

Pharmacokinetic/Pharmacodynamic Evaluation of Ublituximab in Patients With Autoimmune Diseases



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CONCLUSIONS

- SC ublituximab showed an estimated SC bioavailability of 61.9%.
- PK modeling predicted that 400 mg SC every 12 weeks or every 8 weeks delivers 24-week exposure non-inferior to the approved IV regimen (GMR 1.20 and 1.56; 90% CI lower bounds 1.14 and 1.48, both >0.80).

- 100% of participants treated with 400 mg fully SC regimens were depleted by Day 4 and remained depleted throughout the study.
- 400 mg fully SC regimens (undergoing Phase 3 evaluation) were well-tolerated with injection reactions occurring only during the first two injections (1 participant Day 1, 2 participants Day 15) all of which were Grade 1.
- No T1 Gd-enhancing lesions were seen at Week 24 or Week 48 with fully SC regimens.

- These results support SC ublituximab as an alternative to IV administration, with non-inferior predicted exposure, rapid and sustained B-cell depletion, and a well-tolerated safety profile.

REFERENCES:

- Steinman L, et al. N Engl J Med. 2022;387(8):704-714.
- Babiker HM, et al. Expert Opin Investig Drugs. 2018;27(4):407-412.
- BRIUMVI® (ublituximab-xlyi) Prescribing Information. TG Therapeutics, Inc. 2026.

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DISCLOSURES:

KS has received honoraria for speaking, consulting and serving on advisory boards for Merck, Novartis, Roche, Biogen, Celgene, Bristol Myers Squibb and TG Therapeutics. JI has nothing to disclose. JZ has nothing to disclose. HM, TT, JP, and CR are employees of and hold stock or stock options in TG Therapeutics, Inc. EK has received honoraria for speaking, consulting, and serving on advisory boards for Merck, Novartis, Roche, and Biogen. This study was funded by TG Therapeutics, Inc.

BACKGROUND

- Ublituximab is a glycoengineered, chimeric anti-CD20 IgG1 monoclonal antibody that targets a unique epitope of CD20; its low-fucose Fc region enhances FcγRIIIa binding and antibody-dependent cellular cytotoxicity (ADCC) relative to other approved anti-CD20 antibodies.^{1,2}
- Ublituximab IV is approved for adults with relapsing forms of multiple sclerosis (RMS): 150 mg on Day 1 (4-hour infusion), 450 mg on Day 15 (1-hour infusion), then 450 mg every 24 weeks.³
- Subcutaneous (SC) formulations of ublituximab were developed to expand administration options.
- TG1101-RMS-SC101 is a Phase 1, two-part study evaluating the PK, PD, safety and clinical effects of SC ublituximab in participants with RMS or MG who are ublituximab-naïve. This presentation reports data on the RMS population.

METHODS

Phase 1, open-label, two-part dose-finding study of SC ublituximab

PART 1 · Initial-dose SC replacement	PART 2 · Fully SC regimen
- Single SC dose on Day 1 in place of 150 mg IV, then approved IV regimen (450 mg Day 15, q24w) - Sequential dose escalation: 50, 100, 150, 225, 300 mg SC - IV reference cohort for relative bioavailability	- Day 1 (300 or 400 mg) and Day 15 (400 mg), then 400 mg SC every 12 weeks or every 8 weeks - Doses selected to match 24-week exposure of the approved IV regimen
Administration	Assessments
- SC doses given by study staff as a single injection (≤2 mL) into the lower abdomen - IV doses per approved regimen 1-hour post-dose monitoring on Day 1 and Day 15	- PK: AUC and relative bioavailability by cohort - PD: proportion of participants with B-cell counts <10 cells/μL - Safety: AEs, and injection- and infusion-related reactions - MRI (Part 2 only): collected at Week 24 and Week 48

AE, adverse event; AUC, area under the concentration–time curve; EDSS, Expanded Disability Status Scale; GMR, geometric mean ratio; IV, intravenous; PD, pharmacodynamics; PK, pharmacokinetics; RMS, relapsing multiple sclerosis; SC, subcutaneous.

