

## ***Supplementary Materials***

### **Safety and Effectiveness of Satralizumab in Japanese Patients with Neuromyelitis Optica Spectrum Disorder: A 6-month Interim Analysis of Post-marketing Surveillance**

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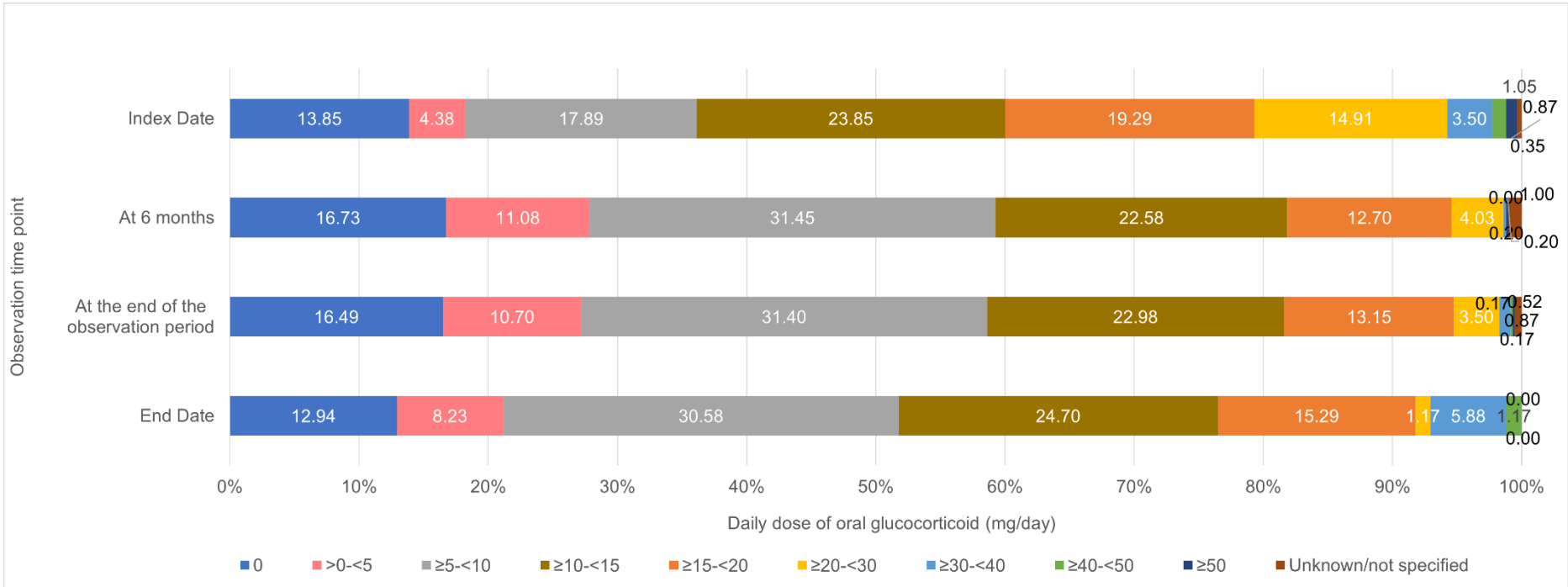
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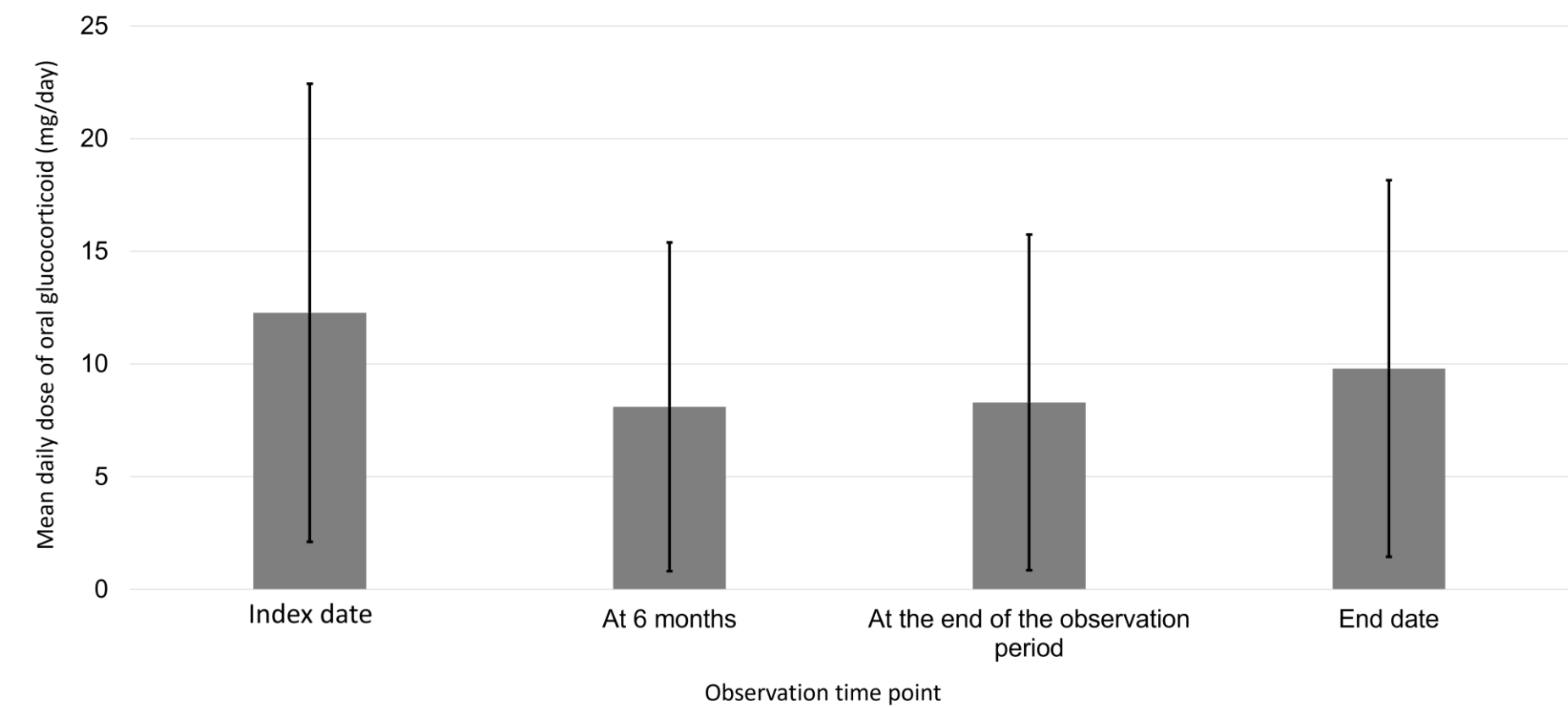
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Figures and tables

