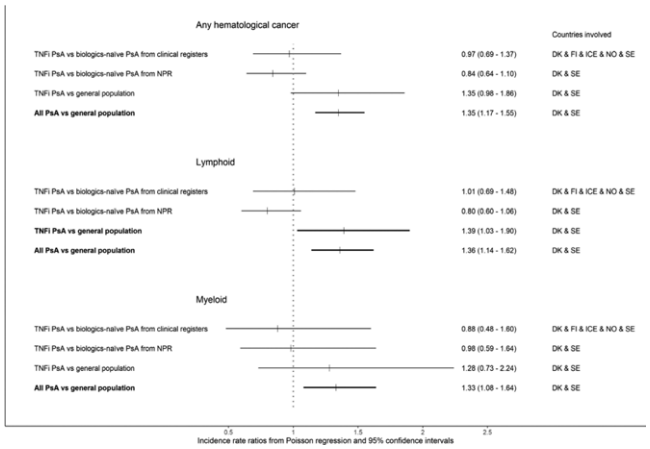

Figure 1. Pooled incidence rate ratios (IRRs) (95% CI) of haematological malignancy overall and by lymphoid and myeloid types, in first ever TNFi treated versus biologics-naïve patients with PsA, and versus general population comparators. **Legend:** Lymphoid malignancies include international classification of diseases (ICD) 10 codes C81-86, C88, C90-91. Myeloid malignancies include ICD10 codes C92-95, D45-D46, D47.1, D47.3-5. Incidence rate ratios adjusted for age (18-55, 56-65, 66-70, >70 years), sex, calendar period (2006-2010, 2011-2019) and country, and using robust standard errors.

Conclusion: In this large five-country cohort study, we did not observe any increased risk of haematological malignancies overall, nor for lymphoid and myeloid types, in patients with PsA treated with TNFi. By contrast, there were signals of a moderately increased underlying risk of haematological malignancies, both of lymphoid and myeloid types, in patients with PsA overall as compared to the general population. The findings are of importance from a patient information perspective.

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OP0258

IZOKIBEP (ABY-035) IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS – 16-WEEK RESULTS FROM A PHASE 2 STUDY

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Background: Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory disease with heterogenous musculoskeletal manifestation (arthritis, spondylitis, enthesitis, dactylitis) and extra-musculoskeletal manifestation (skin and nail psoriasis). In addition, PsA is commonly associated with comorbidities such as metabolic syndrome and cardiovascular diseases where IL-17 is a key driver of this disease.

Izokibep is a unique IL-17A inhibitor with extraordinary potency and small molecular size designed to overcome the limitations of monoclonal antibodies such as poor tissue distribution.

Here, we report 16-week phase 2 results in patients with active PsA.

Objectives: To assess efficacy, safety, pharmacokinetics and immunogenicity of izokibep versus placebo.

Methods: This is a prospective, multicenter, randomized, double-blind, placebo-controlled, parallel-groups, dose-finding trial studying bi-weekly 80 mg or 40 mg izokibep administered subcutaneously versus placebo until Week 16 (Period 1) and dose-controlled treatment until Week 46 (Period 2). PsA patients had to have ≥3 swollen and ≥3 tender joints of the 66/68 joint count, and an inadequate response to previous NSAIDs, csDMARDs or TNF inhibitor therapy. The primary endpoint was to evaluate ACR50 responses of 80 mg bi-weekly versus placebo at Week 16. Key secondary endpoints were ACR20/70, MDA, DAS28, DAPSA, SPARCC, LDI, PASI as well as tolerability and safety. Efficacy outcome measures were assessed in all patients who received at least one dose of study treatment. This trial is registered with ClinicalTrials.gov, NCT04713072.

Results: 135 patients were randomized and treated between June 2020 and July 2021 in 22 European sites located in Austria, Belgium, Czech Republic, Germany, Hungary, Poland and Spain.

