Clinical Responses in Patients with Moderate-to-Severe Plaque Psoriasis Following Withdrawal and Re-treatment with Risankizumab or Switching from Ustekinumab to Risankizumab

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Presented at the Fall Clinical Dermatology Conference - 36th Anniversary • Las Vega, Nevada • October 12 – 15, 2017

INTRODUCTION

- Risankizumab is a humanized IgG1 monoclonal antibody that inhibits IL-23 by binding its p19 subunit.
- In a phase 2 trial, risankizumab demonstrated superiority over ustekinumab in patients with moderate-to-severe plaque psoriasis.

OBJECTIVE

- To assess the efficacy following drug withdrawal and re-treatment with risankizumab or switching from ustekinumab to risankizumab at week 24 of the open label extension (OLE).

MATERIALS & METHODS

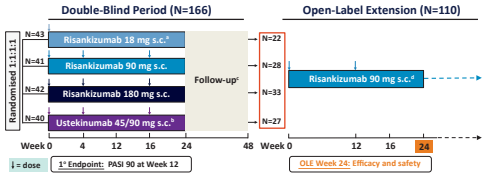
STUDY DESIGN AND PATIENTS

- In the phase 2 ("parent") study,[1] 166 patients with moderate-to-severe plaque psoriasis were randomized to receive subcutaneous injections of risankizumab (18 mg single dose at week 0, or 90 or 180 mg at weeks 0, 4, and 16) or ustekinumab (45 or 90 mg, based on body weight at weeks 0, 4, and 16).
- Patients were followed up through week 48 during the double-blind period.
- Patients (N=110) who completed 48 weeks in the parent study or who failed to achieve 50% improvement in psoriasis area and severity index (PASI 50) response between weeks 24 and 48 were eligible to enter the OLE (**Figure 1**).
- In this ongoing OLE, all patients received 90 mg risankizumab at baseline and every 12 weeks thereafter, regardless of their response level at the end of the parent study.
- Patients who failed to achieve PASI 90 responses in the OLE could increase their dose to 180 mg risankizumab starting at week 12; however, all patients received 90 mg risankizumab for the study period reported here.

EFFICACY AND SAFETY ANALYSES

- In this preliminary analysis, data through week 24 of the OLE from all entering patients were included.
- The following efficacy endpoints were assessed at week 24 of OLE:
  - PASI 90, 90% improvement in Psoriasis Area and Severity Index
  - PASI 100, 100% improvement in Psoriasis Area and Severity Index
  - sPGA 0/1, static Physician Global Assessment score of clear or almost clear
  - sPGA 0, static Physician Global Assessment score of clear
- Non-responder imputation (NRI) was used for missing efficacy data.
- Treatment-emergent adverse events (TEAE) were defined as any adverse events occurring after the first dose of the study drug in the OLE through 24 weeks of OLE and within 105 days after the last dose of study drug (if the patient discontinued treatment during OLE).

Figure 1. Study Design of Phase 2 Trial of Risankizumab in Psoriasis Patients



a. Placebo only at weeks 4 and 16. b. Used as per label (45 mg or 90 mg in patients with body weight ≤100 kg or >100 kg at randomization, respectively). c. Patients completing week 48 of the "parent" study (NCT02054481) were eligible to enroll in the OLE (NCT02203851). Patients who failed to achieve at least 50% improvement from baseline in PASI (<PASI 50) during the follow-up period (indicated by gray shading) were eligible to enter the OLE without completing the "parent" study. d. Patients who failed to achieve PASI 90 response in the OLE could increase their dose to 180 mg risankizumab starting at week 12; however, all patients received 90 mg risankizumab for the study period reported here. Abbreviations: OLE=open-label extension; PASI=Psoriasis Area and Severity Index; s.c.=subcutaneous.

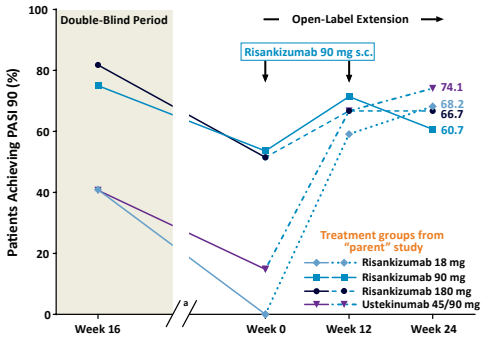
RESULTS

- Of the 166 patients randomized in the phase 2 ("parent") study, 110 (66.3%) patients enrolled in the OLE and received 90 mg risankizumab (**Figure 1**).

