Disclosure of Interests: Philip J Mease Consultant of: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Immagen, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Grant/research support from: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Immagen, Janssen, Novartis, Pfizer, SUN Pharma, and UCB, Aboole Cottrell Shareholder of: Xbiotech (stock options only), Consultant of: Anaptys Bio, Aventis Therapeutics, Beiersdorf, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Inoya, Janssen, LEO Pharma, Novartis, Pfizer, Sun Pharmaceuticals, UCBI, Grant, research support from: Boehringer Ingelheim, Janssen, Novartis, Sun Pharmaceuticals, UCBI, and Xbiotech, lain McInnes Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Peter Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Peter Rahman Speakers bureau: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB, Grant/research support from: Janssen and Novartis, Alex Kollmeier Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, Xie Lu Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, Yusang Jiang Employee of: Cylet, Inc., Shihong Sheng Shareholder of: Johnson & Johnson, Employee of: Janssen Research and Development, LLC, may Shai Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Soumya D Chakravarty Employee of: Janssen Scientific Affairs, LLC, Frederic Lave Shareholder of: Johnson & Johnson, Employee of: Janssen Global Services, LLC, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyno, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB Pharma, Employee of: Director of Imaging and Rheumatology BV

BACKGROUND: RZB, a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits the p19 subunit of the human cytokine interleukin-23, is being investigated as a treatment for PsA.

OBJECTIVE: Evaluate longer-term safety and efficacy of RZB in patients with active PsA who experienced inadequate response or intolerance to 1 or 2 biologic therapies and/or to at least 1 csDMARD therapy.

METHODS: KEEPSAKE 2 (NCT03671148) is an ongoing, phase 3, multicenter study that includes a screening period; a 24-week double-blind, randomized, placebo-controlled, parallel-group period (period 1); and an open-label extension period (period 2). Eligible patients were ≥18 years of age with active PsA (symptom onset ≥6 months before screening, meeting Classification Criteria for PsA [CASPAR], and ≥5 tender and ≥5 swollen joints) and had inadequate response or intolerance to 1 or 2 biologic therapies (Bio-IR) and/or ≥1 conventional synthetic disease modifying antirheumatic drug (csDMARD-IR). Patients received RZB 150 mg or placebo (PBO) at weeks 0, 4, and 16 (1:1). The primary endpoint was the proportion of patients achieving ACR20 response at week 24. Period 2 started at week 24, and patients were switched to receive open-label RZB 150 mg every 12 weeks through week 108.

RESULTS: Efficacy and safety were analyzed in patients who received ≥1 dose of study drug through week 52. Mixed-effect model with repeated measures and nonresponder imputation methods were used to assess continuous and binary variables, respectively. Treatment-emergent adverse events (TEAEs) were summarized using exposure-adjusted event rates (EAERs; events/100 patient-year [PY]).

CONCLUSION: Continuous RZB treatment resulted in maintained efficacy responses with a consistent safety profile through 52 weeks of treatment in patients with active PsA who were Bio-IR and/or csDMARD-IR.

Acknowledgements: AbbVie, Inc. participated in the study design; study research; collection, analysis, and interpretation of data. AbbVie funded the study and provided writing support for this article. Medical writing assistance, funded by AbbVie, was provided by Jay Parekh, PharmD, of JB Ashlin.

Disclosure of Interests: A. Ostor, F. Van den Bosch, C. Asnal, R. Blanco, J. Aelion, W. Lu, Z. Wang, A. M. Soliman, A. Eldred, B. Padilla, A. Kivitz, Monash University, Cabriini Hospital, Melbourne, Australia; Department of Rheumatology, Ghent University, Ghent, Belgium; Proisy Medical Research, K Papp, Clinical Research, Waterlo, Canada; DOM Centro, de Reumatologia, Buenos Aires, Argentina; Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain; Arthritis Clinic, West Tennessee Research Institute, Jackson, United States of America; AbbVie Inc., Immunology, North Chicago, United States of America; Arthritis Center, Clinical Research, Duncansville, United States of America


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RESULTS: At week 24, 58.5% of patients who were randomized to RZB and 55.7% of patients who were randomized to PBO and then switched to RZB at week 24 achieved ACR20. In patients with ≤30% of body surface area affected at baseline, 50.5% of RZB-treated patients (N=123) and 10.2% of PBO-treated patients (N=119) achieved PASI 90 at week 24. At week 52, 64.2% of patients randomized to RZB and 56.2% of patients randomized to PBO and then switched to RZB at week 24 achieved PASI 90. For other efficacy measures, similar trends were observed. RZB was well tolerated through 52 weeks of treatment, and EAERs of adverse events were stable between weeks 24 and 52. At the week 52 data cutoff (19 April 2021), the total EAER of any TEAE in patients receiving RZB was 184.2/100 PY.

CONCLUSION: Continuous RZB treatment resulted in maintained efficacy responses with a consistent safety profile through 52 weeks of treatment in patients with active PsA who were Bio-IR and/or csDMARD-IR.

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Background: Gusekumab (GUS), a selective IL-23p19 inhibitor, showed greater mean improvements in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores vs placebo (PBO) at Week (W) 24 in patients (pts) with active PsA and investigator-confirmed sacroiliitis in pooled post hoc analyses of data from phase 3 DISCOVER (D)-1 & 2 trials. Improvements in symptoms of axial involvement were maintained through 1 year.1

Objectives: To assess maintenance of GUS effect on symptoms of axial involvement in biologic-naive PsA pts with investigator-confirmed sacroiliitis through 2 years of D-2.

