys and Vedolizumab in patients with ulcerative colitis refractory to anti-TNFs: AVE-UC Study Protocol

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Background and aims

The recruitment of leukocytes has become a target for IBD therapy from leukocytoapheresys to anti-integrins and SP1-inhibitors. Combining multiple therapies with different mechanisms of action to get a deeper control of inflammation is receiving growing attention by medical researchers, but safety concerns are an issue. Being a non-pharmacological approach, with no relevant safety signal, the adjunct of apheresis (GMA) to biologics could represent a valid option in patients with UC with inadequate response to biologics, and should reduce the need of colectomy. This hybrid approach has been used in small case series in combination with anti-TNF, especially adalimumab, and recently in Crohn's disease with ustekinumab. Two case reports (one from our group) have been published reporting combo therapy with the antiintegrin vedolizumab. This association has a more appealing rationale due to the synergistic mechanism and on the basis of the slow onset of action of vedolizumab observed in everyday practice. Apheresis can speed up the response to vedolizumab by selective depletion of activated leukocytes, further reducing cell trafficking.

The aim of this study will be the assessment of efficacy and safety of combo therapy with leucocytoapheresys and vedolizumab in patients with UC refractory to conventional therapy and anti-TNFs.

Methods

This open label multicentre study will recruit patients 18-75 years with steroid-dependent/resistant UC refractory to conventional therapy and failure or intolerant to anti-TNFs , who have completed vedolizumab induction therapy (week 8), with inadequate response (Mayo score > 4).

The study protocol will be structured in 2 consecutive phases: Vedolizumab monotherapy administration followed by GMA therapy according to standard protocol (1 per week apheresis sessions in 5 weeks, 1.8 L of peripheral blood treated per session). The apheresis therapies will be performed using LA- 25 (Leukocyte Adsorber 25, Leucapher).

Assessment of disease activity (at induction, at week 8, at the end of GMA, at 52 weeks): Mayo score full and endoscopic subscore.
The IBDQ score will be also assessed at the beginning and after GMA sessions.

The Primary objective of the study is to achieve steroid-free remission at week 16 and 52.
The Secondary objectives are:

- **to assess mucosal healing rate at week 52**
- **to evaluate safety and the impact on quality of life of GMA plus vedolizumab.**

Results and Conclusion

We aim to demonstrate an adjuvant role of GMA in combination therapy with vedolizumab in moderate-to-severe UC who have failed conventional therapies and are refractory or intolerant to anti-TNFs. The ultimate goal will be the avoidance of colectomy, which still has disabling sequelae and a significant impact on quality of life.