Risankizumab
M16-009 Abbreviated Clinical Study Report
R&D/18/0553

2.0 Synopsis

<table>
<thead>
<tr>
<th>AbbVie Inc.</th>
<th>Individual Study Table Referring to Part of Dossier:</th>
<th>(For National Authority Use Only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of Study Drug:</td>
<td>Risankizumab (BI 655066, ABBV-066)</td>
<td></td>
</tr>
<tr>
<td>Name of Active Ingredient:</td>
<td>Risankizumab</td>
<td></td>
</tr>
<tr>
<td>Title of Study:</td>
<td>An Open Label Extension Trial Assessing the Safety and Efficacy of BI 655066/ABBV-066/Risankizumab Administered Subcutaneously in Patients with Moderate to Severe Chronic Plaque Psoriasis</td>
<td></td>
</tr>
<tr>
<td>Rationale for Abbreviated Clinical Study Report:</td>
<td>With the acquisition of risankizumab and transition of responsibilities to AbbVie, it was planned to transfer subjects in Boehringer Ingelheim-sponsored Study M16-009 (Study 1311.13) into Study M15-997, an open-label extension (OLE) study sponsored and conducted by AbbVie. Because Study M16-009 has been closed and its subjects and data are being transferred to another study (Study M15-997), Study M16-009 data are being summarized in an abbreviated clinical study report (CSR).</td>
<td></td>
</tr>
<tr>
<td>Coordinating Investigator:</td>
<td>Kim Alexander Papp, MD</td>
<td></td>
</tr>
<tr>
<td>Study Sites:</td>
<td>A total of 22 sites in 4 countries (Canada, France, Germany, and United States) enrolled subjects in Study M16-009. A total of 24 sites in 4 countries were planned, based on the number of sites from the preceding Study 1311.2.</td>
<td></td>
</tr>
<tr>
<td>Publications:</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Studied Period (Years):</td>
<td></td>
<td>Phase of Development: 2</td>
</tr>
<tr>
<td>First Subject First Visit:</td>
<td>20 November 2014</td>
<td></td>
</tr>
<tr>
<td>Last Subject Last Visit:</td>
<td>04 September 2018</td>
<td></td>
</tr>
<tr>
<td>Objectives:</td>
<td>The primary objective of Study M16-009 was to investigate the safety of risankizumab in subjects with moderate to severe chronic plaque psoriasis who were receiving long-term treatment. Additional study objectives were to further investigate the long-term efficacy, tolerability, pharmacokinetics, pharmacodynamics, and immunogenicity of risankizumab.</td>
<td></td>
</tr>
</tbody>
</table>


Methodology:
This Phase 2, multicenter, OLE study assessed the safety and efficacy of risankizumab in subjects with moderate to severe chronic plaque psoriasis who had successfully completed the preceding BI study, Study 1311.2. Subjects who had successfully completed Study 1311.2 and met the eligibility criteria for Study M16-009 (Study 1311.13) had the option to sign the informed consent form (ICF) and enter Study M16-009. Subjects were allowed to have Extended Visit 1 (EV1) of Study M16-009 as a combined visit on the same day as the end of study (EOS) visit for Study 1311.2 or preferably within an interim period of 6 weeks maximum thereafter.
Subjects in Study M16-009 were scheduled to receive risankizumab 90 mg subcutaneously (SC) beginning at EV1 and then every 12 weeks (q12w) during the study. At Extended Visit 2 (EV2), if the subject had a lack of response (defined as < 90% improvement in Psoriasis Area Severity Index [PASI 90]), the subject's dose could be increased to risankizumab 180 mg for the remainder of the study.

Number of Subjects (Planned and Analyzed):
100 subjects planned; 110 analyzed

Diagnosis and Main Criteria for Inclusion:
Subjects enrolled in this study had moderate to severe chronic plaque psoriasis and had successfully completed the preceding Study 1311.2. Subjects who had experienced any drug-related serious adverse event (SAE); developed guttate, erythrodermic or pustular psoriasis, or drug-induced psoriasis (as diagnosed by the investigator); were taking restricted medications; had chronic or relevant acute infections (e.g., human immunodeficiency virus [HIV], viral hepatitis, or active tuberculosis [TB]); or developed active or suspected malignancy during the preceding study were excluded.

