Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Kastritis E, Palladini G, Minnema MC, et al. Daratumumab-based treatment for immunoglobulin light-chain amyloidosis. N Engl J Med 2021;385:46-58. DOI: 10.1056/NEJMoa2028631

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Collaborators

The following principal investigators participated in the ANDROMEDA study:

Australia: Bradley Augustson, Fiona Kwok, Peter Mollee, Simon Gibbs; **Belgium:** Chantal Doyen, Greet Bries, Isabelle Vande Broek, Ka Lung Wu, Koen Theunissen, Koen Van Eygen, Michel Delforge, Nathalie Meuleman, Philip Vlummens; **Brazil:** Angelo Maiolino, Breno Moreno de Gusmão, Carlos Eduardo Miguel, Edvan Crusoe, Fernanda Moura, Fernanda Seguro, Jandey Bigonha, Juliane Musacchio, Karla Zanella, Laura Garcia, Marcelo Eduardo Zanella Capra, Reijane Alves de Assis, Rosane Bittencourt, Vania Hungria, Walter Braga, Wolney Barreto; **Canada:** Christopher Venner, Donna Reece, Emilie Lemieux-Blanchard, Kevin Song, Michael Sebag, Selay Lam, Victor Zepeda; **China:** Haitao Zhang, Jianda Hu, Jin Lu, Juan Li, Songfu Jiang, Ting Niu, Wenming Chen, Xiaonong Chen, Zhen Cai, Zhou Fude; **Denmark:** Maja Oelholm Vase, Morten Salomo, Niels Abildgaard; **France:** Alain Fuzibet, Anne-Marie Stoppa, Arnaud Jaccard, Bertrand Arnulf, Bruno Moulin, Bruno Royer, David Ghez, Denis Caillot, Dominique Chauveau, Franck Bridoux, Lauriane Clement-Filliatre, Lionel Karlin, Lotfi Benboubker, Mamoun Dib, Margaret Macro, Mohamad Mohty, Olivier Decaux, Olivier Hermine, Olivier Tournilhac, Philippe Moreau, Salomon Manier, Sylvain Choquet, Véronique Dorvaux; **Germany:** Alexander Carpinteiro, Axel Nogai, Britta Besemer, Christoph Roellig, Roland Fenk, Stefan Knop, Stefan Schönland, Timon Hansen; **Greece:** Argiris Symeonidis, Efstathios Kastritis; **Hungary:** Gabor Mikala, Tamás Masszi, Zsolt Nagy; **Israel:** Celia Suriu, Hila Magen, Iuliana Vaxman, Lev Shvidel, Meir Preis, Moshe Gatt, Noa Lavi, Osnat Jarchowsky, Tamar Tadmor, Yael Cohen; **Italy:** Angelo Vacca, Giovanni Palladini, Mario Boccadoro, Maurizio Martelli, Maurizio Musso, Michele Cavo; **Japan:** Chihiro Shimazaki, Hiroyuki Takamatsu, Kazutaka Sunami, Kenshi Suzuki, Nagaaki Katoh, Shinsuke Iida, Takayuki Ikezoe, Tomoaki Fujisaki, Yuta Katayama; **Republic of Korea:** Chang Ki Min, Ho-Jin Shin, Jin seok Kim, Jung Yong Hong, Ki Hyun Kim, Sung-Soo Yoon; **Mexico:** Aline Ramirez, Alvaro Cabrera, Christian Ramos, David Gomez Almaguer, Deborah Martinez, Guillermo Ruiz, Helen Dayani Caballero, Juan Antonio Flores Jimenez; **Netherlands:** Annemiek Broijl, Laurens Nieuwenhuizen, Monique Minnema, Paula Ypma, Wilfried Roeloffzen; **Poland:** Dominik Dytfeld, Grzegorz Charlinski, Grzegorz Helbig, Krzysztof Jamroziak, Sebastian Grosicki, Wieslaw Jedrzejczak; **Spain:** Albert Oriol Rocafiguera, Elham Askari, Fernando Escalante Barrigon, Isabel Krsnik Castello, Javier De la Rubia Comos, Jesus Martin Sanchez, Joaquin Martinez Lopez, Jose Angel Hernandez Rivas, Luis Felipe Casado Montero, Maria Jesus Blanchard Rodriguez, Maria Teresa Cibeira Lopez, Maria Victoria Mateos Manteca, Marta Sonia Gonzalez Perez, Mercedes Gironella Mesa, Rafael Rios Tamayo, Ramon Lecumberri Villamediana, Ricarda Garcia Sanchez, Sunil Lakhwani, Yolanda Gonzalez; **Sweden:** Hareth Nahi, Kristina Carlsson, Markus Hansson, Ulf-Henrik Mellqvist; **Turkey:** Ali Unal, Burhan Ferhanoglu, Hayri Ozsan, Levent Undar, Mehmet Turgut, Mehmet Yilmaz, Meral Beksac, Muhlis Cem Ar, Muzaffer Demir, Sevgi Besisik; **United Kingdom of Great Britain and Northern Ireland:** Ashutosh Wechalekar, Jamie Cavenagh, Jim Cavet, Mark Cook, Rachel Hall; **United States of America:** Adam Waxman, Anuj Mahindra, Cesar Rodriguez Valdes, Christine Ye, Craig Reeder, Daphne Friedman, David Siegel, Divaya Bhutani, Edward Libby, Eva Medvedova, Frank Passero, Giada Bianchi, Giampaolo Talamo, Guido Tricot, Hans Lee,

Heather Landau, Jan Moreb, Jason Valent, Jeffrey Matous, Jeffrey A. Zonder, Jesus Berdeja, Jonathan Kaufman, Keith Stockerl-Goldstein, Keren Osman, Ketan Doshi, Kevin Barton, Larry Anderson, Manisha Bhutani, Mehmet Kocoglu, Michael Rosenzweig, Michael Schuster, Michaela Liedtke, Morie Gertz, Naresh Bumma, Natalie Callander, Raymond Comenzo, Robert Vescio, Roger Pearse, Sandy W. Wong, Stacey A. Goodman, Stefano Tarantolo, Taimur Sher, Tibor Kovacsovics, Tomer Mark, Vaishali Sanchorawala, William Bensinger.

Additional Methods

Preinfusion and Postinfusion Medications

All patients who received daratumumab also received medications to prevent administration-related reactions. Pre-infusion medications were administered 1 to 3 hours before each daratumumab subcutaneous (SC) injection (1 hour preferred), and included dexamethasone (20 mg intravenously [IV] or orally [PO], or equivalent); acetaminophen (650 to 1000 mg IV or PO, or equivalent); an antihistamine (diphenhydramine 25 to 50 mg IV or PO, or equivalent); and montelukast (10 mg PO or equivalent), which is optional on cycle 1 day 1 and could have been administered up to 24 hours before SC infusion, per investigator discretion. Dexamethasone was given as part of the weekly dose, so that on daratumumab dosing days, patients received 20 mg on the day of daratumumab infusion as premedication and the remaining 20 mg on the day after daratumumab dosing. On weeks that daratumumab was not administered, patients in the daratumumab group could take their weekly dose (40 mg) on one day or divided by 2 days.

Postinfusion medications included a low-dose oral methylprednisolone (≤20 mg) or equivalent, the day after the daratumumab SC infusion. However, if the background regimen-specific corticosteroid (eg, dexamethasone) was administered on the day after the infusion, the additional postinfusion steroids are not required, but may be considered by the investigator. Patients who continued daratumumab monotherapy after completing the first six cycles of treatment could discontinue postinfusion corticosteroids in the absence of administration-related reactions per investigator discretion.

Patients with a high risk of respiratory complications (eg, mild asthma or patients with chronic obstructive pulmonary disorder with an forced expiratory volume in 1 second [FEV1] <80% at screening or those who developed FEV1 <80% during the study) were advised to consider the following postinfusion medications: antihistamine (diphenhydramine or equivalent), leukotriene inhibitor (montelukast or equivalent), short-acting β2 adrenergic receptor agonist (eg, salbutamol aerosol), and/or control medications for lung disease.

Disease Evaluation and Definitions of Efficacy End Points

Disease evaluations were performed centrally every 4 weeks during cycles 1 through 6 and every 8 weeks starting at cycle 7 and through the posttreatment observation phase until disease progression (as defined by the major organ deterioration–progression-free survival end point, calculated after adjusting for dependent censoring due to the initiation of non–cross-resistant subsequent therapy), death, or withdrawal from study. Non–cross-resistant subsequent therapy included any anti–plasma cell agent not included in the original protocol-assigned treatment.

Primary End Point

Overall hematologic complete response rate: proportion of patients who achieve a hematologic complete response according to the consensus guidelines for AL amyloidosis[1] with clarifications (ie, if involved FLC [iFLC] is lower than the upper limit of normal [ULN], normalization of uninvolved FLC [uFLC] level and FLC ratio are not required when determining hematologic complete response),[2-8] as assessed per the Independent Review Committee. The overall hematologic complete response rate was calculated for each treatment group based on the intention-to-treat population.

Secondary End Points

Major organ deterioration–progression-free survival: This is a composite endpoint of clinically observable endpoints and was defined from randomization to any one of the following events, whichever comes first:

- Death
- Clinical manifestation of cardiac failure
    - Defined as need for cardiac transplant, left ventricular assist device (LVAD), or intra-aortic balloon pump (IABP)
- Clinical manifestation of renal failure
    - Defined as the development of end-stage renal disease (need for hemodialysis or renal transplant)
- Development of hematologic progressive disease as per consensus guidelines
    - From hematologic complete response, abnormal free light chain ratio (light chain ratio must double), or from any response, a 50% increase in serum M-protein to >0.5 g/dL or 50% increase in urine M-protein to >200 mg/day (a visible peak must be present)
    - Free light chain increase of 50% to >100 mg/L

Organ response rate: for kidney, heart, liver was defined as the proportion of baseline organ involved patients who achieved organ response in each corresponding organ.

Overall survival: the time from the date of randomization to the date of the patient's death. If the patient was alive or the vital status was unknown, then the patient's data were censored at the date the patient was last known to be alive.

Rate of hematologic complete response at 6 months: the proportion of patients who achieve a hematologic complete response at 6 months, according to the consensus guidelines for AL amyloidosis during or after the study treatment.

Improvement in fatigue: the change from baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30.

Improvement in mental functioning: the change from baseline in the 36-Item Short Form Survey version 2 (SF-36v2) Mental Component Summary (MCS).

Improvement in health-related quality of life: the change from baseline in the EORTC QLQ-C30 Global Health Status scale score.

Time to next treatment: the time from the date of randomization to the start date of subsequent AL amyloidosis (non-protocol) treatment. Death due to progressive disease prior to subsequent therapy was considered as an event. Otherwise, patients were censored at the date of death or the last date known to be alive.

Rate of hematologic very good partial response or better: the proportion of patients who achieved hematologic complete response or very good partial response.

Time to response (hematologic complete response or very good partial response): the time between the date of randomization and the first efficacy evaluation at which the patient had met all criteria for hematologic response (hematologic complete response or very good partial response).

Duration of response (hematologic complete response or very good partial response): the time between the date of initial documentation of response to the date of first documented

evidence of hematologic progressive disease. For patients who have not progressed, data were censored at the last disease assessment.

Time to organ response: the time between the date of randomization and the first efficacy evaluation at which the patient had each corresponding organ response.

Time to organ progression: the time from the date of randomization to the date of each corresponding organ progression per consensus guidelines.

