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Disclosure of Conflicts of Interest

Robert Bissonnette, MD

[A Phase 2, Randomized, Placebo-Controlled, Dose-Ranging Study of Oral JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis: Efficacy of Overall and Scalp Psoriasis Responses From FRONTIER 1]

R. Bissonnette is an Advisory Board Member, Consultant, Speaker and/or Investigator for and received honoraria and/or grants from, AbbVie, Alumis, Amgen, AnaptysBio, Bausch Health, Boston, BMS/Celgene, Dermavant, Eli Lilly, Janssen, LEO Pharma, Nimbus, Novartis, Pfizer, Regeneron, UCB, VentyxBio and Xencor; also an employee and shareholder of Innovaderm Research.

Disclosure of Conflicts of Interest

- **A. Pinter** served as an advisor and/or received speaker's honoraria and/or received grants and/or participated in clinical trials for, AbbVie, Almirall Hermal, Amgen, Biogen Idec, BioNTech, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Galderma, GSK, Hexal, Janssen-Cilag GmbH, Klinge Pharma, LEO Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi Genzyme, Schering-Plough, Tigercat Pharma, and UCB Pharma.
- **L. Ferris** served as an investigator for AbbVie, Bristol-Myers Squibb, DermTech, Castle Biosciences, Arcutis, Amgen, Janssen, Eli Lilly, Novartis, UCB, Moberg, Aristea, Acelyrin, Cara Therapeutics, Leo Pharma, Regeneron, Amgen, SkinAnalytics, Acelyrin, Boehringer-Ingelheim, Mobius, Castle Biosciences, Galderma; consultant for Boehringer-Ingelheim, AbbVie, Bristol-Myers Squibb, DermTech, Arcutis, Dermavant, Cara Therapeutics, Leo Pharma, Pfizer, Regeneron, Amgen, Janssen, Novartis; speaker for Boehringer-Ingelheim, Bristol-Myers Squibb, Arcutis, Regeneron, Abbvie.
- **S. Gerdes** served as an advisor and/or received speaker's honoraria and/or received grants and/or participated in clinical trials for, AbbVie, Acelyrin, Affibody AB, Akari Therapeutics Plc, Almirall Hermal, Amgen, Argenx BV, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly, Galderma, Hexal AG, Incyte Inc., Janssen-Cilag, Klinge Pharma, Kymab, LEO Pharma, Medac, Neubourg Skin Care GmbH, Novartis, Pfizer, Pierre Fabre, Principia Biopharma, Regeneron Pharmaceuticals, Sandoz Biopharmaceuticals, Sanofi-Aventis, Trevi Therapeutics and UCB Pharma.
- **P. Rich** served as a principal investigator for Abbvie, Acelyrin, Alfasigma, Allakos, Amgen, Arcutis, Aslan, Atacama, Brickell, Bristol Myers-Squibb, Dermbiont, Dermavant, Dong-A, Eli Lilly, Galderma, Hallux, Incyte, Janssen, Leo, Moberg, Ortho, Pfizer, Sun Pharma, Technoderma, UCB; on advisory board for Cara Therapeutics, Ortho Dermatologics, Bristol Myers-Squibb, La Roche Posay; consultant for Bristol Myers-Squibb, Hexima.
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- **Y.-W. Yang** is an employee of Immunology Global Medical Affairs, Janssen Pharmaceutical Companies of Johnson & Johnson, and **M. Miller**, **Y.-K. Shen**, and **C. DeKlotz** are employees of Janssen Research & Development, LLC; employees may own stock/stock options in Johnson & Johnson, of which Janssen is a subsidiary.
- **K.A. Papp** has received clinical research grants from, honoraria from, and/or served as a consultant, scientific advisor, investigator, speaker, and/or medical officer for AbbVie, Acelyrin, Akros, Amgen, Anacor, Aralez Pharmaceuticals, Arcutis, Avillion, Bausch Health/Valeant, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite Biopharma, Celgene, Celltrion, Coherus, Dermavant, Dermira, Dice Pharmaceuticals, Dow Pharma, Eli Lilly, Evelo, Forbion, Galderma, Gilead, GSK, Incyte, Janssen, Kyowa Hakko Kirin, Leo, Meiji Seika Pharma, Merck (MSD), Mitsubishi Pharma, Novartis, Pfizer, Regeneron, Reistone, Roche, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, UCB, vTv Therapeutics, Xencor.

