

Superior Efficacy of the Oral Phosphodiesterase 4B (PDE4B)-Selective Inhibitor Prifemilast Versus Apremilast in Moderate to Severe Plaque Psoriasis: Top-Line Results of a Head-to-Head Phase 3 Trial

Lin Cai,¹ Guoqiang Zhang,² Lihua Wang,³ Hui Xu,⁴ Xinsuo Duan,⁵ Litao Zhang,⁶ Xiaoyong Zhou,⁷ Huiming Zeng,⁸ Ningning Dang,⁹ Jianyun Lu,¹⁰ Liming Wu,¹¹ Aihua Wei,¹² Qinghua Zhu,¹³ Qian Zhu,¹³ Weifen Zhou,¹³ Jianzhong Zhang¹

¹Peking University People's Hospital, Beijing, China; ²The First Hospital of Hebei Medical University, Shijiazhuang, China; ³Jinan Central Hospital, Jinan, China; ⁴Affiliated Hospital of Jiangsu University, Zhenjiang, China; ⁵Affiliated Hospital of Chengde Medical College, Chengde, China; ⁶Affiliated Hospital of Tianjin Academy of Traditional Chinese Medicine, Tianjin, China; ⁷Wuhan No. 1 Hospital, Wuhan, China; ⁸Hainan Fifth People's Hospital, Haikou, China; ⁹Shandong Provincial Hospital, Jinan, China; ¹⁰Third Xiangya Hospital of Central South University, Changsha, China; ¹¹Hangzhou First People's Hospital, Hangzhou, China; ¹²Beijing Tongren Hospital, Capital Medical University, Beijing, China; ¹³Newsoara Biopharma Co., Ltd, Shanghai, China

SYNOPSIS

- Current therapies for plaque psoriasis have meaningful limitations: conventional systemic medications carry a risk of drug interactions and cumulative toxicity,^{1,2} while biologics are associated with high costs, access barriers, and parenteral administration³⁻⁵
- The oral phosphodiesterase 4 (PDE4) inhibitor apremilast is approved (twice daily [BID]) for psoriasis and has demonstrated modest efficacy⁶
- Prifemilast (HPP737), an investigational oral PDE4B-selective inhibitor, is being evaluated for the treatment of immune-mediated inflammatory diseases (IMIDs; eg, psoriasis, inflammatory bowel disease)
 - Prifemilast has an extended half-life (~21.2 hours) and slow systemic absorption, supporting once-daily (QD) dosing and limited central nervous system penetration⁷
- This phase 3 head-to-head trial demonstrated superior efficacy versus apremilast with a favorable safety and tolerability profile in adults with moderate to severe plaque psoriasis

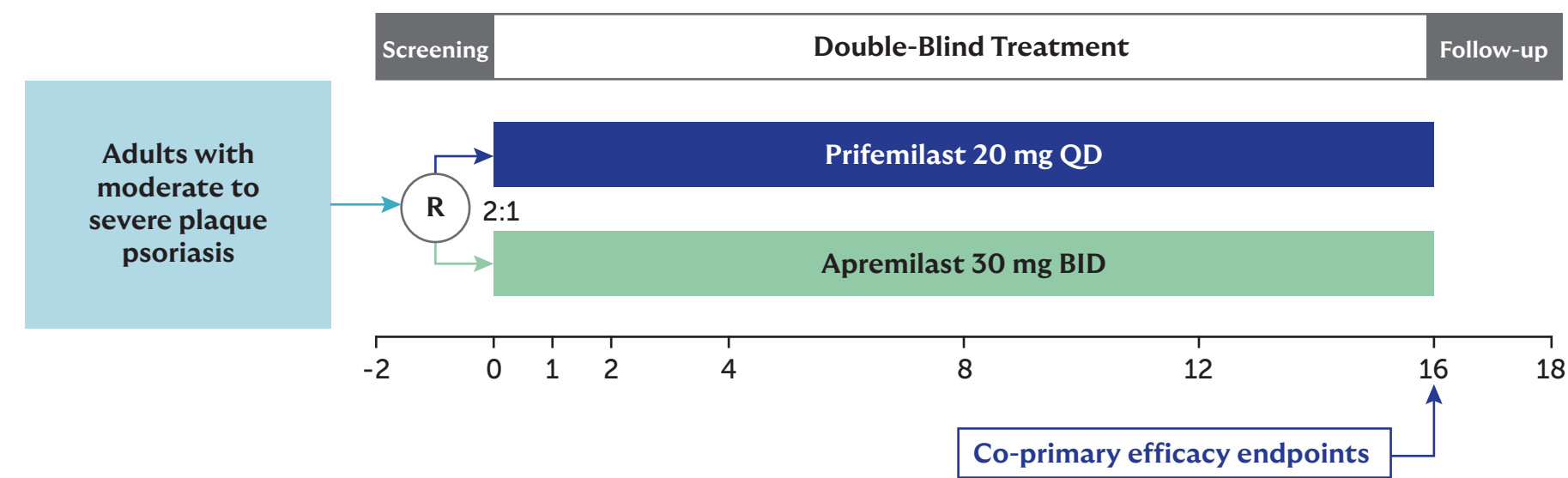
OBJECTIVE

- To evaluate the efficacy and safety of prifemilast versus apremilast in adults with moderate to severe plaque psoriasis