Figure S1. Daily oral glucocorticoid dose over time



**Figure S2.** Changes in oral glucocorticoid dose (at the index date and every 6 months)



**Table S1.** Patient characteristics (analysis set, N=570)

| Characteristic <sup>a</sup>                                            | Categories            | n (%)                  |
|------------------------------------------------------------------------|-----------------------|------------------------|
| Sex                                                                    | Male                  | 47 (8.24)              |
|                                                                        | Female <sup>b</sup>   | 523 (91.75)            |
| Age (years)                                                            | Mean (SD)             | 52.4 (14.1)            |
|                                                                        | <12                   | 2 (0.35)               |
|                                                                        | ≥12-<50               | 233 (40.87)            |
|                                                                        | ≥50-<75               | 306 (53.68)            |
|                                                                        | ≥75                   | 29 (5.08)              |
| Comorbidities (All)                                                    | Yes                   | 276 (48.42)            |
|                                                                        | Diabetes mellitus     | 60 (10.52)             |
|                                                                        | Hypertension          | 45 (7.89)              |
|                                                                        | Dyslipidemia          | 41 (7.19)              |
|                                                                        | Osteoporosis          | 37 (6.49)              |
|                                                                        | Hyperlipidemia        | 26 (4.56)              |
|                                                                        | Sjogren's syndrome    | 23 (4.03)              |
| Specific comorbidities: Hepatic impairment                             | Yes                   | 20 (3.50) <sup>c</sup> |
| Specific comorbidities: Renal impairment                               | Yes                   | 6 (1.05) <sup>c</sup>  |
| History of prior treatment<br>(immunosuppressants and other biologics) | Yes                   | 366 (64.21)            |
|                                                                        | Azathioprine          | 184 (32.28)            |
|                                                                        | Tacrolimus hydrate    | 182 (31.92)            |
|                                                                        | Cyclosporine          | 15 (2.63)              |
|                                                                        | Mycophenolate mofetil | 7 (1.22)               |

