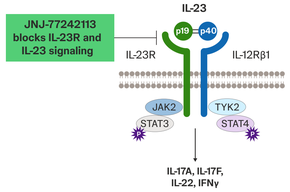
A Phase 2b, Long-term Extension, Dose-ranging Study of Oral JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis: FRONTIER-2

Laura K. Ferris,[1] Jerry Bagel,[2] Yu-Huei Huang,[3] Andrew Pink,[4] Stephen K. Tyring,[5] Georgios Kokolakis,[6] Amy M. DeLozier,[7] Shu Li,[8] Yaung-Kaung Shen,[8] Anthony Todd,[9] Takayuki Ota,[7] Robert Bissonnette[10]

[1]University of Pittsburgh, Pittsburgh, PA, USA; [2]Psoriasis Treatment Center of Central NJ, East Windsor, NJ, USA; [3]Department of Dermatology at Chang Gung Memorial Hospital and the School of Medicine at Chang Gung University, Taoyuan City, Taiwan; [4]NHS Foundation Trust Great Maze Pond, London, England; [5]Center for Clinical Studies, Webster, TX, USA; [6]Psoriasis Research and Treatment Center, Department of Dermatology, Venereology and Allergology, Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [7]Janssen Research and Development, LLC, San Diego, CA, USA; [8]Janssen Research and Development, LLC, Spring House, PA, USA; [9]Janssen Scientific Affairs, LLC, Horsham, PA, USA; [10]Innovaderm Research, Montreal, Quebec, Canada

Background

- FRONTIER 1, a randomized, double-blind, placebo (PBO)-controlled, dose-ranging, phase 2 study, evaluated the efficacy and safety of JNJ-77242113 in patients (pts) with moderate-to-severe plaque psoriasis (PsO)
  - JNJ-77242113 showed superior efficacy and similar safety compared to PBO at Week 16[1]
- In the FRONTIER 2 long-term extension (LTE) study, FRONTIER 1 participants who entered the LTE were evaluated through 1 year



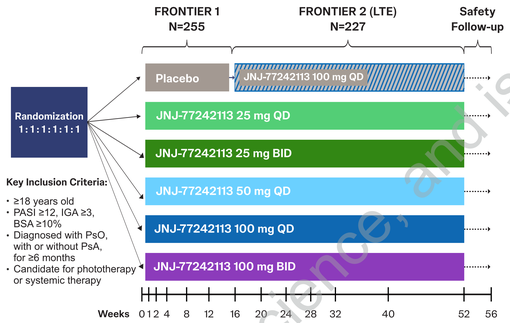
IFN=Interferon; IL=Interleukin; JAK=Janus kinase; STAT=Signal transducers and activators of transcription; TYK=Tyrosine kinase.

Objective

The efficacy and safety of JNJ-77242113, orally administered across a range of doses, were assessed through 1 year in pts with moderate-to-severe plaque PsO

Methods

- In FRONTIER 2, pts randomized to a JNJ-77242113 dosing group in FRONTIER 1 continued treatment through Week 52
- Pts from the FRONTIER 1 PBO group crossed over to JNJ-77242113 100 mg daily (QD) at Week 16 (PBO→100 mg QD)
- Efficacy endpoints (dichotomous and continuous endpoints utilized non-responder imputation [NRI] and mixed models for repeated measures [MMRM], respectively):
  - All JNJ-77242113-randomized pts
  - 35 PBO→100 mg QD pts
  - Scalp-specific Investigator's Global Assessment (ss-IGA): assessed in pts with a ss-IGA ≥2 at baseline (BL)
- Adverse events (AEs): assessed in pts who entered the LTE and received ≥1 dose of JNJ-77242113 treatment



BID=Twice daily; BSA=Body surface area; IGA=Investigator's Global Assessment; LTE=Long-term extension; PASI=Psoriasis Area and Severity Index; PsA=Psoriatic arthritis; PsO=Psoriasis; QD=Once daily.