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

<table>
<thead>
<tr>
<th>Study Drug</th>
<th>Dosage Form</th>
<th>Formulation</th>
<th>Manufacturer</th>
<th>Bulk Lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risankizumab</td>
<td>Injection solution for SC use</td>
<td>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 syringe prefilled with 0.87 mL. Dispensed volume is ≥ 0.83 mL.</td>
<td>BI Pharma &amp; Co. KG</td>
<td>E3744S03</td>
</tr>
</tbody>
</table>

Duration of Treatment:
The planned duration of treatment is up to 4 years.

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number:
Not applicable.
Criteria for Evaluation

Efficacy:
The following key efficacy variables were summarized at Week 48:

- Proportion of subjects achieving ≥ 90% reduction in PASI score (PASI 90)
- Proportion of subjects achieving an sPGA score of clear or almost clear
- Proportion of subjects achieving ≥ 50% reduction in PASI score (PASI 50)
- Proportion of subjects achieving ≥ 75% reduction in PASI score (PASI 75)
- Proportion of subjects achieving 100% reduction in PASI score (PASI 100)
- Proportion of subjects achieving an sPGA score of clear.

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

Safety:
Safety was assessed by reporting of adverse events (AEs), laboratory data, physical examinations (including vital signs), and local tolerability.

Statistical Methods

Efficacy:
Since Study M16-009 is a single-arm, open-label continuation study, no statistical tests were performed, and only summary statistics were to be provided. Data from this study used the Baseline from lead-in Study 1311.2 and were summarized by the treatment groups from Study 1311.2. All efficacy analyses were performed for the intent-to-treat (ITT) population, defined as all subjects who received at least 1 dose of study drug in the study, and based on observed cases (OC); therefore, subjects who did not have an evaluation at the analysis time point were not included. No missing data imputation was applied.

Pharmacokinetic:
Individual concentration-time data with descriptive statistics for trough concentrations were determined for this study. Summary of incidence of ADA and NAb was also provided.

Safety:
Safety analyses included adverse events, clinical laboratory, local tolerability, and vital sign measurements. Safety summaries are based on the Safety Population, defined as the same as the ITT population for this study. All AEs described in this report, except for 1 pretreatment SAE, were considered treatment-emergent, defined as any event with an onset after the first dose of risankizumab in Study M16-009 and with an onset date within 105 days after the last dose of study drug in the analysis period. A listing and descriptive statistics of clinical laboratory and vital sign values over time and extreme abnormal values on treatment were also provided. Local tolerability was assessed by the investigator and summarized.
Summary/Conclusions

Efficacy Results:
Subject response to risankizumab achieved in lead-in Study 1311.2 was generally maintained or improved in Study M16-009, as demonstrated by the proportion of subjects with PASI 90/100 response and responses of sPGA clear/sPGA clear or almost clear, both at Week 48 and at the majority of dosing visits. Improvements in subjects' quality of life were also observed, based on increases in the proportion of subjects achieving DLQI response of 0 or 1 at the majority of dosing visits and decreases in subjects' Baseline DLQI scores at all dosing visits. For those subjects with diagnosed or suspected psoriatic arthritis, improvements were observed in pain VAS scores at a majority of dosing visits.

Pharmacokinetic Results:
Following administration of risankizumab 90 mg or 180 mg SC doses every 12 weeks in this study, risankizumab plasma exposures were consistent with those observed in the randomized controlled lead-in Study 1311.2. The incidence of ADAs and NAbs to risankizumab (treatment-emergent) was 34% (37/109) and 22% (24/109), respectively. Development of ADAs did not have a consistent, apparent impact on risankizumab plasma exposures.

Safety Results:
Risankizumab was safe and well-tolerated in Study M16-009. While over 75% of subjects in this OLE study experienced AEs, the majority of events were mild to moderate in severity and were considered to have no reasonable possibility of being related to study drug. There were no subject deaths and no AEs leading to discontinuation of study drug. Fourteen (12.7%) subjects experienced ≥ 1 SAE. Of these, 2 subjects had SAEs that were considered to have a reasonable possibility of being related to study drug, but neither subject discontinued from study drug as the result of SAEs. Few subjects experienced AEs in pre-specified areas of safety interest, and there were no notable changes in laboratory, vital signs, or local tolerability assessments during the study.

Conclusions:
Long-term treatment with risankizumab in the Phase 2 OLE Study M16-009 was shown to maintain or improve efficacy results previously achieved in subjects with moderate to severe plaque psoriasis in Study 1311.2. Risankizumab was safe and well-tolerated in Study M16-009. Overall, the benefit-risk profile for risankizumab was favorable and consistent with that shown in the lead-in Study 1311.2.