Statistical Methods

In the calculation of hematologic complete response rate, the denominator includes all randomized patients. If a patient dies without achieving a hematologic complete response, this patient will be included in the denominator, however, if the patient achieves hematologic complete response then dies, the patient will be included in both the denominator and numerator of the calculation of hematologic complete response rate. Major organ deterioration–progression-free survival was analyzed by employing inverse probability of censoring weight method to adjust estimates of a treatment effect in the presence of subsequent therapy (any anti–plasma cell agent not included in the original protocol assigned treatment).[9] Continuous variables were summarized using descriptive statistics, and categorical variables were summarized using frequency and percentage. Hazard ratios and corresponding 95% confidence intervals were estimated with the use of a Cox regression model. All statistical hypothesis tests and 95% confidence intervals presented were two-sided. If the testing of the primary end point was found to be statistically significant (alpha level <0.0499 after adjusting for interim analysis), the following secondary end points, as ordered here, were to be tested sequentially each with an

overall two-sided alpha of 0.05: major organ deterioration–progression-free survival and overall survival. The O'Brien–Fleming stopping boundary at the time of the primary analysis for the end points listed above was calculated with the use of a Lan-DeMets alpha-spending function on the basis of the number of events observed.

The primary hypothesis (ie, hypothesis on overall hematologic complete response rate) was tested at the 0.05 significance level (overall). The alpha spent at the second interim analysis was 0.0001 (2-sided). The significance level for the primary analysis was 0.0499 (2-sided) after adjusting for the interim analysis. Testing of the primary and key secondary endpoints was performed using a hierarchical testing approach as proposed by Tang and Geller[10] that strongly controls Type I error rate, in the order of MOD-PFS and OS, such that the overall Type I error rate was strongly controlled under 0.05 (2-sided). If the testing of the primary endpoint rate was statistically significant, then MOD-PFS was to be tested with an overall alpha of 0.05 (2-sided). Specifically, at the primary analysis, MOD-PFS was to be tested at P=0.00136 significance level at the interim analysis for this endpoint using O'Brien-Fleming spending function. If hematologic complete response and MOD-PFS were all statistically significant, then OS was to be tested with an overall alpha of 0.05 (2-sided) using O'Brien-Fleming spending function.

Of the two planned interim analyses, the first evaluated only safety after approximately 30 patients had received at least one cycle of treatment, and the second interim analysis evaluated efficacy and safety after at least 180 patients were treated for at least six cycles.

Figure S1. Study Design.

C denotes cyclophosphamide, d dexamethasone, DARA daratumumab; MOD-PFS major organ deterioration–progression-free survival, QW weekly, Q2W every 2 weeks, Q4W every 4 weeks, SC subcutaneous, V bortezomib.

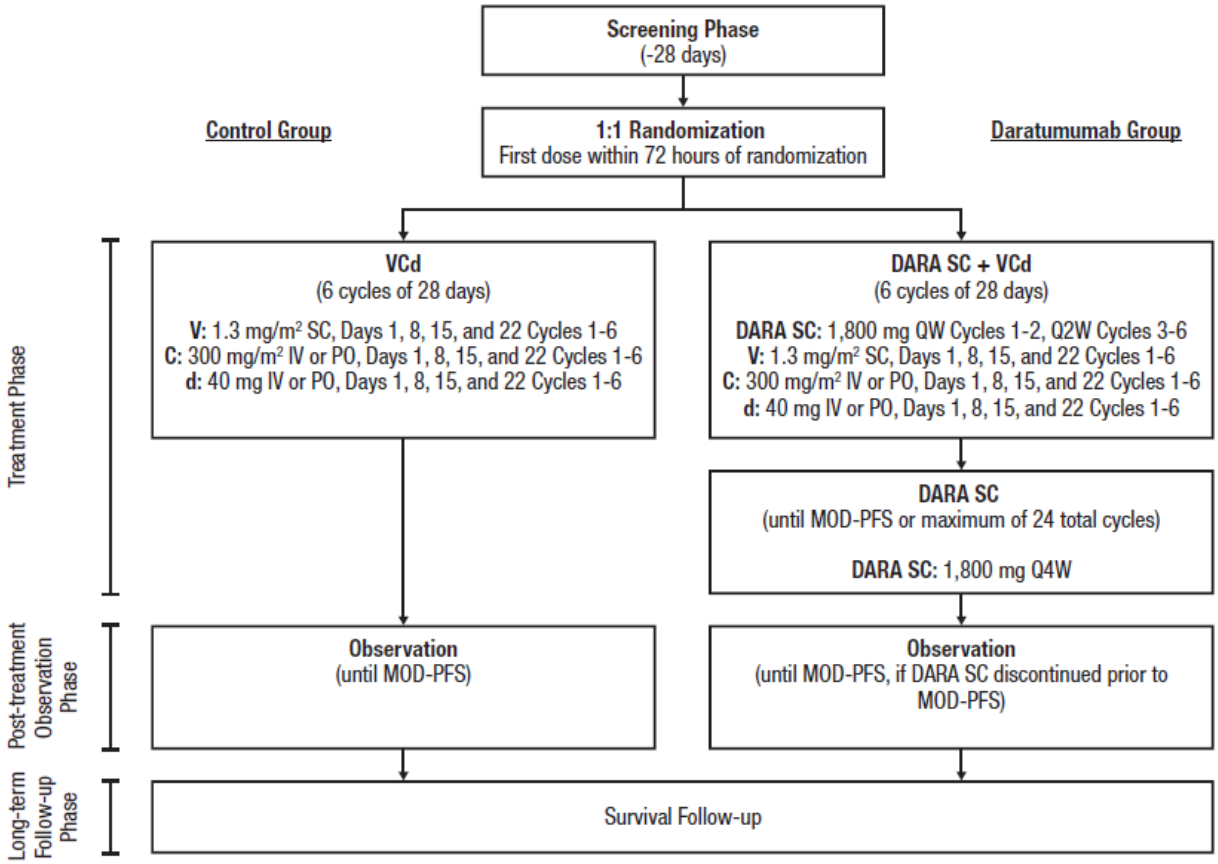
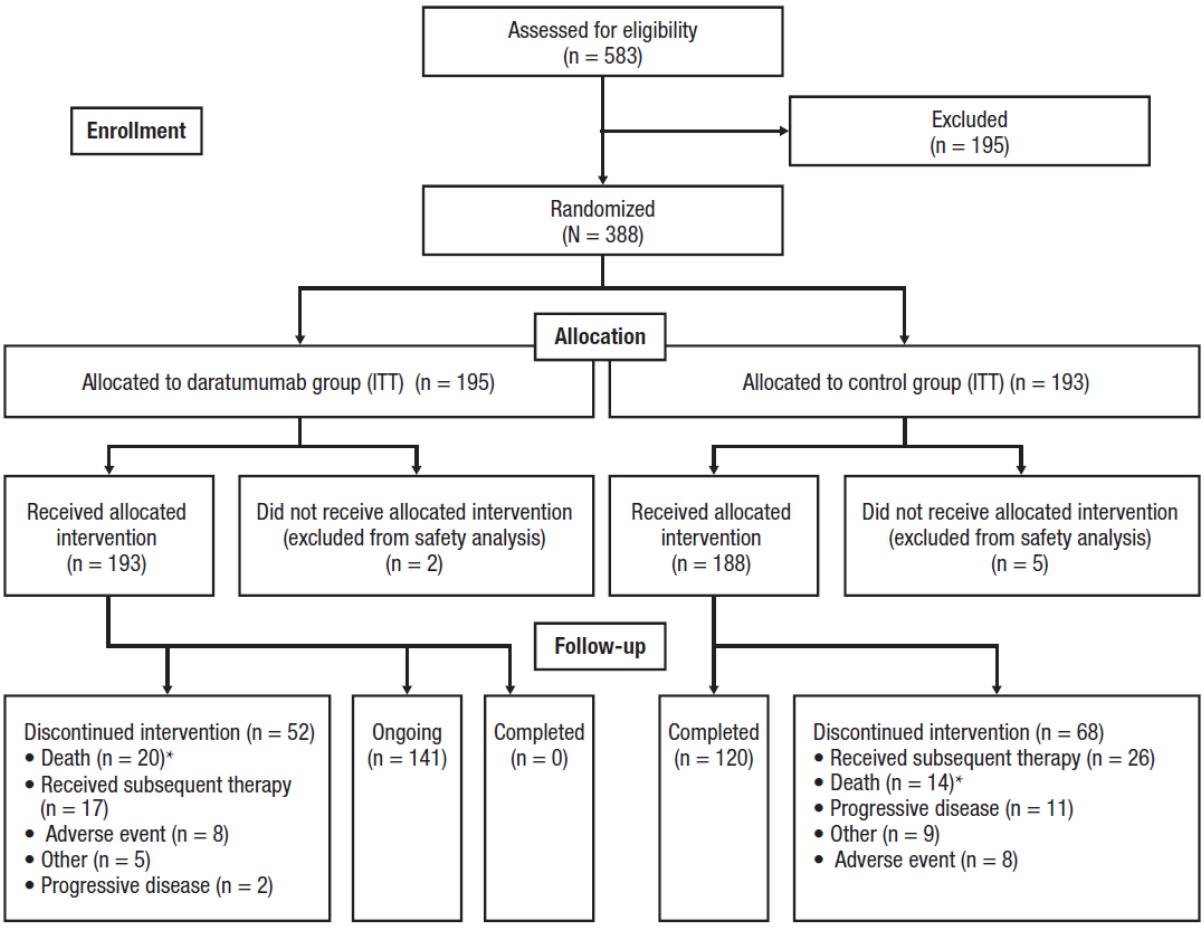


Figure S2. CONSORT Patient Flow Diagram.



*Deaths include only those that were the primary reason for treatment discontinuation, and do not represent the total number of deaths during the study period.

Figure S3. Reduction in iFLC and dFLC During Study.

Mean (A) iFLC levels and (B) dFLC levels achieved by patients during the study, assessed while on treatment and at subsequent disease evaluation. iFLC denotes involved free light chain, dFLC difference between involved and uninvolved free light chain, SE standard error, C cycle, D day, DE disease evaluation.

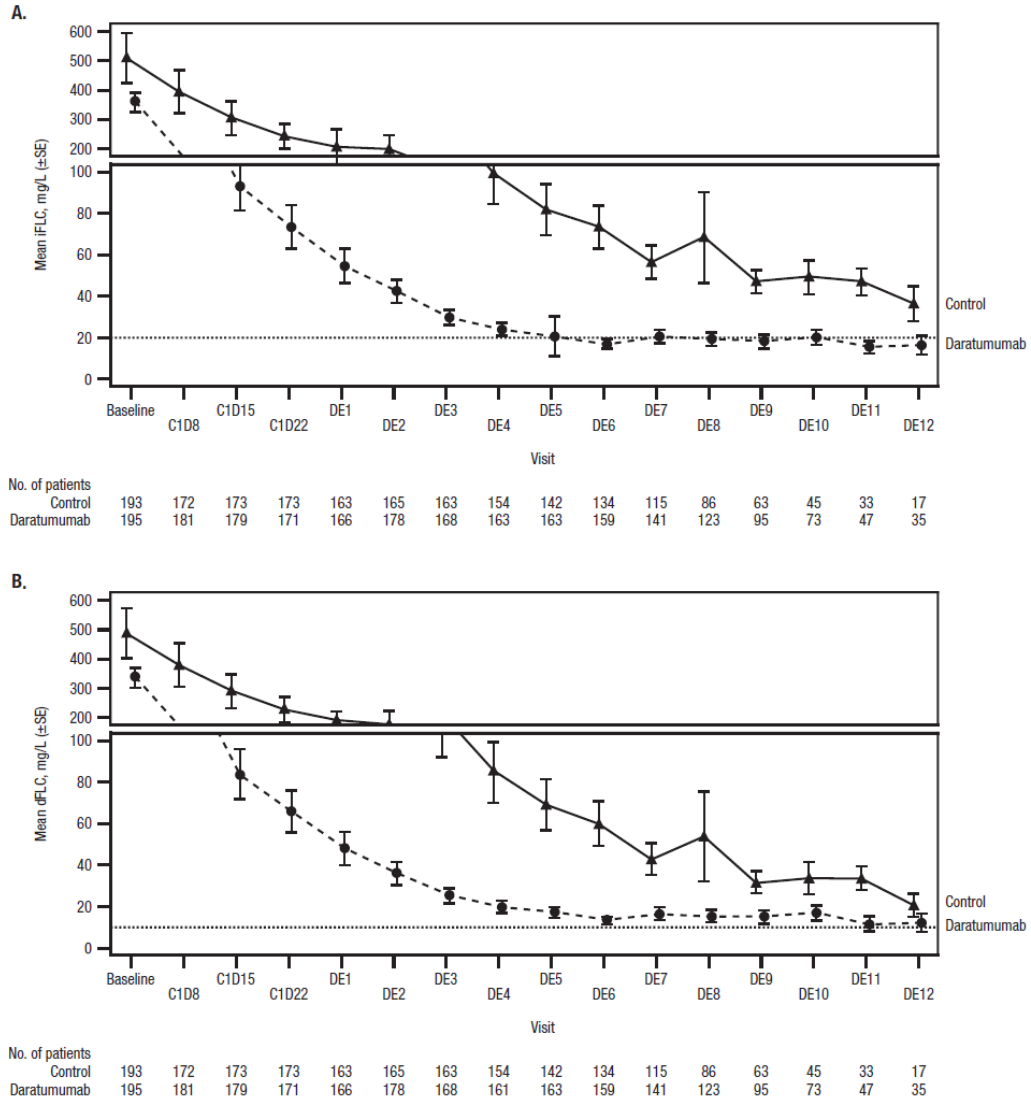


Figure S4. Overall Survival.

