Phase 3 trial demonstrates that MC2-01 cream has improved treatment efficacy compared to calcipotriene plus betamethasone dipropionate topical suspension in patients with mild to moderate psoriasis vulgaris

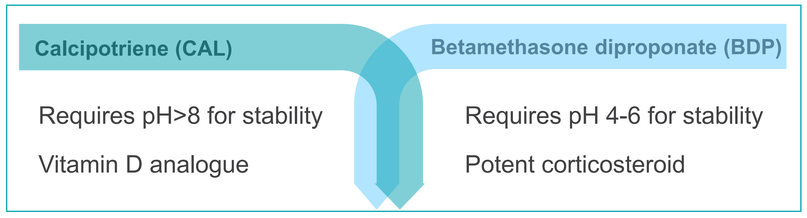
Johan Selmer[1], Birgitte Vestbjerg[1], Morten Præstegaard[1], Linda Stein Gold[2]

[1]MC2 Therapeutics, Hørsholm, Denmark; [2]Dermatology Clinical Research, Henry Ford Health System, Detroit, Michigan

INTRODUCTION:

MC2-01 cream is a novel topical treatment of psoriasis containing the active ingredients calcipotriene and betamethasone dipropionate (0.005% / 0.064% w/w, CAL/BDP). MC2-01 cream is based on PAD™ Technology contributing high penetration of the actives combined with excellent cosmetic elegance. Data from a phase 3 trial is presented comparing efficacy of MC2-01 cream to vehicle and to the comparator CAL/BDP topical suspension ("CAL/BDP TS") in adults with mild to moderate psoriasis vulgaris on the body. The trial enrolled 796 patients at 55 clinical sites across the United States.

Figure 1: Rationale for MC2-01 cream



- **Dual additive efficacy** of CAL and BDP
- **Improved safety** profile compared to the individual actives alone
  - BDP counteracts potential skin irritation of CAL
  - CAL mitigates potential skin atrophogenic effect of BDP
- PAD™ Technology uniquely enables stable aqueous cream combining CAL and BDP

METHODS:

The phase 3, randomized, multicenter, investigator-blind, parallel-group trial evaluated the efficacy and safety of MC2-01 cream compared to MC2-01 vehicle and CAL/BDP TS (sourced as Taclonex® Topical Suspension) in adult patients with psoriasis vulgaris on the body. The 796 enrolled patients were distributed in three arms: MC2-01 cream (n=343), CAL/BDP TS (n=338), MC2-01 vehicle (n=115). Patients applied trial medication once daily for eight weeks. Eligible patients were ≥18 years with a clinical diagnosis of psoriasis vulgaris of at least 6 months duration with mild-moderate disease severity according to the 5-point Physician's Global Assessment (PGA) scale, involving 2-30% body surface area (BSA) and with a mPASI of at least 2. The primary efficacy endpoint was the proportion of subjects with treatment success at Week 8, defined as a minimum two-point decrease from baseline in PGA score. Table 1 demonstrates that patient demographics and baseline disease characteristics (ITT population) were comparable across the treatment groups.

Figure 2: Phase 3 trial design

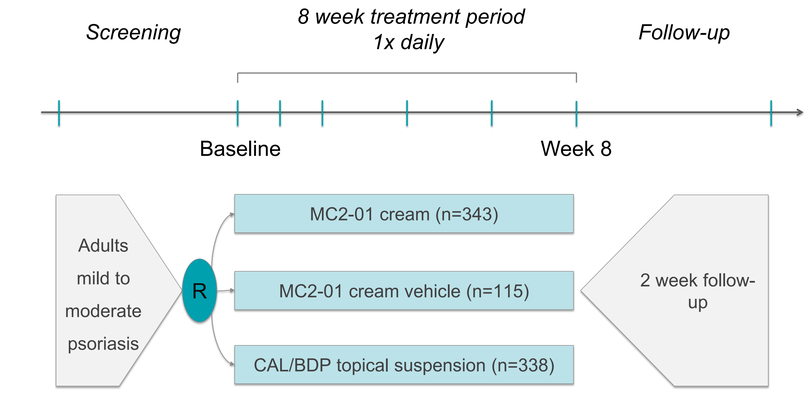


Table 1: Summary of Patient Demographics and Baseline Disease Characteristics (ITT population)

