Autologous Cellular Therapy Open Label Phase I Study in Crohn's Disease With Type 1 Regulatory (Tr1) Lymphocytes (CATS1)

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Tr1 lymphocytes are IL-10 producing cells known to inhibit inflammatory colitis in mice. Ovasave is the first human systemic autologous Tr1 lymphocyte immunomodulating cell therapy for patients with chronic active Crohn's Disease (CACD).Ovasave was produced from patient PBMC exposed to ovalbumin with subsequent cloning and.expansion. The activated, IL-10 producing, antigen-specific Tr1 clones, where used in a phase I open label 12-week study (CATS1), to assess safety and explore efficacy of Ovasave in patients with CACD refractory to existing therapy. After pre-study washout, concomitant use of immunosupressors and anti-TNF was not allowed. Safety was assessed with clinical and laboratory parameters and efficacy with CDAI (response: decrease e100; remission: <150) and IBDQ (response: increase e16).

Eighteen patients (6 male; mean age 33; mean disease duration 12 years) were distributed in 4 single injection dose groups (106 cells n=7; 107 cells n=3; 108cells n=3 and 109 cells n=5). All had previous failure to immunosupressors and anti-TNF (IFX 2/18; IFX and ADA 6/18; IFX, ADA,CZP 10/18) and 10 had previous surgery. Disease was extensive with 13/18 patients with ileum and colon involvement. Ovasave was well tolerated with 53 adverse events (18 possibly related; 1 related) which recovered completely and 12 serious adverse events (3 possibly related with complete recovery). In the overall population, response was observed in 39% (7/18) of patients at weeks 5 and 8 and remission in 11% (2/18) at week 5 and 6% (1/18) at week 8. In the 106 cells group, response was seen in 71% (5/7) at weeks 5 and 8 and remission in 29% (2/7) and 14% (1/7) at weeks 5 and 8 respectively. In this group, the mean CDAI reduction at weeks 5 and 8 was 140.1±112.5 (p=0.0165) and 133.7±84.4 (p=0.0119), respectively, and IBDQ response was seen in 83% (5/6) and 50% (3/6) and mean IBDQ improvement was 44.7±29.9 (p=0.0147) and 35.8±39.3 (p=0.0758) at weeks 5 and 8 respectively.

These preliminary results using Tr1 autologous cells show good tolerability and suggest a dose related efficacy signal, supporting further work and presenting a new therapeutic opportunity for patients with Crohn's Disease.