A Phase 2, Randomized, Placebo-Controlled, Dose-Ranging Study of Oral JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis: Efficacy of Overall and Scalp Psoriasis Responses From FRONTIER 1

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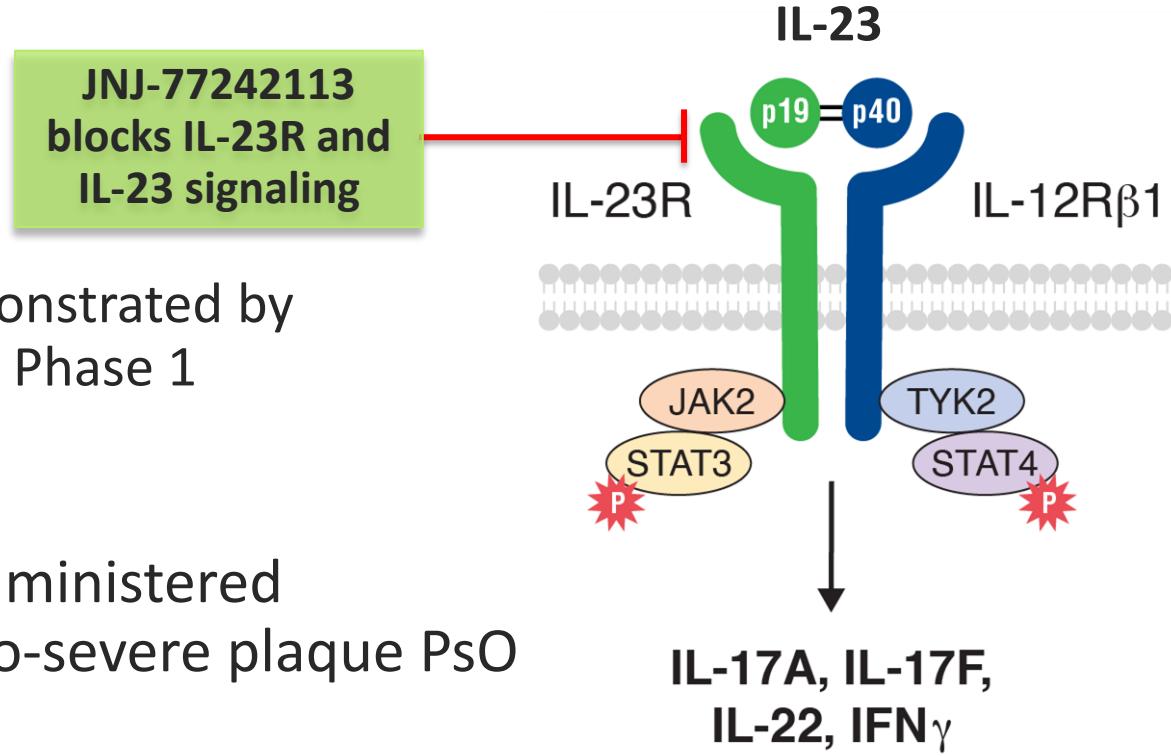
Introduction

- Current therapies targeting the interleukin (IL)-23 pathway are effective in the treatment of immune mediated diseases, such as psoriasis (PsO)
- There are currently no orally delivered therapeutics selectively targeting this pathway
- JNJ-77242113 is a first-in-class oral IL-23R antagonist peptide that selectively and potently blocks IL-23 signaling and downstream inflammatory cytokine production[1]
- Due to its GI stability and exquisite potency, JNJ-77242113 is able to provide systemic IL-23 pathway blockade through oral dosing[1]
  - Robust systemic IL-23 pathway inhibition demonstrated by pharmacodynamic activity upon oral dosing in Phase 1



Objective

- To evaluate the efficacy and safety of orally administered JNJ-77242113 in the treatment of moderate-to-severe plaque PsO

1. Fourie A, et al. Presented at ISID Meeting; May 10-13, 2023; Tokyo, Japan. ID 1109.

Bissonnette R, et al. EADV Congress; October 11-14, 2023; Berlin, Germany.

