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

NON-CLINICAL AND HUMAN PHARMACOLOGY OF THE POTENT AND SELECTIVE TOPICAL RARγ AGONIST TRIFAROTENE

J Aubert\textsuperscript{(1)} - D Piwnicka\textsuperscript{(1)} - B Bertino\textsuperscript{(1)} - S Blanchet-réthoré\textsuperscript{(1)} - I Carlavan\textsuperscript{(1)} - S Deret\textsuperscript{(1)} - B Dréno\textsuperscript{(2)} - B Gamboa\textsuperscript{(1)} - A Jomard\textsuperscript{(1)} - Ap Luzy\textsuperscript{(1)} - P Mauvais\textsuperscript{(1)} - C Mounier\textsuperscript{(1)} - J Pascau\textsuperscript{(1)} - I Pelisson\textsuperscript{(1)} - T Portal\textsuperscript{(1)} - M Rivier\textsuperscript{(1)} - P Rossio\textsuperscript{(1)} - E Thoreau\textsuperscript{(1)} - E Vial\textsuperscript{(1)} - Jj Voegel\textsuperscript{(1)}

Nestlé Skin Health Galderma R&d, Pharmacology, Sophia Antipolis, France\textsuperscript{(1)} - University Hospital Nantes, Chu Nantes, Nantes, France\textsuperscript{(2)}

Introduction: Retinoids have a dominant role in topical acne therapy and to date, only RARβ and RARγ dual agonists have reached the market.

Objectives: to confirm the hypothesis that developing RARγ–selective agonists could yield a new generation of topical acne treatments that would increase safety margins while maintaining the robust efficacy of previous drugs.

Materials and Methods: Structural knowledge derived from the X-Ray structure of known RARγ–selective molecule. Design, synthesis and in vitro evaluation of a novel triaryl series of RARγ agonists were performed including structure activity and property relationship.

Results: Results revealed an unique and isotype specific pocket in the RARγ ligand binding domain thus enabling the optimization of a novel triaryl series of RARγ selective agonist for topical administration.

Conclusions: Structural information led to the discovery of Trifarotene, a new RARγ–selective agonist as a potential new generation of topical acne treatments.