An overview of TEAEs by treatment received during the study is presented in Table 1. All but 1 subject had 1 or more reported TEAE (99%). Of all treated subjects, 95 (77%) had TEAEs that were considered by the investigator to be related to daratumumab; 14 subjects (78%) in the 8 mg/kg and 81 subjects (76%) in the 16 mg/kg group. Of all treated subjects, 38 (31%) subjects experienced 1 or more serious TEAEs; 8 subjects (7%) had serious TEAEs that were considered by the investigator to be drug‑related. Six subjects (33%) in the 8 mg/kg group and 32 subjects (30%) in the 16 mg/kg group experienced 1 or more serious TEAEs. No subject in the 8 mg/kg group and 8 subjects (8%) in the 16 mg/kg group had serious TEAEs considered by the investigator to be related to daratumumab.

In the 16 mg/kg group, 9 subjects (9%) had TEAEs with an outcome of death (Grade 5).

| Table : Overview of Treatment-emergent Adverse Events; All Treated Analysis Set (Study 54767414MMY2002) | | | | | |
| --- | --- | --- | --- | --- | --- |
|  | | 16 mg/kg | | |  |
|  | 8 mg/kg | Part 1 | Part 2 | Total | Total |
| **Analysis set: all treated** | **18** | **41** | **65** | **106** | **124** |
|  |  |  |  |  |  |
| Any TEAE | 18 (100.0%) | 40 (97.6%) | 65 (100.0%) | 105 (99.1%) | 123 (99.2%) |
| Drug-related | 14 (77.8%) | 27 (65.9%) | 54 (83.1%) | 81 (76.4%) | 95 (76.6%) |
|  |  |  |  |  |  |
| Any serious TEAE | 6 (33.3%) | 11 (26.8%) | 21 (32.3%) | 32 (30.2%) | 38 (30.6%) |
| Drug-related | 0 | 2 (4.9%) | 6 (9.2%) | 8 (7.5%) | 8 (6.5%) |
|  |  |  |  |  |  |
| Maximum severity of any TEAE |  |  |  |  |  |
| Grade 1 | 2 (11.1%) | 5 (12.2%) | 3 (4.6%) | 8 (7.5%) | 10 (8.1%) |
| Grade 2 | 5 (27.8%) | 5 (12.2%) | 21 (32.3%) | 26 (24.5%) | 31 (25.0%) |
| Grade 3 | 8 (44.4%) | 22 (53.7%) | 26 (40.0%) | 48 (45.3%) | 56 (45.2%) |
| Grade 4 | 3 (16.7%) | 4 (9.8%) | 10 (15.4%) | 14 (13.2%) | 17 (13.7%) |
| Grade 5 | 0 | 4 (9.8%) | 5 (7.7%) | 9 (8.5%) | 9 (7.3%) |
|  |  |  |  |  |  |
| Treatment discontinuation due to TEAEa | 0 | 1 (2.4%) | 4 (6.2%) | 5 (4.7%) | 5 (4.0%) |
| Drug-related | 0 | 0 | 0 | 0 | 0 |
|  |  |  |  |  |  |
| Death due to TEAEb | 0 | 1 (2.4%) | 1 (1.5%) | 2 (1.9%) | 2 (1.6%) |
| Drug-related | 0 | 0 | 0 | 0 | 0 |
| Keys: TEAE = treatment-emergent adverse event.  aTreatment discontinuation due to adverse event on the end of treatment CRF page.  bDeath due to adverse event on the death CRF page. Percentages are calculated with the number of subjects in each group as denominator. | | | | | |
| Modified from Attachment TSFAE01 | | | | | |

**Find incidence ≥20% by preferred term**

Data presentation in descending order: xx% in all treated subjects; xx% in the 16 mg/kg group

The most frequently reported TEAEs across all treated subjects were fatigue (40%; 40% in the 16 mg/kg group); anemia (36%; 33% in the 16 mg/kg group), nausea (28%; 29% in the 16 mg/kg group); thrombocytopenia (27%; 26% in the 16 mg/kg group); back pain (23%; 22% in the 16 mg/kg group); cough (23%; 21% in the 16 mg/kg group); and neutropenia (20%; 23% in the 16 mg/kg group) (Table 2).