Methods: In D-2, 739 bio-naïve pts with active PsA (≥5 swollen + ≥5 tender joints, CRP > 1 mg/dL, despite standard therapy) were randomized 1:1:1 to GUS 100 mg every 4 W (Q4W, n=245), GUS 100 mg at W0, W4, then Q8W (n=248), or PBO (n=246) with PBO→GUS 100 mg Q4W at W24. Pts with investigator-identified axial symptoms and sacroiliitis (prior x-ray or MRI, or pelvic x-ray at screening) were evaluated. Efficacy was assessed by changes in BASDAI, modified BASDAI (mBASDAI, excluding Q3 [peripheral joint pain]), and BASDAI Q2 (Spinal Pain) scores, and proportions of pts achieving BASDAI 50, Spinal Pain score ≤2, and AS Disease Activity Score (ASDAS) LDA and Spinal Pain responses through W100. Through W24, pts with met treatment failure criteria or had missing data were considered nonresponders.

At W24, missing data were imputed as nonresponse for binary endpoints or no change from baseline for continuous endpoints (nonresponder imputation [NRI]). Axial-related outcomes were also summarized by HLA-B27 status (+/-).

Results: 246 pts had investigator-confirmed sacroiliitis. Baseline characteristics were similar across treatment groups (62% male; mean age 44.4 years; mean BASDAI scores 6.5-6.6). At W24, LS mean/mean changes in BASDAI (-2.4/-2.6) and ASDAS (-1.3/-1.5) scores were greater in GUS- vs PBO-treated pts. Improvements were maintained through W100 in GUS-treated pts: BASDAI, -3.1; Spinal Pain, -3.1; mBASDAI, -3.1; ASDAS, -1.7. Response patterns were similar for BASDAI 50 response rates in GUS-treated pts (W24 38-40%; W100 49-54%). At W24, GUS-treated pts had higher response rates for achievement of ASDAS inactive disease, major improvement, and clinically important improvement vs PBO; response rates (NRI) were maintained, or in some cases further increased, at 2 years. Results were consistent for achievement of ASDAS LDA and Spinal Pain score ≤2 (data not shown). BASDAI-related improvements in axial symptoms through W100 were generally consistent in HLA-B27+/- pts (data not shown).

Conclusion: In bio-naive PsA pts with active PsA and investigator-confirmed sacroiliitis, GUS provided durable improvements in axial symptoms through W100, with substantial proportions of pts achieving and maintaining clinically meaningful improvements.

REFERENCES:

Table 1. Axial symptom assessments through W100 in PsA pts with investigator-confirmed sacroiliitis in DISCOVER-2 (NRI)

<table>
<thead>
<tr>
<th>Change in BASDAI score</th>
<th>W24, LS mean 95% CI</th>
<th>W24, MED mean 95% CI</th>
<th>W100, MED mean 95% CI</th>
<th>W24, MED mean 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Change in mBASDAI (excludes Q3) score</td>
<td>W24, LS mean 95% CI</td>
<td>W24, MED mean 95% CI</td>
<td>W100, MED mean 95% CI</td>
<td>W24, MED mean 95% CI</td>
<td>W24, MED mean 95% CI</td>
<td>W100, MED mean 95% CI</td>
</tr>
<tr>
<td>Change in Spinal Pain (ASDAS (Q2) score)</td>
<td>W24, LS mean 95% CI</td>
<td>W24, MED mean 95% CI</td>
<td>W100, MED mean 95% CI</td>
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GUS Q4W N=82 GUS Q8W N=68 PBO→GUS Q4W N=96
Change in BASDAI score
W24, LS mean (95% CI) -2.5 (-2.9, -2.0) -2.4 (-3.0, -1.8) -1.2 (-1.7, -0.7)
Mean (SD) -2.5 (2.0) -2.6 (2.4) -1.4 (2.4)
W52, mean (SD) -2.2 (2.3) -2.9 (2.6) -1.9 (2.6)
W100, mean (SD) -3.0 (2.3) -3.1 (2.6) -3.3 (2.6)
Change in mBASDAI (excludes Q3) score
W24, LS mean (95% CI) -2.4 (-2.9, -1.9) -2.4 (-2.9, -1.8) -1.2 (-1.7, -0.7)
Mean (SD) -2.5 (2.1) -2.6 (2.5) -1.3 (2.3)
W52, mean (SD) -2.7 (2.6) -2.6 (2.5) -2.9 (2.4)
W100, mean (SD) -3.3 (2.6) -3.1 (2.6) -3.0 (2.4)
Change in Spinal Pain (ASDAS (Q2) score)
W24, LS mean (95% CI) -2.2 (-2.7, -1.7) -2.3 (-2.9, -1.7) -0.9 (-1.5, -0.4)
Mean (SD) -2.3 (2.6) -2.5 (2.8) -1.1 (2.5)
W52, mean (SD) -2.5 (2.7) -2.5 (2.7) -2.5 (2.7)
W100, mean (SD) -2.8 (2.7) -3.1 (2.8) -3.0 (2.8)
Change in ASDAS score
W24, LS mean (95% CI) -1.3 (-1.6, -1.1) -1.3 (-1.6, -1.1) -0.6 (-0.8, -0.4)
Mean (SD) -1.4 (1.0) -1.5 (1.3) -0.7 (1.1)
W52, mean (SD) -1.5 (1.1) -1.5 (1.3) -1.5 (1.3)
W100, mean (SD) -1.6 (1.2) -1.7 (1.2) -1.6 (1.2)