| Characteristic <sup>a</sup>                                    | Categories                                                                                                               | n (%)       |
|----------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------|
|                                                                | Cyclophosphamide hydrate                                                                                                 | 5 (0.87)    |
|                                                                | Eculizumab                                                                                                               | 10 (1.75)   |
|                                                                | Inebilizumab                                                                                                             | 0 (0.00)    |
|                                                                | Rituximab                                                                                                                | 14 (2.45)   |
|                                                                | Satralizumab                                                                                                             | 7 (1.22)    |
| Details of NMOSD                                               |                                                                                                                          |             |
| Anti-AQP4 antibody                                             | Positive                                                                                                                 | 560 (98.24) |
|                                                                | Negative                                                                                                                 | 4 (0.70)    |
|                                                                | No measurement                                                                                                           | 3 (0.52)    |
|                                                                | Unknown/not specified                                                                                                    | 3 (0.52)    |
| Anti-MOG antibody                                              | Positive                                                                                                                 | 4 (0.70)    |
|                                                                | Negative                                                                                                                 | 99 (17.36)  |
|                                                                | No measurement                                                                                                           | 411 (72.10) |
|                                                                | Unknown/not specified                                                                                                    | 56 (9.82)   |
| Clinical manifestations of NMOSD                               |                                                                                                                          |             |
| Specific clinical manifestations of NMOSD (multiple responses) | Optic neuritis                                                                                                           | 354 (62.10) |
|                                                                | Acute myelitis                                                                                                           | 419 (73.50) |
|                                                                | An episode of the area postrema syndrome causing hiccups or nausea and vomiting that cannot be explained by other causes | 71 (12.45)  |
|                                                                | Acute brainstem syndrome                                                                                                 | 47 (8.24)   |

| Characteristic <sup>a</sup>                                     | Categories                                                                                           | n (%)       |
|-----------------------------------------------------------------|------------------------------------------------------------------------------------------------------|-------------|
|                                                                 | Symptomatic narcolepsy or acute diencephalic syndrome with diencephalic MRI lesions typical of NMOSD | 10 (1.75)   |
|                                                                 | Symptomatic cerebral syndrome with brain MRI lesions typical of NMOSD                                | 41 (7.19)   |
| Time from diagnosis to the index date with satralizumab (years) | Mean (SD)                                                                                            | 7.3 (6.4)   |
|                                                                 | <2                                                                                                   | 113 (19.82) |
|                                                                 | ≥2-<5                                                                                                | 112 (19.64) |
|                                                                 | ≥5-<10                                                                                               | 152 (26.66) |
|                                                                 | ≥10                                                                                                  | 174 (30.52) |
|                                                                 | Unknown/not specified                                                                                | 19 (3.33)   |
| Number of relapses within 2 years                               | Mean (SD)                                                                                            | 0.9 (1.3)   |
|                                                                 | 0                                                                                                    | 256 (44.91) |
|                                                                 | 1                                                                                                    | 157 (27.54) |
|                                                                 | 2                                                                                                    | 90 (15.78)  |
|                                                                 | ≥3                                                                                                   | 51 (8.95)   |
|                                                                 | Unknown/not specified                                                                                | 16 (2.80)   |
| EDSS score                                                      | Mean (SD)                                                                                            | 4.19 (2.19) |
|                                                                 | 0                                                                                                    | 18 (3.15)   |
|                                                                 | 1.0                                                                                                  | 22 (3.85)   |
|                                                                 | 1.5                                                                                                  | 12 (2.10)   |
|                                                                 | 2.0                                                                                                  | 74 (12.98)  |
|                                                                 | 2.5                                                                                                  | 41 (7.19)   |
|                                                                 | 3.0                                                                                                  | 42 (7.36)   |

