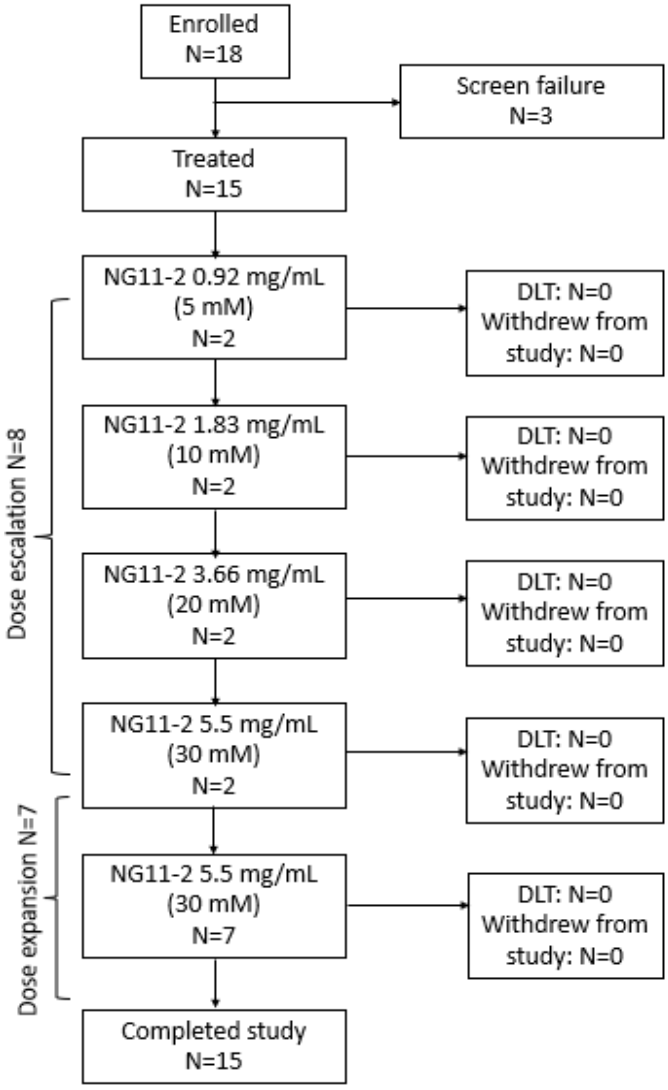
## Participant FlowChart



## Baseline Characteristics

BMI=body mass index; NC=not calculated; SD=standard deviation.

**Table 1: Demographic Characteristics (Full Analysis Set)**

| Demographic Characteristic | 0.92mg/mL (5mM) NG11-2 (N=2) | 1.83mg/mL (10mM) NG11-2 (N=2) | 3.66mg/mL (20mM) NG11-2 (N=2) | 5.5mg/mL (30mM) NG11-2 (N=9) | Total (N=15) |
|---|---|---|---|---|---|
| **Age** | | | | | |
| Mean (SD) | NC | NC | NC | 64.3 (7.62) | 64.6 (6.34) |
| Median (range) | NC (60, 66) | NC (69, 71) | NC (61, 63) | 66.0 (52, 76) | 66.0 (52, 76) |
| **Sex** | | | | | |
| Male, n (%) | 1 (50.0) | 0 | 2 (100.0) | 9 (100.0) | 12 (80.0) |
| Female, n (%) | 1 (50.0) | 2 (100.0) | 0 | 0 | 3 (20.0) |
| **BMI** ($kg/m^2$) | | | | | |
| Mean (SD) | NC | NC | NC | 27.027 (3.7490) | 27.804 (3.3710) |
| Median (Range) | NC (24.17, 29.04) | NC (28.84, 31.60) | NC (29.56, 30.61) | 26.589 (21.63, 35.11) | 28.089 (21.63, 35.11) |
| **Karnofsky performance status** | | | | | |
| Mean (SD) | NC | NC | NC | 94.4 (5.27) | 94.0 (6.32) |
| Median (range) | NC (80, 90) | NC (100, 100) | NC (90, 100) | 90.0 (90, 100) | 90.0 (80, 100) |