At the time of clinical cutoff, a total of 56 deaths (27 in the daratumumab group and 29 in the control group) were observed. One patient in the control group died before receiving treatment. Results for overall survival were immature, and will be analyzed after approximately 200 major organ deterioration-progression–free survival events have occurred. Final overall survival analysis to occur 5 years after date of last patient randomization if overall survival results have not yet crossed the prespecified statistical boundary at prior analysis.

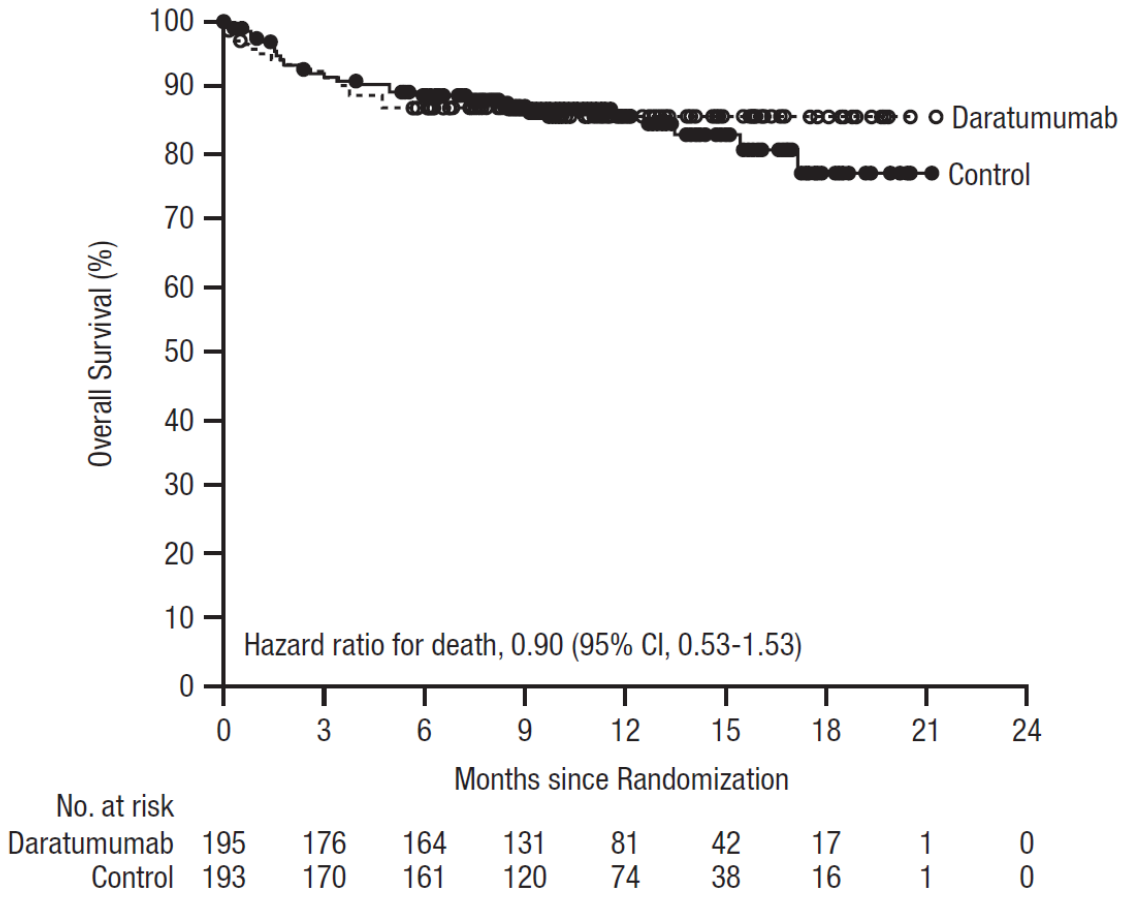


Table S1. Hematologic Response and Progression Criteria

Response Category	*Criteria*
Complete response	• Per consensus guidelines,[1] negative serum and urine immunofixation and normalization of free light chain levels and free light chain ratios • Per clarifications during the trial based on recent evidence[2-4] (recommended by the Steering Committee and agreed upon by the Independent Review Committee), if involved free light chain is lower than upper limit of normal, normalization of uninvolved free light chain level and free light chain ratio is not required when determining hematologic complete response
Very good partial response	• Baseline* dFLC ≥50 mg/L: reduction in dFLC <40 mg/L • Baseline* dFLC <50 mg/L: ≥90% reduction in serum M-protein plus urine M-protein <100 mg/24 hours
Partial response	• Baseline* dFLC ≥50 mg/L: a greater than 50% reduction in the dFLC • Baseline* dFLC <50 mg/L: ≥50% reduction in serum M-protein plus reduction in 24-hour urine M-protein by ≥90% or to <200 mg/24 hours
No response	• Less than a partial response
Progression	• From complete response, abnormal free light chain ratio (light chain must double) • From any response, 50% increase in serum M-protein to >0.5 g/dL or 50% increase in urine M-protein to >200 mg/day (a visible peak must be present) • Involved free light chain increase of 50% to >100 mg/L

dFLC denotes difference between involved and uninvolved free light chain.
*Baseline measurement is defined as the closest non-missing measurement taken on or prior to the first study treatment administration.

Table S2. Organ Response and Progression Criteria

Organ	Response	Progression
Heart[11]	NT-proBNP response (>30% and >300 ng/L decrease in patients with baseline NT-proBNP ≥650 ng/L) or NYHA class response (≥2 class decrease in patients with baseline NYHA class 3 or 4)	NT-proBNP progression (>30% and >300 ng/L increase*) or cTn progression (≥33% increase) or ejection fraction progression (≥10% decrease)
Kidney[12]	≥30% decrease in proteinuria or drop in proteinuria below 0.5 g/24 hours in the absence of renal progression	≥25% decrease in eGFR
Liver[1]	50% decrease in abnormal ALP value	50% increase of ALP above the lowest value

ALP denotes alkaline phosphatase, cTn cardiac troponin, eGFR estimated glomerular filtration rate, NT-proBNP N-terminal pro b-type natriuretic peptide, NYHA New York Heart Association.

*Patients with progressive worsening renal function cannot be scored for NT-proBNP progression.

Table S3. Events for Major Organ Deterioration–Progression-free Survival* and Major Organ Deterioration–Event-free Survival†

Events‡ — no. (%)	Daratumumab Group (N=195)	Control Group (N=193)
MOD-PFS		
Hematologic progression	8 (4.1)	25 (13)
Major organ deterioration	1 (0.5)	7 (3.6)
Death	25 (12.8)	21 (10.9)
MOD-EFS		
Hematologic progression	7 (3.6)	22 (11.4)
Major organ deterioration	1 (0.5)	6 (3.1)
Death	25 (12.8)	19 (9.8)
Subsequent therapy§	13 (6.7)	45 (23.3)

MOD-EFS denotes major organ deterioration–event-free survival, MOD-PFS major organ deterioration–progression-free survival.

*Defined as hematologic progression (assessed by Independent Review Committee), end-stage cardiac or renal disease, or death, whichever comes first (regardless of subsequent therapy).

†Defined as hematologic progression (assessed by Independent Review Committee), end-stage cardiac or renal disease, initiation of subsequent non–cross-resistant anti–plasma cell therapy, or death, whichever comes first.

‡Patients may have had more than one event; for MOD-EFS, the earliest event date was used.

§Subsequent therapy was adjudicated by the Independent Review Committee and was defined as subsequent non–cross-resistant anti–plasma cell therapy (ie, any anti–plasma cell agent not included in the original protocol-assigned treatment).

Table S4. Supportive Analyses of Major Organ Deterioration–Progression-free Survival.

	Daratumumab Group (N=195)	Control Group (N=193)
MOD-PFS, Investigator Assessed*		
Events — no. (%)	37 (19.0)	57 (29.5)
Hematologic progression	11 (5.6)	29 (15.0)
Major organ deterioration	1 (0.5)	7 (3.6)
Death	25 (12.8)	21 (10.9)
Hazard ratio (95% CI)	0.43 (0.28-0.67)	
P value	<0.0001	
MOD-PFS, Naïve Analysis†		
Events — no. (%)	32 (16.4)	43 (22.3)
Hazard ratio (95% CI)	0.57 (0.36-0.91)	
P value	0.0161	
MOD-PFS, Without Censoring for Subsequent Therapy‡		
Events — no. (%)	34 (17.4)	53 (27.5)
Hazard ratio (95% CI)	0.57 (0.37-0.87)	
P value	0.0094	

CI denotes confidence interval, IRC Independent Review Committee, MOD-PFS major organ deterioration–progression-free survival.

*Defined as hematologic progression (assessed by the investigator), end-stage cardiac or renal disease, or death, whichever comes first. Calculated using inverse probability of censoring weighting method as in primary MOD-PFS analysis.

†Defined as hematologic progression (assessed by the IRC), end-stage cardiac or renal disease, or death, whichever comes first. Calculated based on IRC assessment by using naïve censoring method (ie, censoring patients at the last disease assessment before start of subsequent non–cross-resistant, anti–plasma cell therapy). Based on stratified Cox model.

‡Defined as hematologic progression (assessed by the IRC), end-stage cardiac or renal disease, or death, whichever comes first. Calculated based on IRC assessment without censoring for subsequent non–cross-resistant, anti–plasma cell therapy (ie, not censoring patients at the last disease assessment before start of subsequent non–cross-resistant, anti–plasma cell therapy), if a patient receives subsequent non-cross resistant, anti-plasma cell therapy prior to hematologic progression or major organ deterioration. Based on stratified Cox model.

Table S5. Systemic Administration-related Reactions and Local Injection-site Reactions.

Events* — no. (%)	Daratumumab Group (N=193)	Control Group (N=188)
Systemic Administration-related Reactions†	14 (7.3)	–
Events Occurring in >1 Patient		
Chills	3 (1.6)	–
Pyrexia	3 (1.6)	–
Dizziness	2 (1.0)	–
Nausea	2 (1.0)	–
Overall Local Injection-site Reactions (Any Agent)	54 (27.9)	45 (23.9)
Events Occurring in >1 Patient		
Injection-site erythema	18 (9.3)	21 (11.2)
Injection-site pain	7 (3.6)	2 (1.1)
Injection-site bruising	4 (2.1)	0
Infusion-site pain	2 (1.0)	1 (0.5)
Injection-site discoloration	2 (1.0)	1 (0.5)
Local Injection-site Reactions Related to Daratumumab†	21 (10.9)	–
Events Occurring in >1 Patient		
Injection-site erythema	10 (5.2)	–
Injection-site pain	6 (3.1)	–
Infusion-site pain	2 (1.0)	–

*In the safety population, including all patients who received ≥1 dose of study treatment.
†Events related to daratumumab. All events were grade 1 or 2.

