Sustained Improvements in Psoriasis Area and Severity Index and in Percent Body Surface Area of Psoriasis With JNJ-77242113 in Patients With Moderate-to-Severe Plaque Psoriasis: Treat-to-Target Analyses in the FRONTIER 1 & 2 Studies

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Background

- Defined thresholds for Psoriasis Area and Severity Index (PASI) and psoriatic body surface area (BSA) are relevant disease endpoints that inform treat-to-target (T2T) management strategies in psoriasis (PsO)[1,2]
- Interleukin (IL)-23 pathway inhibition via monoclonal antibodies has demonstrated efficacy and safety in patients with moderate-to-severe PsO[3]
- Currently, no oral therapies selectively target the IL-23 pathway

JNJ-77242113 (JNJ-2113)

- First and only targeted oral peptide that inhibits IL-23 signaling by binding to the IL-23 receptor
- Showed superior clinical efficacy vs placebo (PBO) in the phase 2 FRONTIER 1 study, which was durable through 1 year of the FRONTIER 2 long-term extension (LTE) study, in patients with moderate-to-severe plaque PsO[4,5]

Objectives

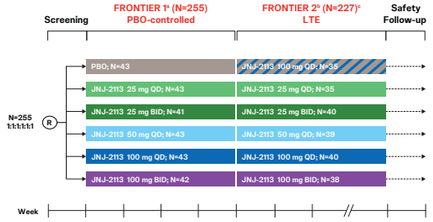
To assess the effect of JNJ-2113 on the achievement of defined treatment goals in patients with moderate-to-severe plaque PsO through 1 year in FRONTIER 1 and 2

Methods

FRONTIER 1 & FRONTIER 2 Study Designs

Key inclusion criteria:

- Moderate-to-severe plaque PsO
  - ≥18 years old
  - PASI ≥12
  - IGA ≥3
  - BSA ≥10%
- Diagnosed with PsO, with or without psoriatic arthritis, for ≥6 months
- Candidate for phototherapy or systemic therapy



[a]NCT05223868. [b]NCT05364554. [c]At W16, 227 participants from FRONTIER 1 entered FRONTIER 2 LTE study. [d]Final safety follow-up for participants who did not enter the LTE. Those not participating in the LTE completed 4 weeks of safety follow-up to complete the FRONTIER 1 study. BID=Twice daily; BSA=Body surface area; IGA=Investigator's Global Assessment; LTE=Long-term extension; PASI=Psoriasis Area and Severity Index; PBO=Placebo; PsO=Psoriasis; QD=Once daily; R=Randomization; W=Week.

Assessments & Analyses

Percent change from baseline in the PASI score through W52

The PASI assesses PsO severity based on three PsO symptoms (erythema, induration, and desquamation)[6]

- Least squares (LS) means and p-values are based on mixed models for repeated measures (MMRM) with treatment group, visit, treatment group-by-visit interaction, baseline weight category (≤90 kg, >90 kg), baseline weight category-by-visit interaction, baseline PASI total score, and baseline PASI total score-by-visit interaction as covariates
- Patients who discontinued study agent due to lack of efficacy, worsening of PsO, or initiation of a prohibited PsO treatment were considered to have zero change from baseline after the occurrence
- Missing data were handled by MMRM under missing at random assumption

Achievement of PASI and BSA treatment targets through W52

Absolute PASI thresholds of ≤5, ≤3, ≤2, ≤1, and 0

- PASI ≤5, ≤3, and ≤2 represent moderate disease control
- PASI ≤2 is a relevant T2T endpoint in the clinical setting[1]
- PASI ≤1 and 0 represent stringent disease control

PsO BSA thresholds of ≤3% and ≤1%

- BSA ≤3% represents acceptable response at W12 of treatment[2]
- BSA ≤1% represents a target response at W12 of treatment[2]

JNJ-2113 vs PBO at W12 and/or W16: Cochran-Mantel-Haenszel chi-square test stratified by baseline weight (≤90 kg vs >90 kg); nominal p-values

Nonresponder imputation (NRI):

- Patients who discontinued study agent due to lack of efficacy, worsening of PsO, or initiation of a prohibited PsO treatment were considered nonresponders after the occurrence
- Remaining patients with missing data were considered nonresponders

Among PBO-randomized patients, only those who crossed over from PBO to JNJ-2113 (PBO→100 mg QD) were included beyond W16