**Table 2: Exposure to Study Intervention and Radiotherapy (Full Analysis Set)**

| Radiation Dosing | 0.92mg/mL (5mM) NG11-2 (N=2) | 1.83mg/mL (10mM) NG11-2 (N=2) | 3.66mg/mL (20mM) NG11-2 (N=2) | 5.5mg/mL* (30mM) NG11-2 (N=9) |
|---|---|---|---|---|
| Number of days NG11-2 dose was received | | | | |
| Mean (SD) | NC | NC | NC | 27.3 (4.77) |
| Median (Range) | NC (27, 27) | NC (29, 30) | NC (17, 30) | 29.0 (15, 30) |
| Number of days radiotherapy received | | | | |
| Mean (SD) | NC | NC | NC | 29.8 (0.44) |
| Median (Range) | NC (29, 34) | NC (30, 30) | NC (30, 30) | 30.0 (29, 30) |
| Mean daily dose of NG11-2 (mg/mL) | | | | |
| Mean (SD) | NC | NC | NC | 5.050 (0.8844) |
| Median (Range) | NC (0.73, 0.86) | NC (1.77, 1.83) | NC (2.07, 3.66) | 5.317 (2.75, 5.50) |
| Participants with at least 1 NG11-2 dose interruption | 2 (100.0) | 0 | 0 | 3 (33.3) |

* In this group, one participant had accelerated radiotherapy with 2 fractional irradiation and 2 NG11-2 treatments on one day of each week from Week 2 to Week 6 of radiotherapy.

Mean daily dose of NG11-2 (mg/mL) was calculated per participant as the total exposure of NG11-2 (mg/mL) during the study divided by the number of days radiotherapy was received.

**Table 3: Diagnosis of Study Participants (Full Analysis Set)**

| Dose Level | Diagnosis | TNM Stage or p16 Status |
|---|---|---|
| 0.92mg/mL (5mM) | Oral cavity<br>Nasopharynx | T4 N3B M0<br>T3 (involving clivus) N0 M0, P16-Positive EBER-Negative |
| 1.83mg/mL (10mM) | Oropharynx<br>Oropharynx | T4 N2A M0, HPV Associated<br>T2 N1 M0, HPV Positive |
| 3.66mg/mL (20mM) | Oropharynx<br>Oropharynx | T2 N1 M0, P16 Positive<br>T2 N1, P16 Positive |
| 5.5mg/mL (30mM) | Oropharynx<br>Oral cavity<br>Oropharynx<br>Oropharynx<br>Oropharynx<br>Oropharynx<br>Oropharynx<br>Oropharynx<br>Oral cavity | T2 N1 M0, P16 Positive<br>T2 N1 M0<br>P16 Positive<br>T2 N1 M0 P16 Positive<br>T1 N2B M0, P16 Positive<br>T2 N1 M0, P16 Positive<br>T2N1M0, P16 Positive<br>T2 N1 M0 P16 Positive T2 N1 |

## Outcome Measures

**Table 4: Duration of Severe RIOM by Oral Mucositis Scale (Full Analysis Set)**

| Duration in Days | 0.92mg/mL (5mM) NG11-2 (N=2) | 1.83mg/mL (10mM) NG11-2 (N=2) | 3.66mg/mL (20mM) NG11-2 (N=2) | 5.5mg/mL (30mM) NG11-2 (N=9) |
|---|---|---|---|---|
| WHO, n | 2 | 1 | 2 | 6 |
| Mean (SD)[a] | NC | NC | NC | 17.3 (10.80) |
| Median (range)[a] | NC (19, 39) | NC (21, 21) | NC (10, 14) | 15.5 (3, 36) |
| Kaplan-Meier estimate of the median (95% CI) | NC (NC, NC) | NC (NC, NC) | NC (NC, NC) | 15.5 (3.0, NC) |
| RTOG, n | 2 | 1 | 1 | 3 |
| Mean (SD)[a] | NC | NC | NC | 12.7 (NC) |
| Median (range)[a] | NC (39, 46) | NC (33, 33) | NC (13, 13) | 14.0 (3, 21) |
| Kaplan-Meier estimate of the median (95% CI) | NC (NC, NC) | NC (NC, NC) | NC (NC, NC) | 14.0 (3.0, NC) |
| NCI-CTCAE, n | 2 | 1 | 1 | 5 |
| Mean (SD)[a] | NC | NC | NC | 17.6 (3.78) |
| Median (range)[a] | NC (18, 39) | NC (33, 33) | NC (7, 7) | 17.0 (14, 22) |
| Kaplan-Meier estimate of the median (95% CI) | NC (NC, NC) | NC (NC, NC) | NC (NC, NC) | 17.0 (14.0, NC) |