| Characteristic <sup>a</sup>                                                                             | Categories               | n (%)       |
|---------------------------------------------------------------------------------------------------------|--------------------------|-------------|
|                                                                                                         | 3.5                      | 51 (8.94)   |
|                                                                                                         | 4.0                      | 33 (5.78)   |
|                                                                                                         | 4.5                      | 30 (5.26)   |
|                                                                                                         | 5.0                      | 41 (7.19)   |
|                                                                                                         | 5.5                      | 18 (3.15)   |
|                                                                                                         | 6.0                      | 61 (10.70)  |
|                                                                                                         | 6.5                      | 24 (4.21)   |
|                                                                                                         | 7.0                      | 20 (3.50)   |
|                                                                                                         | 7.5                      | 23 (4.03)   |
|                                                                                                         | 8.0                      | 7 (1.22)    |
|                                                                                                         | 8.5                      | 17 (2.98)   |
|                                                                                                         | 9.0                      | 5 (0.87)    |
|                                                                                                         | 9.5                      | 3 (0.52)    |
|                                                                                                         | Unknown/not specified    | 28 (4.91)   |
| Status of concomitant therapy at the index date (oral glucocorticoids other than steroid pulse therapy) | Yes                      | 490 (85.96) |
| Use of concomitant therapies at the index date (immunosuppressants)                                     | Yes                      | 277 (48.59) |
| Details of concomitant immunosuppressant therapies                                                      | Azathioprine             | 112 (19.64) |
|                                                                                                         | Tacrolimus Hydrate       | 144 (25.26) |
|                                                                                                         | Cyclosporine             | 11 (1.92)   |
|                                                                                                         | Mycophenolate mofetil    | 6 (1.05)    |
|                                                                                                         | Cyclophosphamide hydrate | 0 (0.00)    |

| Characteristic <sup>a</sup> | Categories               | n (%)     |
|-----------------------------|--------------------------|-----------|
|                             | Immunosuppressants other | 12 (2.10) |
|                             | Mizoribine               | 5 (0.87)  |
|                             | Methotrexate             | 7 (1.22)  |

All data are represented as n (%)

<sup>a</sup>n=570 for all characteristics except time from diagnosis to the start of treatment with satralizumab (years) (n=551), and number of relapses within 2 years (n=554), and EDSS score (n=542)

<sup>b</sup>Of the 523 female subjects, pregnancy occurred in 2 (0.35%), and pregnancy related details of 2 (0.35%) other female subjects were unknown

<sup>c</sup>Comorbidities in all patients excluding 1 with unspecified/details unknown. Comorbidities included ongoing comorbid conditions or diseases (possibly under treatment) at the index date.

AQP4, aquaporin-4; EDSS, Expanded Disability Status Scale; MRI, magnetic resonance imaging; NMOSD, neuromyelitis optica spectrum disorder; SD, standard deviation

**Table S2a.** Number of days from the index date to onset of initial adverse reactions

| Adverse reaction                       | Number of subjects showing adverse reaction | Number of days from the index date to onset of the first adverse reaction |                  |
|----------------------------------------|---------------------------------------------|---------------------------------------------------------------------------|------------------|
|                                        |                                             | Mean (SD)                                                                 | Median (min-max) |
| Total                                  | 114 <sup>a</sup>                            | 54.6 (64.9)                                                               | 29.0 (1-296)     |
| Infections                             | 26                                          | 84.7 (78.9)                                                               | 79.0 (1-296)     |
| Neutropenia/leukopenia/agranulocytosis | 8                                           | 58.5 (33.3)                                                               | 63.0 (15-113)    |
| Thrombocytopenia                       | 2                                           | 113.0 (138.5)                                                             | 113.0 (15-211)   |
| Hypersensitivity                       | 6                                           | 59.3 (75.3)                                                               | 22.0 (1-169)     |
| Hepatic impairment                     | 21                                          | 29.6 (29.6)                                                               | 15.0 (1-92)      |
| Cardiac disorders                      | 7                                           | 80.4 (63.9)                                                               | 83.0 (16-197)    |