Key Takeaways

- **In the FRONTIER 2 study, which evaluated the efficacy and safety of JNJ-77242113 in pts with moderate-to-severe plaque PsO through 1 year:**
  - **The proportions of pts achieving the FRONTIER 1 primary efficacy endpoint were maintained from Week 16 to Week 52**
  - **At Week 52, 76% of pts receiving 100 mg BID achieved PASI 75 response**
  - **Across all efficacy endpoints, the highest response rates at Week 52 were achieved in the JNJ-77242113 100 mg BID group, including response rates of:**

Near Complete Clearance	Complete Clearance
– PASI 90: 64%	– PASI 100: 40%
– IGA 0/1: 74%	– IGA 0: 43%
– ss-IGA 0/1: 75%	– ss-IGA 0: 67%

- **Pt-reported improvements in PsO symptoms and signs were sustained through Week 52**
- **At Week 52, response rates increased substantially in pts who crossed over from PBO to JNJ-77242113 100 mg QD at Week 16**
- **In the context of data through Week 16[1], during which the combined JNJ-77242113 and PBO groups showed similar safety profiles, JNJ-77242113 remained well-tolerated; no safety signals were identified through Week 56**

Results

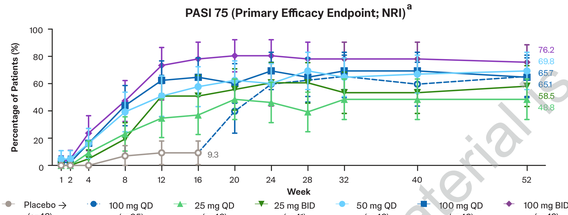
FRONTIER 2 assessed FRONTIER 1 pts with moderate-to-severe plaque PsO entering the LTE

FRONTIER 1 BL Characteristics	PBO (N=43)	JNJ-77242113 25 mg QD (N=43)	JNJ-77242113 25 mg BID (N=41)	JNJ-77242113 50 mg QD (N=43)	JNJ-77242113 100 mg QD (N=43)	JNJ-77242113 100 mg BID (N=42)	JNJ-77242113 Combined[a] (N=212)	Total (N=255)
Pt Demographics								
Age, yrs	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)**
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)**
PsO Characteristics								
PsO disease duration, yrs	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 total score [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)**
BSA [0-100], %	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 3 or 4,* %	88.4/11.6	69.8/30.2	80.5/19.5	83.7/16.3	81.4/18.6	71.4/28.6	77.4/22.6	**79.2/20.8**
ss-IGA ≥2 (mild-severe),[b] %	81.4	86.0	80.0	93.0	93.0	87.8	88.1	**87.0**
PROs								
PSSD symptom score [0-100]	47.3 (20.7)	59.0 (23.6)	51.9 (24.0)	53.9 (24.5)	43.0 (21.3)	55.9 (26.3)	52.7 (24.4)	**51.8 (23.8)**
PSSD sign score [0-100]	62.9 (16.6)	69.5 (16.5)	64.1 (18.9)	64.7 (19.4)	60.4 (18.6)	66.3 (19.1)	65.0 (18.6)	**64.6 (18.3)**
Prior Medications								
Prior Biologics,[c] %	16.3	16.3	31.7	25.6	20.9	21.4	23.1	**22.0**

*Data shown are mean (SD), unless otherwise indicated. *IGA 3/4=moderate/severe; [a]Includes all JNJ-77242113 treatment columns; *25 mg BID, n=40; 100 mg BID, n=41; Combined, n=212; Total, n=253; [b]Includes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, certolizumab pegol. BID=Twice daily; BL=Baseline; BSA=Body surface area; IGA= Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; PROs=Patient-reported outcomes; PsO=Psoriasis; PSSD=Psoriasis Symptoms and Signs Diary; QD=Once daily; SD=Standard deviation; ss-IGA=Scalp-specific IGA.*

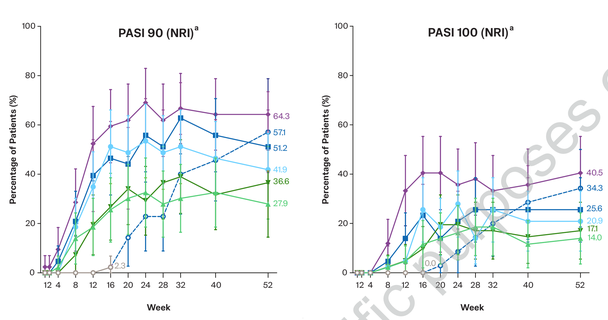
PASI 75 response rates at Week 16 were maintained through Week 52

