Joint Meeting
SFI & DGfI
26-29 SEPTEMBER 2023
Palais de la Musique et des Congrès STRASBOURG

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IL-23 inhibitors in psoriasis, what are the effects on local and systemic immune responses?

MEZGHICHE I. [1], LELOUP C. [1], DANGIEN A. [1,2], YAHIA-CHERBAL H. [1], CAMARD L. [1], PIETROSEMOLI N. [3], CHICA C. [3], CUA D. [4], FOURIE A. [5], GREVING C. [5], SHAIKH B. [5], PARKER R. [6], OUL B. [2], GUAN S. [2], ARACTINGI S. [2], ROGGE L. [1], BIANCHI E. [1]

[1] Institut Pasteur, Universitde Paris, Immunoregulation Unit, Department of Immunology, Paris, France; [2] Department of Dermatology, Hital Cochin, AP-HP, AP-HP Centre-Universitde Paris, Paris, France; [3] Bioinformatics and Biostatistics Hub, Institut Pasteur, Universitde Paris, Paris, France; [4] Janssen Research & Development, LLC, Spring House, Pennsylvania, United States; [5] Janssen Research & Development, LLC, San Diego, California, USA, California, United States; [6] Janssen Research & Development, Janssen-Cilag, Paris, France

Objectives.
The importance of the IL-23/IL-17 signaling pathway in the pathogenesis of chronic inflammatory diseases, including psoriasis has been clearly established. Therapies targeting IL-23 show high efficacy for the treatment of psoriasis. Here we investigate the in vivo effects of IL-23-blockade on systemic and local immune responses in psoriasis patients.

Methods.
31 psoriasis patients were recruited for this study. Blood samples were obtained before and 12 weeks after initiation of anti-IL-23 therapy. To assess the effects of IL-23-inhibitors on systemic immune responses we performed immunophenotyping of circulating immune cells using spectral flow cytometry and whole blood stimulation assays. For local immune responses, skin biopsies were collected from 3 psoriasis patients, and analyzed by Cellular Indexing of Transcriptome and Epitopes sequencing (CITEseq).

Results.
Investigation of IL-23R expression on immune cell populations from psoriasis patients showed that MAIT cells are the population with the highest frequency of IL-23R+ cells, followed by NKT cells and Vd2+ gd T cells. Only few CD4+, CD8+ T cells, or NK cells express detectable levels of IL-23R. We next investigated if anti-IL-23 therapy has an impact on immune cell populations. Whole blood counts showed a statistically significant increase in lymphocyte numbers and a trend for reduction of neutrophil and monocyte counts. We noted a decrease in the fraction of IL-23R expressing Th17 cells. Gene expression analysis of stimulated whole blood cultures showed a significant decrease in inflammatory cytokines genes after treatment. Our investigation of local immune responses at the skin tissue level, showed a higher CD45+ cell infiltration in lesional compared to non-lesional skin, which was reduced after 12 weeks of treatment. The ongoing single cell analysis of these infiltrating cells will identify the main cell subsets involved in psoriasis local pathogenesis.

Conclusions.
IL-23 inhibitors impact both local and systemic immune responses in psoriasis patients.