Data were tabulated excluding patients previously treated with this drug

Calculated with the start date of administration as Day 1

System organ class and preferred term as per MedDRA/J ver. 25.1

<sup>a</sup>Excluding 2 patients whose number of days from the start of this drug treatment was unknown/not recorded (1 patient with infection and 1 patient with poor healing)

None of the subjects showed following adverse reactions: hepatitis B virus reactivation, immunogenicity, malignancies, intestinal perforation, interstitial pneumonia  
max, maximum; MedDRA/J, Medical Dictionary for Regulatory Activities Japanese edition; min, minimum; SD, standard deviation

**Table S2b.** Number of days from the index date to onset of initial adverse reactions

| Adverse reaction                           | Onset of the first adverse reaction from the index date (days) |       |       |        |         |         |         |         |          |           |           |           |       |                              | Total |
|--------------------------------------------|----------------------------------------------------------------|-------|-------|--------|---------|---------|---------|---------|----------|-----------|-----------|-----------|-------|------------------------------|-------|
|                                            | ≤30                                                            | 31-60 | 61-90 | 91-120 | 121-150 | 151-180 | 181-360 | 361-720 | 721-1080 | 1081-1440 | 1441-1800 | 1801-2160 | >2160 | Unknown/<br>not<br>specified |       |
| Total                                      | 68                                                             | 5     | 14    | 10     | 5       | 7       | 5       | 0       | 0        | 0         | 0         | 0         | 0     | 2                            | 116   |
| Infections                                 | 9                                                              | 2     | 4     | 4      | 3       | 2       | 2       | 0       | 0        | 0         | 0         | 0         | 0     | 1                            | 27    |
| Neutropenia/leukopenia/<br>agranulocytosis | 3                                                              | 0     | 3     | 2      | 0       | 0       | 0       | 0       | 0        | 0         | 0         | 0         | 0     | 0                            | 8     |
| Thrombocytopenia                           | 1                                                              | 0     | 0     | 0      | 0       | 0       | 1       | 0       | 0        | 0         | 0         | 0         | 0     | 0                            | 2     |
| Hypersensitivity                           | 4                                                              | 0     | 0     | 0      | 1       | 1       | 0       | 0       | 0        | 0         | 0         | 0         | 0     | 0                            | 6     |
| Hepatic impairment                         | 17                                                             | 0     | 3     | 1      | 0       | 0       | 0       | 0       | 0        | 0         | 0         | 0         | 0     | 0                            | 21    |
| Cardiac disorders                          | 3                                                              | 0     | 1     | 2      | 0       | 0       | 1       | 0       | 0        | 0         | 0         | 0         | 0     | 0                            | 7     |

Data were tabulated excluding patients previously treated with this drug

MedDRA/J version (25.1)