| Table : Most Common (At Least 10%) Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Study 54767414MMY2002) | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | 8 mg/kg | | 16 mg/kg | | Total | |
|  | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 |
| Analysis set: all treated | 18 |  | 106 |  | 124 |  |
| Total number of subjects with TEAE | 18 (100.0%) | 11 (61.1%) | 105 (99.1%) | 70 (66.0%) | 123 (99.2%) | 81 (65.3%) |
| MedDRA system organ class/Preferred term |  |  |  |  |  |  |
| General Disorders And Administration Site Conditions | 12 (66.7%) | 2 (11.1%) | 74 (69.8%) | 7 (6.6%) | 86 (69.4%) | 9 (7.3%) |
| Fatigue | 7 (38.9%) | 0 | 42 (39.6%) | 3 (2.8%) | 49 (39.5%) | 3 (2.4%) |
| Pyrexia | 5 (27.8%) | 0 | 17 (16.0%) | 0 | 22 (17.7%) | 0 |
| Asthenia | 2 (11.1%) | 0 | 12 (11.3%) | 1 (0.9%) | 14 (11.3%) | 1 (0.8%) |
| Respiratory, Thoracic And Mediastinal Disorders | 8 (44.4%) | 1 (5.6%) | 65 (61.3%) | 7 (6.6%) | 73 (58.9%) | 8 (6.5%) |
| Cough | 6 (33.3%) | 0 | 22 (20.8%) | 0 | 28 (22.6%) | 0 |
| Nasal Congestion | 1 (5.6%) | 0 | 19 (17.9%) | 0 | 20 (16.1%) | 0 |
| Dyspnoea | 3 (16.7%) | 0 | 16 (15.1%) | 1 (0.9%) | 19 (15.3%) | 1 (0.8%) |
| Gastrointestinal Disorders | 9 (50.0%) | 1 (5.6%) | 64 (60.4%) | 3 (2.8%) | 73 (58.9%) | 4 (3.2%) |
| Nausea | 4 (22.2%) | 1 (5.6%) | 31 (29.2%) | 0 | 35 (28.2%) | 1 (0.8%) |
| Vomiting | 3 (16.7%) | 1 (5.6%) | 19 (17.9%) | 0 | 22 (17.7%) | 1 (0.8%) |
| Diarrhoea | 4 (22.2%) | 0 | 18 (17.0%) | 0 | 22 (17.7%) | 0 |
| Constipation | 2 (11.1%) | 0 | 17 (16.0%) | 0 | 19 (15.3%) | 0 |
| Musculoskeletal And Connective Tissue Disorders | 10 (55.6%) | 2 (11.1%) | 64 (60.4%) | 10 (9.4%) | 74 (59.7%) | 12 (9.7%) |
| Back Pain | 5 (27.8%) | 2 (11.1%) | 23 (21.7%) | 3 (2.8%) | 28 (22.6%) | 5 (4.0%) |
| Arthralgia | 1 (5.6%) | 0 | 20 (18.9%) | 0 | 21 (16.9%) | 0 |
| Pain In Extremity | 1 (5.6%) | 0 | 18 (17.0%) | 1 (0.9%) | 19 (15.3%) | 1 (0.8%) |
| Musculoskeletal Chest Pain | 2 (11.1%) | 0 | 13 (12.3%) | 2 (1.9%) | 15 (12.1%) | 2 (1.6%) |
| Blood And Lymphatic System Disorders | 12 (66.7%) | 9 (50.0%) | 61 (57.5%) | 44 (41.5%) | 73 (58.9%) | 53 (42.7%) |
| Anaemia | 9 (50.0%) | 4 (22.2%) | 35 (33.0%) | 25 (23.6%) | 44 (35.5%) | 29 (23.4%) |
| Thrombocytopenia | 6 (33.3%) | 4 (22.2%) | 27 (25.5%) | 20 (18.9%) | 33 (26.6%) | 24 (19.4%) |
| Neutropenia | 1 (5.6%) | 1 (5.6%) | 24 (22.6%) | 13 (12.3%) | 25 (20.2%) | 14 (11.3%) |
| Infections And Infestations | 8 (44.4%) | 0 | 54 (50.9%) | 12 (11.3%) | 62 (50.0%) | 12 (9.7%) |
| Upper Respiratory Tract Infection | 3 (16.7%) | 0 | 19 (17.9%) | 1 (0.9%) | 22 (17.7%) | 1 (0.8%) |
| Metabolism And Nutrition Disorders | 11 (61.1%) | 5 (27.8%) | 53 (50.0%) | 11 (10.4%) | 64 (51.6%) | 16 (12.9%) |
| Decreased Appetite | 4 (22.2%) | 0 | 19 (17.9%) | 1 (0.9%) | 23 (18.5%) | 1 (0.8%) |
| Hypercalcaemia | 2 (11.1%) | 1 (5.6%) | 18 (17.0%) | 5 (4.7%) | 20 (16.1%) | 6 (4.8%) |
| Hypokalaemia | 4 (22.2%) | 1 (5.6%) | 11 (10.4%) | 0 | 15 (12.1%) | 1 (0.8%) |
| Vascular Disorders | 8 (44.4%) | 4 (22.2%) | 25 (23.6%) | 9 (8.5%) | 33 (26.6%) | 13 (10.5%) |
| Hypertension | 8 (44.4%) | 4 (22.2%) | 12 (11.3%) | 7 (6.6%) | 20 (16.1%) | 11 (8.9%) |
| Renal And Urinary Disorders | 9 (50.0%) | 1 (5.6%) | 22 (20.8%) | 6 (5.7%) | 31 (25.0%) | 7 (5.6%) |
| Renal Impairment | 7 (38.9%) | 0 | 11 (10.4%) | 2 (1.9%) | 18 (14.5%) | 2 (1.6%) |
| Keys: TEAE = treatment-emergent adverse event. Adverse events are reported using MedDRA version 17.0. Percentages are calculated with the number of subjects in each group as denominator. | | | | | | |
| [TSFAE02C1.rtf] [JNJ-54767414\MMY2002\DBR\_CSR\RE\_CSR\tsfae02c1.sas] 13FEB2015, 14:08 | | | | | | |

Most Common (At Least 1%) treatment-emergent Grade 3 or 4 AEs are provided in Table 3. Of all treated subjects, 81 (65%) had Grade 3 or 4 TEAEs. The occurrence of Grade 3 or 4 TEAEs was similar in both the 8 mg/kg and 16 mg/kg groups (61% versus 66%). The incidence of all Grade 3 or 4 TEAEs is presented in Attachment TSFAE03.