Table S6. Complete Response Outcomes by International Society of Amyloidosis Criteria.

	Daratumumab Group (N=195)		Control Group (N=193)
Complete Response Defined as Negative Immunofixation and FLC Ratio Normalization Without Confirmation*			
Events — %	47.2		22.8
Relative risk ratio (95% CI)		2.1 (1.5-2.8)	
Odds ratio (95% CI)		3.1 (2.0-4.8)	
P value		<0.0001	
Complete Response Defined as Negative Immunofixation and FLC Ratio Within the Reference Range or Abnormal FLC Ratio, if Uninvolved FLC is Higher Than Involved FLC†			
Events — %	54.4		26.9
Relative risk ratio (95% CI)		2.0 (1.5-2.6)	
Odds ratio (95% CI)		3.1 (2.1-4.8)	
P value		<0.0001	

*Palladini G, et al. *J Clin Oncol*. 2012;30:4541-4549.
†Palladini G, et al. *Amyloid.* 2021:1-2.
CI denotes confidence interval.

Table S7. Exposure-adjusted Incidence Rates of Overall and Grade 3 or 4 Adverse Events in the Safety Population.*

Event	Daratumumab Group (N=193)		Control Group (N=188)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	Events per 100 patient-months at risk			
Any adverse event	154.23	10.55	217.92	18.96
Diarrhea	5.26	0.61	8.87	0.88
Peripheral edema	5.75	0.33	10.81	1.38
Constipation	5.07	0.16	8.45	0
Peripheral sensory neuropathy	4.40	0.27	5.14	0.49
Fatigue	3.58	0.44	8.10	0.73
Nausea	3.67	0.16	8.10	0
Upper respiratory tract infection	3.40	0.05	2.74	0.12
Lymphopenia	2.24	1.46	3.74	2.42
Neutropenia	1.22	0.55	1.54	0.62
Pneumonia	1.18	0.83	1.49	0.99
Syncope	0.79	0.56	1.50	1.50
Cardiac failure	0.88	0.54	1.25	0.61
Hypokalemia	1.39	0.16	3.71	1.26

*The safety population included patients who received one or more administration of study treatment. Adverse events shown are those of any grade occurring in more than 25% of the patients in either group, or grade 3 or 4 events occurring in at least 5% of patients in either group.

