2.0 Synopsis

AbbVie Inc.	**Individual Study Table Referring to Part of Dossier:** **Volume:** **Page:**	**(For National Authority Use Only)**
Name of Study Drug: Risankizumab (BI 655066, ABBV-066)		
Name of Active Ingredient: Risankizumab		
Title of Study: A Randomized, Open-Label Study to Assess Efficacy and Safety of Two Different Dose Regimens of Risankizumab Administered Subcutaneously in Japanese Subjects with Generalized Pustular Psoriasis or Erythrodermic Psoriasis		
Investigator: [redacted] MD, PhD		
Study Sites: 9 sites in Japan		
Publications: None		
Studied Period (Years): First Subject First Visit: 26 January 2017 Last Subject Last Visit: 18 November 2020	**Phase of Development:** 3/Post-Marketing Clinical Study	
Objectives: The objective of this study was to investigate the safety and efficacy of 2 different dose regimens of risankizumab for Japanese subjects with generalized pustular psoriasis (GPP) or erythrodermic psoriasis (EP).		
Methodology: This Phase 3 randomized, open-label, parallel-design study compared 2 different dose regimens of risankizumab (75 mg and 150 mg) in subjects with GPP or EP. The primary efficacy endpoint was evaluated at Week 16. Additional endpoints were evaluated at Week 52. Subjects were to continue to receive treatment through Week 160 and were to be followed through at least 20 weeks after the last injection of study drug. This clinical study report presents all the data for the study through the end of study. After marketing approval of risankizumab in Japan (March 2019), the study continued as a post-marketing study.		
Number of Subjects (Planned and Analyzed): Approximately 16 subjects, 8 with GPP and 8 with EP, were planned for this study; 17 were analyzed.		

Diagnosis and Main Criteria for Inclusion:

Subjects enrolled in this study were to be adults ≥ 20 years of age with a clinical diagnosis of GPP for at least 60 days or of EP and were candidates for systemic therapy or phototherapy.

Subjects with GPP were to have ≥ 10% of the body surface area (BSA) involvement for erythema area with pustules and a Japanese Dermatological Association (JDA) total score < 14. Subjects with EP were to have ≥ 80% BSA involvement for inflammatory erythema. Subjects were to be excluded if they had an active ongoing inflammatory disease other than GPP or EP that might confound trial evaluations; had been diagnosed with medication-induced or medication-exacerbated EP; were taking restricted medications, had chronic or relevant acute infections such as human immunodeficiency virus, viral hepatitis, or active tuberculosis (TB); or prior exposure to risankizumab.

Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number:

Study Drug	Dosage Form	Formulation	Manufacturer	Bulk Lot Number
Risankizumab	Injection solution for subcutaneous (SC) use	Injection solution of risankizumab in 4.4 mM succinate buffer, pH 6.2, 225 mM sorbitol and 0.02% polysorbate 20, presented in a 1-mL prefilled syringe (PFS) with 0.87 mL (total dispensed volume was 0.83 mL).	Boehringer Ingelheim Pharma GmbH & Co. KG	16-005253 17-005977 19-001855

Duration of Treatment:

Up to 160 weeks

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number:

Not applicable

Criteria for Evaluation

Efficacy:

For GPP subjects, the primary endpoint was the proportion of subjects achieving a GPP Clinical Response according to JDA total score, defined as at least "Slightly Improved" in the overall improvement rating from baseline at Week 16. For EP subjects, the primary endpoint was the proportion of subjects achieving an EP Clinical Response, defined as at least "Minimally Improved" in Clinical Global Impression-Global Improvement (CGI-GI) at Week 16.

Secondary endpoints for GPP subjects included the following:

- Proportion of subjects achieving a GPP Clinical Response at Week 52
- Proportion of subjects achieving ≥ 90% reduction from baseline Psoriasis Area and Severity Index (PASI) score (PASI 90) at Week 16
- Proportion of subjects achieving PASI 90 at Week 52

Criteria for Evaluation (Continued)

Efficacy (Continued):

Secondary endpoints for EP subjects included the following:

- Proportion of subjects achieving an EP Clinical Response at Week 52
- Proportion of subjects achieving PASI 90 at Week 16
- Proportion of subjects achieving PASI 90 at Week 52

Other efficacy endpoints for GPP subject included the following:

- Proportion of subjects achieving a GPP Clinical Response, defined at least "Slightly Improved" according to JDA total score in the overall improvement rating from baseline.
- Change from baseline in each of the JDA component scores
- Change and Percent change from baseline in JDA score
- Change and Percent change from baseline in PASI
- Change from baseline in BSA
- Proportion of subjects achieving PASI 50/75/90/100 response
- Proportion of subjects achieving Dermatology Life Quality Index (DLQI) of 0/0 or 1
- Change from baseline in DLQI
- Proportion of subjects achieving at least 2 grades of improvement in Physician's Global Assessment of Generalized Pustular Psoriasis (PGA-GPP).