The most frequently reported TEAEs with a severity of Grade 3 or Grade 4 in ≥10% subjects in the 16 mg/kg group were anemia (24%), thrombocytopenia (19%), and neutropenia (12%) (Table 3).

| Table : Most Common (At Least 1%) Treatment-Emergent Grade 3 or 4 Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set (Study 54767414MMY2002) | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | 8 mg/kg | | 16 mg/kg | | Total | |
|  | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 |
| Analysis set: all treated | 18 |  | 106 |  | 124 |  |
| Total number of subjects with TEAEs | 18 (100.0%) | 11 (61.1%) | 105 (99.1%) | 70 (66.0%) | 123 (99.2%) | 81 (65.3%) |
| MedDRA system organ class/Preferred term |  |  |  |  |  |  |
| Blood And Lymphatic System Disorders | 12 (66.7%) | 9 (50.0%) | 61 (57.5%) | 44 (41.5%) | 73 (58.9%) | 53 (42.7%) |
| Anaemia | 9 (50.0%) | 4 (22.2%) | 35 (33.0%) | 25 (23.6%) | 44 (35.5%) | 29 (23.4%) |
| Thrombocytopenia | 6 (33.3%) | 4 (22.2%) | 27 (25.5%) | 20 (18.9%) | 33 (26.6%) | 24 (19.4%) |
| Neutropenia | 1 (5.6%) | 1 (5.6%) | 24 (22.6%) | 13 (12.3%) | 25 (20.2%) | 14 (11.3%) |
| Lymphopenia | 3 (16.7%) | 3 (16.7%) | 4 (3.8%) | 4 (3.8%) | 7 (5.6%) | 7 (5.6%) |
| Leukopenia | 2 (11.1%) | 0 | 7 (6.6%) | 2 (1.9%) | 9 (7.3%) | 2 (1.6%) |
| Infections And Infestations | 8 (44.4%) | 0 | 54 (50.9%) | 12 (11.3%) | 62 (50.0%) | 12 (9.7%) |
| Pneumonia | 1 (5.6%) | 0 | 8 (7.5%) | 5 (4.7%) | 9 (7.3%) | 5 (4.0%) |
| Lobar Pneumonia | 0 | 0 | 3 (2.8%) | 2 (1.9%) | 3 (2.4%) | 2 (1.6%) |
| Soft Tissue Infection | 0 | 0 | 2 (1.9%) | 2 (1.9%) | 2 (1.6%) | 2 (1.6%) |
| Metabolism And Nutrition Disorders | 11 (61.1%) | 5 (27.8%) | 53 (50.0%) | 11 (10.4%) | 64 (51.6%) | 16 (12.9%) |
| Hypercalcaemia | 2 (11.1%) | 1 (5.6%) | 18 (17.0%) | 5 (4.7%) | 20 (16.1%) | 6 (4.8%) |
| Hyperglycaemia | 3 (16.7%) | 0 | 9 (8.5%) | 3 (2.8%) | 12 (9.7%) | 3 (2.4%) |
| Musculoskeletal And Connective Tissue Disorders | 10 (55.6%) | 2 (11.1%) | 64 (60.4%) | 10 (9.4%) | 74 (59.7%) | 12 (9.7%) |
| Back Pain | 5 (27.8%) | 2 (11.1%) | 23 (21.7%) | 3 (2.8%) | 28 (22.6%) | 5 (4.0%) |
| Musculoskeletal Chest Pain | 2 (11.1%) | 0 | 13 (12.3%) | 2 (1.9%) | 15 (12.1%) | 2 (1.6%) |
| Neck Pain | 0 | 0 | 2 (1.9%) | 2 (1.9%) | 2 (1.6%) | 2 (1.6%) |
| Pathological Fracture | 0 | 0 | 2 (1.9%) | 2 (1.9%) | 2 (1.6%) | 2 (1.6%) |
| Vascular Disorders | 8 (44.4%) | 4 (22.2%) | 25 (23.6%) | 9 (8.5%) | 33 (26.6%) | 13 (10.5%) |
| Hypertension | 8 (44.4%) | 4 (22.2%) | 12 (11.3%) | 7 (6.6%) | 20 (16.1%) | 11 (8.9%) |
| General Disorders And Administration Site Conditions | 12 (66.7%) | 2 (11.1%) | 74 (69.8%) | 7 (6.6%) | 86 (69.4%) | 9 (7.3%) |
| Fatigue | 7 (38.9%) | 0 | 42 (39.6%) | 3 (2.8%) | 49 (39.5%) | 3 (2.4%) |
| Respiratory, Thoracic And Mediastinal Disorders | 8 (44.4%) | 1 (5.6%) | 65 (61.3%) | 7 (6.6%) | 73 (58.9%) | 8 (6.5%) |
| Bronchospasm | 0 | 0 | 5 (4.7%) | 2 (1.9%) | 5 (4.0%) | 2 (1.6%) |
| Nervous System Disorders | 10 (55.6%) | 2 (11.1%) | 37 (34.9%) | 6 (5.7%) | 47 (37.9%) | 8 (6.5%) |
| Headache | 1 (5.6%) | 0 | 10 (9.4%) | 2 (1.9%) | 11 (8.9%) | 2 (1.6%) |
| Renal And Urinary Disorders | 9 (50.0%) | 1 (5.6%) | 22 (20.8%) | 6 (5.7%) | 31 (25.0%) | 7 (5.6%) |
| Renal Impairment | 7 (38.9%) | 0 | 11 (10.4%) | 2 (1.9%) | 18 (14.5%) | 2 (1.6%) |
| Gastrointestinal Disorders | 9 (50.0%) | 1 (5.6%) | 64 (60.4%) | 3 (2.8%) | 73 (58.9%) | 4 (3.2%) |
| Abdominal Pain | 1 (5.6%) | 0 | 8 (7.5%) | 2 (1.9%) | 9 (7.3%) | 2 (1.6%) |
| Keys: TEAE = treatment-emergent adverse event. Adverse events are reported using MedDRA version 17.0. Percentages are calculated with the number of subjects in each group as denominator. | | | | | | |
| [TSFAE05B.rtf] [JNJ-54767414\MMY2002\DBR\_CSR\RE\_CSR\tsfae05b.sas] 25MAR2015, 16:34 | | | | | | |