Figure 1. Study Schema



RESULTS

Baseline Characteristics

Characteristic	Part 1 IV N = 17	Part 1 SC/IV N = 45	Part 2 SC N = 28
Follow-up, months, mean (SD)	21.4 (2.6)	20.0 (4.1)	11.7 (4.7)
Age, years, mean (SD)	39.4 (9.7)	37.3 (11.6)	41.5 (11.3)
Female, n (%)	13 (76.5)	35 (77.8)	18 (64.3)
Race, White, n (%)	17 (100)	45 (100)	28 (100)
Weight, kg, mean (SD)	73.9 (21.5)	70.9 (17.5)	77.2 (20.0)
BMI, kg/m², mean (SD)	25.2 (6.6)	24.8 (4.9)	26.6 (6.5)
Years since diagnosis, mean (SD)	7.2 (8.1)	6.1 (7.8)	5.8 (8.1)
≥1 relapse in 2 years prior to screening, n (%)	16 (94.1)	37 (82.2)	21 (75.0)
EDSS score, median (range)	3.5 (1.0–5.5)	2.0 (0–5.5)	2.0 (1.0–5.5)
Baseline B-cells, cells/μL, median (IQR)	135.0 (106.0–215.0)	188.0 (135.0–227.0)	207.5 (140.0–269.5)
Previously treated with DMT, n (%)	9 (52.9)	24 (53.3)	12 (42.9)
Prior anti-CD20, n (%) ^a	0	3 (6.7)	1 (3.6)

Data cut-off 30 June 2026. Part 1 SC pools cohorts SC1–SC5 and the model-informed 300 mg cohort; Part 2 SC pools the 300/400 mg Q12W, 400/400 mg Q12W and 400 mg Q8W cohorts. ^aOcrelizumab was the only prior anti-CD20 agent received. BMI, body mass index; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; IQR, interquartile range; IV, intravenous; SC, subcutaneous; SD, standard deviation.

- Baseline demographics and disease characteristics were balanced across each population.

Exposure

Table 2. Model-Predicted AUC(0–W24): SC Q12W and Q8W Regimens vs Approved IV Regimen