Key Takeaways

- **Treatment with JNJ-2113 provided robust and sustained skin improvements, consistent with achievement of important treatment targets, in patients with moderate-to-severe PsO**
- **The highest levels of improvement and response rates were observed with JNJ-2113 100 mg BID, with two-thirds of patients achieving PASI ≤2 or BSA ≤3% and approximately half achieving PASI ≤1 or BSA ≤1% at W16**
- **Patient- and group-level data indicated maintenance of JNJ-2113 stringent response through W52**

Results

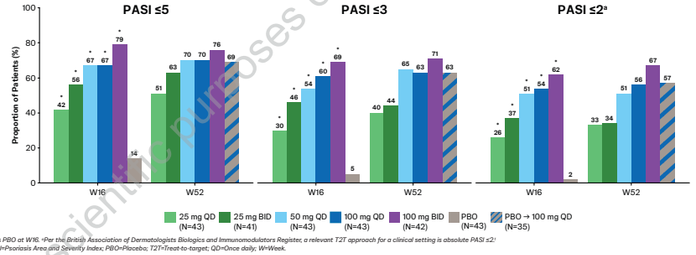
FRONTIER 1 participants had established, moderate-to-severe plaque PsO

		PBO (N=43)	JNJ-2113 25 mg QD (N=43)	JNJ-2113 25 mg BID (N=41)	JNJ-2113 50 mg QD (N=43)	JNJ-2113 100 mg QD (N=43)	JNJ-2113 100 mg BID (N=42)	JNJ-2113 All (N=212)	All Groups (N=255)
Demographics									
	Age, years	43.9 (14.7)	44.5 (12.7)	45.7 (11.9)	45.1 (11.1)	44.7 (14.1)	42.0 (11.3)	44.4 (12.2)	44.3 (12.6)
	Female	42%	26%	27%	37%	26%	29%	29%	31%
	White/Asian	86%/12%	70%/28%	66%/17%	72%/21%	81%/16%	71%/21%	72%/21%	74%/19%
	Weight, kg	92.1 (24.7)	89.0 (19.4)	90.8 (22.1)	87.6 (19.2)	85.4 (22.5)	88.5 (16.9)	88.2 (20.0)	88.9 (20.9)
Disease Characteristics									
	PsO disease duration, years	17.9 (14.4)	15.5 (11.8)	18.1 (11.8)	21.5 (11.2)	19.5 (13.3)	16.7 (13.8)	18.3 (12.5)	18.2 (12.8)
	PASI (0-72)	19.0 (5.3)	18.9 (5.3)	18.5 (5.8)	19.2 (5.1)	18.4 (6.9)	20.3 (6.5)	19.1 (5.9)	19.0 (5.8)
	Psoriatic BSA, %	26.1 (15.7)	21.1 (9.3)	20.9 (11.9)	23.9 (13.6)	20.5 (13.7)	24.2 (12.6)	22.1 (12.3)	22.8 (13.0)
	IGA								
	Moderate (3)/Severe (4)	88%/12%	70%/30%	80%/20%	84%/16%	81%/19%	71%/29%	77%/23%	79%/21%
Medication use at baseline									
	Phototherapy[a]	44%	40%	37%	56%	49%	33%	43%	43%
	Biologics[b]	16%	16%	32%	26%	21%	21%	23%	22%
	Systemics[c]	79%	77%	80%	81%	79%	74%	78%	78%

Data shown are mean (SD) or percentage, unless otherwise indicated. [a]Includes PUVA or UVB. [b]Includes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, certolizumab pegol. [c]Includes conventional nonbiologic systemic therapies, novel nonbiologic systemic therapies, 1,25-vitamin D3 and analogs, phototherapy, and biologics. BID=Twice daily; BSA=Body surface area; IGA=Investigator's Global Assessment; JNJ-2113=JNJ-77242113; PASI=Psoriasis Area and Severity Index; PBO=Placebo; PsO=Psoriasis; PUVA=Psoralen plus ultraviolet A; SD=Standard deviation; QD=Once daily; UVB=Ultraviolet B.

Greater proportions of JNJ-2113-treated vs PBO-treated patients achieved absolute PASI thresholds of ≤5, ≤3, and ≤2 at W16; rates were maintained at W52

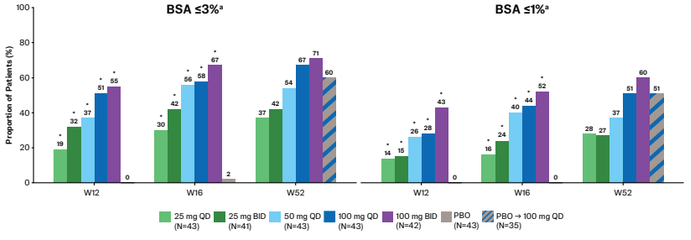
- 67% of patients receiving JNJ-2113 100 mg twice daily (BID) achieved PASI ≤2 at W52, a clinically relevant T2T threshold
- Response rates at W52 following PBO→100 mg once daily (QD) reached those with JNJ-2113 100 mg QD across absolute PASI thresholds