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Analysis set: safety	188	188	163	193	193	177	149
Subjects with 1 or more TEAEs	185 (98.4%)	175 (93.1%)	150 (92.0%)	189 (97.9%)	180 (93.3%)	167 (94.4%)	121 (81.2%)
System organ class							
Preferred term							
General disorders and administration site conditions	138 (73.4%)	107 (56.9%)	86 (52.8%)	147 (76.2%)	117 (60.6%)	90 (50.8%)	34 (22.8%)
Edema peripheral	68 (36.2%)	45 (23.9%)	28 (17.2%)	69 (35.8%)	54 (28.0%)	35 (19.8%)	10 (6.7%)
Fatigue	53 (28.2%)	36 (19.1%)	26 (16.0%)	52 (26.9%)	38 (19.7%)	24 (13.6%)	6 (4.0%)
Asthenia	20 (10.6%)	12 (6.4%)	12 (7.4%)	31 (16.1%)	22 (11.4%)	11 (6.2%)	6 (4.0%)
Pyrexia	16 (8.5%)	8 (4.3%)	10 (6.1%)	25 (13.0%)	15 (7.8%)	9 (5.1%)	4 (2.7%)
Injection site erythema	21 (11.2%)	17 (9.0%)	5 (3.1%)	18 (9.3%)	16 (8.3%)	4 (2.3%)	1 (0.7%)
Chills	4 (2.1%)	3 (1.6%)	1 (0.6%)	10 (5.2%)	8 (4.1%)	2 (1.1%)	0
Injection site pain	2 (1.1%)	2 (1.1%)	0	7 (3.6%)	4 (2.1%)	3 (1.7%)	0
Malaise	5 (2.7%)	4 (2.1%)	1 (0.6%)	7 (3.6%)	4 (2.1%)	2 (1.1%)	2 (1.3%)
Pain	3 (1.6%)	3 (1.6%)	0	7 (3.6%)	5 (2.6%)	2 (1.1%)	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Influenza like illness	3 (1.6%)	0	3 (1.8%)	6 (3.1%)	1 (0.5%)	3 (1.7%)	3 (2.0%)
Localized edema	6 (3.2%)	4 (2.1%)	4 (2.5%)	6 (3.1%)	3 (1.6%)	3 (1.7%)	0
Sudden death	3 (1.6%)	3 (1.6%)	0	6 (3.1%)	4 (2.1%)	2 (1.1%)	0
Generalized edema	6 (3.2%)	3 (1.6%)	3 (1.8%)	5 (2.6%)	2 (1.0%)	3 (1.7%)	0
Chest discomfort	3 (1.6%)	2 (1.1%)	1 (0.6%)	4 (2.1%)	3 (1.6%)	1 (0.6%)	0
Injection site bruising	0	0	0	4 (2.1%)	3 (1.6%)	1 (0.6%)	0
Non-cardiac chest pain	9 (4.8%)	4 (2.1%)	7 (4.3%)	4 (2.1%)	3 (1.6%)	1 (0.6%)	1 (0.7%)
Face edema	3 (1.6%)	0	3 (1.8%)	3 (1.6%)	2 (1.0%)	1 (0.6%)	0
Swelling face	1 (0.5%)	1 (0.5%)	0	3 (1.6%)	1 (0.5%)	2 (1.1%)	0
Gait disturbance	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Infusion site pain	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Injection site discoloration	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Injection site hematoma	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Edema	2 (1.1%)	0	2 (1.2%)	2 (1.0%)	1 (0.5%)	2 (1.1%)	0
Peripheral swelling	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Application site erythema	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Catheter site erythema	0	0	0	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Catheter site pain	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Chest pain	4 (2.1%)	2 (1.1%)	2 (1.2%)	1 (0.5%)	1 (0.5%)	0	0
Cyst	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Discomfort	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Drug intolerance	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Exercise tolerance decreased	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Feeling cold	0	0	0	1 (0.5%)	0	1 (0.6%)	0
General physical health deterioration	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Gravitational edema	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Hyperpyrexia	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Hypothermia	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Injection site dryness	0	0	0	1 (0.5%)	1 (0.5%)	1 (0.6%)	0
Injection site pruritus	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	0
Injection site reaction	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Injection site swelling	0	0	0	1 (0.5%)	1 (0.5%)	1 (0.6%)	0
Mucosal dryness	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Mucosal inflammation	0	0	0	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Edema due to cardiac disease	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Temperature intolerance	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Ulcer hemorrhage	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Administration site erythema	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Administration site irritation	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Facial pain	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Feeling abnormal	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Infusion site extravasation	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Injection site discomfort	2 (1.1%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Injection site exfoliation	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Injection site induration	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Injection site inflammation	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Injection site rash	4 (2.1%)	3 (1.6%)	1 (0.6%)	0	0	0	0
Sudden cardiac death	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Xerosis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Gastrointestinal disorders	134 (71.3%)	109 (58.0%)	68 (41.7%)	142 (73.6%)	118 (61.1%)	80 (45.2%)	40 (26.8%)
Diarrhea	57 (30.3%)	40 (21.3%)	24 (14.7%)	69 (35.8%)	42 (21.8%)	31 (17.5%)	18 (12.1%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Constipation	54 (28.7%)	43 (22.9%)	14 (8.6%)	66 (34.2%)	52 (26.9%)	20 (11.3%)	7 (4.7%)
Nausea	52 (27.7%)	39 (20.7%)	19 (11.7%)	52 (26.9%)	33 (17.1%)	21 (11.9%)	7 (4.7%)
Vomiting	21 (11.2%)	9 (4.8%)	15 (9.2%)	26 (13.5%)	15 (7.8%)	9 (5.1%)	6 (4.0%)
Abdominal pain	18 (9.6%)	6 (3.2%)	12 (7.4%)	18 (9.3%)	10 (5.2%)	4 (2.3%)	5 (3.4%)
Abdominal pain upper	13 (6.9%)	10 (5.3%)	3 (1.8%)	16 (8.3%)	12 (6.2%)	5 (2.8%)	1 (0.7%)
Abdominal distension	12 (6.4%)	8 (4.3%)	6 (3.7%)	13 (6.7%)	5 (2.6%)	5 (2.8%)	3 (2.0%)
Flatulence	0	0	0	7 (3.6%)	5 (2.6%)	1 (0.6%)	1 (0.7%)
Dyspepsia	12 (6.4%)	8 (4.3%)	4 (2.5%)	6 (3.1%)	4 (2.1%)	1 (0.6%)	1 (0.7%)
Dysphagia	2 (1.1%)	1 (0.5%)	1 (0.6%)	6 (3.1%)	5 (2.6%)	2 (1.1%)	0
Hemorrhoids	3 (1.6%)	1 (0.5%)	2 (1.2%)	6 (3.1%)	4 (2.1%)	2 (1.1%)	0
Dry mouth	6 (3.2%)	3 (1.6%)	3 (1.8%)	5 (2.6%)	2 (1.0%)	2 (1.1%)	1 (0.7%)
Gastroesophageal reflux disease	1 (0.5%)	0	1 (0.6%)	5 (2.6%)	3 (1.6%)	3 (1.7%)	0
Abdominal discomfort	2 (1.1%)	2 (1.1%)	0	4 (2.1%)	1 (0.5%)	2 (1.1%)	1 (0.7%)
Ascites	2 (1.1%)	0	2 (1.2%)	4 (2.1%)	2 (1.0%)	1 (0.6%)	1 (0.7%)
Hematochezia	0	0	0	4 (2.1%)	2 (1.0%)	2 (1.1%)	0
Mouth hemorrhage	1 (0.5%)	0	1 (0.6%)	4 (2.1%)	1 (0.5%)	4 (2.3%)	0
Stomatitis	5 (2.7%)	4 (2.1%)	2 (1.2%)	4 (2.1%)	3 (1.6%)	1 (0.6%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Odynophagia	0	0	0	3 (1.6%)	0	2 (1.1%)	1 (0.7%)
Aphthous ulcer	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Dental caries	0	0	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Gastric ulcer	0	0	0	2 (1.0%)	1 (0.5%)	2 (1.1%)	0
Gingival pain	0	0	0	2 (1.0%)	0	2 (1.1%)	0
Inguinal hernia	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Mouth ulceration	3 (1.6%)	1 (0.5%)	2 (1.2%)	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Abdominal hernia	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Abdominal pain lower	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Abdominal wall edema	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Anal fissure	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Angular cheilitis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Cheilitis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Chronic gastritis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Colitis ischemic	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Epigastric discomfort	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Food poisoning	0	0	0	1 (0.5%)	0	0	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Gastritis	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Gastrointestinal disorder	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Gastrointestinal hemorrhage	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Gastrointestinal toxicity	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Glossitis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Impaired gastric emptying	0	0	0	1 (0.5%)	1 (0.5%)	1 (0.6%)	0
Lip hematoma	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Melena	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	0
Oral mucosal blistering	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Oral pain	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	0
Pancreatitis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Paresthesia oral	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Rectal hemorrhage	2 (1.1%)	2 (1.1%)	0	1 (0.5%)	0	0	1 (0.7%)
Salivary hypersecretion	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Tongue discoloration	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Tongue ulceration	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Tooth loss	0	0	0	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Toothache	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Trichoglossia	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Upper gastrointestinal hemorrhage	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Acquired macroglossia	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Diarrhea hemorrhagic	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Gastric antral vascular ectasia	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Gastrointestinal motility disorder	2 (1.1%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Gastrointestinal pain	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Gastrointestinal wall thickening	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Hemorrhoidal hemorrhage	2 (1.1%)	2 (1.1%)	0	0	0	0	0
Hypoesthesia oral	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Ileus	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Esophageal oedema	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Esophageal spasm	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Oral disorder	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Salivary gland enlargement	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Infections and infestations	101 (53.7%)	50 (26.6%)	74 (45.4%)	127 (65.8%)	57 (29.5%)	89 (50.3%)	59 (39.6%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Upper respiratory tract infection	21 (11.2%)	10 (5.3%)	13 (8.0%)	50 (25.9%)	14 (7.3%)	27 (15.3%)	26 (17.4%)
Pneumonia	12 (6.4%)	3 (1.6%)	9 (5.5%)	21 (10.9%)	7 (3.6%)	9 (5.1%)	6 (4.0%)
Nasopharyngitis	11 (5.9%)	3 (1.6%)	8 (4.9%)	19 (9.8%)	4 (2.1%)	11 (6.2%)	8 (5.4%)
Conjunctivitis	5 (2.7%)	1 (0.5%)	5 (3.1%)	12 (6.2%)	3 (1.6%)	9 (5.1%)	2 (1.3%)
Herpes zoster	12 (6.4%)	4 (2.1%)	8 (4.9%)	10 (5.2%)	6 (3.1%)	3 (1.7%)	1 (0.7%)
Bronchitis	5 (2.7%)	2 (1.1%)	4 (2.5%)	9 (4.7%)	2 (1.0%)	1 (0.6%)	6 (4.0%)
Oral candidiasis	2 (1.1%)	1 (0.5%)	1 (0.6%)	9 (4.7%)	2 (1.0%)	6 (3.4%)	4 (2.7%)
Hordeolum	11 (5.9%)	4 (2.1%)	9 (5.5%)	8 (4.1%)	5 (2.6%)	4 (2.3%)	0
Rhinitis	2 (1.1%)	0	2 (1.2%)	8 (4.1%)	2 (1.0%)	3 (1.7%)	3 (2.0%)
Sepsis	0	0	0	7 (3.6%)	1 (0.5%)	5 (2.8%)	1 (0.7%)
Urinary tract infection	6 (3.2%)	3 (1.6%)	4 (2.5%)	7 (3.6%)	2 (1.0%)	4 (2.3%)	1 (0.7%)
Gastroenteritis	3 (1.6%)	0	3 (1.8%)	6 (3.1%)	1 (0.5%)	4 (2.3%)	2 (1.3%)
Lower respiratory tract infection	4 (2.1%)	2 (1.1%)	2 (1.2%)	6 (3.1%)	3 (1.6%)	2 (1.1%)	3 (2.0%)
Sinusitis	2 (1.1%)	2 (1.1%)	0	5 (2.6%)	1 (0.5%)	1 (0.6%)	3 (2.0%)
Influenza	9 (4.8%)	5 (2.7%)	4 (2.5%)	4 (2.1%)	0	1 (0.6%)	3 (2.0%)
Otitis media	0	0	0	4 (2.1%)	0	3 (1.7%)	1 (0.7%)
Pharyngitis	1 (0.5%)	1 (0.5%)	0	4 (2.1%)	1 (0.5%)	1 (0.6%)	2 (1.3%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Respiratory tract infection	2 (1.1%)	0	2 (1.2%)	4 (2.1%)	1 (0.5%)	1 (0.6%)	2 (1.3%)
Ear infection	0	0	0	3 (1.6%)	0	2 (1.1%)	1 (0.7%)
Tooth infection	1 (0.5%)	0	1 (0.6%)	3 (1.6%)	1 (0.5%)	2 (1.1%)	0
Cellulitis	5 (2.7%)	0	5 (3.1%)	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Gingivitis	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Infection	0	0	0	2 (1.0%)	2 (1.0%)	0	1 (0.7%)
Esophageal candidiasis	0	0	0	2 (1.0%)	0	2 (1.1%)	0
Respiratory syncytial virus infection	0	0	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Septic shock	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	0	2 (1.1%)	0
Tooth abscess	0	0	0	2 (1.0%)	0	2 (1.1%)	0
Vulvovaginal candidiasis	0	0	0	2 (1.0%)	0	2 (1.1%)	0
Abscess of external auditory meatus	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Adenovirus infection	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Bacterial infection	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Body tinea	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Campylobacter gastroenteritis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Campylobacter infection	0	0	0	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Candida sepsis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Chronic sinusitis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Clostridium difficile infection	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Conjunctivitis bacterial	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Cytomegalovirus enterocolitis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Diverticulitis	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Enteritis infectious	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Epididymitis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Erysipelas	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Escherichia bacteremia	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Eye infection	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Eye infection bacterial	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Folliculitis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Fungal skin infection	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Gastroenteritis viral	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Gastrointestinal candidiasis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Gastrointestinal infection	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Helicobacter gastritis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Herpes virus infection	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0
Laryngitis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Localized infection	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Lower respiratory tract infection viral	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Lymphangitis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Neutropenic sepsis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Onychomycosis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Oral fungal infection	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Osteomyelitis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Otitis media viral	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Parainfluenzae virus infection	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Peritonitis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Pertussis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Pneumonia pneumococcal	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Pulmonary sepsis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Pyelonephritis acute	0	0	0	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Rash pustular	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Respiratory tract infection viral	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Rhinovirus infection	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Sinusitis bacterial	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Skin infection	2 (1.1%)	2 (1.1%)	0	1 (0.5%)	0	1 (0.6%)	0
Tinea infection	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	0
Tinea versicolor	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Tonsillitis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Vaginal infection	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Viral upper respiratory tract infection	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Wound infection	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Asymptomatic bacteriuria	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Candida infection	2 (1.1%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Clostridium bacteremia	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Cystitis	2 (1.1%)	0	2 (1.2%)	0	0	0	0
Diarrhea infectious	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Escherichia urinary tract infection	1 (0.5%)	0	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Herpes dermatitis	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Herpes simplex	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Paronychia	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Postoperative wound infection	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Pulpitis dental	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Serratia infection	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Tinea pedis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Tracheitis	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Upper respiratory tract infection bacterial	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Viral infection	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Vulvovaginal mycotic infection	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Nervous system disorders	103 (54.8%)	68 (36.2%)	64 (39.3%)	116 (60.1%)	83 (43.0%)	67 (37.9%)	25 (16.8%)
Peripheral sensory neuropathy	37 (19.7%)	18 (9.6%)	24 (14.7%)	60 (31.1%)	20 (10.4%)	39 (22.0%)	13 (8.7%)
Dizziness	26 (13.8%)	18 (9.6%)	8 (4.9%)	29 (15.0%)	24 (12.4%)	5 (2.8%)	1 (0.7%)
Headache	18 (9.6%)	12 (6.4%)	7 (4.3%)	25 (13.0%)	22 (11.4%)	3 (1.7%)	6 (4.0%)
Dysgeusia	11 (5.9%)	5 (2.7%)	6 (3.7%)	15 (7.8%)	10 (5.2%)	5 (2.8%)	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Paresthesia	12 (6.4%)	6 (3.2%)	6 (3.7%)	15 (7.8%)	10 (5.2%)	5 (2.8%)	1 (0.7%)
Syncope	12 (6.4%)	9 (4.8%)	4 (2.5%)	14 (7.3%)	10 (5.2%)	5 (2.8%)	0
Neuralgia	4 (2.1%)	1 (0.5%)	3 (1.8%)	11 (5.7%)	3 (1.6%)	6 (3.4%)	2 (1.3%)
Tremor	2 (1.1%)	1 (0.5%)	1 (0.6%)	10 (5.2%)	5 (2.6%)	5 (2.8%)	0
Presyncope	3 (1.6%)	2 (1.1%)	1 (0.6%)	7 (3.6%)	4 (2.1%)	2 (1.1%)	1 (0.7%)
Hypoesthesia	3 (1.6%)	2 (1.1%)	1 (0.6%)	6 (3.1%)	1 (0.5%)	4 (2.3%)	1 (0.7%)
Neuropathy peripheral	1 (0.5%)	0	1 (0.6%)	4 (2.1%)	2 (1.0%)	2 (1.1%)	0
Restless legs syndrome	2 (1.1%)	1 (0.5%)	1 (0.6%)	3 (1.6%)	3 (1.6%)	0	0
Somnolence	2 (1.1%)	1 (0.5%)	1 (0.6%)	3 (1.6%)	2 (1.0%)	1 (0.6%)	0
Taste disorder	6 (3.2%)	4 (2.1%)	2 (1.2%)	3 (1.6%)	1 (0.5%)	2 (1.1%)	0
Cerebral infarction	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	2 (1.0%)	0	0
Dizziness postural	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	2 (1.0%)	0	0
Dysesthesia	0	0	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Facial paralysis	0	0	0	2 (1.0%)	2 (1.0%)	0	0
Lethargy	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Post herpetic neuralgia	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	0	2 (1.1%)	0
Areflexia	0	0	0	1 (0.5%)	0	1 (0.6%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Autonomic nervous system imbalance	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Autonomic neuropathy	3 (1.6%)	2 (1.1%)	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Balance disorder	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	0
Carpal tunnel syndrome	1 (0.5%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Cerebrovascular accident	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	0	1 (0.7%)
Cervicobrachial syndrome	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Extrapyramidal disorder	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Hemiparesis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Lacunar infarction	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Loss of consciousness	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Migraine	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Migraine with aura	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Peripheral motor neuropathy	3 (1.6%)	0	3 (1.8%)	1 (0.5%)	0	0	1 (0.7%)