Overall Study Design

Primary Objective & Primary Endpoint:

- To evaluate the dose-response of JNJ-77242113 treatment at Week 16 in patients with moderate-to-severe plaque PsO
- Proportion of patients achieving PASI 75 at Week 16

Patient Population:

- ≥18 years old
- PASI ≥12, IGA ≥3 & BSA ≥10%
- Diagnosed with PsO, with or without PsA, for ≥6 months
- Candidate for phototherapy or systemic therapy

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; QD=Once daily.

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Demographics and Disease Characteristics at Baseline

	Placebo	JNJ-77242113						Total
		25 mg QD	25 mg BID	50 mg QD	100 mg QD	100 mg BID	Combined*	
Full analysis set, n	43	43	41	43	43	42	212	255
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 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	18.99 (5.3)	18.90 (5.3)	18.46 (5.8)	19.23 (5.1)	18.42 (6.9)	20.33 (6.5)	19.07 (5.9)	19.05 (5.8)
IGA score, n (%)								
Severe (4)	5 (11.6%)	13 (30.2%)	8 (19.5%)	7 (16.3%)	8 (18.6%)	12 (28.6%)	48 (22.6%)	53 (20.8%)
Moderate (3)	38 (88.4%)	30 (69.8%)	33 (80.5%)	36 (83.7%)	35 (81.4%)	30 (71.4%)	164 (77.4%)	202 (79.2%)
ss-IGA score, n	43	43	40	43	43	41	210	253
Severe (4), n (%)	5 (11.6%)	7 (16.3%)	2 (5.0%)	6 (14.0%)	7 (16.3%)	8 (19.5%)	30 (14.3%)	35 (13.8%)
Moderate (3), n (%)	24 (55.8%)	23 (53.5%)	24 (60.0%)	25 (58.1%)	24 (55.8%)	22 (53.7%)	118 (56.2%)	142 (56.1%)
Mild (2), n (%)	6 (14.0%)	7 (16.3%)	6 (15.0%)	9 (20.9%)	9 (20.9%)	6 (14.6%)	37 (17.6%)	43 (17.0%)
Very Mild (1), n (%)	2 (4.7%)	1 (2.3%)	0	1 (2.3%)	0	2 (4.9%)	4 (1.9%)	6 (2.4%)
Absence (0), n (%)	6 (14.0%)	5 (11.6%)	8 (20.0%)	2 (4.7%)	3 (7.0%)	3 (7.3%)	21 (10.0%)	27 (10.7%)
Previous Psoriasis Medications/Therapies, n (%)								
Phototherapy**	19 (44.2%)	17 (39.5%)	15 (36.6%)	24 (55.8%)	21 (48.8%)	14 (33.3%)	91 (42.9%)	110 (43.1%)
Biologics†	7 (16.3%)	7 (16.3%)	13 (31.7%)	11 (25.6%)	9 (20.9%)	9 (21.4%)	49 (23.1%)	56 (22.0%)
Systemics‡	34 (79.1%)	33 (76.7%)	33 (80.5%)	35 (81.4%)	34 (79.1%)	31 (73.8%)	166 (78.3%)	200 (78.4%)

PUVA=Psoralen plus ultraviolet A; ss-IGA=Scalp-specific Investigator's Global Assessment; UVB=Ultraviolet B. Data shown are mean (SD), unless otherwise indicated. *Includes all JNJ-77242113 treatment columns. **Includes PUVA or UVB. †Includes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, certolizumab pegol. ‡Includes conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, biologics.