At baseline, patients had a mean age of 48.5 (SD 12.0) years, a mean BMI of 29.0 (SD 4.8) kg/m^2, a mean swollen joint count (SJC) of 9.9 (SD 6.6), and a mean tender joint count (TJC) of 16.7 (SD 10.4). The mean PsA disease duration was 7.1 (SD 7.8) years. 13% failed previous TNF inhibitor treatment and 80% received a concomitant csDMARD.

At Week 16, the confirmatory primary endpoint ACR50 response rate was met (p=0.0003). ACR50 response rate was 52% in the 80 mg group, 48% in the 40 mg and 13% in the placebo group. The ACR20/50/70 response rates up to Week 16 by treatment group are presented in Figure 1.

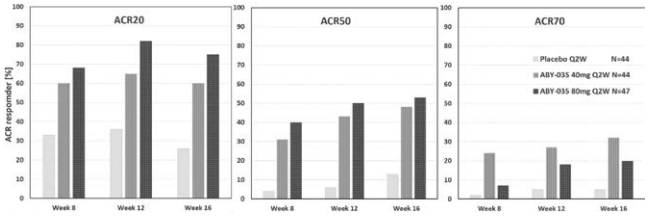

Figure 1. ACR20/50/70 response rates

SJC and TJC rapidly decreased with active treatment as indicated in Table 1.

Table 1. SJC and TJC by visit until Week 16

	Mean SJC (SD)			Mean TJC (SD)		
Study Week	Placebo Q2W N=44	40 mg Q2W N=44	80 mg Q2W N=47	Placebo Q2W N=44	40 mg Q2W N=44	80 mg Q2W N=47
BL	9.2 (6.4)	10.1 (7.0)	10.4 (6.4)	16.4 (11.3)	16.7 (10.3)	17.0 (9.7)
2	8.4 (6.1)	7.3 (6.5)	7.6 (7.6)	14.9 (10.0)	13.3 (9.5)	13.8 (10.7)
4	7.7 (7.7)	6.0 (7.0)	5.6 (6.2)	14.1 (11.8)	12.5 (11.6)	11.2 (9.2)
8	6.0 (6.2)	3.5 (4.1)	3.7 (4.7)	10.5 (7.5)	9.0 (10.5)	7.4 (7.2)
12	5.1 (5.2)	2.6 (3.4)	2.3 (3.4)	10.9 (8.7)	8.1 (8.9)	6.0 (6.7)
16	5.0 (5.7)	2.4 (3.7)	1.7 (2.7)	10.7 (9.1)	7.1 (7.7)	5.6 (6.8)

There was a dose-response relationship and a fast onset of response.

No serious or severe adverse events occurred during Period 1. The three most frequently affected System Organ Classes (SOCs) were SOC General disorders and administration site conditions comprising mainly mild injection site reactions or erythema followed by SOC Infections and infestations and SOC Metabolism and nutrition disorders. One mild, transient vulvovaginal *Candida* infection with active treatment was reported. Apart from injection site reactions there were no apparent differences in the occurrence of adverse events between active and placebo patients.

Conclusion: In this phase 2 study, izokibep showed a dose-dependent high degree of efficacy in patients with active PsA having failed previous treatment. Overall, izokibep was well tolerated.

These data strongly support further clinical development.