METHODS

- Adults with body mass index 18 to 35 kg/m² and a history of stable plaque psoriasis for ≥6 months that was moderate to severe (Psoriasis Area and Severity Index [PASI] score ≥10, static Physician's Global Assessment [sPGA] score ≥3, and body surface area [BSA] involvement ≥10%) at baseline were included
- This phase 3, randomized, double-blind, active-controlled, double-dummy, multicenter trial was conducted in China (NCT07712731)
- Patients were randomly assigned 2:1 to prifemilast 20 mg QD or apremilast 30 mg BID for 16 weeks (**Figure 1**)
 - Apremilast was titrated from 10 mg QD to 30 mg BID over 6 days, per US adult prescribing information; prifemilast did not require titration

Figure 1. Study Design



BID = twice daily; QD = once daily; R = randomization.

- Co-primary endpoints: percentage of patients achieving ≥75% improvement from baseline in PASI score (PASI 75) and sPGA score of 0 (clear) or 1 (almost clear) at Week 16
- Secondary endpoints included changes from baseline in PASI 90 (≥90% improvement), PASI 100 (100% improvement), and Dermatology Life Quality Index (DLQI) score
- The safety analysis set included all randomized patients who received ≥1 dose of study drug, and the full analysis set included all randomized patients with ≥1 postbaseline efficacy assessment
- Superiority of prifemilast over apremilast was determined using the Mantel-Haenszel common risk difference between groups for the co-primary endpoint, with the lower limit of the 95% CI required to be >0%

DISCLOSURES:

LC, GZ, L Wang, HX, XD, LZ, XZ, HZ, ND, JL, L Wu, AW, and JZ report being clinical trial investigators for Newsoara Biopharma Co., Ltd. Qinghua Zhu, Qian Zhu, and WZ are employees of Newsoara Biopharma Co., Ltd.

RESULTS

- The safety analysis set included 607 patients treated with prifemilast (n=405) or apremilast (n=202); the full analysis set included 602 patients (prifemilast [n=401]; apremilast [n=201])
 - Study completion rates were similar in both treatment groups (90%)
- Demographics and baseline characteristics were balanced between groups, with the exception of mean age ($P<0.01$; **Table 1**)

Table 1. Demographics and Baseline Characteristics

Parameter	Prifemilast 20 mg QD (n=401)	Apremilast 30 mg BID (n=201)
Age, mean (SD), y	49.4 (13.2)	46.4 (12.8)
Male, n (%)	326 (81.3)	160 (79.6)
BMI, mean (SD), kg/m ²	25.8 (3.5)	25.8 (3.8)
Duration of psoriasis, mean (SD), y	9.04 (9.17) ^a	9.92 (9.65) ^a
sPGA score category, n (%)		
3	225 (56.1)	107 (53.2)
4	152 (37.9)	81 (40.3)
5	24 (6.0)	13 (6.5)
PASI score, mean (SD)	20.2 (9.0)	19.9 (8.5)
BSA involvement, mean (SD), %	28.4 (17.4)	29.1 (17.8)
DLQI score, mean (SD)	12.4 (7.6)	12.8 (7.9)

Full analysis set.

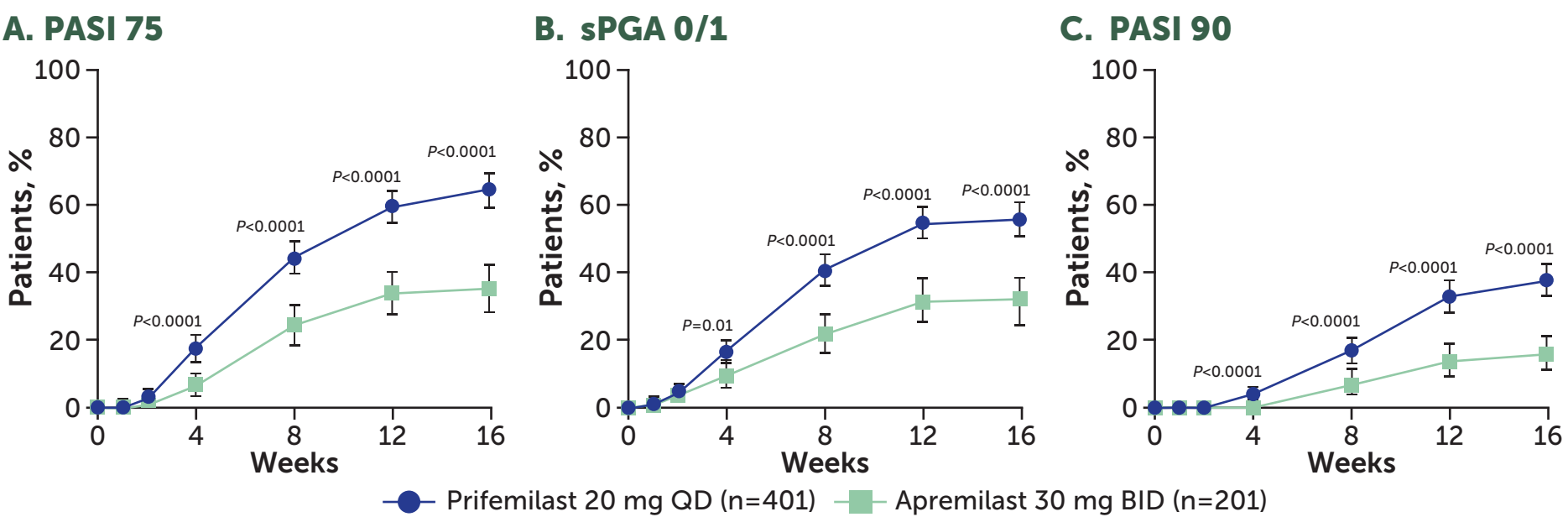
^aData were missing for 1 patient in the prifemilast group and for 3 patients in the apremilast group.