[a] Only participants who reached severe RIOM and were no longer experiencing severe RIOM are included. Severe RIOM was defined as a WHO, RTOG or NCI-CTCAE score of Grade 3 and above. Duration of severe RIOM (days) was defined as the cumulative time spent with severe RIOM.

CI=confidence interval; NC=not calculated; NCI-CTCAE=National Cancer Institute-Common Terminology Criteria for Adverse Events; RIOM=radiation-induced oral mucositis; RTOG=Radiation Therapy Oncology Group; SD=standard deviation; WHO=World Health Organization.

**Table 5: Incidence and Time to Onset of Severe RIOM by Oral Mucositis Scale (Full Analysis Set)**

| Incidence and Time to Onset in Days | 0.92mg/mL (5mM) NG11-2 (N=2) | 1.83mg/mL (10mM) NG11-2 (N=2) | 3.66mg/mL (20mM) NG11-2 (N=2) | 5.5mg/mL (30mM) NG11-2 (N=9) |
|---|---|---|---|---|
| WHO | | | | |
| Incidence of severe RIOM[a], n | 2 (100.0) | 0 | 2 (100.0) | 4 (44.4) |
| Time to onset of severe RIOM[b], n | 2 | 1 | 2 | 6 |
| Mean (SD)[b] | NC | NC | NC | 37.5 (13.53) |
| Median (range)[b] | NC (32, 39) | NC (47, 47) | NC (36, 37) | 33.0 (22, 54) |
| Kaplan-Meier estimate of the median time to onset (95% CI) | NC (NC, NC) | NC (NC, NC) | NC (NC, NC) | 54.0 (22.0, NC) |
| RTOG | | | | |
| Incidence of severe RIOM[a], n | 2 (100.0) | 0 | 1 (50.0) | 3 (33.3) |
| Time to onset of severe RIOM[b], n | 2 | 1 | 1 | 3 |
| Mean (SD)[b] | NC | NC | NC | 30.3 (NC) |
| Median (range)[b] | NC (22, 39) | NC (47, 47) | NC (22, 22) | 33.0 (22, 36) |
| Kaplan-Meier estimate of the median time to onset (95% CI) | NC (NC, NC) | NC (NC, NC) | NC (NC, NC) | NC (22.0, NC) |
| NCI-CTCAE | | | | |
| Incidence of severe RIOM[a], n | 2 (100.0) | 0 | 1 (50.0) | 3 (33.3) |
| Time to onset of severe RIOM[b], n | 2 | 1 | 1 | 5 |
| Mean (SD)[b] | NC | NC | NC | 40.4 (13.05) |
| Median (range)[b] | NC (36, 39) | NC (47, 47) | NC (25, 25) | 36.0 (25, 54) |
| Kaplan-Meier estimate of the median time to onset (95% CI) | NC (NC, NC) | NC (NC, NC) | NC (NC, NC) | 54.0 (25.0, NC) |

[a] Only participants who reached severe RIOM during the treatment period are included.

[b] Only participants who reached severe RIOM are included.

Severe RIOM was defined as a WHO, RTOG or NCI-CTCAE score of Grade 3 and above. Time to onset of severe RIOM (days) was defined as the first date of severe RIOM – date of first dose + 1.

CI=confidence interval; NC=not calculated; NCI-CTCAE=National Cancer Institute-Common Terminology Criteria for Adverse Events; RIOM=radiation-induced oral mucositis; RTOG=Radiation Therapy Oncology Group; SD=standard deviation; WHO=World Health Organization.

