Distribution of Improvements in Psoriasis Area and Severity Index from the Phase 2 Trial of Risankizumab in Moderate to Severe Plaque Psoriasis

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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.[1]
- Response rates derived from dichotomizing a continuous variable at a certain threshold (eg, 90% improvement in Psoriasis Area and Severity Index, PASI 90) are often used as primary endpoints in clinical trials to demonstrate efficacy of investigational products.
- However, additional visualization of the cumulative distribution of responses can help assess the consistency of PASI improvement at the population level.

OBJECTIVE

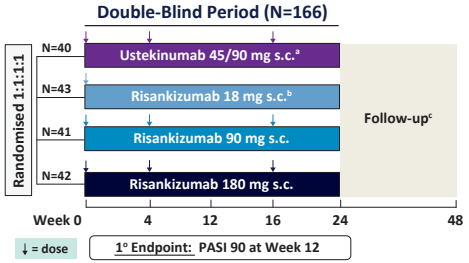
- The objective of this analysis was to examine the distribution of PASI responses in patients from the phase 2 trial treated with risankizumab versus ustekinumab.

MATERIALS & METHODS

STUDY DESIGN AND PATIENTS

- Patients (N=166) with moderate to severe plaque psoriasis were randomized to receive subcutaneous injections of risankizumab (18 mg single dose, 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, **Figure 1**).

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



a. Used as per label (45 mg or 90 mg in patients with body weight ≤100 kg or >100 kg at randomization, respectively). b. Placebo only at weeks 4 and 16. c. 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 (NCT02203851). Abbreviations: PASI=Psoriasis Area and Severity Index; q12w=every 12 weeks; s.c.=subcutaneous.

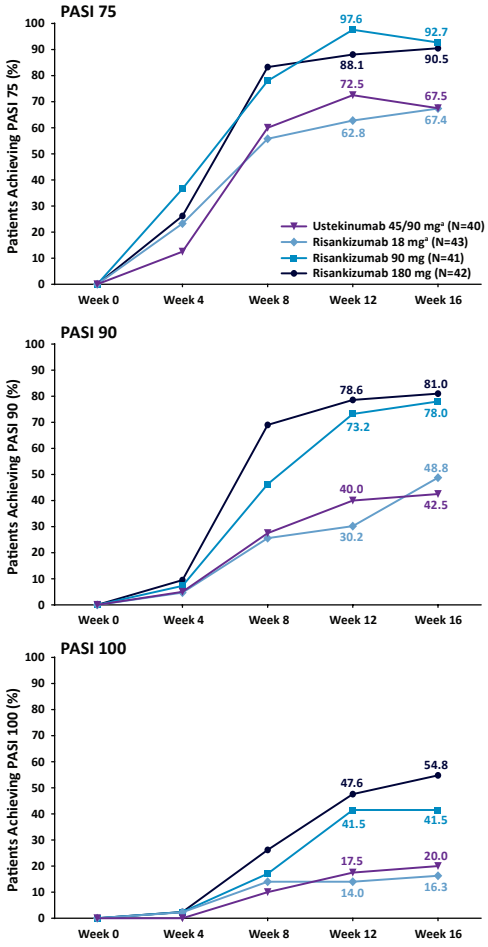
EFFICACY ANALYSES

- The proportions of patients achieving different levels of PASI responses were assessed at weeks 12 and 16 in an intent-to-treat population.
- Patients with a missing assessment were counted as non-responders for that assessment.
- Cumulative probability plots were generated to assess the distribution of changes from baseline in PASI score across treatment groups.

RESULTS

- The proportions of patients achieving PASI 75, PASI 90, and PASI 100 responses are shown in **Figure 2**.
- At week 12, the proportions of patients achieving the primary end point of PASI 90 response were 30.2% (13/43), 73.2% (30/41), and 78.6% (33/42) for 18 mg, 90 mg, and 180 mg risankizumab groups, respectively, compared with 40% (16/40) for ustekinumab-treated patients (**Figure 2**).[1]

