MEDICAL THERAPIES AND PHARMACOLOGY

# OX40L BLOCKING MONOCLONAL ANTIBODY KY1005 STRONGLY SUPPRESSES THE DELAYED-TYPE HYPERSENSITIVITY SKIN RESPONSE TO KLH IN HEALTHY VOLUNTEERS

*M Saghari Md [1] - J Powell Mbchb Ffpm [2] - R Wilson Phd [2] - S Gilbert Phd [2] - R Rissman Phd [3] - M Moerland Md Phd [3] - Mba Van Doorn Md Phd [4] - N Brennan Bsc [2] - B Porter-brown Mbbs Ffpm [2] - S Quaratino Md Phd [2] - M Yateman Phd [2] - P Gal Md Phd [3] - J Burggraaf Md Phd [5]*

*Center For Humab Drug Research, Dermatology, Leiden, Netherlands [1] - Kymab, Clinical Development, Cambridge, United Kingdom [2] - Chdr, Dermatology, Leiden, Netherlands [3] - Erasmus Medical Center, Dermatology, Rotterdam, Netherlands [4] - Leiden Academic Center For Drug Research, Univerity Of Leiden, Leiden, Netherlands [5]*

Introduction: KY1005 is a human non-depleting monoclonal antibody blocking OX40L interaction with OX40, inhibiting Teff response and maintaining Treg activity. In a phase 1 healthy volunteer study, skin delayed type hypersensitivity (DTH) assessment was implemented to assess pharmacodynamic activity of KY1005.

Objective: To explore the DTH immune response after KY1005 treatment followed by immunization challenges with a neo-antigen (keyhole limpet hemocyanin, KLH).

Materials and Methods: Five cohorts of 8 male subjects each in a 6:2 active vs. placebo ratio received three doses of KY1005 at 4-week intervals at ascending doses. Subjects were vaccinated with 0.1mg KLH seven days after the third dose. Twenty-one days later, subjects received 0.001mg KLH intradermally in the left forearm and saline control in the right forearm. Forty-eight hours after intradermal KLH administration, the DTH response was quantified by multispectral imaging (Antera 3D, Miravex, Dublin, Ireland) and laser speckle contrast imaging (LSCI, PeriCam PSI System, Perimed AB, Järfälla, Sweden) recordings.

Results: KY1005 treatment suppressed KLH-induced dermal erythema quantified by multispectral imaging in 0.45 mg/kg, 4 mg/kg, and 12 mg/kg cohorts compared to placebo reaching $P<0.05$ (estimated differences: 0.20 AU (95% CI 0.09 – 0.31, effect size (estimated difference/SD) 1.95), 0.15 AU (95% CI 0.04 – 0.26, effect size 1.46), and 0.22 AU (95% CI 0.11 – 0.33, effect size 2.14), respectively) and the cutaneous blood flow by LSCI in 0.45 mg/kg and 4 mg/kg treatment groups compared to placebo reaching $P<0.05$ (estimated differences: 11.6 AU (95% CI 3.1 – 20.0, effect size 1.62), and 10.2 AU (95% CI

2.1 – 18.3, effect size 1.43), respectively).

Conclusion: The anti-OX40L monoclonal antibody KY1005 suppressed the T-cell mediated delayed type hypersensitivity response quantified by multispectral and laser speckle contrast imaging. KY1005 shows potential to serve as a novel treatment modality in cutaneous T-cell dependent disorders. A phase 2a study in atopic dermatitis is ongoing.