Guselkumab Shows Strong Long-Term Effectiveness and High Drug Survival in Patients With Moderate-to-Severe Psoriasis Across Different Treatment Lines – First Interim Results of the Non-Interventional German G-REAL Study

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Background

- Psoriasis (Pso) is a chronic, immune-mediated disease characterized by red, scaly plaques and driven by the interleukin(IL)-23/IL-17 inflammatory pathway[1]
- Guselkumab (GUS), a selective, p19 subunit-targeted IL-23 inhibitor, has demonstrated significant and durable efficacy in patients with moderate-to-severe Pso[2,3]
- Previously, ECLIPSE, a phase 3, double-blind trial in Pso, showed that GUS is superior to secukinumab (SEC; an IL-17A inhibitor) in reaching a Psoriasis Area and Severity Index (PASI) 90 response at 1-year post-treatment initiation[4]
- G-REAL is a prospective, non-interventional, multicenter study assessing the long-term effectiveness and impact of GUS and SEC on health-related quality of life in patients with plaque Pso across different treatment lines in routine clinical care in Germany

Objectives

This first interim analysis from the G-REAL study assessed GUS effectiveness, patient-reported outcomes (PROs), and drug survival over 84 weeks (W) across treatment lines, and it evaluated effectiveness and safety with GUS and SEC over 84W

Key Takeaways

- **Guselkumab (GUS) demonstrated robust long-term clinical effectiveness, marked quality of life improvements, and high drug survival rates through 84 weeks (W) in patients with moderate-to-severe Pso irrespective of prior biological treatment in the G-REAL study**
- **Bionaïve patients achieved the highest response and drug survival rates, highlighting the benefits of GUS when used as a first line biologic**
- **Onset of response was similar with GUS and secukinumab (SEC); however, higher PASI 90 and complete skin clearance response rates were achieved with GUS from W28 through W84**

Methods

Study Design

- Adult patients had a confirmed diagnosis of moderate-to-severe Pso and PASI score >5 at baseline
- Patients were treated per routine clinical care (GUS Q8W or SEC Q4W) and data were collected at W0, W4, W12, W20, W28, W52, and W84

Primary Outcomes

- **PASI 90** at W84 with GUS across treatment lines
- **DLQI 0/1** at W84 with GUS across treatment lines

Current Interim Analysis

- 332 of 650 planned patients were enrolled from November 2021 to December 2022 (Phase 1 of enrollment was pre-defined to allow for timely balanced enrollment across treatment groups [GUS and SEC] and lines[a])
- Of these 332 patients, 239 initiating GUS and 87 initiating SEC had analyzable clinical data at baseline and at least one visit post-baseline[b]
- Final analysis is planned with all enrolled patients

Analyzed Parameters

- **Impact of GUS through W84 across treatment lines**
  - Rates of PASI 90 and PASI ≤3 response
  - Improvements in DLQI score
  - Drug survival[c]
- **Impact of GUS vs SEC through W84 in the total population**
  - Rates of PASI 90 and PASI 0 response
  - Incidence of AEs

Statistics

- **Impact of GUS:**
  - Clinical effectiveness and PRO data were analyzed as observed
  - Drug survival was analyzed using Kaplan-Meier methodology[c]
- **Impact of GUS vs SEC:** Effectiveness data were analyzed using nonresponder imputation after applying treatment failure rules[d]
- Group comparisons, when performed, were exploratory. Nominal p-values are reported

*[a]Treatment lines based on previous biological treatment: GUS: bionaïve, 1 prior biologic, and ≥2 prior biologics; SEC: bionaïve and ≥1 prior biologic. [b]Full Analysis Set definition. [c]In the absence of confirmation of treatment discontinuation (including patients lost to follow-up), the time to event was censored on the last documented study date. [d]Patients were considered treatment failures when (1) GUS or SEC was discontinued due to lack of effectiveness, loss of effectiveness, or an AE of psoriasis worsening, or (2) a new therapy other than the therapy at baseline was started. **AE**=adverse event, **DLQI**=Dermatology Life Quality Index, **Q4W**=every 4 weeks, **Q8W**=every 8 weeks.*