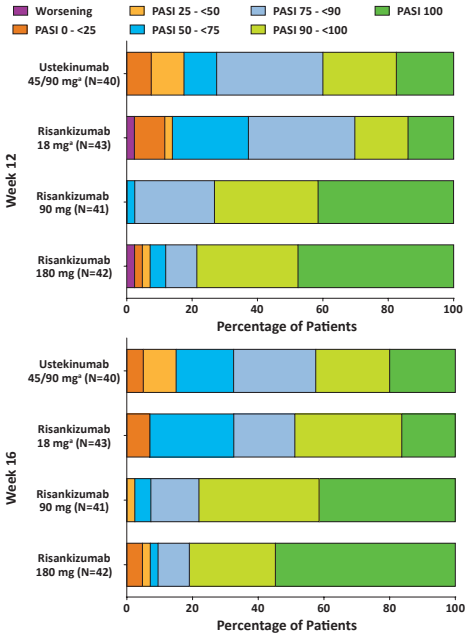
Figure 2. PASI 75, PASI 90, and PASI 100 Response Rates Through Week 16 (NRI)



[a]One patient each with missing response in risankizumab 18 mg and ustekinumab 45/90 mg groups, and were imputed as non-responders. Abbreviations: NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index.

- Patients treated with 90 mg or 180 mg of risankizumab achieved higher response rates across all levels of PASI improvement when compared with patients treated with 18 mg risankizumab (single dose) or ustekinumab (**Figure 3**).

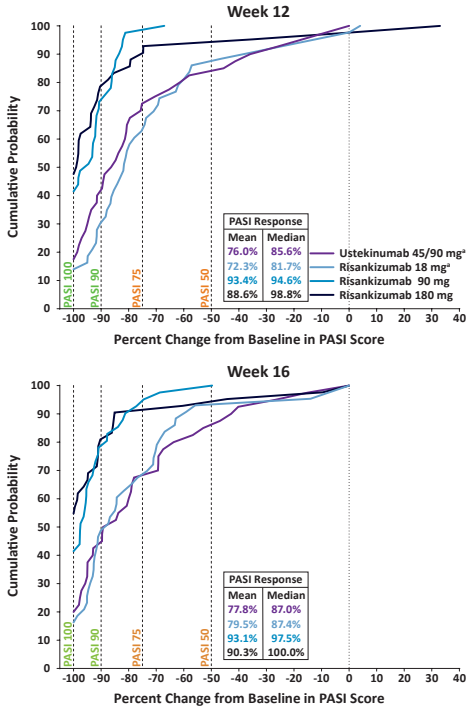
Figure 3. Distribution of Changes in PASI Responses from Baseline at Weeks 12 and 16 (NRI)



a. One patient each with missing response in risankizumab 18 mg and ustekinumab 45/90 mg groups, and were imputed as having no (0%) improvement. Abbreviations: NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index.

- The cumulative probability plot demonstrated that patients treated with 90 or 180 mg of risankizumab had a higher likelihood of achieving greater improvements from baseline in PASI score compared with patients treated with 18 mg risankizumab or ustekinumab (**Figure 4**).
  - Median values for improvement in PASI scores at week 12 were 81.7%, 94.6%, and 98.8% in patients treated with 18 mg, 90 mg, and 180 mg of risankizumab, respectively, compared with 85.6% in ustekinumab-treated patients.
  - At week 16, median values for improvement in PASI scores were 87.4%, 97.5%, and 100.0% in patients treated with 18 mg, 90 mg, and 180 mg of risankizumab, respectively, compared with 87.0% in ustekinumab-treated patients.

Figure 4. Cumulative Probability of Percent Change from Baseline in PASI Scores at Weeks 12 and 16 (NRI)



a. One patient each with missing response in risankizumab 18 mg and ustekinumab 45/90 mg groups, and were imputed as having no (0%) improvement. Abbreviations: NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index.

CONCLUSIONS

- The overall improvements in PASI scores at weeks 12 and 16 were higher in patients treated with 90 or 180 mg risankizumab compared with ustekinumab.
- Patients treated with 90 or 180 mg risankizumab showed a greater shift in PASI distribution towards PASI 90-100 response rates compared with ustekinumab-treated patients.

REFERENCES

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

DISCLOSURES

B Strober has received honoraria or fees for serving on advisory boards and as a consultant for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Janssen-Ortho, Leo Pharma, Maruho, Merck, Novartis, Pfizer, Sanofi/Regeneron, Sun Pharma, and UCB. He is a scientific director for the CORRONA-NPF Psoriasis Registry. **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. **M Flack** is a full-time employee of Boehringer Ingelheim. **Y Gu, EHZ Thompson,** and **WC Valdecantos** are full-time salaried employees of AbbVie and may own stock/options. Boehringer Ingelheim funded the study (NCT02054481), 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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