- Among pts who crossed over from PBO→100 mg QD at Week 16, PASI 75 response rates rapidly converged with those of JNJ-77242113-randomized pts



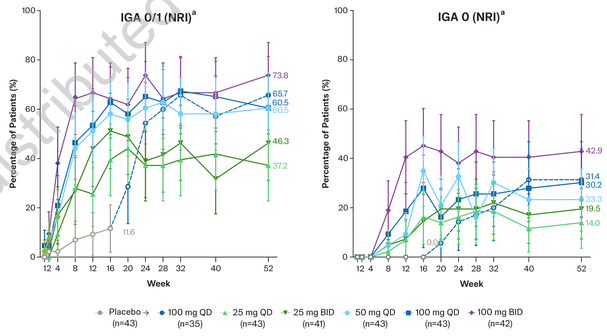
[a]Pts who discontinued study agent due to lack of efficacy/worsening of PsO, or who initiated a prohibited PsO treatment were considered non-responders after the occurrence. Pts with missing data were considered non-responders. BID=Twice daily; NRI=Non-responder imputation; PASI=Psoriasis Area and Severity Index; PsO=Psoriasis; Pts=Patients; QD=Once daily.

PASI 90 and PASI 100 response rates were generally maintained from Week 16 through Week 52



[a]Pts who discontinued study agent due to lack of efficacy/worsening of PsO, or who initiated a prohibited PsO treatment were considered non-responders after the occurrence. Pts with missing data were considered non-responders. BID=Twice daily; IGA=Investigator's Global Assessment; NRI=Non-responder imputation; PsO=Psoriasis; Pts=Patients; QD=Once daily.

IGA 0/1 and IGA 0 response rates were generally maintained from Week 16 through Week 52



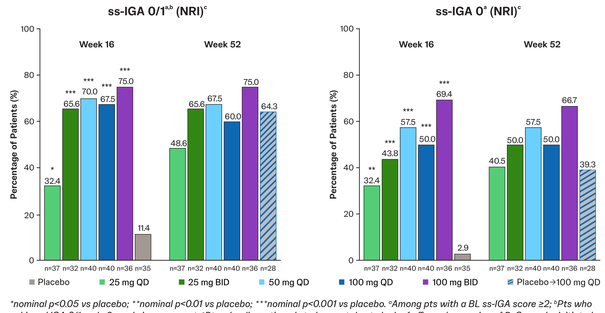
[a]Pts who discontinued study agent due to lack of efficacy/worsening of PsO, or who initiated a prohibited PsO treatment were considered non-responders after the occurrence. Pts with missing data were considered non-responders. BID=Twice daily; IGA=Investigator's Global Assessment; NRI=Non-responder imputation; PsO=Psoriasis; Pts=Patients; QD=Once daily.

Improvements in Psoriasis Symptoms and Signs Diary (PSSD) scores at Week 16 were generally maintained through Week 52

[a]LSM are based on the MMRM model with treatment group, visit, treatment group by visit interaction, BL weight category (≤90 kg, >90 kg), BL weight category by visit interaction, BL PSSD symptom/sign score, and BL PSSD symptom/sign score by visit interaction as covariates. Zero change was assigned after pts discontinued study agent due to lack of efficacy/worsening of PsO or initiated a prohibited PsO treatment. Missing data was handled by MMRM under missing at random assumption. BID=Twice daily; BL=Baseline; LSM=Least square mean; MMRM=Mixed models for repeated measurements; NRI=Non-responder imputation; PsO=Psoriasis; PSSD=Psoriasis Symptoms and Signs Dairy; Pts=Patients; QD=Once daily.

ss-IGA 0/1 and ss-IGA 0 response rates were generally maintained from Week 16 through Week 52

- In pts who crossed over from PBO→100 mg QD at Week 16, ss-IGA 0/1 and ss-IGA 0 response rates substantially increased by Week 52