Table 4 summarizes the primary cause of death in all treated subjects. Twelve subjects died within 30 days of the last dose of study drug; all 12 were in the 16 mg/kg group. Ten of the deaths were due to progressive disease, and 2 of the deaths were due to a TEAE.

| Table : Death and Primary Cause of Death; All Treated Analysis Set (Study 54767414MMY2002) | | | |
| --- | --- | --- | --- |
|  | 8 mg/kg | 16 mg/kg | Total |
| Analysis set: all treated | 18 | 106 | 124 |
| Total number of subjects died | 7 (38.9%) | 31 (29.2%) | 38 (30.6%)\* |
| Progressive disease | 5 (27.8%) | 29 (27.4%) | 34 (27.4%) |
| Adverse event | 0 | 2 (1.9%) | 2 (1.6%) |
| Other | 2 (11.1%) | 0 | 2 (1.6%) |
| Death within 30 days of last dose | 0 | 12 (11.3%) | 12 (9.7%) |
| Progressive disease | 0 | 10 (9.4%) | 10 (8.1%) |
| Adverse event | 0 | 2 (1.9%) | 2 (1.6%) |
| Other | 0 | 0 | 0 |
| Percentages are calculated with the number of subjects in each group as denominator. | | | |
| \* One additional death was identified after the database lock, see [ERRATA](#ERRATA) Section for details. | | | |
| Modified from Attachment TSFDTH01 | | | |

**Data presentation: Overall vs 16 mg/kg group**

**Find AE incidences and present them in a descending order**

Thirty-eight (38) subjects (31%; 32 subjects [30%] in the 16 mg/kg group) had a serious TEAE (Grade 1 to 4). The most frequently reported serious TEAEs that occurred in all treated subjects at a 3% or higher frequency were; general physical health deterioration (6 subjects; 5%), pneumonia (4 subjects, 3%), and hypercalcaemia (4 subjects, 3%) (Table 5).