EFFICACY

- At OLE entry, PASI 90 response rates for patients previously treated with 18 mg, 90 mg, or 180 mg risankizumab or ustekinumab were 0% (0/22), 53.6% (15/28), 51.5% (17/33), and 14.8% (4/27), respectively, reflecting residual benefit from study drug in the parent study (**Figure 2**).
- At week 24 of the OLE, PASI 90 response rates increased to 68.2% (15/22), 60.7% (17/28), 66.7% (22/33), and 74.1% (20/27) in patients initially treated with 18 mg, 90 mg, or 180 mg risankizumab or ustekinumab, respectively.

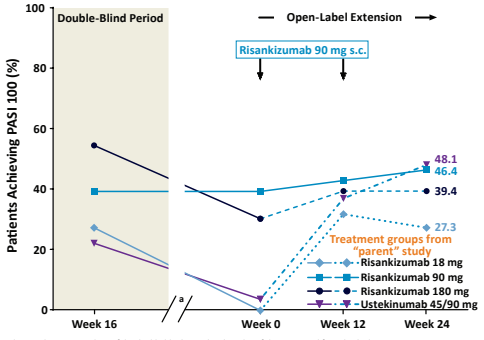
Figure 2. PASI 90 Responses Through Week 24 of OLE (NRI)



a. The time between week 16 of the double-blind period and week 0 of the OLE varied for individual patients. Abbreviations: NRI=non-responder imputation; OLE=open-label extension; PASI=Psoriasis Area and Severity Score; s.c.=subcutaneous.

- At OLE entry, PASI 100 response rates for patients previously treated with 18 mg, 90 mg, or 180 mg risankizumab or ustekinumab were 0% (0/22), 39.3% (11/28), 30.3% (10/33), and 3.7% (1/27), respectively, and increased to 27.3% (6/22), 46.4% (13/28), 39.4% (12/33), and 48.1% (13/27), respectively, at week 24 of the OLE (**Figure 3**).

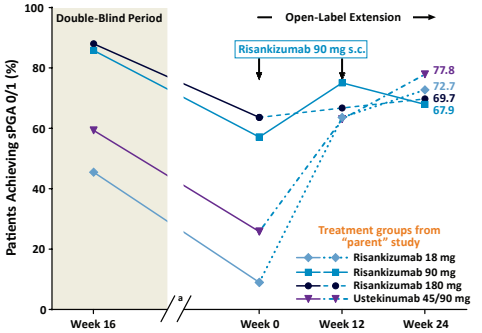
Figure 3. PASI 100 Responses Through Week 24 of OLE (NRI)



a. The time between week 16 of the double-blind period and week 0 of the OLE varied for individual patients. Abbreviations: NRI=non-responder imputation; OLE=open-label extension; PASI=Psoriasis Area and Severity Score; s.c.=subcutaneous.

- The proportions of patients previously treated with 18 mg, 90 mg, or 180 mg risankizumab or ustekinumab achieving static Physician's Global Assessment scores of 0 or 1 (sPGA 0/1) at OLE entry were 9.1% (2/22), 57.1% (16/28), 63.6% (21/33), and 25.9% (7/27), respectively, and improved to 72.7% (16/22), 67.9% (19/28), 69.7% (23/33), and 77.8% (21/27), respectively, at week 24 of the OLE (**Figure 4**).

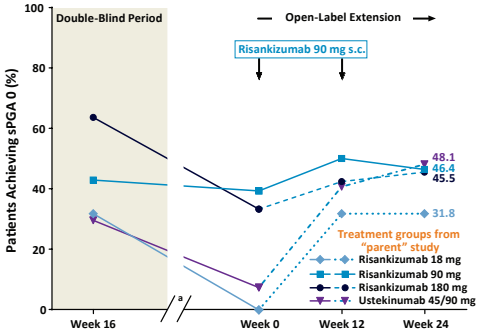
Figure 4. sPGA Scores of 0/1 Through Week 24 of OLE (NRI)



a. The time between week 16 of the double-blind period and week 0 of the OLE varied for individual patients. Abbreviations: NRI=non-responder imputation; OLE=open-label extension; s.c.=subcutaneous; sPGA=static Physician's Global Assessment.

- At OLE entry, sPGA scores of 0 for patients previously treated with 18 mg, 90 mg, or 180 mg risankizumab or ustekinumab were 0% (0/22), 39.3% (11/28), 33.3% (11/33), and 7.4% (2/27), respectively, and improved to 31.8% (7/22), 46.4% (13/28), 45.5% (15/33), and 48.1% (13/27), respectively, at week 24 of the OLE (**Figure 5**).