MedDRA/J, Medical Dictionary for Regulatory Activities Japanese edition

**Table S3.** Individual adverse reactions: infections by seriousness (safety analysis set, N=570)

| Event term                          | Serious                        |                      |                                  | Total                          |                      |                                  |
|-------------------------------------|--------------------------------|----------------------|----------------------------------|--------------------------------|----------------------|----------------------------------|
|                                     | Number of subjects with events | Incidence % (95% CI) | Events/100 person-years (95% CI) | Number of subjects with events | Incidence % (95% CI) | Events/100 person-years (95% CI) |
| Total adverse reactions             | 29                             | 5.08 (3.43-7.22)     | 17.35 (12.70-23.15)              | 118                            | 20.70 (17.44-24.26)  | 76.22 (66.07-87.48)              |
| Infections and infestations         | 18                             | 3.15 (1.88-4.94)     | 9.05 (5.80-13.47)                | 28                             | 4.91 (3.28-7.02)     | 13.58 (9.51-18.80)               |
| Breast abscess                      | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Cellulitis                          | 2                              | 0.35 (0.04-1.26)     | 0.75 (0.09-2.72)                 | 2                              | 0.35 (0.04-1.26)     | 0.75 (0.09-2.72)                 |
| Cystitis                            | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 3                              | 0.52 (0.10-1.53)     | 1.13 (0.23-3.30)                 |
| Escherichia sepsis                  | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Gastroenteritis                     | 0                              | 0.00 (0.00-0.64)     | 0.00 (-1.39)                     | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Herpes simplex                      | 0                              | 0.00 (0.00-0.64)     | 0.00 (-1.39)                     | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Herpes zoster                       | 0                              | 0.00 (0.00-0.64)     | 0.00 (-1.39)                     | 2                              | 0.35 (0.04-1.26)     | 0.75 (0.09-2.72)                 |
| Mastitis                            | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Nasopharyngitis                     | 0                              | 0.00 (0.00-0.64)     | 0.00 (-1.39)                     | 1                              | 0.17 (0.00-0.97)     | 0.75 (0.09-2.72)                 |
| Paronychia                          | 0                              | 0.00 (0.00-0.64)     | 0.00 (-1.39)                     | 2                              | 0.35 (0.04-1.26)     | 0.75 (0.09-2.72)                 |
| Pneumonia                           | 3                              | 0.52 (0.10-1.53)     | 1.13 (0.23-3.30)                 | 3                              | 0.52 (0.10-1.53)     | 1.13 (0.23-3.30)                 |
| Pneumonia aspiration <sup>a</sup>   | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Pulmonary tuberculosis              | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Sepsis                              | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Septic shock                        | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Sinusitis                           | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Urinary tract infection             | 3                              | 0.52 (0.10-1.53)     | 1.13 (0.23-3.30)                 | 3                              | 0.52 (0.10-1.53)     | 1.13 (0.23-3.30)                 |
| Vulvovaginal candidiasis            | 0                              | 0.00 (0.00-0.64)     | 0.00 (--1.39)                    | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Escherichia urinary tract infection | 2                              | 0.35 (0.0-1.26)      | 0.75 (0.09-2.72)                 | 2                              | 0.35 (0.04-1.26)     | 0.75 (0.09-2.72)                 |
| Jaw abscess                         | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |
| Pneumococcal infection              | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 | 1                              | 0.17 (0.00-0.97)     | 0.37 (0.00-2.10)                 |

|                                   |   |                  |                  |   |                  |                  |
|-----------------------------------|---|------------------|------------------|---|------------------|------------------|
| Atypical mycobacterial infection  | 1 | 0.17 (0.00-0.97) | 0.37 (0.00-2.10) | 1 | 0.17 (0.00-0.97) | 0.37 (0.00-2.10) |
| Oral herpes                       | 0 | 0.00 (0.00-0.64) | 0.00 (--1.39)    | 1 | 0.17 (0.00-0.97) | 0.37 (0.00-2.10) |
| Medical device site abscess       | 1 | 0.17 (0.00-0.97) | 0.37 (0.00-2.10) | 1 | 0.17 (0.00-0.97) | 0.37 (0.00-2.10) |
| Necrotizing soft tissue infection | 1 | 0.17 (0.00-0.97) | 0.37 (0.00-2.10) | 1 | 0.17 (0.00-0.97) | 0.37 (0.00-2.10) |

If the same event (with the same MedDRA SOC and PT code) occurred more than once but if the seriousness levels of the event were different (1 serious and other nonserious event), each event was counted separately but the total number of subjects was considered as 1

Adverse events other than “progression/recurrence of NMOSD (including neuromyelitis optica)” were tabulated

<sup>a</sup>Adverse reactions that cannot be predicted from the current “Precautions for Use”

CI, confidence interval; MedDRA, Medical Dictionary for Regulatory Activities; NMOSD, neuromyelitis optica spectrum disorder; PT, preferred term; SOC, system organ class