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.

Figure 1. IGA Success at week 16

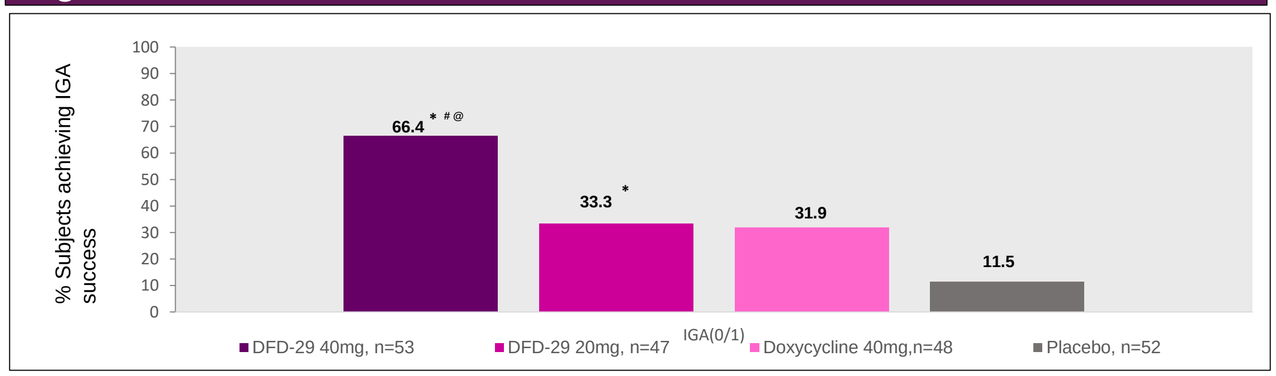
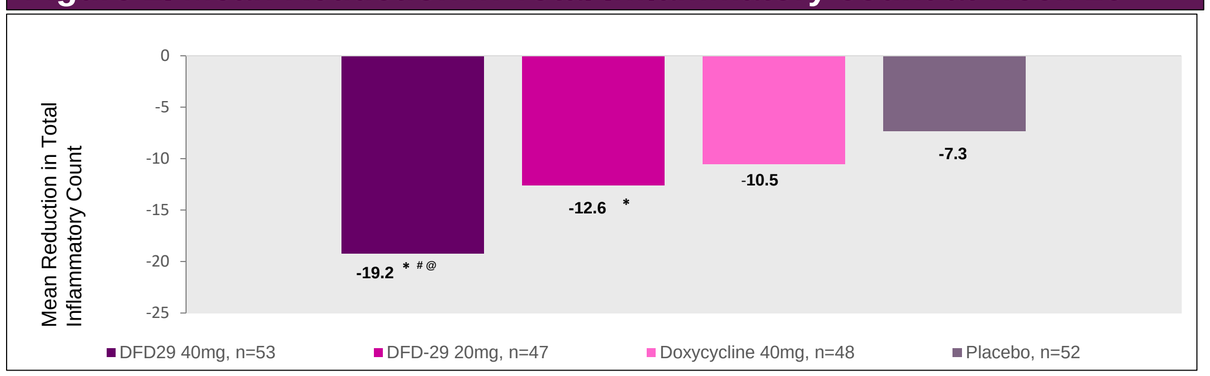


Figure 2. Mean Reduction in Total Inflammatory count at week 16



*Statistical significance reported vs placebo, # Statistical significance reported vs Doxycycline, @ Statistical significance reported vs DFD-29 20mg

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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