INNOVATIVE THERAPEUTIC STRATEGIES IN GENODERMATOSIS: AN ITALIAN MULTICENTRE STUDY

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Background. Genodermatoses are a group of rare inherited disorders affecting the skin and its adnexa. Their clinical presentation is heterogeneous, reflecting the wide underlying genetic heterogeneity. The manifestations have a strong impact on the quality of life and on the duration. To date, there are no therapeutic tools available to treat the condition but we focus on the best possible symptomatic management through topical or systemic therapies.

Aims. The primary aim of the study is to evaluate the clinical efficacy of the biologic agents dupilumab (anti-IL-4/IL-13) and secukinumab (anti-IL-17A) in patients with genodermatosis using two validated scales: the Dermatology Life Quality Index (DLQI) and the Numeric Rating Scale for itch (NRS-itch). Secondary objectives were to assess treatment effectiveness in the two main genodermatosis subgroups, namely skin fragility disorders and keratinization disorders, and to evaluate treatment safety.

Materials and Methods. This Italian multicenter retrospective study involved 8 centers coordinated by the Regional Referral Center for Pediatric Dermatology and Rare Cutaneous Diseases of the University Hospital of Padua. 47 patients with a mean age of 31.6 years were enrolled: 32 patients were given dupilumab and the remaining 15 secukinumab according to the doses indicated in each data sheet. Efficacy was assessed through DLQI and NRS-itch scores recorded at baseline and during follow-up visits at 3, 6, 9, 12, 18 and 24 months.

Results. A progressive reduction in both DLQI and NRS-itch scores was observed from treatment initiation. At 6 months, DLQI decreased by 54.6% and NRS-itch by 46.8%, corresponding to an approximately 50% reduction in perceived disease burden. Only two patients developed mild adverse reactions, one treated with dupilumab (3.1%) and one with secukinumab (6.7%). Five patients (10.6%) discontinued treatment, mainly because of lack of efficacy.

Conclusions. This multicenter retrospective study, the first reported in the literature with a cohort of 47 patients, demonstrates the relevant and sustained clinical benefit of dupilumab and secukinumab in genodermatoses. After 24 months, DLQI decreased from 19.35 to 7.00 (-63.8%) and NRS-pruritus from 7.96 to 3.00 (-62.3%). The safety profile was favorable, with only two mild adverse events reported. These findings support the need for prospective controlled studies in larger cohorts stratified according to genetic and cytokine-related disease phenotypes.