DFD-29, a low dose oral minocycline, demonstrates superior efficacy as compared to placebo and Oraycea® Capsules (doxycycline HCl) in subjects with papulopustular rosacea

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Introduction

- Rosacea is a chronic, inflammatory skin disease that affects primarily the cheeks, nose, chin, and forehead, mainly in adults. Papulopustular rosacea is the second most common subtype.

Methods

- In a phase 2, randomized, double-blind, parallel group trial enrolling adults (n=205) with mild, moderate or severe papulopustular rosacea, subjects were randomized to receive DFD-29 (minocycline HCl), 40 mg extended release (ER) capsules, DFD-29, 20 mg ER capsules, Oraycea® (doxycycline HCl), 40 mg capsules (anti-inflammatory dose with modified release) or placebo, one capsule a day for 16 weeks.

- The co-primary endpoints were proportion of subjects achieving treatment success (IGA – ‘0’/ ‘1’ with ≥ 2-grade reduction), and mean reduction in total inflammatory lesion counts at Week 16 compared, in the DFD-29 compared to placebo and doxycycline groups.

- An earlier phase 1 study, the dermal Interstitial Space Fluid (dISF) levels of doxycycline and minocycline were measured, using Open-Flow Microperfusion (OFM) in healthy human subjects.

Results

- The Full Analysis Set (FAS) included 200 subjects. Of these, 53 subjects were in DFD-29 (40 mg) group, 47 in DFD-29 (20 mg), 48 in doxycycline (40 mg) and 52 in the placebo group.

- The proportion of subjects achieving IGA treatment success was 66.04% in DFD-29 (40 mg), 33.33% in doxycycline (40 mg), 31.91% in DFD-29 (20 mg) and 11.54% in the placebo group (Fig.1). Highly statistically significant treatment differences (p<0.0001) were demonstrated for DFD-29 (40 mg) vs placebo and doxycycline (40 mg), as well as for DFD-29 (20 mg) versus Placebo. Highly statistically significant treatment differences were demonstrated for DFD-29 (40 mg) versus placebo (p<0.0001), versus doxycycline 40 mg (p=0.0010) and versus DFD-29 (20 mg) (p=0.0007).

- The mean reduction in total inflammatory lesion count from Baseline was 19.2 lesions in DFD-29 (40 mg), 12.6 lesions in DFD-29 (20 mg), 10.5 lesions in doxycycline (40 mg) and 7.3 lesions in placebo groups (Fig.2). Highly statistically significant treatment differences were demonstrated for DFD-29 (40 mg) versus Placebo (p<0.0001), versus doxycycline (p=0.0004) and versus DFD-29 (20 mg) (p=0.0070).

- The proportion of subjects experiencing at least one TEAE was 73.58% in DFD-29 (40 mg), 83.33% in DFD-29 (20 mg), 77.08% in doxycycline (40 mg) and 67.31% in the placebo groups. Overall, most of the reported TEAEs were of mild or moderate intensity and were not or possibly related to the study treatment per investigator.

- The OFM study demonstrated that DFD-29 (40 mg) and oral doxycycline 40 mg, provide similar dermal interstitial space fluid (dISF) levels of minocycline and doxycycline, respectively.

Conclusions

- DFD-29, low dose minocycline, could become another option in treatment of inflammatory lesions of rosacea, for patients with mild, moderate or severe rosacea.

- Despite similar dISF levels, DFD-29 (40 mg) has greater efficacy compared to doxycycline 40 mg, probably due to greater lipophilicity resulting in higher intracellular concentrations.

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