REFERENCES: None

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Boehringer Ingelheim, Flexion, Janssen, Pfizer, Sanofi, Regeneron, SUN Pharma Advanced Research, Gilead Sciences, Inc., Grant/research support from: Pfizer, Janssen, Chugai, Celgene, Roche, Alan Kivitz, Peter C. Taylor Consultant of: AbbVie, Biogen, Bristol Myers Squibb, Fresenius, Galapagos, Gilead, GlaxoSmithKline, Janssen, Lilly, Nordic Pharma, Pfizer, Roche, Sanofi, and UCB, Grant/research support from: Celgene and Galapagos, Dieter Wetzel Consultant of: Acino, Affibody, Biotest, Cheplapharm, CSL Behring, Mundipharma, Roche, Sandoz, Temmler, Nikolai C Brun Employee of: Affibody AB, Jan Brandt-Juergens Speakers bureau: Abbvie, Pfizer, Roche, Sanofi-Aventis, Novartis, Lilly, MSD, UCB, BMS, Janssen, Medac, Gilead, Affibody, Paid instructor for: Abbvie, Pfizer, Roche, Sanofi-Aventis, Novartis, Lilly, MSD, UCB, BMS, Janssen, Medac, Gilead, Affibody, Edit Drescher: None declared, Eva Dokoupilova: None declared, Anna Rowińska-Osuch: None declared, Nadia Abdel-Kader Martin Speakers bureau: Pfizer in 2011, Kurt de Vlam Speakers bureau: AbbVie, Amgen, Eli Lilly, Novartis, UCB, Paid instructor for: Amgen, Galapagos, UCB, Consultant of: Eli Lilly, Johnson &Johnson, Novartis Galapagos, UCB, Grant/research support from: Celgene

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OP0259 MINIMAL DISEASE ACTIVITY RESPONSE PATTERNS IN BIO-NAIVE PATIENTS TREATED WITH GUSELKUMAB: A MACHINE LEARNING ANALYSIS

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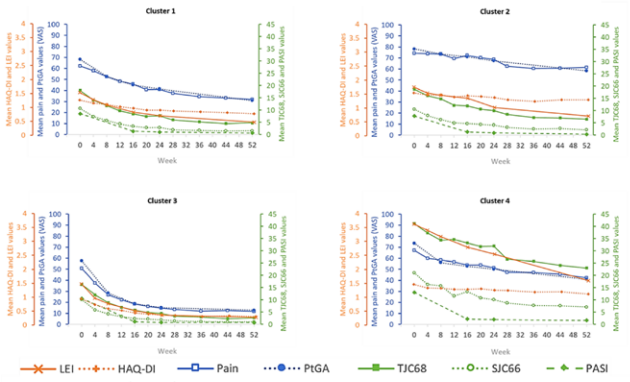
Background: Guselkumab (GUS), a human monoclonal antibody targeting the interleukin-23p19 subunit, demonstrated joint and skin efficacy in patients with active psoriatic arthritis (PsA) in the Phase III DISCOVER-1/-2 trials.[1,2] Minimal disease activity (MDA), a multi-domain composite outcome, is a clinically relevant measure of therapeutic response in PsA.[3] However, response dynamics and the effect of individual domains on achieving MDA are not well understood.
Objectives: Characterise response patterns in MDA domains over time and identify potential baseline (BL) response predictors using machine learning.
Methods: Data from bio-naïve patients with active PsA receiving GUS 100 mg every 4 or 8 weeks were pooled across DISCOVER-1/-2. Eligibility criteria are described elsewhere.[1,2] Unsupervised machine learning using the time-series K-means clustering algorithm was performed to identify clusters according to MDA domain responses over 52 weeks. MDA domain thresholds were tender joint count (TJC), swollen joint count (SJC), Psoriasis Area and Severity Index (PASI) and Leeds Enthesitis Index (LEI) each ≤1; patient global assessment (PtGA) visual analogue scale (VAS) ≤20; patient pain VAS ≤15 and Health Assessment Questionnaire-Disability Index (HAQ-DI) ≤0.5. BL characteristics were described for each cluster (Table 1). Missing data were not imputed.

Table 1. BL characteristics of four MDA response clusters (C1–4) in bio-naïve patients with active PsA treated with GUS 100 mg every 4 or 8 weeks