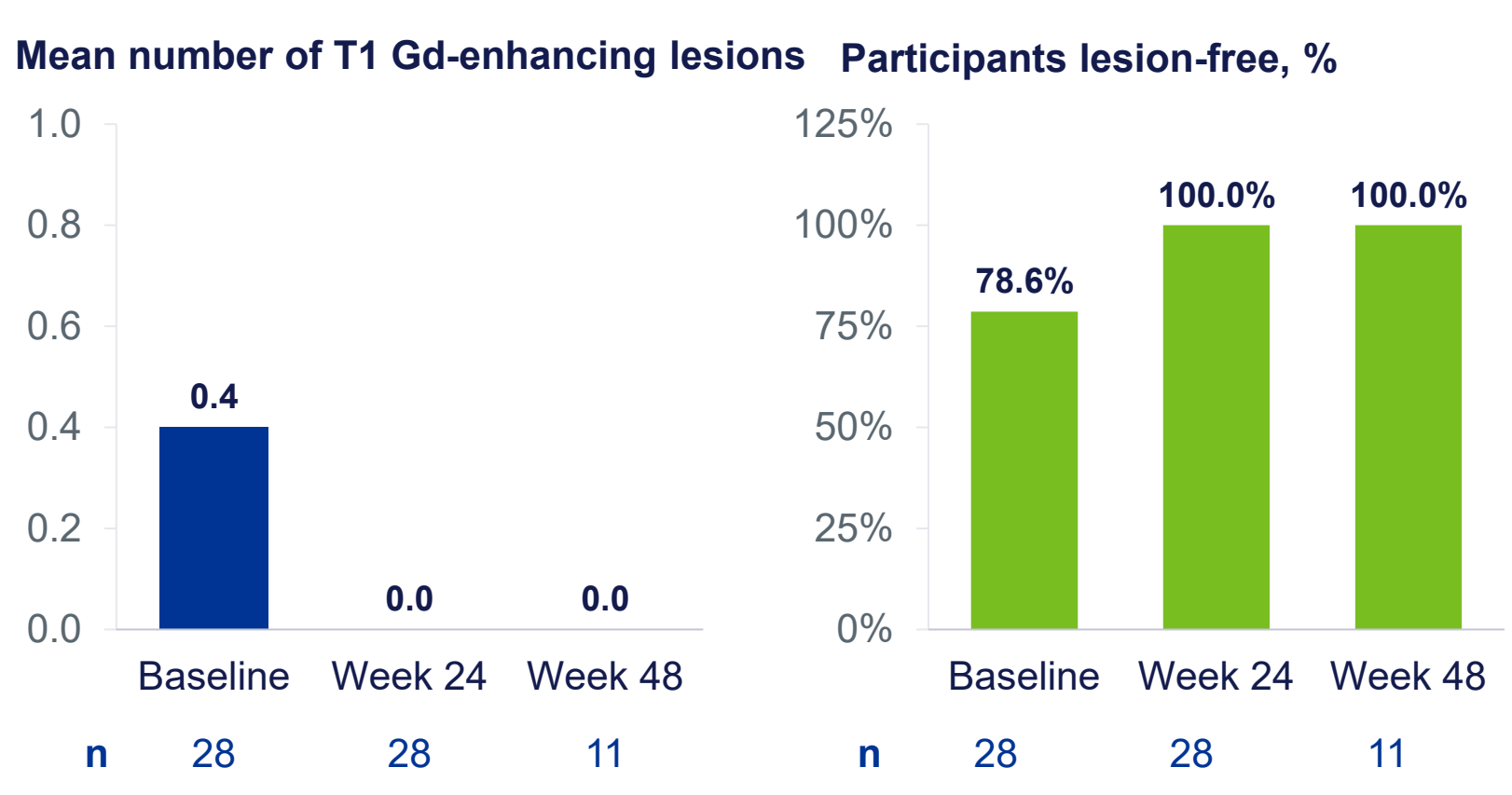
Regimen	N	Mean (SD)	Median [range]	GMR vs IV (90% CI)
Approved IV regimen	120	52,260 (12,830)	50,820 [20,410–114,300]	Reference
400 mg SC Q12W	120	62,650 (14,850)	61,120 [20,570–134,400]	1.20 (1.14–1.26)
400 mg SC Q8W	120	81,000 (18,830)	79,260 [24,900–171,600]	1.56 (1.48–1.64)

Simulated exposures, N=120 per regimen. AUC, area under the concentration–time curve; CI, confidence interval; GMR, geometric mean ratio; IV, intravenous; PK, pharmacokinetic; Q8W/Q12W, every 8/12 weeks; SC, subcutaneous; SD, standard deviation.

- Data represents 120 unique patients simulated from the population PK model.
- Estimated SC bioavailability, mean (95% CI): 61.9% (55.1%–68.7%).
- PK modeling and simulation predicted non-inferior 24-week exposure for both fully SC regimens relative to the approved IV regimen.
- Both lower bounds exceed the 0.80 non-inferiority threshold that defines the primary endpoint of the ongoing Phase 3 trial.