Peripheral sensorimotor neuropathy	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Poor quality sleep	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Radiculopathy	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Akinesthesia	1 (0.5%)	0	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Altered state of consciousness	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Amnesia	2 (1.1%)	0	2 (1.2%)	0	0	0	0
Burning sensation	3 (1.6%)	1 (0.5%)	2 (1.2%)	0	0	0	0
Cerebral thrombosis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Cognitive disorder	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Depressed level of consciousness	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Disturbance in attention	4 (2.1%)	3 (1.6%)	1 (0.6%)	0	0	0	0
Focal dyscognitive seizures	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Hypogeusia	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Ischemic stroke	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Memory impairment	2 (1.1%)	2 (1.1%)	0	0	0	0	0
Neurological decompensation	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Psychomotor hyperactivity	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Seizure	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Status epilepticus	1 (0.5%)	0	1 (0.6%)	0	0	0	0
VIth nerve disorder	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Vagus nerve disorder	1 (0.5%)	0	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Respiratory, thoracic and mediastinal disorders	74 (39.4%)	44 (23.4%)	45 (27.6%)	105 (54.4%)	62 (32.1%)	47 (26.6%)	32 (21.5%)
Dyspnea	32 (17.0%)	19 (10.1%)	16 (9.8%)	44 (22.8%)	24 (12.4%)	15 (8.5%)	11 (7.4%)
Cough	19 (10.1%)	8 (4.3%)	11 (6.7%)	32 (16.6%)	10 (5.2%)	12 (6.8%)	14 (9.4%)
Oropharyngeal pain	5 (2.7%)	3 (1.6%)	2 (1.2%)	12 (6.2%)	7 (3.6%)	4 (2.3%)	3 (2.0%)
Productive cough	1 (0.5%)	0	1 (0.6%)	12 (6.2%)	3 (1.6%)	6 (3.4%)	3 (2.0%)
Epistaxis	3 (1.6%)	1 (0.5%)	2 (1.2%)	10 (5.2%)	5 (2.6%)	7 (4.0%)	0
Pleural effusion	10 (5.3%)	6 (3.2%)	5 (3.1%)	10 (5.2%)	5 (2.6%)	5 (2.8%)	1 (0.7%)
Nasal congestion	2 (1.1%)	0	2 (1.2%)	9 (4.7%)	1 (0.5%)	5 (2.8%)	3 (2.0%)
Dysphonia	4 (2.1%)	1 (0.5%)	3 (1.8%)	7 (3.6%)	5 (2.6%)	2 (1.1%)	0
Dyspoea exertional	6 (3.2%)	2 (1.1%)	4 (2.5%)	7 (3.6%)	5 (2.6%)	2 (1.1%)	1 (0.7%)
Hiccups	2 (1.1%)	2 (1.1%)	0	7 (3.6%)	7 (3.6%)	0	0
Rales	1 (0.5%)	0	1 (0.6%)	6 (3.1%)	3 (1.6%)	1 (0.6%)	2 (1.3%)
Rhinorrhea	2 (1.1%)	0	2 (1.2%)	5 (2.6%)	1 (0.5%)	2 (1.1%)	2 (1.3%)
Hypoxia	1 (0.5%)	0	1 (0.6%)	3 (1.6%)	2 (1.0%)	0	1 (0.7%)
Pneumothorax	1 (0.5%)	1 (0.5%)	1 (0.6%)	3 (1.6%)	0	2 (1.1%)	1 (0.7%)
Sleep apnea syndrome	1 (0.5%)	0	1 (0.6%)	3 (1.6%)	0	2 (1.1%)	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Asthma	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Chronic obstructive pulmonary disease	0	0	0	2 (1.0%)	0	2 (1.1%)	1 (0.7%)
Orthopnea	4 (2.1%)	4 (2.1%)	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Pulmonary oedema	8 (4.3%)	5 (2.7%)	3 (1.8%)	2 (1.0%)	0	2 (1.1%)	0
Upper-airway cough syndrome	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	0	2 (1.1%)	0
Apnea	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Asthma-chronic obstructive pulmonary disease overlap syndrome	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Bronchial hyperreactivity	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Bronchospasm	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Hydrothorax	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Laryngeal inflammation	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Lung disorder	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Pneumonia aspiration	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Pneumonitis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Pulmonary embolism	2 (1.1%)	2 (1.1%)	0	1 (0.5%)	0	1 (0.6%)	0
Pulmonary hemorrhage	0	0	0	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Respiratory symptom	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Rhinitis allergic	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Sinus pain	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Throat tightness	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Wheezing	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Acute pulmonary edema	2 (1.1%)	1 (0.5%)	2 (1.2%)	0	0	0	0
Acute respiratory distress syndrome	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Atelectasis	3 (1.6%)	2 (1.1%)	1 (0.6%)	0	0	0	0
Dry throat	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Dyspnea paroxysmal nocturnal	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Hemoptysis	2 (1.1%)	0	2 (1.2%)	0	0	0	0
Laryngeal pain	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Nasal edema	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Respiratory failure	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Tachypnea	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Throat irritation	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Metabolism and nutrition disorders	84 (44.7%)	56 (29.8%)	47 (28.8%)	95 (49.2%)	58 (30.1%)	58 (32.8%)	28 (18.8%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Hypokalemia	28 (14.9%)	11 (5.9%)	20 (12.3%)	24 (12.4%)	12 (6.2%)	13 (7.3%)	5 (3.4%)
Decreased appetite	23 (12.2%)	15 (8.0%)	9 (5.5%)	19 (9.8%)	11 (5.7%)	8 (4.5%)	1 (0.7%)
Hyponatremia	7 (3.7%)	3 (1.6%)	5 (3.1%)	16 (8.3%)	8 (4.1%)	9 (5.1%)	2 (1.3%)
Hyperglycemia	7 (3.7%)	5 (2.7%)	5 (3.1%)	12 (6.2%)	4 (2.1%)	9 (5.1%)	4 (2.7%)
Hyperkalemia	7 (3.7%)	6 (3.2%)	3 (1.8%)	12 (6.2%)	8 (4.1%)	4 (2.3%)	5 (3.4%)
Hypocalcemia	9 (4.8%)	6 (3.2%)	6 (3.7%)	11 (5.7%)	7 (3.6%)	5 (2.8%)	2 (1.3%)
Hyperuricemia	8 (4.3%)	4 (2.1%)	4 (2.5%)	10 (5.2%)	4 (2.1%)	6 (3.4%)	3 (2.0%)
Hypertriglyceridemia	4 (2.1%)	3 (1.6%)	3 (1.8%)	9 (4.7%)	1 (0.5%)	6 (3.4%)	4 (2.7%)
Hypoalbuminemia	11 (5.9%)	7 (3.7%)	7 (4.3%)	9 (4.7%)	8 (4.1%)	1 (0.6%)	1 (0.7%)
Fluid retention	5 (2.7%)	3 (1.6%)	3 (1.8%)	8 (4.1%)	5 (2.6%)	3 (1.7%)	0
Hypoglycemia	3 (1.6%)	1 (0.5%)	2 (1.2%)	7 (3.6%)	4 (2.1%)	2 (1.1%)	1 (0.7%)
Hypercholesterolemia	5 (2.7%)	3 (1.6%)	5 (3.1%)	6 (3.1%)	3 (1.6%)	5 (2.8%)	1 (0.7%)
Hypomagnesemia	3 (1.6%)	1 (0.5%)	2 (1.2%)	6 (3.1%)	4 (2.1%)	3 (1.7%)	1 (0.7%)
Dehydration	4 (2.1%)	3 (1.6%)	1 (0.6%)	4 (2.1%)	2 (1.0%)	1 (0.6%)	1 (0.7%)
Fluid overload	7 (3.7%)	6 (3.2%)	2 (1.2%)	3 (1.6%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Folate deficiency	0	0	0	2 (1.0%)	2 (1.0%)	0	0
Hyperamylasemia	0	0	0	2 (1.0%)	0	2 (1.1%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Hypernatremia	0	0	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Hypophosphatemia	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Iron deficiency	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Acidosis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Alkalosis hypochloremic	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Diabetes mellitus	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Diabetic metabolic decompensation	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Hypercalcemia	2 (1.1%)	0	2 (1.2%)	1 (0.5%)	1 (0.5%)	0	1 (0.7%)
Hyperchloremia	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Increased appetite	3 (1.6%)	2 (1.1%)	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Malnutrition	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Metabolic alkalosis	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Starvation	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Tetany	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Type 2 diabetes mellitus	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Vitamin B12 deficiency	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0
Vitamin D deficiency	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Zinc deficiency	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Gout	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Hyperphosphatemia	2 (1.1%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Metabolic acidosis	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Steroid diabetes	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Tumor lysis syndrome	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Blood and lymphatic system disorders	77 (41.0%)	51 (27.1%)	51 (31.3%)	86 (44.6%)	57 (29.5%)	69 (39.0%)	25 (16.8%)
Anemia	44 (23.4%)	34 (18.1%)	21 (12.9%)	47 (24.4%)	27 (14.0%)	34 (19.2%)	5 (3.4%)
Lymphopenia	28 (14.9%)	16 (8.5%)	23 (14.1%)	36 (18.7%)	24 (12.4%)	28 (15.8%)	15 (10.1%)
Thrombocytopenia	22 (11.7%)	10 (5.3%)	15 (9.2%)	33 (17.1%)	21 (10.9%)	23 (13.0%)	3 (2.0%)
Neutropenia	12 (6.4%)	5 (2.7%)	10 (6.1%)	21 (10.9%)	13 (6.7%)	14 (7.9%)	4 (2.7%)
Leukopenia	7 (3.7%)	5 (2.7%)	4 (2.5%)	11 (5.7%)	9 (4.7%)	7 (4.0%)	1 (0.7%)
Febrile neutropenia	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Disseminated intravascular coagulation	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Hemorrhagic diathesis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Leukocytosis	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	0	1 (0.7%)
Lymphadenopathy	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Lymphocytosis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Microcytic anemia	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Normocytic anemia	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Blood loss anemia	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Hemolysis	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Iron deficiency anemia	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Spontaneous hematoma	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Thrombocytosis	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Skin and subcutaneous tissue disorders	42 (22.3%)	27 (14.4%)	23 (14.1%)	86 (44.6%)	49 (25.4%)	47 (26.6%)	21 (14.1%)
Rash	13 (6.9%)	11 (5.9%)	4 (2.5%)	17 (8.8%)	9 (4.7%)	5 (2.8%)	6 (4.0%)
Erythema	3 (1.6%)	2 (1.1%)	1 (0.6%)	11 (5.7%)	9 (4.7%)	3 (1.7%)	1 (0.7%)
Pruritus	8 (4.3%)	4 (2.1%)	5 (3.1%)	10 (5.2%)	6 (3.1%)	2 (1.1%)	4 (2.7%)
Dry skin	2 (1.1%)	1 (0.5%)	1 (0.6%)	9 (4.7%)	1 (0.5%)	6 (3.4%)	2 (1.3%)
Rash maculo-papular	2 (1.1%)	2 (1.1%)	1 (0.6%)	8 (4.1%)	5 (2.6%)	4 (2.3%)	0
Alopecia	5 (2.7%)	4 (2.1%)	1 (0.6%)	7 (3.6%)	1 (0.5%)	6 (3.4%)	0
Hyperhidrosis	1 (0.5%)	0	1 (0.6%)	5 (2.6%)	3 (1.6%)	0	2 (1.3%)
Decubitus ulcer	0	0	0	4 (2.1%)	1 (0.5%)	4 (2.3%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Pain of skin	0	0	0	4 (2.1%)	2 (1.0%)	1 (0.6%)	1 (0.7%)
Actinic keratosis	0	0	0	3 (1.6%)	1 (0.5%)	2 (1.1%)	1 (0.7%)
Skin lesion	2 (1.1%)	0	2 (1.2%)	3 (1.6%)	1 (0.5%)	1 (0.6%)	2 (1.3%)
Urticaria	2 (1.1%)	1 (0.5%)	1 (0.6%)	3 (1.6%)	0	2 (1.1%)	1 (0.7%)
Blister	0	0	0	2 (1.0%)	1 (0.5%)	2 (1.1%)	0
Dermatitis allergic	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Dermatitis bullous	0	0	0	2 (1.0%)	0	2 (1.1%)	0
Nail discoloration	0	0	0	2 (1.0%)	0	2 (1.1%)	0
Nail disorder	0	0	0	2 (1.0%)	1 (0.5%)	2 (1.1%)	0
Night sweats	4 (2.1%)	0	4 (2.5%)	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Papule	0	0	0	2 (1.0%)	0	2 (1.1%)	0
Petechiae	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	0	2 (1.1%)	0
Rash pruritic	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	2 (1.0%)	0	0
Sensitive skin	0	0	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Skin erosion	0	0	0	2 (1.0%)	0	2 (1.1%)	0
Dermatitis acneiform	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Ecchymosis	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Eczema	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Erythema multiforme	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0
Hemorrhage subcutaneous	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Intertrigo	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Photosensitivity reaction	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Purpura	2 (1.1%)	0	2 (1.2%)	1 (0.5%)	1 (0.5%)	0	0
Rash erythematous	2 (1.1%)	2 (1.1%)	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Rash macular	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Rash papular	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Seborrhoeic dermatitis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Skin atrophy	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0
Skin burning sensation	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Skin discoloration	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Skin hyperpigmentation	3 (1.6%)	1 (0.5%)	2 (1.2%)	1 (0.5%)	1 (0.5%)	0	0
Skin irritation	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Telangiectasia	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Asteatosis	1 (0.5%)	1 (0.5%)	0	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Dermatitis exfoliative generalized	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Drug eruption	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Epidermolysis	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Lividity	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Palmoplantar keratoderma	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Pruritus allergic	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Skin exfoliation	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Skin fissures	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Musculoskeletal and connective tissue disorders	52 (27.7%)	29 (15.4%)	29 (17.8%)	83 (43.0%)	51 (26.4%)	39 (22.0%)	34 (22.8%)
Back pain	11 (5.9%)	2 (1.1%)	11 (6.7%)	23 (11.9%)	11 (5.7%)	8 (4.5%)	8 (5.4%)
Arthralgia	9 (4.8%)	1 (0.5%)	8 (4.9%)	20 (10.4%)	9 (4.7%)	1 (0.6%)	11 (7.4%)
Muscle spasms	10 (5.3%)	7 (3.7%)	3 (1.8%)	19 (9.8%)	9 (4.7%)	9 (5.1%)	4 (2.7%)
Myalgia	7 (3.7%)	6 (3.2%)	1 (0.6%)	17 (8.8%)	13 (6.7%)	3 (1.7%)	4 (2.7%)
Muscular weakness	11 (5.9%)	8 (4.3%)	4 (2.5%)	16 (8.3%)	7 (3.6%)	10 (5.6%)	0
Pain in extremity	9 (4.8%)	6 (3.2%)	4 (2.5%)	16 (8.3%)	5 (2.6%)	7 (4.0%)	5 (3.4%)
Musculoskeletal chest pain	3 (1.6%)	2 (1.1%)	1 (0.6%)	5 (2.6%)	2 (1.0%)	2 (1.1%)	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Musculoskeletal pain	2 (1.1%)	1 (0.5%)	1 (0.6%)	5 (2.6%)	1 (0.5%)	2 (1.1%)	2 (1.3%)
Pain in jaw	0	0	0	3 (1.6%)	2 (1.0%)	1 (0.6%)	0
Spinal pain	0	0	0	3 (1.6%)	1 (0.5%)	2 (1.1%)	0
Bone pain	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Flank pain	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Intervertebral disc protrusion	0	0	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Jaw cyst	0	0	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Joint swelling	0	0	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Arthritis	0	0	0	1 (0.5%)	0	1 (0.6%)	1 (0.7%)
Bursitis	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Coccydynia	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0
Connective tissue inflammation	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Facet joint syndrome	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Groin pain	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Muscle atrophy	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Muscle contracture	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Muscle tightness	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Musculoskeletal stiffness	2 (1.1%)	2 (1.1%)	0	1 (0.5%)	1 (0.5%)	0	0
Myalgia intercostal	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Myokymia	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Myositis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Neck pain	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Plantar fasciitis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Polymyalgia rheumatica	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Tendonitis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Amyotrophy	2 (1.1%)	0	2 (1.2%)	0	0	0	0
Hypercreatinemia	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Lumbar spinal stenosis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Musculoskeletal discomfort	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Myopathy	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Osteoarthritis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Osteoporosis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Rheumatic disorder	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Rotator cuff syndrome	1 (0.5%)	0	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Tendon disorder	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Investigations	60 (31.9%)	39 (20.7%)	34 (20.9%)	74 (38.3%)	40 (20.7%)	38 (21.5%)	27 (18.1%)
Alanine aminotransferase increased	10 (5.3%)	8 (4.3%)	3 (1.8%)	18 (9.3%)	10 (5.2%)	5 (2.8%)	3 (2.0%)
Blood creatinine increased	16 (8.5%)	11 (5.9%)	8 (4.9%)	17 (8.8%)	10 (5.2%)	6 (3.4%)	4 (2.7%)
Aspartate aminotransferase increased	8 (4.3%)	7 (3.7%)	1 (0.6%)	16 (8.3%)	7 (3.6%)	5 (2.8%)	4 (2.7%)
Gamma-glutamyltransferase increased	11 (5.9%)	7 (3.7%)	7 (4.3%)	12 (6.2%)	7 (3.6%)	6 (3.4%)	4 (2.7%)
Weight decreased	6 (3.2%)	3 (1.6%)	3 (1.8%)	11 (5.7%)	5 (2.6%)	8 (4.5%)	4 (2.7%)
Blood alkaline phosphatase increased	11 (5.9%)	5 (2.7%)	8 (4.9%)	9 (4.7%)	3 (1.6%)	4 (2.3%)	5 (3.4%)
Weight increased	6 (3.2%)	4 (2.1%)	2 (1.2%)	8 (4.1%)	3 (1.6%)	2 (1.1%)	3 (2.0%)
Alpha hydroxybutyrate dehydrogenase increased	2 (1.1%)	1 (0.5%)	1 (0.6%)	4 (2.1%)	2 (1.0%)	2 (1.1%)	1 (0.7%)
Blood lactate dehydrogenase increased	4 (2.1%)	2 (1.1%)	2 (1.2%)	4 (2.1%)	3 (1.6%)	2 (1.1%)	0
Troponin I increased	0	0	0	4 (2.1%)	1 (0.5%)	1 (0.6%)	2 (1.3%)
Blood creatine phosphokinase increased	1 (0.5%)	0	1 (0.6%)	3 (1.6%)	3 (1.6%)	0	0
Lipase increased	0	0	0	3 (1.6%)	2 (1.0%)	1 (0.6%)	0
C-reactive protein increased	3 (1.6%)	1 (0.5%)	2 (1.2%)	2 (1.0%)	0	2 (1.1%)	1 (0.7%)
Electrocardiogram QT prolonged	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	0	0	2 (1.3%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
High density lipoprotein increased	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Occult blood	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Alanine aminotransferase	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Antiphospholipid antibodies positive	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Blood growth hormone increased	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Blood insulin decreased	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Blood thyroid stimulating hormone decreased	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Blood urine present	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Body temperature increased	0	0	0	1 (0.5%)	0	1 (0.6%)	0
C-reactive protein decreased	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Cortisol increased	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Creatinine renal clearance increased	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Cytomegalovirus test positive	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Fibrin D dimer increased	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Glomerular filtration rate decreased	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Glucose urine present	0	0	0	1 (0.5%)	0	1 (0.6%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Immunoglobulins decreased	2 (1.1%)	0	2 (1.2%)	1 (0.5%)	0	1 (0.6%)	0
Influenza A virus test positive	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Low density lipoprotein increased	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Myocardial necrosis marker increased	0	0	0	1 (0.5%)	1 (0.5%)	0	0