| Table : Most Common (At Least 1%) Treatment-emergent Serious Adverse Events by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Study 54767414MMY2002) | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | 8 mg/kg | | 16 mg/kg | | Total | |
|  | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 |
| Analysis set: all treated | 18 |  | 106 |  | 124 |  |
| Total number of subjects with serious TEAEs | 6 (33.3%) | 6 (33.3%) | 32 (30.2%) | 24 (22.6%) | 38 (30.6%) | 30 (24.2%) |
| MedDRA system organ class/Preferred term |  |  |  |  |  |  |
| Infections And Infestations | 0 | 0 | 13 (12.3%) | 10 (9.4%) | 13 (10.5%) | 10 (8.1%) |
| Pneumonia | 0 | 0 | 4 (3.8%) | 3 (2.8%) | 4 (3.2%) | 3 (2.4%) |
| Lobar Pneumonia | 0 | 0 | 2 (1.9%) | 2 (1.9%) | 2 (1.6%) | 2 (1.6%) |
| General Disorders And Administration Site Conditions | 1 (5.6%) | 1 (5.6%) | 8 (7.5%) | 2 (1.9%) | 9 (7.3%) | 3 (2.4%) |
| General Physical Health Deterioration | 1 (5.6%) | 1 (5.6%) | 5 (4.7%) | 0 | 6 (4.8%) | 1 (0.8%) |
| Musculoskeletal And Connective Tissue Disorders | 1 (5.6%) | 1 (5.6%) | 5 (4.7%) | 5 (4.7%) | 6 (4.8%) | 6 (4.8%) |
| Musculoskeletal Chest Pain | 0 | 0 | 2 (1.9%) | 2 (1.9%) | 2 (1.6%) | 2 (1.6%) |
| Metabolism And Nutrition Disorders | 1 (5.6%) | 1 (5.6%) | 4 (3.8%) | 3 (2.8%) | 5 (4.0%) | 4 (3.2%) |
| Hypercalcaemia | 0 | 0 | 4 (3.8%) | 3 (2.8%) | 4 (3.2%) | 3 (2.4%) |
| Blood And Lymphatic System Disorders | 0 | 0 | 2 (1.9%) | 2 (1.9%) | 2 (1.6%) | 2 (1.6%) |
| Anaemia | 0 | 0 | 2 (1.9%) | 2 (1.9%) | 2 (1.6%) | 2 (1.6%) |
| Keys: TEAE = treatment-emergent adverse event. Adverse events are reported using MedDRA version 17.0. Percentages are calculated with the number of subjects in each group as denominator. | | | | | | |
| [TSFAE04A1.rtf] [JNJ-54767414\MMY2002\DBR\_CSR\RE\_CSR\tsfae04a1.sas] 13FEB2015, 14:08 | | | | | | |

Treatment-emergent AEs leading to treatment discontinuation by preferred term is presented in Table 6. Treatment discontinuation due to AE was reported for 5 subjects (4%), all in the 16 mg/kg group (Table 6); no subject discontinued treatment due to an AE related to daratumumab. General physical health deterioration was reported in 2 subjects; the following were reported in 1 subject each (H1N1 influenza, hypercalcemia, and spinal cord compression) (Table 6).

| Table : Treatment Discontinuation due to Treatment-emergent Adverse Events by Preferred Term and Relationship; All Treated Analysis Set (Study 54767414MMY2002) | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | 8 mg/kg | | 16 mg/kg | | Total | |
|  | Total | Related | Total | Related | Total | Related |
| Analysis set: all treated | 18 |  | 106 |  | 124 |  |
| Total number of subjects with treatment discontinuation due to TEAEs | 0 | 0 | 5 (4.7%) | 0 | 5 (4.0%) | 0 |
| Preferred term |  |  |  |  |  |  |
| General Physical Health Deterioration | 0 | 0 | 2 (1.9%) | 0 | 2 (1.6%) | 0 |
| H1N1 Influenza | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Hypercalcaemia | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Spinal Cord Compression | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Keys: TEAE = treatment-emergent adverse event. Adverse events are reported using MedDRA version 17.0. Percentages are calculated with the number of subjects in each group as denominator. Adverse events reported as the reason for treatment discontinuation on the end of treatment CRF page are summarized. | | | | | | |
| [TSFAE07.rtf] [JNJ-54767414\MMY2002\DBR\_CSR\RE\_CSR\tsfae07.sas] 13FEB2015, 14:08 | | | | | | |

Treatment-emergent AEs leading to a skipped infusion by preferred term are presented in Table 7. Skipped infusions due to TEAEs were reported in 10% of all treated subjects; 4 subjects (3%) had skipped infusions that were considered to be related to daratumumab. The following drug-related TEAEs were reported in 1 subject each (1%) and resulted in a skipped infusion (upper respiratory tract infection, herpes zoster, influenza-like illness, and neutropenia).

| Table : Infusion Skip due to Treatment-emergent Adverse Events by Preferred Term and Relationship; All Treated Analysis Set (Study 54767414MMY2002) | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | 8 mg/kg | | 16 mg/kg | | Total | |
|  | Total | Related | Total | Related | Total | Related |
| Analysis set: all treated | 18 |  | 106 |  | 124 |  |
| Total number of subjects with infusion skip due to TEAEs | 1 (5.6%) | 0 | 11 (10.4%) | 4 (3.8%) | 12 (9.7%) | 4 (3.2%) |
| Preferred term |  |  |  |  |  |  |
| Hypercalcaemia | 1 (5.6%) | 0 | 1 (0.9%) | 0 | 2 (1.6%) | 0 |
| Upper Respiratory Tract Infection | 0 | 0 | 2 (1.9%) | 1 (0.9%) | 2 (1.6%) | 1 (0.8%) |
| Conjunctivitis | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Gingival Bleeding | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Headache | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Herpes Zoster | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 1 (0.8%) | 1 (0.8%) |
| Influenza Like Illness | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 1 (0.8%) | 1 (0.8%) |
| Lumbar Vertebral Fracture | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Musculoskeletal Chest Pain | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Neutropenia | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 1 (0.8%) | 1 (0.8%) |
| Parainfluenzae Virus Infection | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Pneumonia | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Pyrexia | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Soft Tissue Infection | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Spinal Pain | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Thrombocytopenia | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Urinary Tract Infection | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Keys: TEAE = treatment-emergent adverse event. Adverse events are reported using MedDRA version 17.0. Percentages are calculated with the number of subjects in each group as denominator. Adverse events reported as the reason for action ‘infusion skipped’ on the Daratumumab infusion CRF page are summarized. | | | | | | |
| [TSFAE08.rtf] [JNJ-54767414\MMY2002\DBR\_CSR\RE\_CSR\tsfae08.sas] 13FEB2015, 14:08 | | | | | | |

