Title:

CATS1 STUDY: IMMUNOMONITORING AND CLINICAL RESULTS OF ANTIGEN-SPECIFIC T REGULATORY (TREG) CELL THERAPY FOR CROHN'S DISEASE (CD)

Author Block:

Nathalie Clerget-Chossat, [1] Valérie Brun,[1] Pierre Desreumaux,[2] Mathieu Allez,[3] Laurent Beaugerie,[4] Xavier Hébuterne,[5] Yoram Bouhnik,[6] Maria Nachury,[7] Agnès Duchange,[8] Arnaud Foussat,[1] Miguel Forte,[1] Jean-Frédéric Colombel,[2]

[1]TxCell, Valbonne Sophia-Antipolis, France, [2]Claude Huriez Hospital, Lille, France, [3]St-Louis Hospital, Paris, France, [4]St-Antoine Hospital, Paris, France, [5]L'Archet 2 Hospital, Nice, France, [6]Beaujon Hospital, Clichy, France, [7]Jean Minjoz Hospital, Besançon, France, [8]Effi-Stat, Paris, France.

Body:

CATS1 study assessed the tolerability and efficacy of Ovasave, an antigen-specific Treg therapy for patients with refractory Crohn's Disease. Treg cells induce immunomodulating effects through cytokines secretion and cell-cell contact.

CATS1 was an open label, 12-week, single injection, phase I/II study in 20 patients with CD and active inflammation (4 doses of 10^6, 10^7, 10^8, 10^9 cells with respectively 8, 3, 3, 6 patients). Ovasave was produced *ex vivo* from patients' PBMCs exposed to ovalbumin followed by cell cloning, expansion and formulation for infusion. Patients were assessed for tolerability and efficacy (CDAI responder: decrease >=100; remission: <150). *In vitro* changes in peripheral blood immune cell populations and PBMCs proliferative response to ovalbumin were also evaluated.

Mean age: 34.5; Baseline CDAI: 364±81 (n=20); 19/20 patients had previous failure to immunosupressors and multiple anti-TNFs; 16/20 had previous CD surgery.

Ovasave injections were well tolerated: 54 adverse events (2 related), 11 serious adverse events (3 possibly related, recovered).

Response was observed in 40% (8/20) patients at weeks 5 and 8. In the best dose group (10^6 cells), response was 75% (6/8) at both time points; remission was 38% (3/8) and 25% (2/8) and the mean CDAI reduction 143.4±105 (p=0.0062) and 131.6.3±65.4 (p=0.002) at weeks 5 and 8 respectively. Immunomonitoring studies revealed that blood CD16+ pro-inflammatory monocytes were selectively decreased 3 weeks after Ovasave administration in the group of responder patients at week 5. In this group, the proliferative response of PBMC to ovalbumin *in vitro* was significantly reduced 3 weeks after treatment, suggesting a direct suppression of ovalbumin-specific immune response.

This first open label study shows that Treg cell therapy is well tolerated and demonstrates a dose related efficacy consistent across multiple clinical and mechanistic immunological assessment methods. Treg cell therapy may represent an innovative value-adding opportunity for refractory CD patients.

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