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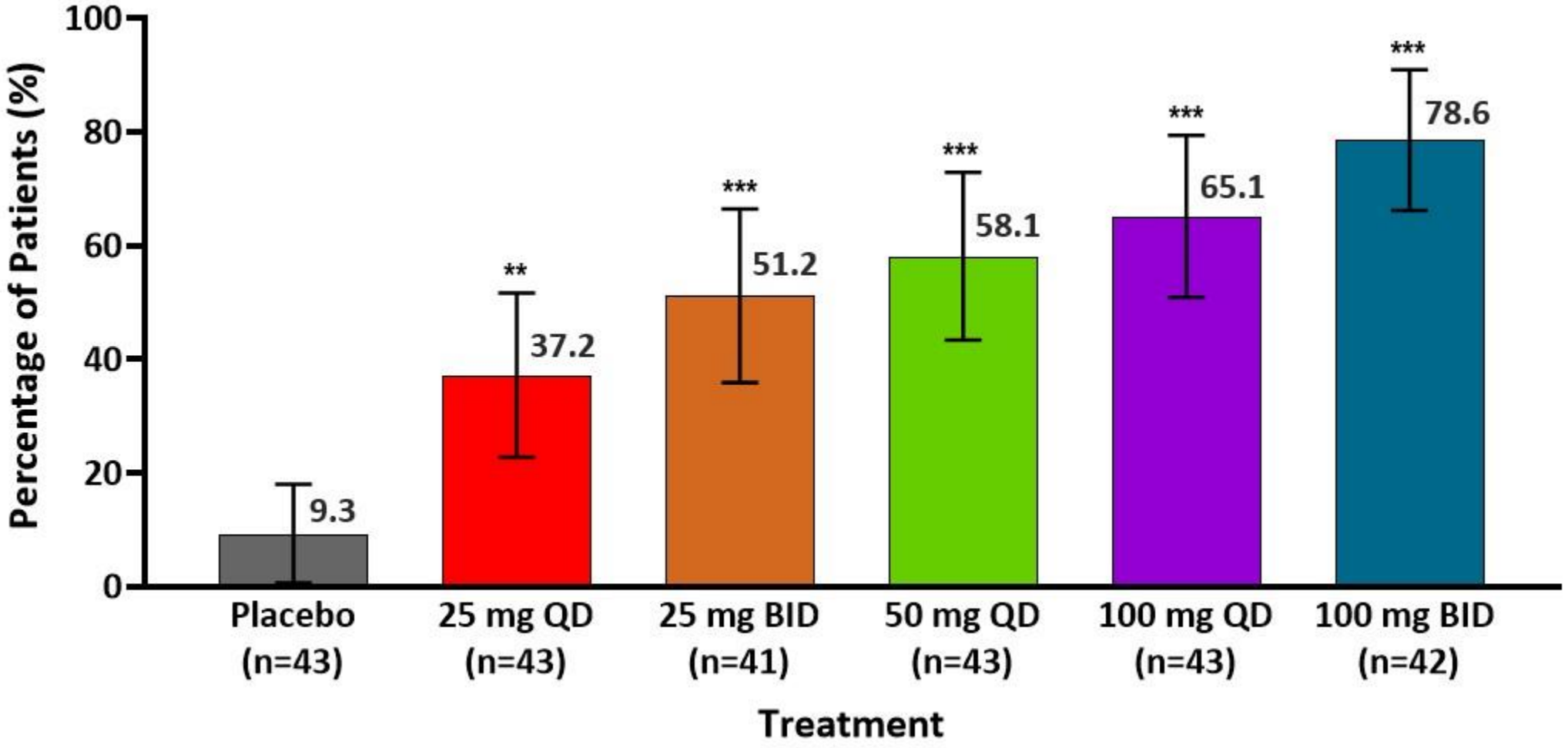
Proportion of Patients Achieving PASI 75 (95% CI) at Week 16



Significant dose-response was detected for PASI 75 at Week 16

*nominal p<0.05 vs placebo; **nominal p<0.01 vs placebo; ***nominal p<0.001 vs placebo. Patients who discontinued study agent due to lack of efficacy, worsening of PsO, or use of a prohibited PsO treatment prior to Week 16 were considered non-responders. Patients with missing data were considered non-responders. Dose-response was tested based on trough levels.