	Cluster			
	C1	C2	C3	C4
Patients, N	201	97	209	64
Age, years	46.1 ± 12.2	45.5 ± 11.5	46.1 ± 11.3	47.0 ± 11.1
Female, %	47.8	55.7	36.4	43.8
BMI, kg/m²	29.4 ± 6.3	29.2 ± 6.5	28.9 ± 5.4	28.7 ± 5.7
CRP, mg/dl	1.8 ± 2.4	1.8 ± 1.6	1.4 ± 2.0	1.9 ± 2.1
PsA disease duration, years	5.5 ± 5.8	5.3 ± 5.7	5.2 ± 5.9	5.8 ± 5.9
SJC (0–66)	10.7 ± 5.4	10.6 ± 5.0	10.1 ± 6.2	21.1 ± 12.2
TJC (0–68)	18.1 ± 9.6	18.8 ± 8.8	16.3 ± 10.7	41.2 ± 13.3
Spondylitis, %	28.9	26.8	29.7	42.2
PASI score (0–72)	8.6 ± 8.9	7.8 ± 8.0	10.6 ± 12.0	13.1 ± 14.6
Dactylitis, %	42.8	42.3	35.4	71.9
Dactylitis score (0–60)	3.7 ± 6.9	1.6 ± 2.9	2.0 ± 4.4	11.7 ± 15.2
Dactylitis count (0–20)	2.1 ± 4.0	0.9 ± 1.7	1.3 ± 2.8	6.0 ± 6.8
Enthesitis, %	62.2	62.9	56.9	89.1
LEI (0–6)	1.5 ± 1.6	1.7 ± 1.8	1.5 ± 1.7	3.6 ± 2.0
HAQ-DI (0–3)	1.3 ± 0.6	1.5 ± 0.5	0.9 ± 0.6	1.5 ± 0.5
PtGA (0–100 VAS)	68.3 ± 17.8	78.2 ± 14.1	57.6 ± 21.6	73.7 ± 15.8
Pain (0–100 VAS)	62.1 ± 17.0	74.3 ± 13.7	50.8 ± 21.3	67.2 ± 15.2

Data are mean ± standard deviation or %. CRP, C-reactive protein.

Figure 1. Response patterns of individual MDA domains from Week 0 to Week 52 in four MDA response clusters (C1–4) of bio-naïve patients with active PsA treated with GUS 100 mg every 4 or 8 weeks



Data points are mean cluster values.
GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PtGA, patient global assessment; SJC66, swollen joint count 0-66; TJC68, tender joint count 0-68; VAS, visual analogue scale.

Results: This analysis included 571 of 669 patients receiving GUS and identified four distinct response clusters (C1–4; Table 1). Mean age and body mass index (BMI) were similar across clusters; C3 had a lower proportion of female patients. Relative to C3, a high burden of BL disease was observed in C4 across clinical measures and patient-reported outcomes (PROs), and across PROs only in C2. Through Week 52, MDA response rates were highest in C3 and lowest in C4, yet all clusters showed continuous improvement in mean values across all MDA domains (Figure 1). In C3, all individual domain thresholds were rapidly reached. C1, 2 and 4, met PASI threshold and showed a substantial reduction in SJC while other domains varied. In C1 and 2, improvement in clinical measures paralleled that of C3; however, PROs appeared to take longer to resolve. Responses were slowest in C4, though improvements were substantial given the high BL disease burden. Improvement in pain, PtGA and HAQ-DI occurred earlier in C1 than C2.
Conclusion: Machine learning identified four clusters of GUS-treated PsA patients based on differing response patterns in individual MDA domains. Response types may differ due to BL disease burden, especially in patients with higher pain, PtGA and functional disability scores. These results offer an innovative, complementary approach to identifying treatment response patterns across diverse clusters of bio-naïve patients with PsA, which may facilitate clinical decision-making.

REFERENCES:

[1] Deodhar et al. *Lancet* 2020; 395: 1115–25.
[2] Mease et al. *Lancet* 2020; 395: 1126–36.
[3] Coates et al. *Ann Rheum Dis* 2010; 69: 48–53.

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OP0260 RESPONSIVENESS OF A COMBINED POWER DOPPLER AND GREYSCALE ULTRASOUND SCORE FOR ASSESSING SYNOVITIS AT JOINT LEVEL IN PSORIATIC ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO CSDMARDS: DATA FROM THE ULTIMATE TRIAL

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