# CRUKD/17/009, BT1718 Basic Results Summary for ISRCTN

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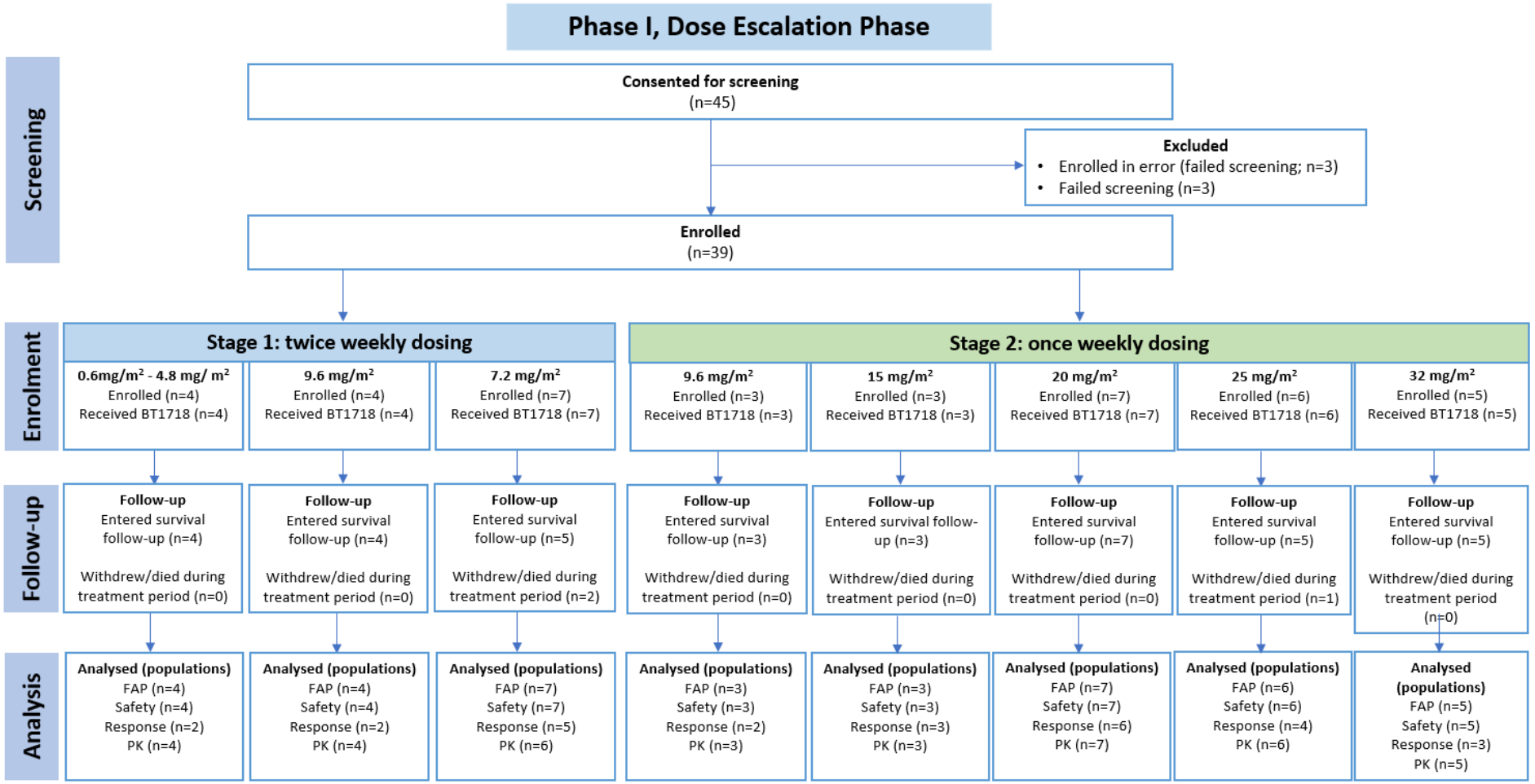
## PARTICIPANT FLOW

### Patient Disposition for the Phase I, Dose Escalation Phase of Trial CRUKD/17/009




*Abbreviations: FAP=Full Analysis Population; n=number of patients with the characteristic of interest; PK=pharmacokinetic.*