BID = twice daily; BMI = body mass index; BSA = body surface area; DLQI = Dermatology Life Quality Index; PASI = Psoriasis Area and Severity Index; QD = once daily; sPGA = static Physician's Global Assessment.

EFFICACY

- Patients treated with prifemilast were **>3 times** more likely to achieve PASI 75 at Week 16 (odds ratio [OR], 3.4; 95% CI, 2.3-4.8) than those treated with apremilast (64.6% vs 35.3%; $P<0.0001$; **Figure 2A**)
- Patients treated with prifemilast were **>2.5 times** more likely to achieve sPGA 0/1 at Week 16 (OR, 2.8; 95% CI, 1.9-4.0) than those treated with apremilast (55.6% vs 31.3%; $P<0.0001$; **Figure 2B**)
- Prifemilast showed significantly higher PASI 90 (**Figure 2C**) and PASI 100 ($P\leq 0.03$ Weeks 4-16) response rates versus apremilast; greater numeric improvements in DLQI scores were also observed with prifemilast (Weeks 1-16)

Figure 2. Percentage of Patients Achieving (A) PASI 75, (B) sPGA 0/1, and (C) PASI 90 Over Time



Full analysis set.

BID = twice daily; PASI = Psoriasis Area and Severity Index; QD = once daily; sPGA = static Physician's Global Assessment.

SAFETY

- Prifemilast was well tolerated, with rates of grade ≥3 treatment-emergent adverse events (AEs), serious AEs, and AE-related discontinuations low and similar between the 2 treatment groups (**Table 2**)
 - Increased triglyceride (including hypertriglyceridemia) and serum uric acid levels were more commonly observed with apremilast
 - Diarrhea occurred more frequently with prifemilast; 98.7% of events were mild or moderate (median onset, 3 days; median duration, 8 days)
 - Weight loss occurred more frequently with prifemilast; all events were grade 1 (5% to <10% decrease from baseline) or grade 2 (10% to <20% decrease), with no treatment interruptions or discontinuations

Table 2. Summary of AEs

Patients with an AE, n (%)	Prifemilast 20 mg QD (n=405)	Apremilast 30 mg BID (n=202)
Any AE	334 (82.5)	153 (75.7)
Treatment-related AEs	275 (67.9)	126 (62.4)
Grade ≥3 AEs	31 (7.7)	13 (6.4)
Serious AEs	16 (4.0)	5 (2.5)
Serious treatment-related AEs	2 (0.5)	1 (0.5)
Deaths	0	0
AEs leading to discontinuation	8 (2.0)	3 (1.5)
Most frequent AEs ^a		
Diarrhea	78 (19.3)	20 (9.9)
Weight loss	62 (15.3)	19 (9.4)
URT ^b	52 (12.8)	21 (10.4)
Decreased serum uric acid level	32 (7.9)	0
Limb pain	26 (6.4)	10 (5.0)
Hypertriglyceridemia	23 (5.7)	15 (7.4)
Nausea	23 (5.7)	11 (5.4)
Loss of appetite	22 (5.4)	2 (1.0)
Protein urine present	21 (5.2)	5 (2.5)
Elevated blood triglyceride level	12 (3.0)	11 (5.4)
Elevated serum uric acid level	11 (2.7)	15 (7.4)

Safety analysis set.

^a≥5.0% of patients in either treatment group.

AE = adverse event; BID = twice daily; QD = once daily; URTI = upper respiratory tract infection.

CONCLUSION

- Prifemilast demonstrated superior efficacy to apremilast in reducing the extent and severity of psoriasis and was well tolerated
- These findings support continued development of prifemilast for psoriasis and other IMIDs, including ulcerative colitis and Crohn's disease

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