In the 16 mg/kg group, 54 subjects (51%) experienced TEAEs of infections/infestations, which included 19/106 subjects (18%) with upper respiratory tract infections. Eight/106 subjects each (8%) had pneumonia and nasopharyngitis, 7/106 subjects (7%) had sinusitis and 6/106 subjects (6%) had urinary tract infections (Table 8).

| Table : Treatment-emergent Adverse Events of Infections/Infestations by Preferred Term and Event Onset Time; All Treated Analysis Set (Study 54767414MMY2002) | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 8 mg/kg | | | | | 16 mg/kg | | | | |
|  | | Event Onset Within | | | |  | Event Onset Within | | | |
|  | Total | ≤8 Weeks | 8 - ≤16 Weeks | 16 - ≤24 Weeks | >24 Weeks | Total | ≤8 Weeks | 8 - ≤16 Weeks | 16 - ≤24 Weeks | >24 Weeks |
| Analysis set: all treated | 18 |  |  |  |  | 106 |  |  |  |  |
| Total number of subjects treated within windowa | 18 | 18 | 10 | 4 | 4 | 106 | 106 | 79 | 45 | 34 |
| Total number of subjects with TEAE of infections/infestations | 8 (44.4%) | 4 (22.2%) | 3 (30.0%) | 1 (25.0%) | 1 (25.0%) | 54 (50.9%) | 31 (29.2%) | 24 (30.4%) | 9 (20.0%) | 12 (35.3%) |
| Upper Respiratory Tract Infection | 3 (16.7%) | 1 (5.6%) | 3 (30.0%) | 0 | 0 | 19 (17.9%) | 10 (9.4%) | 6 (7.6%) | 2 (4.4%) | 5 (14.7%) |
| Nasopharyngitis | 1 (5.6%) | 0 | 0 | 1 (25.0%) | 0 | 8 (7.5%) | 4 (3.8%) | 2 (2.5%) | 2 (4.4%) | 1 (2.9%) |
| Pneumonia | 1 (5.6%) | 1 (5.6%) | 0 | 0 | 0 | 8 (7.5%) | 4 (3.8%) | 2 (2.5%) | 0 | 2 (5.9%) |
| Sinusitis | 1 (5.6%) | 1 (5.6%) | 0 | 0 | 0 | 7 (6.6%) | 2 (1.9%) | 2 (2.5%) | 2 (4.4%) | 2 (5.9%) |
| Urinary Tract Infection | 0 | 0 | 0 | 0 | 0 | 6 (5.7%) | 2 (1.9%) | 2 (2.5%) | 0 | 2 (5.9%) |
| Bronchitis | 0 | 0 | 0 | 0 | 0 | 4 (3.8%) | 0 | 3 (3.8%) | 0 | 2 (5.9%) |
| Influenza | 2 (11.1%) | 1 (5.6%) | 0 | 0 | 1 (25.0%) | 2 (1.9%) | 1 (0.9%) | 1 (1.3%) | 0 | 0 |
| Lobar Pneumonia | 0 | 0 | 0 | 0 | 0 | 3 (2.8%) | 2 (1.9%) | 0 | 1 (2.2%) | 0 |
| Candida Infection | 1 (5.6%) | 1 (5.6%) | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Conjunctivitis | 0 | 0 | 0 | 0 | 0 | 2 (1.9%) | 1 (0.9%) | 0 | 1 (2.2%) | 0 |
| Oral Candidiasis | 0 | 0 | 0 | 0 | 0 | 2 (1.9%) | 0 | 2 (2.5%) | 0 | 0 |
| Parainfluenzae Virus Infection | 0 | 0 | 0 | 0 | 0 | 2 (1.9%) | 1 (0.9%) | 1 (1.3%) | 0 | 0 |
| Soft Tissue Infection | 0 | 0 | 0 | 0 | 0 | 2 (1.9%) | 0 | 2 (2.5%) | 0 | 0 |
| Cellulitis | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 1 (1.3%) | 0 | 0 |
| Device Related Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Ear Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 0 | 1 (2.2%) | 0 |
| Gastroenteritis | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 0 | 0 | 1 (2.9%) |
| Gastroenteritis Viral | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 1 (1.3%) | 0 | 0 |
| Genital Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 1 (1.3%) | 0 | 0 |
| H1n1 Influenza | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Herpes Zoster | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Hordeolum | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Lower Respiratory Tract Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Mucosal Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Ophthalmic Herpes Simplex | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 1 (1.3%) | 0 | 0 |
| Oral Herpes | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 1 (1.3%) | 0 | 0 |
| Paronychia | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 1 (2.9%) |
| Pneumonia Streptococcal | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Pyelonephritis | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 0 | 0 | 1 (2.9%) |
| Respiratory Tract Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 0 | 0 | 1 (2.9%) |
| Sepsis | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 0 | 1 (2.2%) | 0 |
| Streptococcal Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 1 (0.9%) | 0 | 0 | 0 |
| Tooth Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 1 (1.3%) | 0 | 0 |
| Varicella | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 0 | 1 (2.2%) | 0 |
| Vulvovaginal Mycotic Infection | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0 | 1 (1.3%) | 0 | 0 |
| Keys: TEAE = treatment-emergent adverse event.  aIncludes subjects either treated or experienced any TEAE in the SOC of infections/infestations within the specific window. Adverse events are reported using MedDRA version 17.0. Percentages are calculated with the number of subjects treated within each window as denominator. | | | | | | | | | | |
| Modified from Attachment TSFAE22 | | | | | | | | | | |

