PSORIASIS

PRECISION MEDICINE IN PSORIASIS: PHARMACOGENETICS OF USTEKINUMAB AND SECUKINUMAB RESPONSE IN A LARGE COHORT OF PSORIATIC PATIENTS

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Introduction: Nowadays, the core therapeutic approach in psoriasis has shifted in favor of the interleukin (IL)-23/IL-17 axis. Nevertheless, an important quota of patients does not experience disease improvement, even with the most recently introduced compounds acting against these core cytokines.

Objective: We conducted a retrospective study aiming to investigate the possible influence of different genetic polymorphisms or the combination of more polymorphisms on the clinical outcome of the IL12/23-blocking agent (ustekinumab) and of the anti-IL17A (secukinumab).

Materials and Methods: 44 SNPs associated with psoriasis-related risk loci were analysed in a cohort of 188 patients diagnosed with moderate-to-severe chronic plaque-type psoriasis, treated with Secukinumab (n=88) or Ustekinumab (n=100). To this end, targeted sequencing was performed using NGS TruSeq Custom Amplicon (TSCA) Low-Input kit and the MiSeq platform (Illumina, San Diego, USA), according to manufacturer' instructions. Sequencing data were collected, aggregated and filtered by using a set of ad hoc bioinformatics script. Basically, a top-down approach was applied to select all positive calls with a read depth >50x and allelic frequency of 0.3. Variant's annotations were verified with the latest version of ANNOVAR on hg19, and IGV was used to check peculiar variants of

interest.

Results: To evaluate the efficacy of ustekinumab and secukinumab (primary endpoint), the 75%, 90% and 100% improvement in PASI score (PASI 75, 90 and PASI 100) were calculated up to 2 years of treatment. Secondary endpoint was to evaluate the potential effect of genetic polymorphisms in the prediction of “primary inefficacy” or “secondary inefficacy” to ustekinumab and/or secukinumab.
Stepwise multivariate logistic regression models were performed to evaluate the association between dependent variables (e.g. clinical and demographic characteristics, history of previous exposure to biological therapies, SNPs analyzed in the study) and response to treatment.

Conclusion: This study adds new data regarding precision medicine in psoriasis.