Autologous cellular therapy open label phase I/II study in Crohn's Disease with type 1 regulatory (Tr1) lymphocytes (CATS1)

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World Immune regulation Meeting -V 24 - 27 March 2011, Davos Switzerland

Tr1 lymphocytes are IL-10 producing cells known to inhibit inflammatory colitis in mice. *Ovasave* is the first human 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 Tr1 clones, were used in a phase I/II 12-week study (CATS1), to assess safety and explore efficacy in patients with CACD refractory to therapy. Concomitant use of immunosupressors and anti-TNF was not allowed. Safety was assessed with clinical and laboratory parameters and efficacy with CDAI (response: decrease ≥100; remission: <150) and IBDQ (increase ≥16).

Eighteen patients were distributed in 4 single injection groups (10^6 cells n=7; 10^7 cells n=3; 10^8cells n=3 and 10^9 cells n=5). All had previous failure to immunosupressors and anti-TNF, 10 had previous surgery. *Ovasave* was well tolerated with 55 adverse events (18 possibly related; 1 definitely 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, remission in 11% (2/18) at week 5 and 6% (1/18) at week 8. In the 10^6 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.