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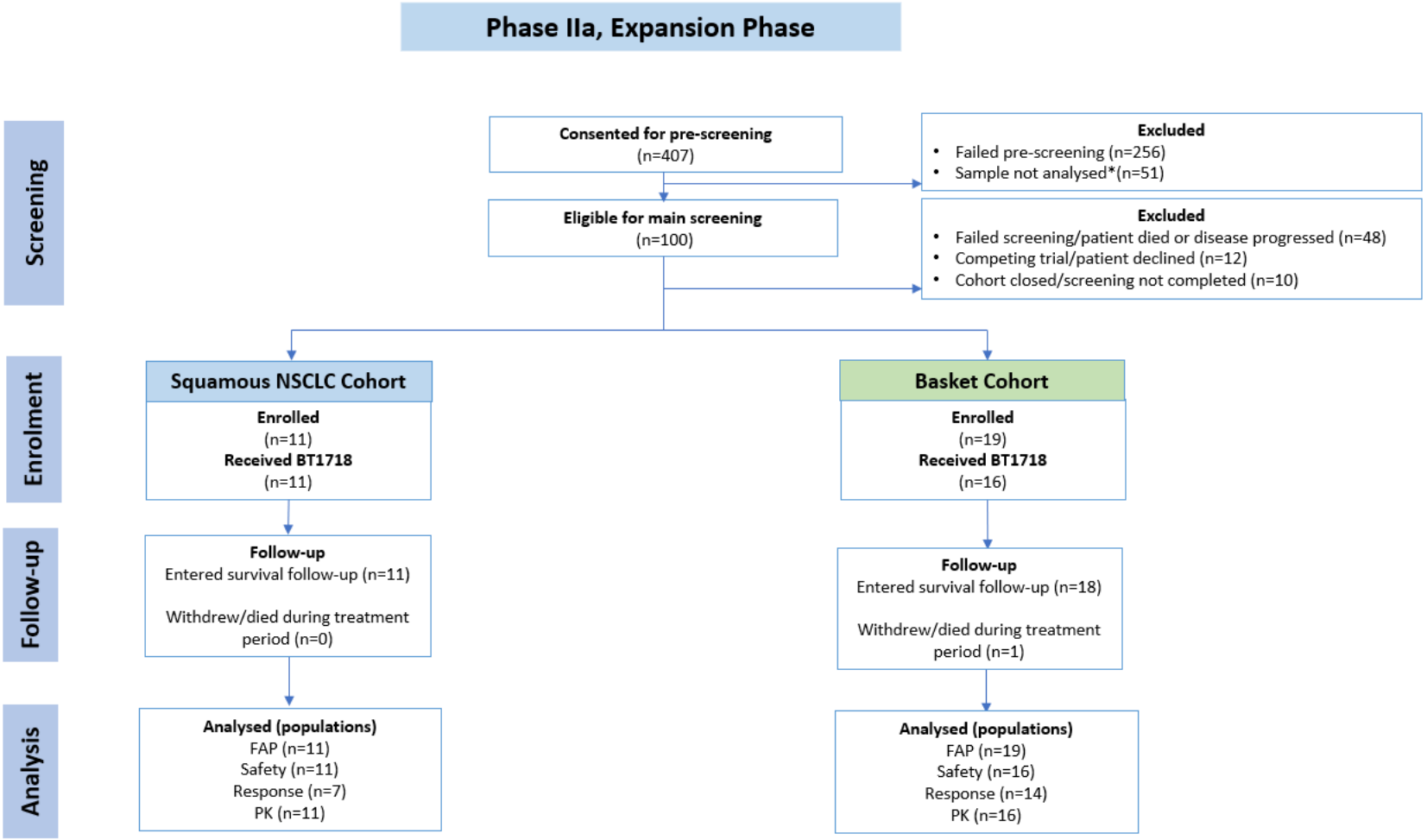
**Patient Disposition for the Phase IIa, Expansion Phase of Trial CRUKD/17/009**