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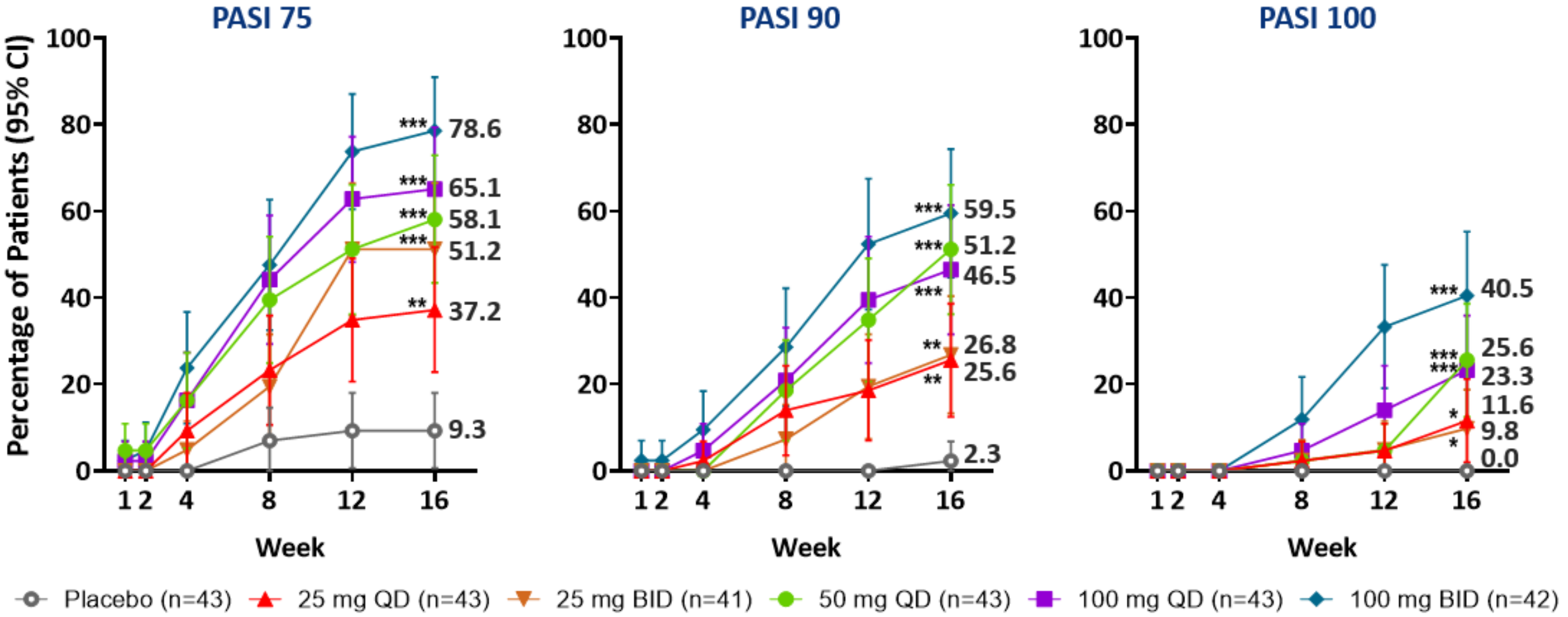
Response rates for PASI 75, PASI 90, and PASI 100 for all JNJ-77242113 doses were significantly higher than placebo at Week 16



*nominal p<0.05 vs placebo; **nominal p<0.01 vs placebo; ***nominal p<0.001 vs placebo. Patients 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. Patients with missing data were considered non-responders.

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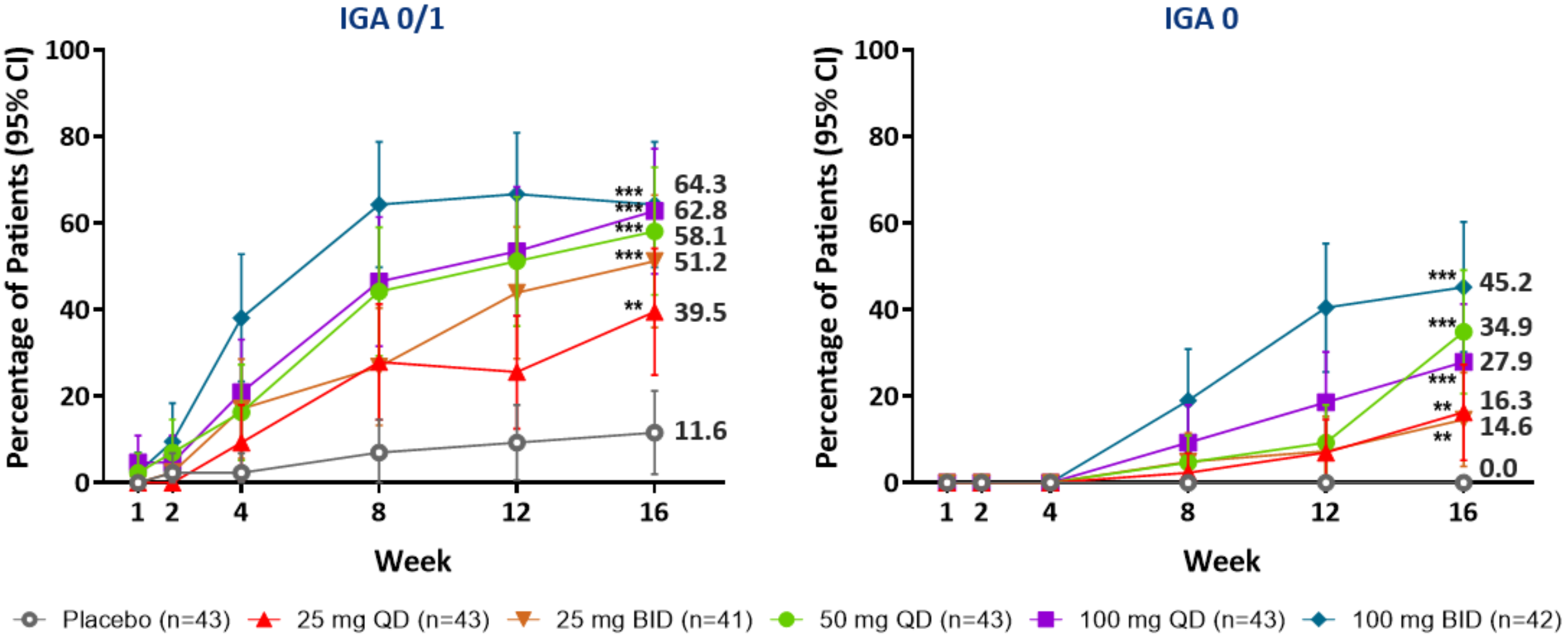
Response rates for IGA scores of 0/1 and 0 for all JNJ-77242113 doses were significantly higher than placebo at Week 16