**Find incidence ≥3% by preferred term, presenting in a descending order**

Infusion-related reactions (IRR any grade) were reported in 43% of all treated subjects (Table 9). The most frequently reported IRRs were nasal congestion (11%), chills (9%), cough (7%), throat irritation, dyspnea and vomiting (6% each), nausea (4%) and bronchospasm (3%). All other IRRs were reported in ≤3 subjects (2%). Six percent (6%) of all treated subjects had Grade 3 or 4 IRRs; bronchospasm and hypertension (each reported in 2%) and anemia, dyspnea, chills, hypertension, and cytokine release syndrome (reported in 1% each).

| Table : Infusion Related Reactions by System Organ Class, Preferred Term and Grade 3/4; All Treated Analysis Set (Study 54767414MMY2002) | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | 8 mg/kg | | 16 mg/kg | | Total | |
|  | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 | Any Grade | Grade 3 or 4 |
| Analysis set: all treated | 18 |  | 106 |  | 124 |  |
| Total number of subjects with infusion related reactions | 8 (44.4%) | 2 (11.1%) | 45 (42.5%) | 5 (4.7%) | 53 (42.7%) | 7 (5.6%) |
| MedDRA system organ class/Preferred term |  |  |  |  |  |  |
| Respiratory, Thoracic And Mediastinal Disorders | 4 (22.2%) | 0 | 28 (26.4%) | 3 (2.8%) | 32 (25.8%) | 3 (2.4%) |
| Nasal Congestion | 1 (5.6%) | 0 | 13 (12.3%) | 0 | 14 (11.3%) | 0 |
| Cough | 3 (16.7%) | 0 | 6 (5.7%) | 0 | 9 (7.3%) | 0 |
| Dyspnoea | 1 (5.6%) | 0 | 6 (5.7%) | 1 (0.9%) | 7 (5.6%) | 1 (0.8%) |
| Throat Irritation | 0 | 0 | 7 (6.6%) | 0 | 7 (5.6%) | 0 |
| Bronchospasm | 0 | 0 | 4 (3.8%) | 2 (1.9%) | 4 (3.2%) | 2 (1.6%) |
| Wheezing | 1 (5.6%) | 0 | 2 (1.9%) | 0 | 3 (2.4%) | 0 |
| Sneezing | 0 | 0 | 2 (1.9%) | 0 | 2 (1.6%) | 0 |
| Laryngeal Oedema | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Oropharyngeal Pain | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| General Disorders And Administration Site Conditions | 6 (33.3%) | 1 (5.6%) | 11 (10.4%) | 0 | 17 (13.7%) | 1 (0.8%) |
| Chills | 5 (27.8%) | 1 (5.6%) | 6 (5.7%) | 0 | 11 (8.9%) | 1 (0.8%) |
| Chest Discomfort | 1 (5.6%) | 0 | 1 (0.9%) | 0 | 2 (1.6%) | 0 |
| Pyrexia | 2 (11.1%) | 0 | 0 | 0 | 2 (1.6%) | 0 |
| Chest Pain | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Fatigue | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Infusion Site Bruising | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Non-Cardiac Chest Pain | 1 (5.6%) | 0 | 0 | 0 | 1 (0.8%) | 0 |
| Pain | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Gastrointestinal Disorders | 1 (5.6%) | 0 | 8 (7.5%) | 0 | 9 (7.3%) | 0 |
| Vomiting | 1 (5.6%) | 0 | 6 (5.7%) | 0 | 7 (5.6%) | 0 |
| Nausea | 0 | 0 | 5 (4.7%) | 0 | 5 (4.0%) | 0 |
| Diarrhoea | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Paraesthesia Oral | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Skin And Subcutaneous Tissue Disorders | 1 (5.6%) | 0 | 5 (4.7%) | 0 | 6 (4.8%) | 0 |
| Pruritus | 1 (5.6%) | 0 | 2 (1.9%) | 0 | 3 (2.4%) | 0 |
| Rash Macular | 1 (5.6%) | 0 | 1 (0.9%) | 0 | 2 (1.6%) | 0 |
| Urticaria | 1 (5.6%) | 0 | 1 (0.9%) | 0 | 2 (1.6%) | 0 |
| Rash | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Eye Disorders | 0 | 0 | 4 (3.8%) | 0 | 4 (3.2%) | 0 |
| Eye Pruritus | 0 | 0 | 2 (1.9%) | 0 | 2 (1.6%) | 0 |
| Cataract | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Vision Blurred | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Musculoskeletal And Connective Tissue Disorders | 2 (11.1%) | 0 | 2 (1.9%) | 0 | 4 (3.2%) | 0 |
| Back Pain | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Flank Pain | 1 (5.6%) | 0 | 0 | 0 | 1 (0.8%) | 0 |
| Groin Pain | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Musculoskeletal Pain | 1 (5.6%) | 0 | 0 | 0 | 1 (0.8%) | 0 |
| Blood And Lymphatic System Disorders | 0 | 0 | 3 (2.8%) | 1 (0.9%) | 3 (2.4%) | 1 (0.8%) |
| Anaemia | 0 | 0 | 2 (1.9%) | 1 (0.9%) | 2 (1.6%) | 1 (0.8%) |
| Red Blood Cell Agglutination | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Cardiac Disorders | 1 (5.6%) | 0 | 2 (1.9%) | 0 | 3 (2.4%) | 0 |
| Tachycardia | 1 (5.6%) | 0 | 1 (0.9%) | 0 | 2 (1.6%) | 0 |
| Palpitations | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Vascular Disorders | 2 (11.1%) | 1 (5.6%) | 1 (0.9%) | 1 (0.9%) | 3 (2.4%) | 2 (1.6%) |
| Hypertension | 1 (5.6%) | 1 (5.6%) | 1 (0.9%) | 1 (0.9%) | 2 (1.6%) | 2 (1.6%) |
| Hypotension | 1 (5.6%) | 0 | 0 | 0 | 1 (0.8%) | 0 |
| Immune System Disorders | 1 (5.6%) | 1 (5.6%) | 1 (0.9%) | 0 | 2 (1.6%) | 1 (0.8%) |
| Cytokine Release Syndrome | 1 (5.6%) | 1 (5.6%) | 0 | 0 | 1 (0.8%) | 1 (0.8%) |
| Seasonal Allergy | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Nervous System Disorders | 0 | 0 | 2 (1.9%) | 0 | 2 (1.6%) | 0 |
| Headache | 0 | 0 | 2 (1.9%) | 0 | 2 (1.6%) | 0 |
| Psychiatric Disorders | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Anxiety | 0 | 0 | 1 (0.9%) | 0 | 1 (0.8%) | 0 |
| Adverse events are reported using MedDRA version 17.0. Percentages are calculated with the number of subjects in each group as denominator. | | | | | | |
| [TSFAE20.rtf] [JNJ-54767414\MMY2002\DBR\_CSR\RE\_CSR\tsfae20.sas] 13FEB2015, 14:09 | | | | | | |