## Adverse Events

**Table 6: Overview of Treatment-Emergent Adverse Events (Full Analysis Set)**

| Adverse event category | 0.92mg/mL (5mM) NG11-2 (N=2) n (%) [events] | 1.83mg/mL (10mM) NG11-2 (N=2) n (%) [events] | 3.66mg/mL (20mM) NG11-2 (N=2) n (%) [events] | 5.5mg/mL (30mM) NG11-2 (N=9) n (%) [events] | Total (N=15) n (%) [events] |
|---|---|---|---|---|---|
| Any TEAE | 2 (100) [23] | 2 (100) [43] | 2 (100) [32] | 9 (100) [213] | 15 (100) [311] |
| Any TEAE of CTCAE Grade 3 or higher | 1 (50.0) [1] | 0 | 0 | 7 (77.8) [25] | 8 (53.3) [26] |
| Any TEAE with outcome of death | 0 | 0 | 0 | 0 | 0 |
| Any treatment-emergent SAE[a] | 2 (100) [4] | 0 | 0 | 6 (66.7) [16] | 8 (53.3) [20] |
| Any treatment-emergent SAE causally related to NG11-2[b] | 0 | 0 | 0 | 0 | 0 |
| Any TEAE leading to discontinuation of NG11-2 | 1 (50.0) [1] | 0 | 1 (50.0) [1] | 0 | 2 (13.3) [2] |
| Any TEAE classified as a DLT[c] | 0 | 0 | 0 | 0 | 0 |
| Any TEAE causally related to NG11-2[b] | 2 (100) [2] | 1 (50.0) [1] | 2 (100) [14] | 7 (77.8) [54] | 12 (80.0) [71] |

[a] Included events with an outcome of death.

[b] Causally related to NG11-2 as assessed by the investigator. Causally related AE/SAEs were those with a relationship of possibly related, probably related and definitely related.

[c] DLTs were only summarised for participants in the dose escalation cohort.

CTCAE=Common Terminology Criteria for Adverse Events; DLT=dose-limiting toxicity; SAE=serious adverse event; TEAE=treatment-emergent adverse event