MRI

Figure 2. T1 Gd-Enhancing Lesions, Part 2 Fully SC Regimens

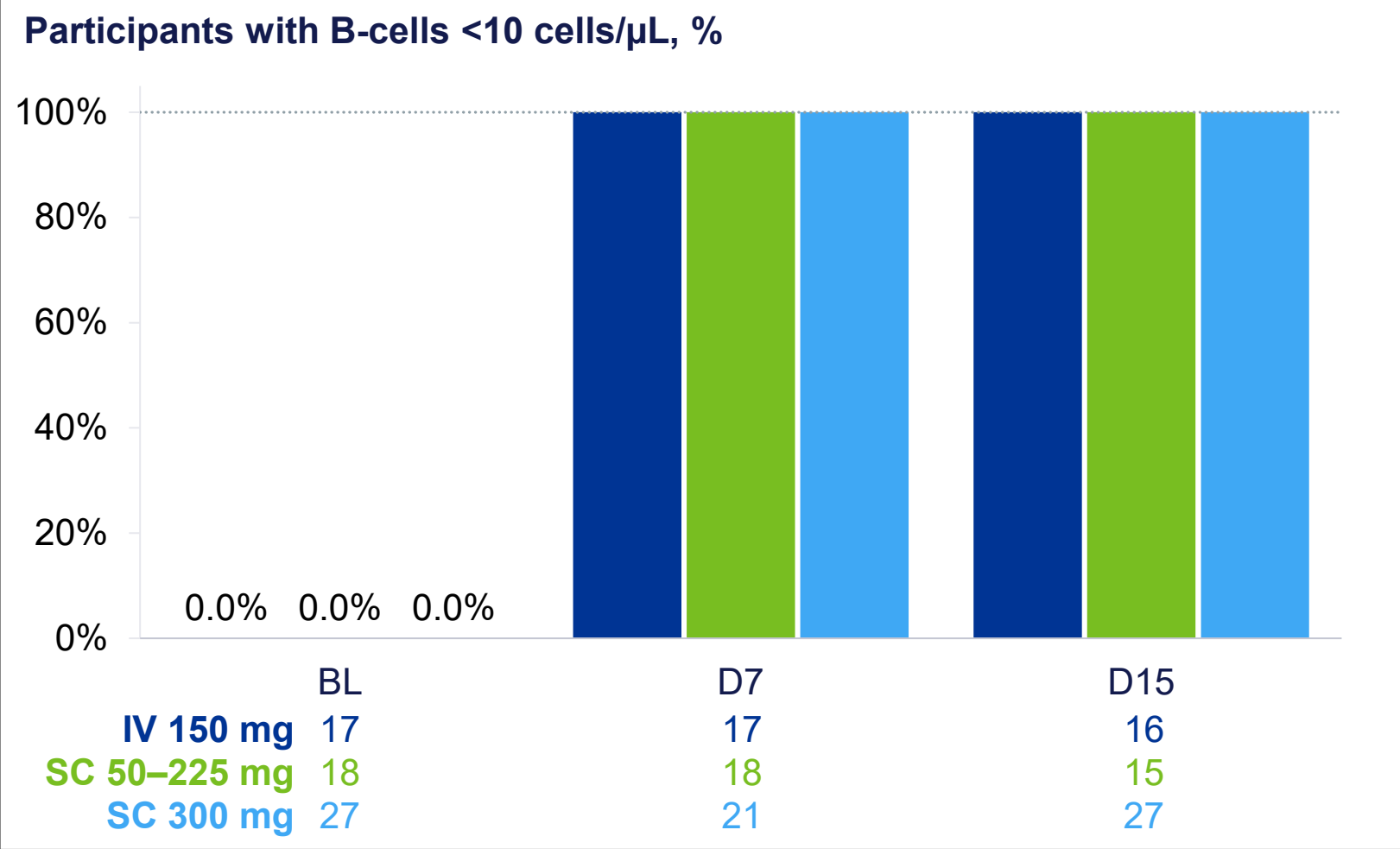


Part 2 SC cohorts pooled. Participants in MRI-mITT: baseline n=28, Week 24 n=28, Week 48 n=11 (Week 48 reached by the 300/400 mg Q12W cohort only). Gd, gadolinium; MRI-mITT, magnetic resonance imaging modified intent-to-treat; SC, subcutaneous.

- Mean T1 Gd-enhancing lesion count fell from 0.4 at baseline to 0.0 at Week 24 and remained 0.0 at Week 48.
- 100% of participants were lesion-free at Week 24 and Week 48.

B-Cell Depletion

Figure 3. B-Cell Depletion After the First Dose (Part 1)



- A single SC injection on Day 1 depleted B-cells as rapidly as the 150 mg IV infusion.