The duration of daratumumab infusions for the first infusion, second infusion, and all subsequent infusions is presented in Table 10. For the 16 mg/kg group, the median duration of infusion decreased with subsequent infusions, ie, the first infusion was 7.0 hours, compared with 4.2 hours for the second, and 3.4 for all subsequent infusions. One subject (Subject 100039) had an infusion stopped due to an IRR of exacerbated hypertension.

| Table 10: Duration of Daratumumab Infusions; All Treated Analysis Set (Study 54767414MMY2002) | | | |
| --- | --- | --- | --- |
|  | 8 mg/kg | 16 mg/kg | Total |
| Analysis set: all treated | 18 | 106 | 124 |
|  |  |  |  |
| Duration of infusions (hours) |  |  |  |
| First infusion |  |  |  |
| N | 18 | 106 | 124 |
| Mean (SD) | 8.16 (3.959) | 7.34 (1.602) | 7.46 (2.108) |
| Median | 7.02 | 6.96 | 6.96 |
| Range | (5.3; 23.5) | (1.5; 14.3) | (1.5; 23.5) |
| Second infusion |  |  |  |
| N | 16 | 103 | 119 |
| Mean (SD) | 4.95 (1.852) | 4.86 (1.309) | 4.87 (1.385) |
| Median | 4.10 | 4.23 | 4.22 |
| Range | (2.4; 8.8) | (2.7; 8.5) | (2.4; 8.8) |
| All subsequent infusions |  |  |  |
| N | 58 | 1105 | 1163 |
| Mean (SD) | 3.69 (0.530) | 3.49 (0.391) | 3.50 (0.401) |
| Median | 3.54 | 3.42 | 3.42 |
| Range | (2.8; 6.2) | (1.1; 6.7) | (1.1; 6.7) |
| Note: Duration of infusion includes both actual infusion time and interruption time, if any. | | | |
| [TSIEXP04.rtf] [JNJ-54767414\MMY2002\DBR\_CSR\RE\_CSR\tsiexp04.sas] 13FEB2015, 14:07 | | | |