**Table 71: Treatment-Emergent Adverse Events Reported in More than 1 Participant Overall (Full Analysis Set)**

| Preferred Term | 0.92mg/mL (5mM) NG11-2 (N=2) n (%) [rate[a]] | 1.83mg/mL (10mM) NG11-2 (N=2) n (%) [rate[a]] | 3.66mg/mL (20mM) NG11-2 (N=2) n (%) [rate[a]] | 5.5mg/mL (30mM) NG11-2 (N=9) n (%) [rate[a]] | Total (N=15) n (%) [rate[a]] |
|---|---|---|---|---|---|
| Participants reporting any TEAE | 2 (100) [419.8] | 2 (100) [459.4] | 2 (100) [405.8] | 9 (100) [447.9] | 15 (100) [439.4] |
| Nausea | 1 (50.0) [209.9] | 1 (50.0) [229.7] | 2 (100) [405.8] | 8 (88.9) [398.1] | 12 (80.0) [351.5] |
| Dysgeusia | 0 | 1 (50.0) [229.7] | 1 (50.0) [202.9] | 8 (88.9) [398.1] | 10 (66.7) [292.9] |
| Constipation | 1 (50.0) [209.9] | 1 (50.0) [229.7] | 1 (50.0) [202.9] | 6 (66.7) [298.6] | 9 (60.0) [263.6] |
| Dry mouth | 0 | 2 (100.0) [459.4] | 2 (100) [405.8] | 5 (55.6) [248.8] | 9 (60.0) [263.6] |
| Oral candidiasis | 2 (100) [419.8] | 1 (50.0) [229.7] | 0 | 6 (66.7) [298.6] | 9 (60.0) [263.6] |
| Weight decreased | 1 (50.0) [209.9] | 1 (50.0) [229.7] | 1 (50.0) [202.9] | 5 (55.6) [248.8] | 8 (53.3) [234.3] |
| Oral dysaesthesia | 1 (50.0) [209.9] | 0 | 1 (50.0) [202.9] | 5 (55.6) [248.8] | 7 (46.7) [205.0] |
| Fatigue | 1 (50.0) [209.9] | 1 (50.0) [229.7] | 0 | 5 (55.6) [248.8] | 7 (46.7) [205.0] |
| Radiation skin injury | 1 (50.0) [209.9] | 1 (50.0) [229.7] | 0 | 5 (55.6) [248.8] | 7 (46.7) [205.0] |
| Oral pain | 1 (50.0) [209.9] | 1 (50.0) [229.7] | 1 (50.0) [202.9] | 3 (33.3) [149.3] | 6 (40.0) [175.7] |
| Oropharyngeal pain | 0 | 1 (50.0) [229.7] | 1 (50.0) [202.9] | 4 (44.4) [199.0] | 6 (40.0) [175.7] |
| Dysphagia | 1 (50.0) [209.9] | 2 (100.0) [459.4] | 0 | 2 (22.2) [99.5] | 5 (33.3) [146.5] |
| Stomatitis | 0 | 1 (50.0) [229.7] | 0 | 4 (44.4) [199.0] | 5 (33.3) [146.5] |
| Dyspepsia | 0 | 0 | 1 (50.0) [202.9] | 3 (33.3) [149.3] | 4 (26.7) [117.2] |
| Vomiting | 1 (50.0) [209.9] | 1 (50.0) [229.7] | 0 | 2 (22.2) [99.5] | 4 (26.7) [117.2] |
| Decreased appetite | 0 | 2 (100.0) [459.4] | 0 | 2 (22.2) [99.5] | 4 (26.7) [117.2] |
| Hypokalaemia | 0 | 2 (100.0) [459.4] | 1 (50.0) [202.9] | 1 (11.1) [49.8] | 4 (26.7) [117.2] |
| Hypophos-phataemia | 0 | 0 | 0 | 3 (33.3) [149.3] | 3 (20.0) [87.9] |
| Abdominal pain | 0 | 0 | 0 | 2 (22.2) [99.5] | 2 (13.3) [58.6] |
| Abdominal pain upper | 0 | 0 | 1 (50.0) [202.9] | 1 (11.1) [49.8] | 2 (13.3) [58.6] |
| Oral discomfort | 1 (50.0) [209.9] | 0 | 1 (50.0) [202.9] | 0 | 2 (13.3) [58.6] |
| Tremor | 0 | 0 | 0 | 2 (22.2) [99.5] | 2 (13.3) [58.6] |
| Dehydration | 0 | 0 | 1 (50.0) [202.9] | 1 (11.1) [49.8] | 2 (13.3) [58.6] |
| Dysphonia | 0 | 0 | 0 | 2 (22.2) [99.5] | 2 (13.3) [58.6] |
| Increased upper airway secretion | 0 | 1 (50.0) [229.7] | 0 | 1 (11.1) [49.8] | 2 (13.3) [58.6] |
| Pain | 0 | 0 | 0 | 2 (22.2) [99.5] | 2 (13.3) [58.6] |
| Pyrexia | 1 (50.0) [209.9] | 0 | 0 | 1 (11.1) [49.8] | 2 (13.3) [58.6] |
| Tinnitus | 0 | 0 | 0 | 2 (22.2) [99.5] | 2 (13.3) [58.6] |

| Preferred Term | 0.92mg/mL (5mM) NG11-2 (N=2) n (%) [rate[a]] | 1.83mg/mL (10mM) NG11-2 (N=2) n (%) [rate[a]] | 3.66mg/mL (20mM) NG11-2 (N=2) n (%) [rate[a]] | 5.5mg/mL (30mM) NG11-2 (N=9) n (%) [rate[a]] | Total (N=15) n (%) [rate[a]] |
|---|---|---|---|---|---|
| Hypertension | 0 | 0 | 0 | 2 (22.2) [99.5] | 2 (13.3) [58.6] |
| Thrombocytopenia | 0 | 0 | 0 | 2 (22.2) [99.5] | 2 (13.3) [58.6] |
| Sinus tachycardia | 1 (50.0) [209.9] | 0 | 0 | 1 (11.1) [49.8] | 2 (13.3) [58.6] |

[a] Rate is the incidence rate of the TEAE per 100 participant years, calculated as the number of participants with TEAEs divided by the total duration of treatment across all participants in a given dose level, multiplied by 100.

Participants with multiple TEAEs are counted once for each preferred term.