Safety

Table 3. Overall Safety Summary

Participants, n (%)	Part 1 IV N = 17	Part 1 SC N = 45	Part 2 SC N = 28
Any AE	13 (76.5)	40 (88.9)	20 (71.4)
Serious AE ^a	0	3 (6.7)	2 (7.1)
AE leading to permanent discontinuation ^b	0	1 (2.2)	0
Treatment-related AE	7 (41.2)	24 (53.3)	13 (46.4)
Any infection	10 (58.8)	26 (57.8)	15 (53.6)
Serious infection	0	1 (2.2)	1 (3.6)
Systemic injection-related reaction	0	10 (22.2)	7 (25.0)
Local injection-site reaction	0	1 (2.2)	1 (3.6)
Infusion-related reaction (IV doses)	2 (11.8)	13 (28.9)	—
Death	0	0	0

^aSerious AEs: Part 1 SC – anal fistula, anal abscess, liver disorder, hydrosalpinx (1 each); Part 2 SC – appendicitis, basal cell carcinoma (1 each). ^bOne infusion-related reaction at Week 24 led to ublituximab discontinuation. Infusion-related reactions in Part 1 SC occurred with IV doses from Day 15 onward. AE, adverse event; IV, intravenous; SC, subcutaneous.

- SC ublituximab was well-tolerated: no deaths, one discontinuation for an AE, and serious AEs in 3 Part 1 SC and 2 Part 2 SC participants, none related to study drug.

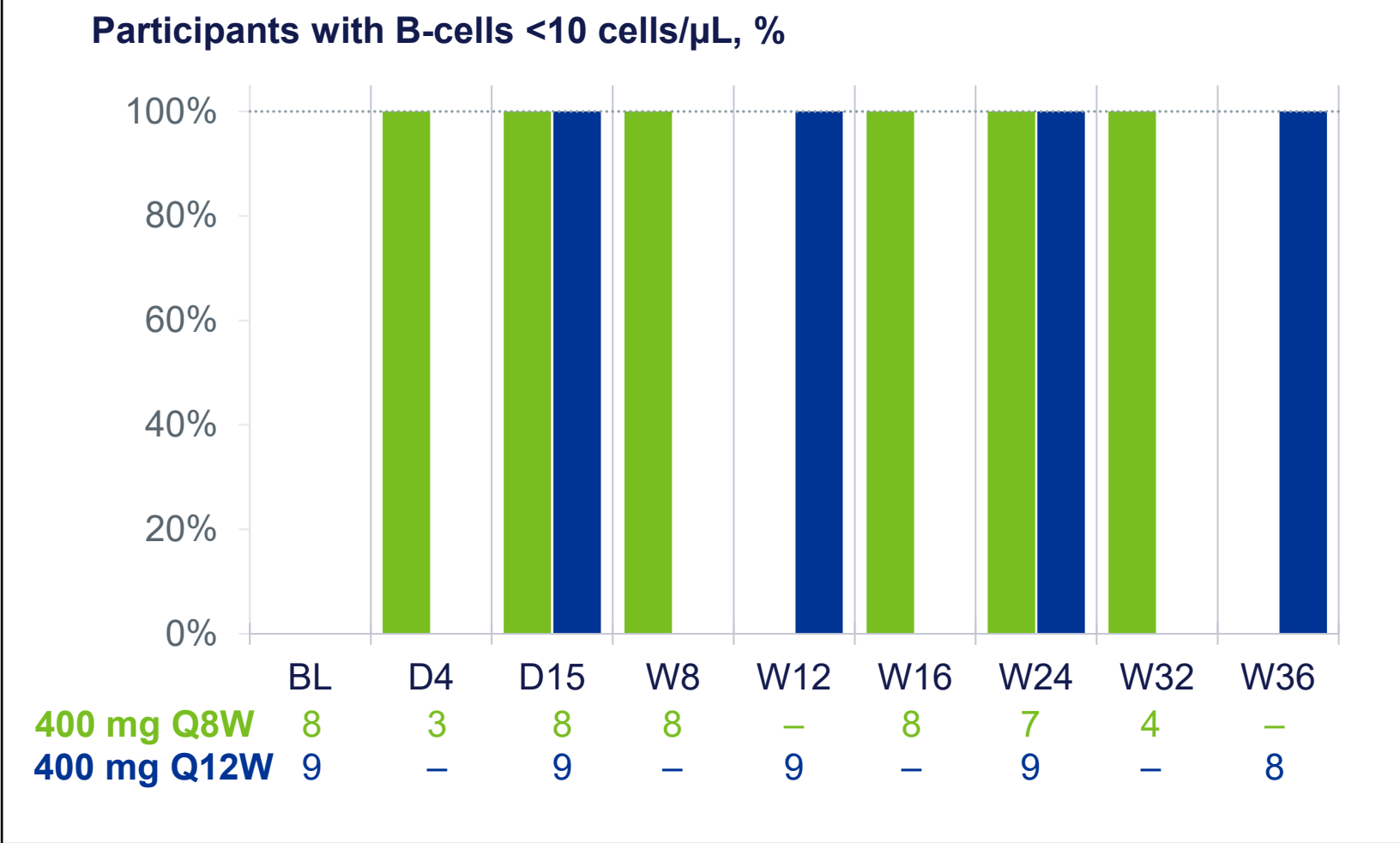
Table 4. AEs Occurring in >10% of Participants in Any Group