*nominal p<0.05 vs placebo; **nominal p<0.01 vs placebo; ***nominal p<0.001 vs placebo. Patients 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. Patients with missing data were considered non-responders.

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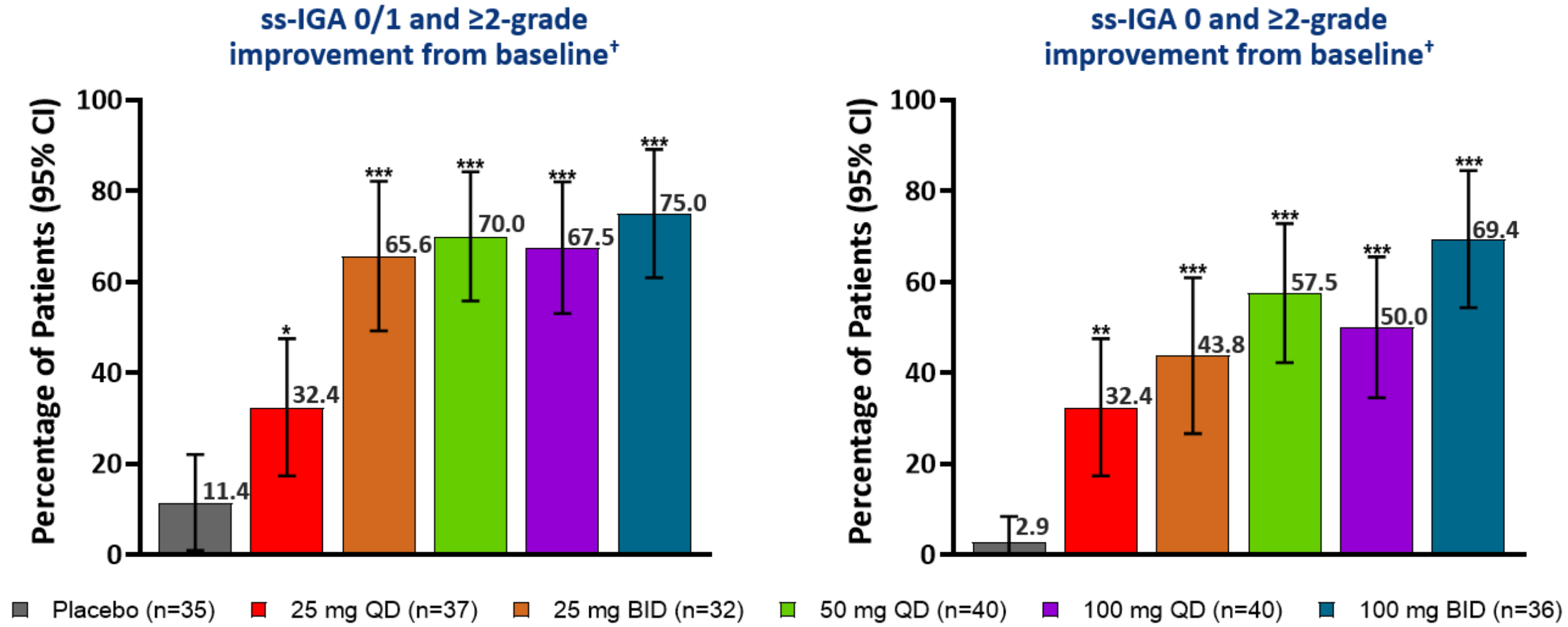
Response rates for scalp PsO for all JNJ-77242113 doses were significantly higher than placebo at Week 16