Other efficacy endpoints for EP subject included the following:

- Proportion of subjects achieving an EP Clinical Response, defined at least "Minimally Improved" in CGI-GI for EP
- Proportion of subjects achieving at least "Much Improved" in CGI-GI for EP
- Percent change from baseline in PASI
- Change from baseline in PASI
- Proportion of subjects achieving PASI 50/75/90/100 response
- Change from baseline in BSA
- Proportion of subjects achieving DLQI of 0/0 or 1
- Change from baseline in DLQI

Pharmacokinetics:

Risankizumab plasma concentrations were determined. For immunogenicity assessment, anti-drug antibodies (ADAs) and neutralizing antibodies (NAb) against risankizumab were determined.

Safety:

Safety evaluations included collection of adverse events (AEs), clinical laboratory values, physical examinations, and local tolerability.

Statistical Methods

Efficacy:

Efficacy analyses were based on the intent-to-treat principle, comprising all subjects who were randomized. Treatment effect was evaluated based on a two-sided significance level of 0.05.

Pharmacokinetics:

Descriptive statistics for risankizumab plasma concentrations for each sampling time (study visit) were calculated. Immunogenicity (ADA) data were summarized during Weeks 0 to 100 as well as by planned visit. Risankizumab plasma concentrations were compared by ADA (positive or negative) by visit.

Safety:

Safety analyses included reporting of AEs, laboratory, physical examination (including vital signs and 12-lead electrocardiogram), and local tolerability. Safety summaries are provided using the Safety Analysis Set, which consists of all subjects who received at least 1 dose of study medication. For safety parameters, the treatment that was actually used by the subject was applied in the analysis (an as-treated analysis). All AEs described in this report were considered treatment-emergent, defined as any event with an onset or worsening after the first dose of study drug and with an onset date within 140 days after the last dose of study drug in the analysis period, or prior to the first dose in the subsequent period for subjects who entered into the subsequent period.

Summary/Conclusions

Efficacy Results:

All subjects achieved a clinical response in both the GP and EP substudies at Week 16. At Week 52, in both the GPP and EP substudies, all subjects who continued on risankizumab maintained a clinical response. A majority of subjects in both the GP and EP substudies achieved a clinically meaningful response for the other efficacy endpoints. For most subjects who continued on treatment, these responses were maintained through Week 160.

Pharmacokinetic and Immunogenicity Results:

Following administration of risankizumab 75 mg and 150 mg SC doses at Weeks 0, 4 and every 12 weeks (q12w) thereafter in subjects with GPP and EP, steady state was approximately achieved by Week 16. Risankizumab trough plasma concentrations were approximately dose proportional across the 75 mg and 150 mg SC doses evaluated in the study. With the 150 mg SC regimen, risankizumab plasma concentrations were comparable to those previously observed in the global Phase 3 trials of risankizumab in subjects with plaque psoriasis.

In subjects who received at least 1 dose of risankizumab during Weeks 0 to 100, the incidence of ADAs to risankizumab (treatment emergent) was approximately 24% (4/17) with only 1 subject positive for NAb (6%; 1/17). Development of ADAs did not appear to have an impact on risankizumab plasma exposures.

Safety Results:

Though the interpretation of rates of SAEs, AEs leading to discontinuation of study drug, and severe AEs in this study of Japanese subjects are limited due to the small sample size, no specific safety concerns were identified. There was 1 death due to an event of cardiac failure; the event was adjudicated as a CV event and was considered unrelated to the study drug by investigator and sponsor.

A comprehensive review of laboratory and vital sign results, including mean changes from Baseline and potentially clinically significant values, did not reveal safety concerns.

Summary/Conclusions (Continued)

Conclusions:

Both risankizumab dosage regimens produced clinically meaningful results for both GPP and EP subjects and all subjects who continued treatment in the study maintained Week 16 results at Week 52. Overall, long-term treatment with risankizumab demonstrated durable high rates of skin clearance in subjects with GPP and EP. All subjects who continued on risankizumab through Week 160 maintained a clinical response. In this study, risankizumab was well tolerated and had an acceptable safety profile at both dosage levels. No Japanese-specific safety issues were identified.