[a]All nominal p<0.01 vs PBO at W16. [b]Per the British Association of Dermatologists Biologics and Immunomodulators Register, a relevant T2T approach for a clinical setting is absolute PASI ≤2.[1] BID=Twice daily; PASI=Psoriasis Area and Severity Index; PBO=Placebo; T2T=Treat-to-target; QD=Once daily; W=Week.

Greater proportions of JNJ-2113-treated vs PBO-treated patients achieved PsO BSA thresholds of ≤3% and ≤1% at W12 and W16; rates were maintained or increased at W52

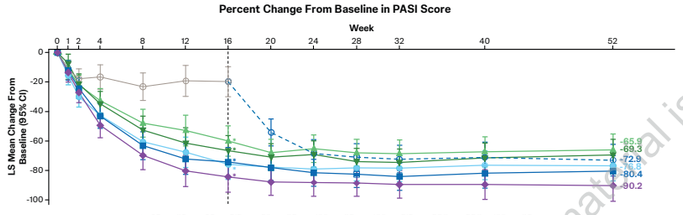
- At W52, 71% and 60% of patients treated with 100 mg BID achieved acceptable (≤3%) and target (≤1%) BSA responses, respectively
- Rates for both BSA thresholds at W52 following PBO→100 mg QD approached those with JNJ-2113 100 mg QD



[a]All nominal ps≤0.01 vs PBO at W16. [b]Per the National Psoriasis Foundation, at W12 (3 months) after treatment initiation, an acceptable response is BSA ≤3% and a target response is ≤1%.[2] BID=Twice daily; BSA=Body surface area; PBO=Placebo; QD=Once daily; W=Week.

Percent improvements in PASI score were greater with JNJ-2113 than PBO as early as W4, with continued and sustained improvement over time

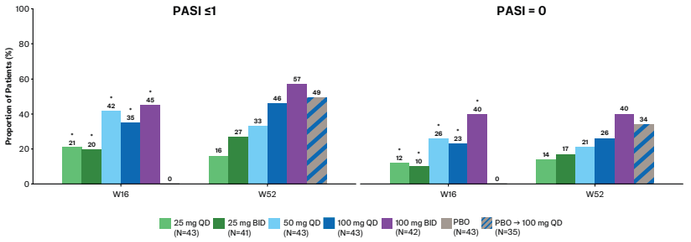
- Highest mean percent improvements in PASI score were seen with JNJ-2113 100 mg BID, with approximately 90% improvement at W52



[a]All nominal p<0.001 vs PBO at W16. Dotted line indicates transition from PBO-controlled FRONTIER 1 to FRONTIER 2 LTE with PBO→100 mg QD. BID=Twice daily; CI=Confidence interval; LS=Least squares; PASI=Psoriasis Area and Severity Index; PBO=Placebo; QD=Once daily; W=Week.

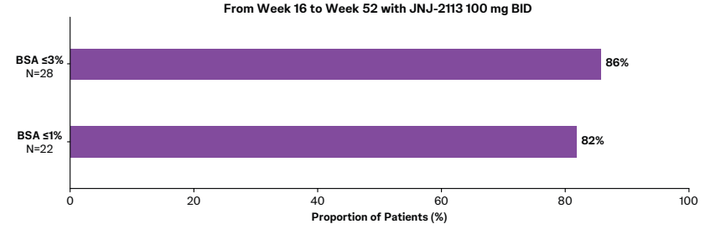
Greater proportions of JNJ-2113-treated vs PBO-treated patients achieved stringent PASI thresholds of ≤1 and 0 at W16; rates were maintained or increased at W52

- 45% and 40% of patients receiving JNJ-2113 100 mg BID achieved PASI ≤1 and PASI=0, respectively, at W16
- Following PBO→100 mg QD, W52 rates for both PASI thresholds approached those with JNJ-2113 100 mg BID



[a]Nominal p<0.05 to <0.01 vs PBO at W16. BID=Twice daily; PASI=Psoriasis Area and Severity Index; PBO=Placebo; QD=Once daily; W=Week.

86% and 82% of patients treated with 100 mg BID achieving BSA ≤3% and ≤1% at W16, respectively, maintained response at W52



BID=Twice daily; BSA=Body surface area.

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