†Among patients with a baseline ss-IGA score ≥2. *nominal p<0.05 vs placebo; **nominal p<0.01 vs placebo; ***nominal p<0.001 vs placebo. Patients 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. Patients with missing data were considered non-responders.

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Number of Patients With ≥1 TEAE With Frequency of ≥5% of Preferred Terms in Any Treatment Group Through End of Study by System Organ Class and Preferred Term

	Placebo	JNJ-77242113					
		25 mg QD	25 mg BID	50 mg QD	100 mg QD	100 mg BID	Combined*
Safety analysis set, n	43	43	41	43	43	42	212
Avg duration of follow-up (weeks)	15.03	15.70	16.20	15.75	16.07	15.81	15.90
Patients with ≥1 AE, n (%)	22 (51.2%)	20 (46.5%)	20 (48.8%)	26 (60.5%)	19 (44.2%)	26 (61.9%)	111 (52.4%)
System organ class/Preferred term, n (%)							
Infections and infestations	12 (27.9%)	15 (34.9%)	14 (34.1%)	17 (39.5%)	7 (16.3%)	11 (26.2%)	64 (30.2%)
COVID-19	5 (11.6%)	5 (11.6%)	8 (19.5%)	3 (7.0%)	3 (7.0%)	4 (9.5%)	23 (10.8%)
Nasopharyngitis	2 (4.7%)	1 (2.3%)	3 (7.3%)	8 (18.6%)	1 (2.3%)	2 (4.8%)	15 (7.1%)
Upper respiratory tract infection	1 (2.3%)	3 (7.0%)	0	0	0	2 (4.8%)	5 (2.4%)
Gastrointestinal disorders	5 (11.6%)	3 (7.0%)	4 (9.8%)	6 (14.0%)	4 (9.3%)	7 (16.7%)	24 (11.3%)
Diarrhoea	1 (2.3%)	2 (4.7%)	2 (4.9%)	4 (9.3%)	1 (2.3%)	1 (2.4%)	10 (4.7%)
Nervous system disorders	1 (2.3%)	0	2 (4.9%)	3 (7.0%)	3 (7.0%)	2 (4.8%)	10 (4.7%)
Headache	1 (2.3%)	0	1 (2.4%)	1 (2.3%)	3 (7.0%)	1 (2.4%)	6 (2.8%)
Respiratory, thoracic and mediastinal disorders	1 (2.3%)	1 (2.3%)	0	1 (2.3%)	3 (7.0%)	2 (4.8%)	7 (3.3%)
Cough	0	1 (2.3%)	0	1 (2.3%)	3 (7.0%)	1 (2.4%)	6 (2.8%)

- There were three serious AEs (n=1 each: COVID-19, infected cyst, suicide attempt; all on active drug and assessed as not related to study intervention by investigators). No dose-dependent relationship was observed.
- A low number of laboratory abnormalities occurred, and were comparable between placebo and JNJ-77242113 groups. There was no evidence of a dose-dependent increase in the occurrence of abnormalities.

AE=Adverse event; TEAE=Treatment-Emergent Adverse Event. *Includes all JNJ-77242113 treatment columns.
Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 25.1.

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Conclusions

- JNJ-77242113 is a first-in-class oral IL-23R antagonist peptide that demonstrated a significant dose-response in PASI 75 at Week 16 and significantly greater efficacy across all doses compared with placebo in patients with moderate-to-severe plaque PsO in a Phase 2b study
  - Significantly greater efficacy across all doses compared with placebo was also observed in the subgroup of patients with baseline scalp PsO
- JNJ-77242113 was generally well-tolerated in all treatment groups

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