N-terminal prohormone brain natriuretic peptide increased	3 (1.6%)	1 (0.5%)	3 (1.8%)	1 (0.5%)	1 (0.5%)	0	0
Neutrophil count increased	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Occult blood positive	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	0
Parasite stool test positive	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Procalcitonin increased	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Protein total decreased	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Specific gravity urine increased	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Troponin T increased	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	0
Venous pressure jugular increased	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
White blood cells urine positive	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Blood pressure orthostatic decreased	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Blood urea increased	1 (0.5%)	1 (0.5%)	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Ejection fraction decreased	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Globulins decreased	1 (0.5%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Inspiratory capacity decreased	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Myocardial strain	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Prothrombin time prolonged	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Respirovirus test positive	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Specific gravity urine decreased	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Venous pressure jugular	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Vitamin D decreased	2 (1.1%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Psychiatric disorders	61 (32.4%)	42 (22.3%)	32 (19.6%)	66 (34.2%)	42 (21.8%)	20 (11.3%)	12 (8.1%)
Insomnia	47 (25.0%)	31 (16.5%)	18 (11.0%)	46 (23.8%)	29 (15.0%)	12 (6.8%)	7 (4.7%)
Anxiety	12 (6.4%)	6 (3.2%)	6 (3.7%)	9 (4.7%)	4 (2.1%)	2 (1.1%)	3 (2.0%)
Agitation	6 (3.2%)	3 (1.6%)	3 (1.8%)	4 (2.1%)	3 (1.6%)	0	1 (0.7%)
Depression	6 (3.2%)	3 (1.6%)	4 (2.5%)	4 (2.1%)	3 (1.6%)	0	1 (0.7%)
Nervousness	0	0	0	3 (1.6%)	2 (1.0%)	0	1 (0.7%)
Confusional state	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	2 (1.0%)	0	0
Depressive symptom	0	0	0	2 (1.0%)	2 (1.0%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Irritability	5 (2.7%)	4 (2.1%)	3 (1.8%)	2 (1.0%)	2 (1.0%)	0	0
Mood swings	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Restlessness	3 (1.6%)	2 (1.1%)	1 (0.6%)	2 (1.0%)	0	2 (1.1%)	0
Delirium	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Hallucination	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Head banging	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Mania	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Mood altered	4 (2.1%)	3 (1.6%)	2 (1.2%)	1 (0.5%)	1 (0.5%)	1 (0.6%)	0
Affect lability	2 (1.1%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Aggression	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Anxiety disorder	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Apathy	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Depressed mood	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Personality change	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Stress	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Substance-induced psychotic disorder	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Suicidal ideation	1 (0.5%)	0	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Cardiac disorders	41 (21.8%)	24 (12.8%)	24 (14.7%)	63 (32.6%)	33 (17.1%)	31 (17.5%)	12 (8.1%)
Cardiac failure	10 (5.3%)	7 (3.7%)	4 (2.5%)	16 (8.3%)	9 (4.7%)	9 (5.1%)	1 (0.7%)
Atrial fibrillation	4 (2.1%)	2 (1.1%)	2 (1.2%)	11 (5.7%)	4 (2.1%)	5 (2.8%)	2 (1.3%)
Palpitations	6 (3.2%)	4 (2.1%)	2 (1.2%)	11 (5.7%)	7 (3.6%)	3 (1.7%)	2 (1.3%)
Cardiac arrest	3 (1.6%)	3 (1.6%)	0	7 (3.6%)	4 (2.1%)	3 (1.7%)	0
Angina pectoris	5 (2.7%)	2 (1.1%)	3 (1.8%)	4 (2.1%)	2 (1.0%)	1 (0.6%)	2 (1.3%)
Sinus tachycardia	2 (1.1%)	0	2 (1.2%)	4 (2.1%)	2 (1.0%)	2 (1.1%)	1 (0.7%)
Pericardial effusion	1 (0.5%)	0	1 (0.6%)	3 (1.6%)	0	3 (1.7%)	0
Atrial flutter	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Bradycardia	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Cardiac failure congestive	4 (2.1%)	1 (0.5%)	3 (1.8%)	2 (1.0%)	0	2 (1.1%)	0
Diastolic dysfunction	0	0	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Supraventricular tachycardia	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Tachycardia	2 (1.1%)	1 (0.5%)	1 (0.6%)	2 (1.0%)	2 (1.0%)	0	0
Arteriospasm coronary	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Bradyarrhythmia	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Bundle branch block left	0	0	0	1 (0.5%)	0	0	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Cardiac discomfort	0	0	0	1 (0.5%)	0	1 (0.6%)	1 (0.7%)
Cardiac disorder	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Cardiac dysfunction	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Cardiac flutter	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Cardiogenic shock	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Cardiovascular insufficiency	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Extrasystoles	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Hepatojugular reflux	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Left ventricular dysfunction	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Pericarditis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Sinus bradycardia	2 (1.1%)	1 (0.5%)	2 (1.2%)	1 (0.5%)	0	1 (0.6%)	0
Sinus node dysfunction	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	1 (0.7%)
Supraventricular extrasystoles	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Ventricular arrhythmia	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Ventricular extrasystoles	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Ventricular hypertrophy	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Acute coronary syndrome	1 (0.5%)	0	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Acute left ventricular failure	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Acute myocardial infarction	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Arrhythmia	3 (1.6%)	1 (0.5%)	2 (1.2%)	0	0	0	0
Atrial tachycardia	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Atrial thrombosis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Cardiac amyloidosis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Cardiomegaly	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Cardiomyopathy	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Defect conduction intraventricular	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Mitral valve incompetence	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Myocardial infarction	2 (1.1%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Ventricular tachycardia	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Vascular disorders	43 (22.9%)	24 (12.8%)	25 (15.3%)	53 (27.5%)	34 (17.6%)	17 (9.6%)	6 (4.0%)
Hypotension	21 (11.2%)	14 (7.4%)	10 (6.1%)	27 (14.0%)	18 (9.3%)	10 (5.6%)	1 (0.7%)
Hypertension	3 (1.6%)	2 (1.1%)	3 (1.8%)	9 (4.7%)	6 (3.1%)	3 (1.7%)	1 (0.7%)
Orthostatic hypotension	11 (5.9%)	3 (1.6%)	8 (4.9%)	8 (4.1%)	4 (2.1%)	2 (1.1%)	2 (1.3%)
Hot flush	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	2 (1.0%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Aortic arteriosclerosis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Circulatory collapse	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0
Deep vein thrombosis	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Embolism	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Flushing	3 (1.6%)	2 (1.1%)	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Hyperemia	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Orthostatic hypertension	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Thrombophlebitis superficial	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Thrombosis	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	0	1 (0.7%)
Varicophlebitis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Varicose vein	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Arteriovenous fistula	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Hematoma	2 (1.1%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Microangiopathy	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Peripheral vascular disorder	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Shock hemorrhagic	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Spider vein	1 (0.5%)	0	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Eye disorders	35 (18.6%)	14 (7.4%)	26 (16.0%)	50 (25.9%)	19 (9.8%)	27 (15.3%)	16 (10.7%)
Vision blurred	8 (4.3%)	4 (2.1%)	4 (2.5%)	10 (5.2%)	6 (3.1%)	3 (1.7%)	1 (0.7%)
Blepharitis	5 (2.7%)	1 (0.5%)	5 (3.1%)	9 (4.7%)	2 (1.0%)	7 (4.0%)	2 (1.3%)
Conjunctival hemorrhage	3 (1.6%)	0	3 (1.8%)	6 (3.1%)	3 (1.6%)	1 (0.6%)	2 (1.3%)
Dry eye	2 (1.1%)	0	2 (1.2%)	5 (2.6%)	0	3 (1.7%)	2 (1.3%)
Cataract	2 (1.1%)	0	2 (1.2%)	4 (2.1%)	0	0	4 (2.7%)
Eye irritation	1 (0.5%)	1 (0.5%)	0	4 (2.1%)	1 (0.5%)	3 (1.7%)	0
Lacrimation increased	1 (0.5%)	1 (0.5%)	0	3 (1.6%)	1 (0.5%)	2 (1.1%)	0
Visual impairment	3 (1.6%)	2 (1.1%)	1 (0.6%)	3 (1.6%)	0	2 (1.1%)	1 (0.7%)
Eyelid hematoma	0	0	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Ocular hyperemia	2 (1.1%)	1 (0.5%)	1 (0.6%)	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Vitreous floaters	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Accommodation disorder	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Amaurosis fugax	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Blepharospasm	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Chalazion	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Conjunctival hyperemia	0	0	0	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Eye discharge	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Eye hemorrhage	0	0	0	1 (0.5%)	1 (0.5%)	0	1 (0.7%)
Eye pruritus	2 (1.1%)	0	2 (1.2%)	1 (0.5%)	0	1 (0.6%)	0
Eye swelling	2 (1.1%)	0	2 (1.2%)	1 (0.5%)	0	1 (0.6%)	0
Ocular discomfort	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Orbital myositis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Periorbital oedema	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Photophobia	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Retinopathy	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Scleral hemorrhage	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Visual acuity reduced	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0
Blindness unilateral	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Eye hematoma	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Eye pain	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Myopia	1 (0.5%)	1 (0.5%)	1 (0.6%)	0	0	0	0
Swelling of eyelid	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Swollen tear duct	1 (0.5%)	1 (0.5%)	0	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Xerophthalmia	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Injury, poisoning and procedural complications	25 (13.3%)	13 (6.9%)	14 (8.6%)	42 (21.8%)	11 (5.7%)	25 (14.1%)	17 (11.4%)
Fall	8 (4.3%)	3 (1.6%)	5 (3.1%)	13 (6.7%)	3 (1.6%)	9 (5.1%)	3 (2.0%)
Contusion	6 (3.2%)	3 (1.6%)	3 (1.8%)	12 (6.2%)	5 (2.6%)	5 (2.8%)	2 (1.3%)
Skin laceration	3 (1.6%)	0	3 (1.8%)	4 (2.1%)	1 (0.5%)	3 (1.7%)	1 (0.7%)
Head injury	0	0	0	3 (1.6%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Subcutaneous hematoma	0	0	0	3 (1.6%)	0	1 (0.6%)	2 (1.3%)
Eye contusion	2 (1.1%)	0	2 (1.2%)	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Facial bones fracture	0	0	0	2 (1.0%)	2 (1.0%)	0	0
Hip fracture	0	0	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Periorbital hemorrhage	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Rib fracture	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Skin abrasion	2 (1.1%)	1 (0.5%)	2 (1.2%)	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Bone contusion	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Delayed engraftment	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Hand fracture	0	0	0	1 (0.5%)	0	0	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Muscle strain	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Periorbital hematoma	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Post-traumatic neck syndrome	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Procedural pain	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Spinal compression fracture	2 (1.1%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Sunburn	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Thermal burn	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Tooth fracture	0	0	0	1 (0.5%)	1 (0.5%)	1 (0.6%)	0
Traumatic fracture	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Upper limb fracture	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Wound	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Eye injury	2 (1.1%)	2 (1.1%)	0	0	0	0	0
Face injury	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Gastrointestinal stoma complication	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Incision site edema	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Joint dislocation	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Nasal injury	1 (0.5%)	1 (0.5%)	0	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Traumatic hematoma	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Traumatic liver injury	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Traumatic ulcer	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Renal and urinary disorders	34 (18.1%)	25 (13.3%)	18 (11.0%)	41 (21.2%)	19 (9.8%)	20 (11.3%)	11 (7.4%)
Renal impairment	11 (5.9%)	9 (4.8%)	5 (3.1%)	9 (4.7%)	3 (1.6%)	5 (2.8%)	1 (0.7%)
Acute kidney injury	7 (3.7%)	6 (3.2%)	3 (1.8%)	7 (3.6%)	4 (2.1%)	2 (1.1%)	1 (0.7%)
Hematuria	0	0	0	6 (3.1%)	2 (1.0%)	4 (2.3%)	1 (0.7%)
Dysuria	4 (2.1%)	1 (0.5%)	4 (2.5%)	5 (2.6%)	2 (1.0%)	2 (1.1%)	2 (1.3%)
Urinary retention	0	0	0	5 (2.6%)	0	3 (1.7%)	2 (1.3%)
Chronic kidney disease	2 (1.1%)	2 (1.1%)	1 (0.6%)	4 (2.1%)	2 (1.0%)	2 (1.1%)	1 (0.7%)
Renal failure	3 (1.6%)	2 (1.1%)	3 (1.8%)	3 (1.6%)	1 (0.5%)	2 (1.1%)	1 (0.7%)
Micturition disorder	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	0
Pollakiuria	4 (2.1%)	1 (0.5%)	3 (1.8%)	2 (1.0%)	2 (1.0%)	0	0
Proteinuria	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	1 (0.5%)	2 (1.1%)	1 (0.7%)
Chromaturia	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Cystitis hemorrhagic	1 (0.5%)	1 (0.5%)	1 (0.6%)	1 (0.5%)	0	1 (0.6%)	0
Glycosuria	0	0	0	1 (0.5%)	1 (0.5%)	1 (0.6%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Micturition urgency	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Nephrolithiasis	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Nephropathy	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Nephrotic syndrome	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Renal pain	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	1 (0.5%)	0	0
Urge incontinence	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Urinary incontinence	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Nocturia	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Polyuria	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Renal cyst	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Renal injury	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Urine flow decreased	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Reproductive system and breast disorders	10 (5.3%)	10 (5.3%)	0	16 (8.3%)	8 (4.1%)	3 (1.7%)	6 (4.0%)
Amenorrhea	0	0	0	2 (1.0%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Breast pain	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	0	0	2 (1.3%)
Erectile dysfunction	4 (2.1%)	4 (2.1%)	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Scrotal edema	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	2 (1.0%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Epididymal cyst	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Gynecomastia	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	0	1 (0.7%)
Pelvic floor muscle weakness	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Penile edema	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Prostatic disorder	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Prostatomegaly	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Testicular microlithiasis	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Vaginal discharge	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Vulval disorder	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Vulvovaginal dryness	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Breast swelling	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Testicular pain	3 (1.6%)	3 (1.6%)	0	0	0	0	0
Ear and labyrinth disorders	5 (2.7%)	3 (1.6%)	3 (1.8%)	15 (7.8%)	6 (3.1%)	8 (4.5%)	5 (3.4%)
Hypoacusis	0	0	0	4 (2.1%)	1 (0.5%)	2 (1.1%)	1 (0.7%)
Tinnitus	0	0	0	4 (2.1%)	0	3 (1.7%)	2 (1.3%)
Vertigo	3 (1.6%)	2 (1.1%)	2 (1.2%)	4 (2.1%)	3 (1.6%)	2 (1.1%)	0
Deafness	0	0	0	3 (1.6%)	1 (0.5%)	2 (1.1%)	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Ear pain	0	0	0	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Eustachian tube dysfunction	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Middle ear effusion	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Middle ear inflammation	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Ear discomfort	1 (0.5%)	1 (0.5%)	0	0	0	0	0
External ear pain	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Hepatobiliary disorders	15 (8.0%)	5 (2.7%)	12 (7.4%)	10 (5.2%)	6 (3.1%)	3 (1.7%)	2 (1.3%)
Hepatomegaly	0	0	0	4 (2.1%)	4 (2.1%)	0	0
Hyperbilirubinemia	9 (4.8%)	3 (1.6%)	8 (4.9%)	4 (2.1%)	2 (1.0%)	2 (1.1%)	0
Cholelithiasis	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Hepatic function abnormal	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	0	1 (0.7%)
Liver injury	1 (0.5%)	0	1 (0.6%)	1 (0.5%)	1 (0.5%)	0	0
Cholestasis	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Diabetic hepatopathy	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Hepatic steatosis	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Hepatocellular injury	1 (0.5%)	0	1 (0.6%)	0	0	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3 (1.6%)	2 (1.1%)	2 (1.2%)	7 (3.6%)	2 (1.0%)	0	5 (3.4%)
Basal cell carcinoma	1 (0.5%)	0	1 (0.6%)	2 (1.0%)	1 (0.5%)	0	1 (0.7%)
Bladder cancer	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Lipoma	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Melanocytic naevus	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Seborrhoeic keratosis	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Skin cancer	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	0	1 (0.7%)
Hemangioma of skin	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Intraductal papillary mucinous neoplasm	1 (0.5%)	0	1 (0.6%)	0	0	0	0
Endocrine disorders	4 (2.1%)	3 (1.6%)	1 (0.6%)	6 (3.1%)	3 (1.6%)	1 (0.6%)	2 (1.3%)
Hypothyroidism	3 (1.6%)	2 (1.1%)	1 (0.6%)	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Adrenocortical insufficiency acute	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Hyperthyroidism	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Steroid withdrawal syndrome	0	0	0	1 (0.5%)	1 (0.5%)	0	0
Thyroid mass	0	0	0	1 (0.5%)	1 (0.5%)	0	0