Preferred term, n (%)	Part 1 IV N = 17	Part 1 SC/IV N = 45	Part 2 SC N = 28
Any AE	13 (76.5)	40 (88.9)	20 (71.4)
Upper respiratory tract infection	4 (23.5)	15 (33.3)	7 (25.0)
Infusion-related reaction (IV doses)	2 (11.8)	13 (28.9)	—
Injection-related reaction (SC doses)	—	10 (22.2)	7 (25.0)
Headache	—	11 (24.4)	3 (10.7)
Urinary tract infection	3 (17.6)	5 (11.1)	2 (7.1)
Pharyngitis	1 (5.9)	5 (11.1)	1 (3.6)
Nasopharyngitis	2 (11.8)	1 (2.2)	4 (14.3)
Influenza	1 (5.9)	—	3 (10.7)
Cough	—	—	3 (10.7)

Preferred terms shown if reported in >10% of participants in any group; sorted by Part 1 SC incidence. In Part 1 SC, infusion-related reactions occurred with IV doses from Day 15 onward. AE, adverse event; IV, intravenous; SC, subcutaneous.

- Upper respiratory tract infection and injection- or infusion-related reactions were the most common AEs.

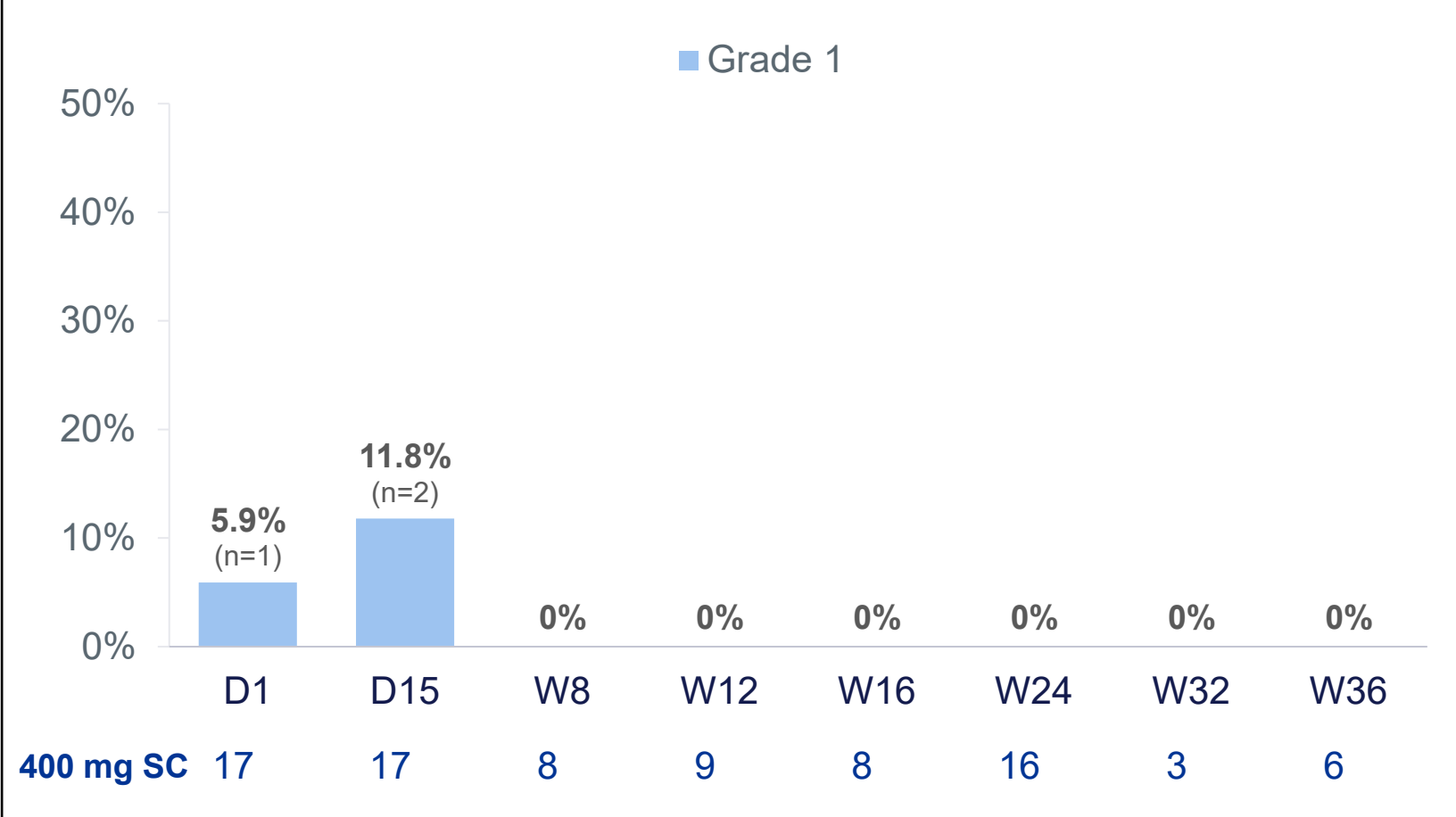
Figure 4. B-Cell Depletion by 400 mg Fully SC Regimens



- 100% of participants treated with 400 mg SC regimens were depleted by Day 4.
- Depletion was sustained through maintenance dosing: 100% at every visit

Tolerability