	MC2-01 cream N=342	CAL/BDP TS N=337	MC2-01 vehicle N=115	Total N=794[1]
Mean age (SD)	52.0 (14.4)	52.8 (13.7)	50.4 (14.3)	52.0 (14.1)
Gender				
Female	40.6	34.4	38.3	37.7
Male	59.4	65.6	61.7	62.3
Race				
White	84.8%	88.7%	88.7%	87.0%
Black or African Americans	9.6%	5.9%	9.6%	8.2%
Asian	2.9%	3.0%	0.9%	2.6%
Other	2.4%	2.4%	0.9%	2.2%
Duration of psoriasis years (SD)	17.7 (13.4)	15.0 (12.7)	16.3 (13.7)	16.3 (13.2)
Baseline PGA				
Mild (%)	19.9	16.9	17.4	18.3
Moderate (%)	80.1	83.1	82.6	81.7
Baseline mean mPASI (SD)	7.3 (3.9)	7.7 (4.1)	7.1 (4.1)	7.4 (4.0)
Baseline mean BSA % (SD)	7.3 (6.0)	8.4 (7.0)	7.5 (6.1)	7.8 (6.5)

[1]Two patients (one in each active arm) were excluded from the ITT population since they did not open the medication

Phase 3 trial met its primary objective and is superior to CAL/BDP TS

Primary objective:

- Non-inferiority of MC2-01 cream versus CAL/BDP TS at Week 8 using PGA treatment success as primary endpoint

Primary analysis:

- Superiority versus MC2-01 vehicle was achieved
- Non-inferiority of MC2-01 cream versus CAL/BDP TS was achieved
- Non-overlapping 95% CI demonstrated superiority of MC2-01 cream versus CAL/BDP TS at Week 8

Table 2: Primary endpoint[1] – PGA Treatment Success at Week 8

	MC2-01 cream (n=302)	CAL/BDP TS (n=279)	MC2-01 vehicle (n=88)
PGA Treatment Success Rate % (CI 95%)	40.1 (34.5 – 45.6)	24.0 (19.0 – 29.0)	4.5 (0.2 – 8.9)

[1]The primary analysis for non-inferiority comparison was conducted on the per protocol analysis set

EFFICACY RESULTS:

The phase 3 trial met its primary objective to demonstrate non-inferiority of MC2-01 cream to CAL/BDP TS on PGA treatment success at Week 8 using the PP analysis set (Table 2). The secondary efficacy endpoint of non-inferiority of % change in mPASI from baseline to Week 8 of MC2-01 cream versus CAL/BDP TS at Week 8 was also met.

Additional analysis of PGA treatment success on the ITT population using multiple imputations showed that MC2-01 cream was superior to CAL/BDP TS at Week 4 ($p<0.0001$) and Week 8 ($p<0.0001$) (Fig. 3). Similar analyses of % change in mPASI from baseline confirmed that MC2-01 cream was superior to CAL/BDP TS throughout treatment from Week 1 (26.2% vs. 18.9%, $p<0.001$) to Week 8 (64.8% vs. 52.3%, $p<0.0001$) (Fig. 4).

MC2-01 cream provided robust reduction in itch vs. vehicle measured by the proportion of patients having ≥4-point improvement on an 11-point numeric rating scale of itch severity (60.2% vs. 21.4% at Week 4, $p<0.01$) (Fig. 5).

SAFETY DATA:

No SAEs with relationship to study medication were observed in the trial. 3.5% of subjects in the MC2-01 cream arm had an AE definitely, probably, or possibly related to treatment compared to 3.3% of in the CAL/BDP TS arm.
The most frequent adverse events in both active arms were application site irritation, application site pruritus, and application site folliculitis; all with an occurrence below 1% in both arms.