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+
Adrenal hematoma	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Immune system disorders	2 (1.1%)	2 (1.1%)	0	5 (2.6%)	1 (0.5%)	2 (1.1%)	2 (1.3%)
Hypogammaglobulinemia	1 (0.5%)	1 (0.5%)	0	3 (1.6%)	1 (0.5%)	1 (0.6%)	1 (0.7%)
Seasonal allergy	1 (0.5%)	1 (0.5%)	0	1 (0.5%)	0	1 (0.6%)	0
Secondary immunodeficiency	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Congenital, familial and genetic disorders	1 (0.5%)	1 (0.5%)	0	2 (1.0%)	0	1 (0.6%)	1 (0.7%)
Hereditary hemorrhagic telangiectasia	0	0	0	1 (0.5%)	0	1 (0.6%)	0
Hydrocele	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Macroglossia	1 (0.5%)	1 (0.5%)	0	0	0	0	0
Social circumstances	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Stress at work	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Surgical and medical procedures	0	0	0	1 (0.5%)	0	0	1 (0.7%)
Cardiac ablation	0	0	0	1 (0.5%)	0	0	1 (0.7%)

Table S8. Treatment-emergent Adverse Events by Cycle.

	Control Group n (%)			Daratumumab Group n (%)			
	Total	Cycles 1-2	Cycles 3-6	Total	Cycles 1-2	Cycles 3-6	Cycles 7+

TEAE denotes treatment-emergent adverse event.

Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 22.1.

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