**Table 8: Treatment-Emergent Adverse Events with Maximum Reported CTCAE Grade 3 or Above (Full Analysis Set)**

| Preferred Term | 0.92mg/mL (5mM) NG11-2 (N=2) n (%) | 1.83mg/mL (10mM) NG11-2 (N=2) n (%) | 3.66mg/mL (20mM) NG11-2 (N=2) n (%) | 5.5mg/mL (30mM) NG11-2 (N=9) n (%) | Total (N=15) n (%) |
|---|---|---|---|---|---|
| All participants reporting a severe TEAE | 2 (100) | 2 (100) | 2 (100) | 9 (100) | 15 (100) |
| Grade 3 | 1 (50.0) | 0 | 0 | 5 (55.6) | 6 (40.0) |
| Grade 4 | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Nausea | 1 (50.0) | 1 (50.0) | 2 (100) | 8 (88.9) | 12 (80.0) |
| Grade 3 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Oropharyngeal pain | 0 | 1 (50.0) | 1 (50.0) | 4 (44.4) | 6 (40.0) |
| Grade 3 | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Stomatitis | 0 | 1 (50.0) | 0 | 4 (44.4) | 5 (33.3) |
| Grade 3 | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Hypertension | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Grade 3 | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Abdominal pain | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Grade 3 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Thrombocytopenia | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Grade 4 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Syncope | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Grade 3 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Hypophagia | 1 (50.0) | 0 | 0 | 0 | 1 (6.7) |
| Grade 3 | 1 (50.0) | 0 | 0 | 0 | 1 (6.7) |
| Aphonia | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Grade 3 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Aspiration | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Grade 3 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Pulmonary embolism | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Grade 3 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Lymphopenia | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Grade 4 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |

| Preferred Term | 0.92mg/mL (5mM) NG11-2 (N=2) n (%) | 1.83mg/mL (10mM) NG11-2 (N=2) n (%) | 3.66mg/mL (20mM) NG11-2 (N=2) n (%) | 5.5mg/mL (30mM) NG11-2 (N=9) n (%) | Total (N=15) n (%) |
|---|---|---|---|---|---|
| Neutropenia | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Grade 3 | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |

Grade 3=moderate, Grade 4=life-threatening.

Each participant was only represented with the maximum reported CTCAE grade for each preferred term.

CTCAE=Common Terminology Criteria for Adverse Events; TEAE=treatment-emergent adverse event.

**Table 29: Treatment-Emergent Adverse Events Considered Related to NG11-2 (Full Analysis Set)**

| Preferred Term | 0.92mg/mL (5mM) NG11-2 (N=2) n (%) | 1.83mg/mL (10mM) NG11-2 (N=2) n (%) | 3.66mg/mL (20mM) NG11-2 (N=2) n (%) | 5.5mg/mL (30mM) NG11-2 (N=9) n (%) | Total (N=15) n (%) |
|---|---|---|---|---|---|
| Any TEAE related to NG11-2 | 2 (100) | 1 (50.0) | 2 (100) | 7 (77.8) | 12 (80.0) |
| Oral dysaesthesia | 1 (50.0) | 0 | 1 (50.0) | 3 (33.3) | 5 (33.3) |
| Oral pain | 0 | 1 (50.0) | 0 | 3 (33.3) | 4 (26.7) |
| Abdominal pain upper | 0 | 0 | 1 (50.0) | 1 (11.1) | 2 (13.3) |
| Nausea | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Oral discomfort | 1 (50.0) | 0 | 1 (50.0) | 0 | 2 (13.3) |
| Tremor | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Pain | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Hypertension | 0 | 0 | 0 | 2 (22.2) | 2 (13.3) |
| Dysphagia | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Gingival pain | 0 | 0 | 1 (50.0) | 0 | 1 (6.7) |
| Oesophageal pain | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Vomiting | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Dysaesthesia | 0 | 0 | 1 (50.0) | 0 | 1 (6.7) |
| Palpitations | 0 | 0 | 0 | 1 (11.1) | 1 (6.7) |
| Candida infection | 0 | 0 | 1 (50.0) | 0 | 1 (6.7) |
| Oropharyngeal pain | 0 | 0 | 1 (50.0) | 0 | 1 (6.7) |
| Rash | 0 | 0 | 1 (50.0) | 0 | 1 (6.7) |

Grade 3=moderate, Grade 4=life-threatening.
Participants with multiple TEAEs are counted once for each preferred term.
TEAE=treatment-emergent adverse event.