Figure 5. Injection Reactions, 400 mg Fully SC Regimens



- All IRRs were Grade 1 and completely resolved without sequela.
- No IRRs were Grade ≥2, serious, or resulted in discontinuation.

Table 5. Injection-Related Reaction Symptoms

Participants, n (%)	Part 1 SC/IV N = 45	Part 2 SC N = 28
Any injection-related reaction	11 (24.4)	8 (28.6)
Systemic injection-related reaction	10 (22.2)	7 (25.0)
Chills	5 (11.1)	0
Headache	4 (8.9)	1 (3.6)
Pyrexia	2 (4.4)	2 (7.1)
Influenza-like illness	2 (4.4)	2 (7.1)
Myalgia	2 (4.4)	1 (3.6)
Local injection-site reaction	1 (2.2) ^a	1 (3.6) ^b

Part 1 SC: reactions to the Day 1 SC injection (subsequent Part 1 doses were IV infusions); Part 2 SC: all SC injections. Symptoms shown if reported in ≥2 participants in any group. ^aInjection site pain (Grade 1). ^bInjection site erythema (Grade 1). IV, intravenous; SC, subcutaneous.

Premedications:

- Part 1 SC: antihistamine, corticosteroid and antipyretic (all oral) 30–60 min before each dose
- Part 2: antihistamine, corticosteroid and antipyretic (all oral) 30–60 min before first dose; antihistamine and antipyretic only for all subsequent doses