ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

MTORC1 PATHWAY IS MODULATED BY BIOLOGICAL THERAPY IN HIDRADENITIS SUPPURATIVA PATIENTS

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Introduction: Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that usually presents with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body. Mechanistic target of rapamycin (mTOR) is a serine/threonine kinase, which acts as the central component of two distinct signalling complexes known as mechanistic target of rapamycin complex (mTORC) 1 and mTORC2. mTOR dysregulation is involved in other skin inflammatory diseases such as acne and psoriasis. Recently, biologics are emerging in the management of HS and, in particular adalimumab (ADA).

Objective: The aim of this study is to analyse the effects of ADA therapy on mTORC1 activity in HS patients.

Materials and Methods: All enrolled subjects received ADA according to the recommended dose for adult patients with HS and underwent a specific anthropometric evaluation. mTOR gene expression analysis was executed on skin biopsies from lesional skin of recruited HS patients at baseline and after 16 weeks of treatment (W16). Immunofluorescence detection of S6K1 and P-S6K1 was carried out in LS skin before and after 16 weeks of ADA.

Results: In this study, we reported a clinical improvement after 16 weeks of ADA therapy with an excellent or medium response in 77% of patients. Moreover, we showed, for the first time, that mTOR espression was strongly reduced after 16 weeks of ADA therapy in HS lesional skin. Immunofluorescence analysis demonstrated that ADA therapy at W16 modulates mTORC1, acting on one of its effector proteins: ribosomal protein S6 kinase 1 (S6K1) and its activated form P-S6K1. Both proteins were found to be increased in HS lesional skin and ADA was able to reduce them at W16. Interestingly, the intensity of staining after therapy correlated with clinical response.

Conclusion: mTORC1 pathway is modulated by anti-TNF-α treatment, highlighting a

possible new mechanism by which TNF-α inhibition improves HS.