Results

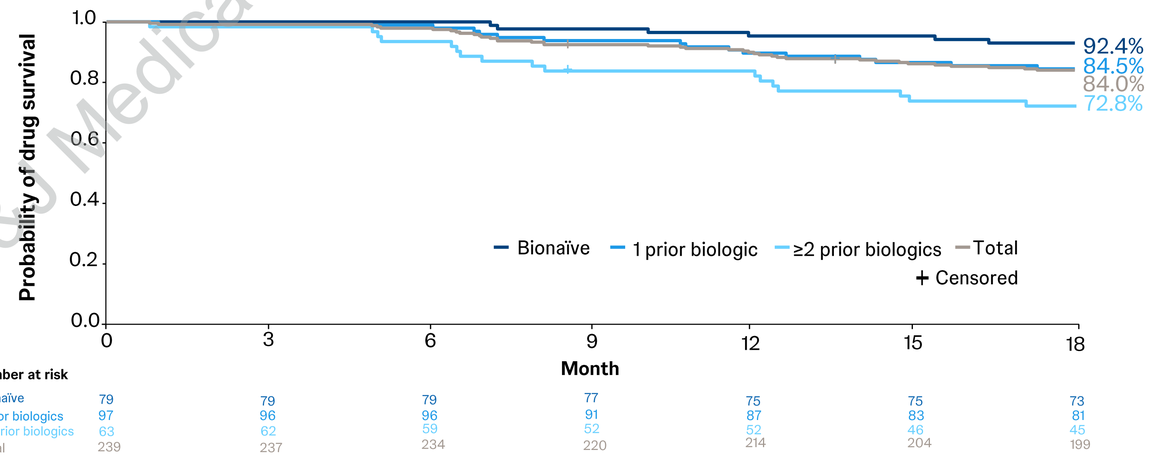
Baseline patient and disease characteristics were generally well balanced between treatment cohorts

Baseline Characteristics		GUS (N = 239[a])	SEC (N = 87[a])
Demographics			
	Mean age, yrs (SD)	48.5 (13.6)	47.3 (13.6)
	Female, n (%)	94 (39.3)	33 (37.9)
	Mean BMI, kg/m² (SD)	29.0 (5.7)	29.5 (6.8)
Disease Characteristics			
	Mean Pso disease duration, yrs (SD)	17.6 (11.9)	13.4 (13.7)
	Mean PASI (0-72) (SD)	14.6 (8.5)	15.2 (7.4)
	Mean DLQI (0-30) (SD)	14.0 (7.8)	14.9 (7.7)
Concomitant Diseases[b], n (%)			
	Arterial hypertension	65 (27.2)	23 (26.4)
	Psoriatic arthritis	61 (25.5)	23 (26.4)
	Hyperlipidaemia	27 (11.3)	6 (6.9)
	Diabetes	15 (6.3)	11 (12.6)
	Obesity	17 (7.1)	7 (8.0)
Prior csDMARDs Use, n (%)			
	Methotrexate	112 (46.9)	37 (42.5)
	Cyclosporine	22 (9.2)	5 (5.7)

*[a]Ns are presented for the full analysis set. [b]Top 5 most frequent concomitant diseases shown. **BMI**=body mass index, **csDMARD**=conventional synthetic disease-modifying antirheumatic drug, **SD**=standard deviation.*

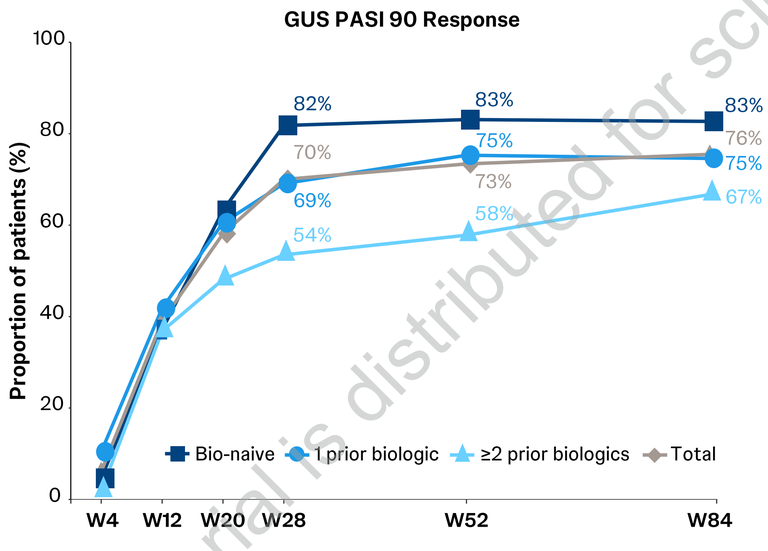
High drug survival rates with GUS were sustained through 18 months across treatment lines