Figure 5. sPGA Scores of 0 Through Week 24 of OLE (NRI)



a. The time between week 16 of the double-blind period and week 0 of the OLE varied for individual patients. Abbreviations: NRI=non-responder imputation; OLE=open-label extension; s.c.=subcutaneous; sPGA=static Physician's Global Assessment.

SAFETY

- An overview of treatment-emergent AEs through 24 weeks of OLE for all patients who entered OLE is presented in **Table 1**.
  - Through 24 weeks of OLE, the overall rates of adverse events (AEs) and serious AEs were 38.2% (42 patients) and 2.7% (3 patients), respectively.
  - The most common AE (occurring in >5% of patients overall) was nasopharyngitis.

Table 2. Summary of Adverse Events Through Week 24 of OLE[a]

Adverse Events, n (%)	Risankizumab 18 mg N=22	Risankizumab 90 mg N=28	Risankizumab 180 mg N=33	Ustekinumab 45/90 mg N=27	Overall N=110
Any AEs	11 (50.0)	11 (39.3)	10 (30.3)	10 (37.0)	42 (38.2)
Drug-related AEs[b]	0	1 (3.6)	0	1 (3.7)	2 (1.8)
Any AE with toxicity of grade 3 or 4	1 (4.5)	1 (3.6)	0	2 (7.4)	4 (3.6)
AE leading to study drug discontinuation	0	0	0	0	0
AEs of special interest	0	0	0	0	0
Infections	5 (22.7)	7 (25.0)	6 (18.2)	4 (14.8)	22 (20.0)
Serious AEs[c]	1 (4.5)[e]	1 (3.6)[f]	1 (3.0)[g]	0	3 (2.7)
Death	0	0	0	0	0
Life-threatening	0	0	0	0	0
Persistent or significant disability or incapacity	0	0	0	0	0
Requires or prolongs hospitalization	1 (4.5)	1 (3.6)	1 (3.0)	0	3 (2.7)
Congenital anomaly or birth defect	0	0	0	0	0
Other medically important serious event	1 (4.5)	0	0	0	1 (0.9)
Most Common AEs[d]					
Nasopharyngitis	0	3 (10.7)	1 (3.0)	2 (7.4)	6 (5.5)
Upper respiratory tract infection	0	0	2 (6.1)	0	2 (1.8)

a. AEs through week 24 in all patients who entered OLE based on their initial treatment groups. b. Investigator assessed AE as possibly or probably related to study drug. c. A serious adverse event was defined as any adverse event that results in death, is immediately life-threatening, results in persistent or significant disability or incapacity, requires or prolongs hospitalization, is a congenital anomaly or birth defect, or is characterized on the basis of appropriate medical judgment as an important medical event that may jeopardize the patient and may require medical or surgical intervention. d. Most common AEs occurring in >5% of patients. e. One patient with basal cell carcinoma, carpal tunnel syndrome, and ulnar neuropathy. f. One patient with arthritis. g. One patient with thyroid goiter.
Abbreviations: OLE=open-label extension; AEs=adverse events.

CONCLUSIONS

- Switching treatment to risankizumab in patients initially treated with ustekinumab resulted in higher clinical responses, as measured by increases in PASI and sPGA responses at 24 weeks.
- Re-treatment with two doses (OLE baseline and week 12) of 90 mg of risankizumab following risankizumab withdrawal also resulted in return of substantial clinical benefit.
- The rates of adverse events through 24 weeks of OLE were as expected for the population and similar to those observed in the parent study.

REFERENCES

1. Papp KA, et al. *N Engl J Med* 2017; 376: 1551-60.

DISCLOSURES

KA Papp has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Amgen, Astellas, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Eli Lilly, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa-Hakko Kirin, Leo Pharma, MedImmune, Merck-Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Sanofi-Genzyme, Stiefel, Sun Pharma, Takeda, UCB, and Valeant. **A Blauvelt** has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, grants as an investigator from AbbVie, Aclaris, Allergan, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, UCB, Valeant, and Vidac. **M Flack** is a full-time employee of Boehringer Ingelheim. **Y Gu** and **EHZ Thompson** are full-time employees of AbbVie and may own stock/options. Boehringer Ingelheim funded the studies (NCT02054481 and NCT02203851), contributed to its design, and participated in data collection. AbbVie participated in data analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.

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