Online Supplement

Supplemental Text

RESULTS

Pharmacokinetics and immunogenicity. Three hundred sixty-seven patients had evaluable serum samples collected following subcutaneous administration of guselkumab 100 mg. Median steady-state trough serum guselkumab concentrations were maintained through Week52 when guselkumab was given every 4 weeks (Q4W; 4.69 µg/mL) or Q8W (1.14 µg/mL).

The overall incidence of antibodies to guselkumab remained low (5% [20 of 367 of guselkumab-treated patients]) through Week52, including two (0.5%) patients possessing guselkumab-neutralizing antibodies. Antibodies to guselkumab were detected in similar proportions of patients with (5%; 12/236) or without (6%; 8/131) non-biologic disease-modifying antirheumatic drug use at baseline, as well as in tumor necrosis factor-inhibitor (TNFi)-naïve (5% [12/256]) and TNFi-experienced (7% [8/111]) patients. The presence of antibodies to guselkumab did not preclude achievement of responses according to American College of Rheumatology criteria.

Noting the limited number of patients who developed antibodies to guselkumab, there was no apparent association between the development of antibodies to guselkumab and the occurrence of injection-site reactions.

Safety

Five events of suicidal ideation were reported through Week60, including one patient in each of the placebo and guselkumab 100 mg Q8W groups during Week0–24[14] and one patient in each of the guselkumab 100 mg Q4W, guselkumab 100 mg Q8W, and placebo followed by guselkumab 100 mg Q4W groups during Week24–60. All five events were level 1 on the electronic Columbia-Suicide Severity Rating Scale questionnaire.

Supplemental Table

Table S1. Number (%) of patients with post-baseline laboratory values by maximum NCI-CTCAE grade through Week 60 of the DISCOVER-1 trial

	Placebo→Guselkumab 100 mg Q4W		Guselkumab 100 mg (Week0–60)		All Guselkumab
	Placebo (Week0–24)	Q4W (Week24–60)[a]	Q4W (Week0–60)	Q8W (Week0–60)	
Treated patients, N	126	114	128	127	369
Weeks of follow-up, mean	24.0	35.3	59.5	58.3	51.6
Patients with post-baseline evaluations, N	124	113	128	126	367
Neutrophil count decreased					
Grade 1 (<LLN to 1.5×10^9/L)	4 (3.2)	4 (3.5)	13 (10.2)	9 (7.1)	26 (7.1)
Grade 2 (<1.5 to 1.0×10^9/L)	0	0	3 (2.3)	1 (0.8)	4 (1.1)
Grade 3 (<1.0 to 0.5×10^9/L)	0	1 (0.9)[b]	0	0	1 (0.3)
Grade 4 (<0.5×10^9/L)	0	0	0	0	0
Platelet count decreased)					
Grade 1 (<LLN to 75.0×10^9/L)	0	3 (2.7)	3 (2.3)	8 (6.3)	14 (3.8)
Grade 2 (<75.0 to 50.0×10^9/L)	0	0	0	1 (0.8)[c]	1 (0.3)
Grade 3 or 4 (<50.0×10^9/L)	0	0	0	0	0
WBC count decreased					
Grade 1 (<LLN to 3.0×10^9/L)	3 (2.4)	5 (4.4)	14 (10.9)	7 (5.6)	26 (7.1)
Grade 2 (<3.0 to 2.0×10^9/L)	1 (0.8)	1 (0.9)	3 (2.3)	1 (0.8)	5 (1.4)[d]
Grade 3 or 4 (<2.0×10^9/L)	0	0	0	0	0
ALT increased					
Grade 1 (>1 to 3×ULN)	41 (33.1)	32 (28.3)	67 (52.3)	43 (34.1)	142 (38.7)
Grade 2 (>3 to 5xULN)	1 (0.8)	4 (3.5)	3 (2.3)	4 (3.2))	11 (3.0)
Grade 3 (>5 to 20×ULN)	1 (0.8)	0	0	1 (0.8)[e]	1 (0.3)
Grade 4 (>20xULN)	0	0	0	0	0
AST increased					
Grade 1 (>1 to 3×ULN)	24 (19.4)	25 (22.1)	42 (32.8)	35 (27.8)	102 (27.8)
Grade 2 (>3 to 5xULN)	2 (1.6)	3 (2.7)	3 (2.3)	4 (3.2)	10 (2.7)
Grade 3 (>5 to 20×ULN)	2 (1.6)	1 (0.9)	1 (0.8)	1 (0.8)	3 (0.8)[f]
Grade 4 (>20xULN)	0	0	0	0	0
Blood bilirubin increased					
Grade 1 (>ULN to 1.5xULN)	1 (0.8)	8 (7.1)	12 (9.4)	1 (0.8)	21 (5.7)
Grade 2 (>1.5 to 3.0xULN)	2 (1.6)	2 (1.8)	0	5 (4.0)[g]	7 (1.9)
Grade 3 or 4 (>3.0xULN)	0	0	0	0	0

[a]These 114 patients received placebo during Week0-24; only abnormalities reported from Week24-52 are summarized.
[b]Resolved in 8 days without treatment; not associated with an infection.
[c]Resolved spontaneously at the subsequent visit without treatment; not associated with a bleeding event.
[d]Associated with infection (pulpitis dental, tooth abscess) before Week24[14] and interruption of guselkumab for one patient; neither associated with infection nor led to study agent discontinuation for other patients.
[e]In a patient with Grade-1 ALT and Grade-2 AST elevations at initial screening and concomitant medications including methotrexate, celecoxib, isoniazid, and epinastine; accompanied by Grade-2 AST increase and AE of ultrasound-confirmed fatty liver at Week 36; ALT and AST decreased to Grade-1 14 days later without interrupting study drug; followed by Grade-2 total bilirubin increase (>2.0×ULN) at Week 52.
[f]All resolved over time; none led to study agent discontinuation.
[g]>2.0×ULN in two patients: 1) Elderly individual with elevated bilirubin at baseline and throughout study; medical history included Gilbert's syndrome; no ALT/AST increase Grade ≥2; no intervention required; 2) see footnote e.
AE – adverse event, ALT – alanine aminotransferase, AST – aspartate aminotransferase, LLN – lower limit of normal, NCI-CTCAE - National Cancer Institute - Common Terminology Criteria for Adverse Events, Q4/8W – every 4/8 weeks, ULN – upper limit of

normal, WBC – white blood cell

Supplemental Figure

Figure S1. Proportions of patients achieving ACR20, ACR50, and ACR70 responses from Week 24 through Week 52. Panels **A**, **C**, and **E** summarize response rates among randomized patients with application of data handling rules and NRI (see *Methods*). Previously reported Week 24 data[14] included for reference. Of 126 patients randomized to receive placebo, 114 crossed over to guselkumab 100 mg Q4W (after Week 24 response assessments); the 12 patients who received only placebo before discontinuing study agent were included as nonresponders through Week52. Panels **B**, **D**, and **F** summarize observed data in patients continuing study treatment at Week 24, as prespecified in the statistical analysis plan. *ACR – American College of Rheumatology, GUS – guselkumab, NRI – nonresponder imputation, PBO – placebo, Q4/8W – every 4/8 weeks*