- Through W84, the highest probability of drug survival was observed among bionaïve patients (92.4%), followed by those with 1 prior biologic (84.5%) and ≥2 prior biologics (72.8%)



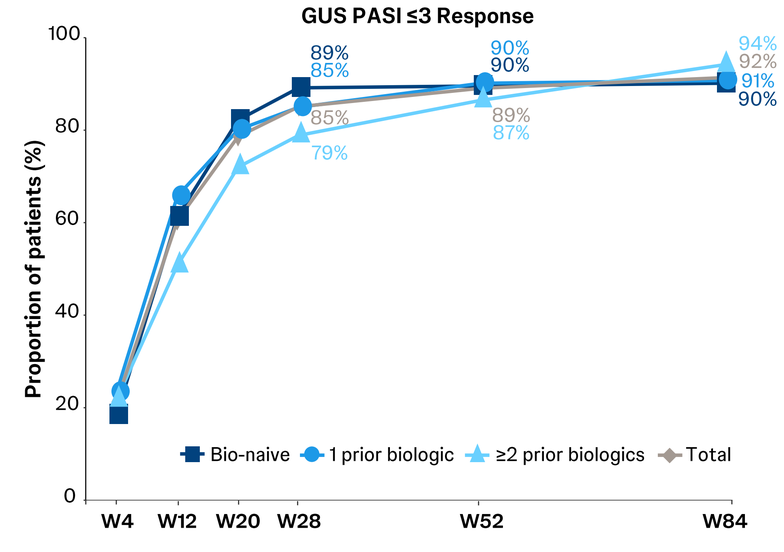
PASI 90 response rates with GUS were highest among bionaïve patients

- High levels of PASI 90 response were generally achieved with GUS and maintained through W84 across treatment lines
- Of those achieving PASI 90 at W52, 92.3% in the GUS total population maintained response at W84; response rates were greater in bionaïve patients (97.4%) compared to those with prior biological treatment (1 prior biologic: 90.9%; ≥2 prior biologics: 86.4%; data not shown in figure)



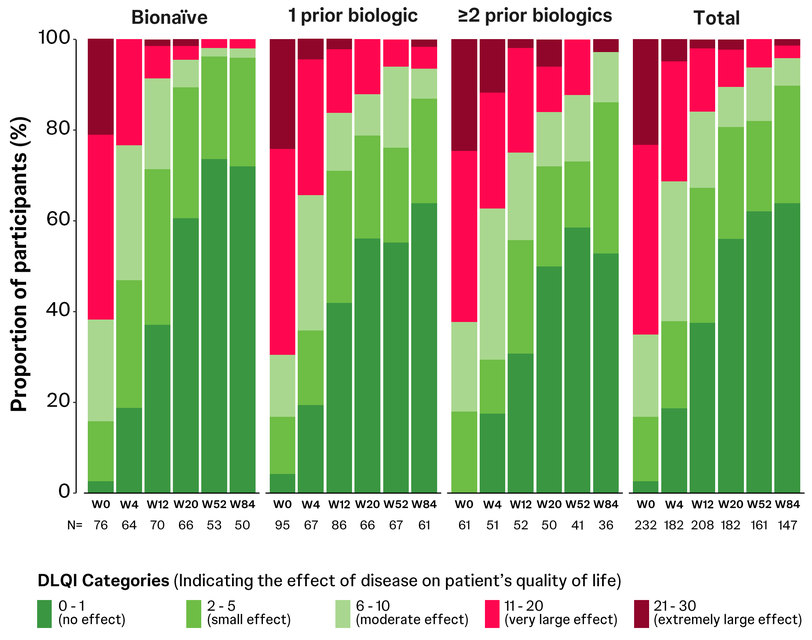
High PASI ≤3 response rates were generally achieved with GUS and maintained through W84 across treatment lines

- Generally comparable PASI ≤3 response rates were observed with GUS across treatment lines