Figure 3: Primary efficacy variable: % PGA Treatment Success

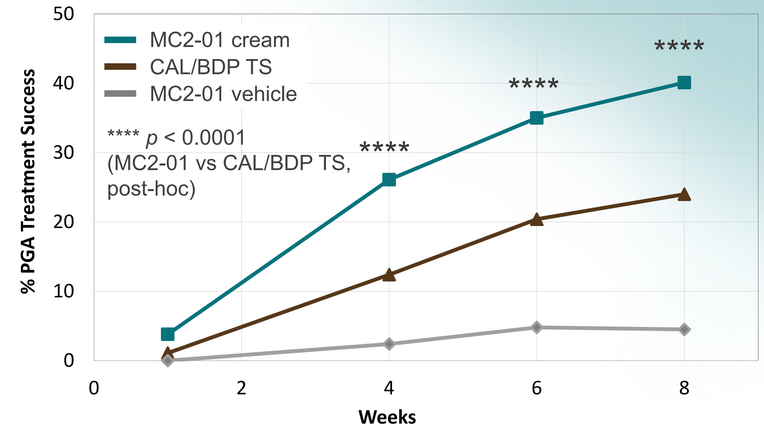


Figure 4: Secondary efficacy variable: % change from baseline in mPASI

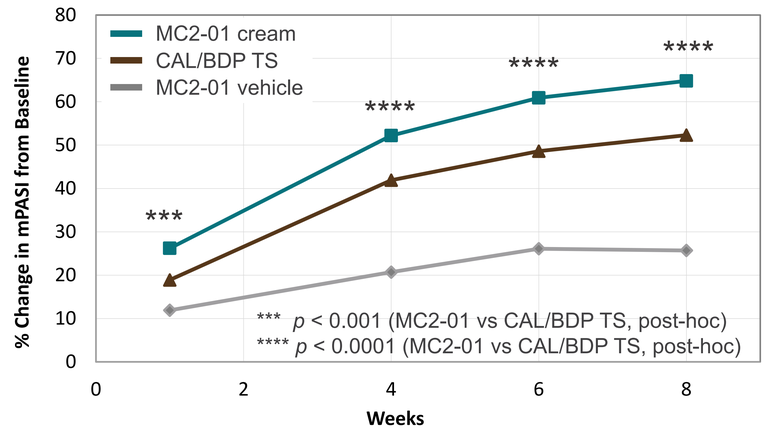
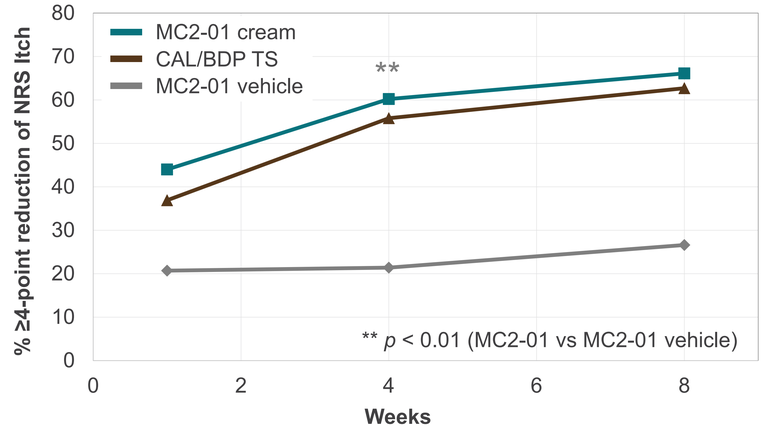


Figure 5: Secondary efficacy PRO: Reduction of itch by proportion of subjects with ≥4-point reduction of itch on 11-point NRS scale



CONCLUSION:

MC2-01 cream demonstrated in the phase 3 trial a substantial improvement in overall efficacy and onset of action for topical treatment of psoriasis compared to CAL/BDP TS without compromising the safety profile of the currently marketed CAL/BDP fixed combinations.

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