**nominal p<0.05 vs placebo; **nominal p<0.01 vs placebo; ***nominal p<0.001 vs placebo. [a]Among pts with a BL ss-IGA score ≥2; [b]Pts who achieved IGA 0/1 and ≥2-grade improvement; [c]Pts who discontinued study agent due to lack of efficacy/worsening of PsO, or who initiated a prohibited PsO treatment were considered non-responders after the occurrence. Pts with missing data were considered non-responders. BID=Twice daily; BL=Baseline; IGA=Investigator's Global Assessment; NRI=Non-responder imputation; PsO=Psoriasis; Pts=Patients; QD=Once daily; ss-IGA=Scalp-specific IGA.*

Among FRONTIER 2 pts who received JNJ-77242113 from Week 16 to Week 52, no safety signals were identified through Week 56

- Rates of gastrointestinal-related AEs did not increase in pts receiving JNJ-77242113 during the LTE (6% in the JNJ-77242113 combined group)
  - FRONTIER 1 Week 16: 12% PBO vs 11% JNJ-77242113 combined group[1]
- No evidence of dose-dependent increase in the occurrence of AEs
- 4% experienced serious AEs
  - All considered not related to the study intervention by investigators
- No deaths occurred during the LTE

Pts With ≥1 TEAE of Frequency ≥5% of Preferred Terms in Any Treatment Group From Week 16 Through Week 56

LTE Safety Analysis Set	Placebo → 100 mg QD (N=35)	JNJ-77242113 25 mg QD (N=35)	JNJ-77242113 25 mg BID (N=40)	JNJ-77242113 50 mg QD (N=39)	JNJ-77242113 100 mg QD (N=40)	JNJ-77242113 100 mg BID (N=38)	JNJ-77242113 Combined[a] (N=227)
Avg duration of follow-up, weeks	37.8	36.6	35.0	38.4	35.9	38.6	37.0
Pts with ≥1 AE, n (%)	23 (65.7)	18 (51.4)	27 (67.5)	19 (48.7)	27 (67.5)	19 (50.0)	133 (58.6)
Nasopharyngitis	9 (25.7)	3 (8.6)	6 (15.0)	7 (17.9)	11 (27.5)	5 (13.2)	41 (18.1)
Upper respiratory tract infection	4 (11.4)	6 (17.1)	3 (7.5)	3 (7.7)	2 (5.0)	4 (10.5)	22 (9.7)
COVID-19	2 (5.7)	1 (2.9)	1 (2.5)	3 (7.7)	2 (5.0)	3 (7.9)	12 (5.3)
Headache	0	2 (5.7)	3 (7.5)	0	3 (7.5)	0	8 (3.5)
Influenza	1 (2.9)	0	3 (7.5)	1 (2.6)	1 (2.5)	1 (2.6)	7 (3.1)
Urinary tract infection	2 (5.7)	1 (2.9)	1 (2.5)	1 (2.6)	0	2 (5.3)	7 (3.1)
ALT increased	2 (5.7)	1 (2.9)	0	1 (2.6)	0	2 (5.3)	6 (2.6)
Bronchitis	1 (2.9)	1 (2.9)	1 (2.5)	3 (7.7)	0	0	6 (2.6)
Hypertension	1 (2.9)	0	2 (5.0)	1 (2.6)	1 (2.5)	1 (2.6)	6 (2.6)
AST increased	1 (2.9)	1 (2.9)	0	1 (2.6)	0	2 (5.3)	5 (2.2)
Arthralgia	1 (2.9)	0	0	1 (2.6)	2 (5.0)	0	4 (1.8)
Meniscus injury	0	1 (2.9)	2 (5.0)	0	0	0	3 (1.3)
Sinusitis	0	0	2 (5.0)	1 (2.6)	0	0	3 (1.3)
Vomiting	0	0	0	0	2 (5.0)	0	2 (0.9)

[a]Includes all JNJ-77242113 treatment columns. Pts are counted only once for any given event, regardless of the number of times they actually experienced the event. AEs are coded using MedDRA Version 25.1. AE=Adverse event; ALT=Alanine aminotransferase; AST=Aspartate aminotransferase; Avg=Average; BID=Twice daily; COVID-19=Coronavirus disease 2019; LTE=Long-term extension; MedDRA=Medical Dictionary for Regulatory Activities; Pts=Patients; QD=Once daily; TEAE=Treatment-emergent adverse event.

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