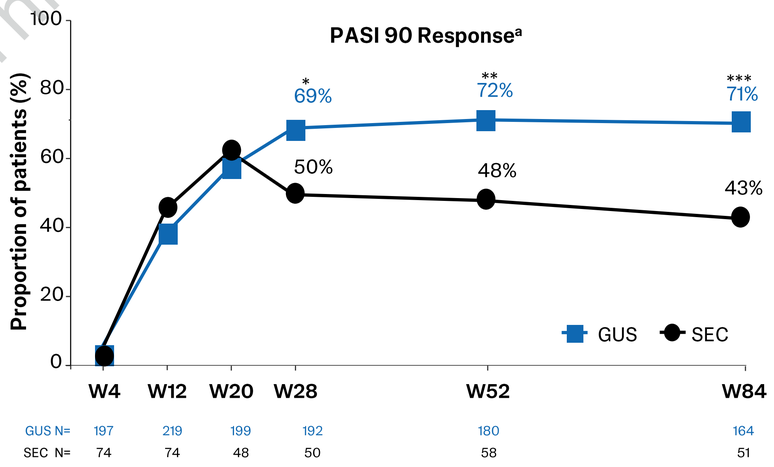


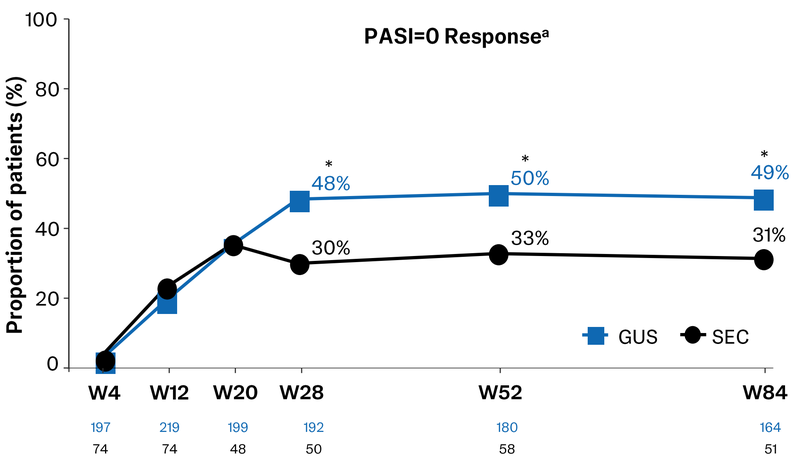
Quality of life improved rapidly and continued to improve with GUS through W84 across treatment lines

- In the total population, DLQI 0/1[a] response rates increased from 2.6% at W0 to 63.9% at W84 with GUS
- Through W84, the highest DLQI 0/1[a] response rates with GUS were seen among bionaïve patients



Total Population: After W20, GUS demonstrated higher PASI 0 and PASI 90 response rates versus SEC through W84





- Treatment failure rates were 5.0% for GUS and 21.8% for SEC

Nominal *$p<0.05$, **$p<0.01$, ***$p<0.001$ vs SEC. *[a]Analyzed after applying treatment failure rules (see Statistics section).*

No new safety signals for GUS were identified through W84

Safety through W84	GUS (N = 244)[a]	SEC (N = 88)[a]
Any AE	140 (57.4%)	46 (52.3%)
ADR[b,c]	22 (9.0%)	13 (14.8%)
Infections and infestations	12 (4.9%)	7 (8.0%)
Skin and subcutaneous tissue disorders	5 (2.0%)	0 (0.0%)
Gastrointestinal disorders	3 (1.2%)	2 (2.3%)
General disorders and administration site conditions	0 (0.0%)	2 (2.3%)
Any SAE	19 (7.8%)	5 (5.7%)
SADR	2 (0.8%)	1 (1.1%)
Infections and infestations	2 (0.8%)	0 (0.0%)
Cardiac disorders	0 (0.0%)	1 (1.1%)
Deaths	0 (0.0%)	0 (0.0%)

*[a]N are presented for the Safety Analysis Set, defined as all enrolled patients who received at least 1 dose of GUS or SEC. [b]Defined as an AE considered related to treatment. [c]Most frequently reported system organ classes for ADRs are shown. **ADR**=adverse drug reaction, **SADR**=serious adverse drug reaction, **SAE**=serious adverse event.*

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