3 COLON TARGETED, LOW SYSTEMIC ABSORPTION SOLUBLE CICLOSPORIN IN ULCERATIVE COLITIS

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Introduction Ciclosporin (CsA) is effective as rescue therapy in approximately 70–80% of patients with severe UC in whom surgery is contemplated. A recent study shows CsA to be as effective as infliximab in inducing remission in UC. However its use is limited by concerns re renal and neurological toxicity and difficulty in measuring drug levels. Thus, a form of CsA that is released predominantly in the colon and exhibits low systemic absorption might be of considerable benefit to UC patients.

CyCol® is a delayed release oral formulation of CsA that targets release into the colon. This compound has been shown both to prevent and heal colitis in the DSS and IL-10 knock out animal models and has no appreciable absorption in human volunteers.

Aims/Background Thus, the aim of this double blind placebo controlled multicentre Irish and UK study was to evaluate the efficacy and safety of CyCol in patients with mild or moderate UC, as defined by a score of 4–10 on a modified DAI.

Method The study period was 4 weeks. Patients on 5ASA compounds, immunomodulatory agents or low dose steroids (<10 mgs prednisolone) were included provided their dosages were

stable for >8 weeks. Patients were excluded if they had previously failed CsA or had received biologic agents within the past 8 weeks. The primary objective of this study was remission, defined as a DAI of <2 with no score >1. The secondary objectives of this study were response (defined as a reduction in DAI of <3), safety and efficacy of CyCol on the mucosal and histological healing.

Results 118 patients were randomised (154 screened) to receive 75 mgs CyCol or placebo daily. More patients on the active ingredient achieved remission (13.6%) than placebo (6.3%) but this was not significant (p=0.22). Likewise, 30.4% of patients on active treatment responded versus 18.8% on placebo (p=0.35). There was no appreciable difference between groups as regards mucosal and histological healing.

A post hoc analysis showed a significant response benefit for CyCol in those patients who were not taking immunomodulatory drugs. Adverse events (AE) were common in both arms and almost invariably related to disease activity. No AE was attributable to CyCol and ciclosporin levels in blood were undetectable.

Conclusion While CyCol® at the dose employed in this study over a 4 week period had numerically better results than did placebo, the results were not statistically superior. Further studies in moderate-severe patients are planned, with FDA approval, using larger doses of CyCol in a tighter patient population over a longer duration.

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