*Patients eligible for main screening includes patients who had retrospective testing for MT1-MMP expression, which was permitted for patients in the sqNSCLC cohort following implementation of CSP Version 8.0 (dated 11 November 2021).*
**Reasons for sample not analysed included cohort closed (n=34); sample requested, not suitable or never sent, including for patients who died/progressed (n=13); temporary halt to recruitment due to COVID-19 (n=2); competing trial (n=2).*
*Abbreviations: COVID-19=coronavirus disease 2019; CSP=Clinical Study Protocol; FAP=Full Analysis Population; n=number of patients with the characteristic of interest; PK=pharmacokinetic; sqNSCLC=squamous non-small cell lung cancer.*

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## BASELINE CHARACTERISTICS (FULL ANALYSIS POPULATION)

| | Overall No. of Patients (N=69) | Dose Escalation Patients - Twice Weekly Dosing (N=15) | Dose Escalation Patients - Once Weekly Dosing (N=24) | Expansion Patients sqNSCLC Cohort (N=11) | Expansion Patients Basket Cohort (N=19) |
|---|---|---|---|---|---|
| **Patients** | | | | | |
| Female | 36 | 7 | 12 | 1 | 16 |
| Male | 33 | 8 | 12 | 10 | 3 |
| **Age (Years)** | | | | | |
| Mean | 56.7 | 53.4 | 57.1 | 59.6 | 57.3 |
| Median | 59 | 56 | 59.5 | 59 | 59 |
| Min | 22 | 27 | 22 | 35 | 38 |
| Max | 78 | 72 | 77 | 78 | 69 |
| **Weight (kg)** | | | | | |
| Mean | 74.9 | 71.5 | 76.3 | 78.3 | 73.9 |
| Median | 74.2 | 69.4 | 76.5 | 76.4 | 74.2 |
| Min | 45 | 45.1 | 45 | 53.4 | 50.1 |
| Max | 126.9 | 122.4 | 120.7 | 126.9 | 104.5 |
| **Height (cm)** | | | | | |
| Mean | 167.6 | 168.7 | 167.3 | 172.6 | 164.1 |
| Median | 165 | 174 | 165 | 174 | 162 |
| Min | 155 | 157 | 155 | 160 | 155 |
| Max | 197 | 178 | 197 | 189 | 184 |
| **WHO Performance Status** | | | | | |
| 0 | 16 | 3 | 6 | 2 | 5 |
| 1 | 53 | 12 | 18 | 9 | 14 |

*Abbreviations: min=minimum; max=maximum; N=number of patients; No.=number; sqNSCLC=squamous non-small cell lung cancer; WHO=World Health Organization.*

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## OUTCOME MEASURES

## PRIMARY OUTCOME MEASURES

### Maximum Tolerated Dose, Maximum Administered Dose and Recommended Phase II Dose (Dose Escalation Phase, Safety Population)

| | Twice Weekly Dosing (N=15) | Once Weekly Dosing (N=24) |
|---|---|---|
| MTD of BT1718 | 7.2 mg/m$^2$ | 20 mg/m$^2$ |
| MAD of BT1718 | 9.6 mg/m$^2$ | 32 mg/m$^2$ |
| RP2D | Not determined* | 20 mg/m$^{2\#}$ |

** Only once weekly dosing was recommended for further evaluation.*
*\# A modified dosing schedule of 15 mg/m$^2$ BT1718 once weekly for Cycle 1 with escalation to 20 mg/m$^2$ BT1718 once weekly from Cycle 2, if tolerated, was the RP2D from the Phase IIa, Expansion Phase of the trial.*
*Abbreviations: MAD=maximum administered dose; MTD=maximum tolerated dose; N=number of patients; RP2D=recommended Phase II dose.*

### Number of Patients who Experienced Dose Limiting Toxicities (Dose Escalation Phase, Safety Population)

| | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
|---|---|---|---|---|---|---|---|---|
| | Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4) | Cohort 5 (9.6 mg/m$^2$) (N=4) | Cohort 6 (7.2 mg/m$^2$) (N=7) | Cohort 1A (9.6 mg/m$^2$) (N=3) | Cohort 2A (15 mg/m$^2$) (N=3) | Cohort 3A (20 mg/m$^2$) (N=7) | Cohort 4A (25 mg/m$^2$) (N=6) | Cohort 5A (32 mg/m$^2$) (N=5) |
| No. of patients evaluable for DLTs | 3* | 3 | 6 | 3 | 3 | 6 | 6$^{\#}$ | 4 |
| No. of patients with DLT | 0 | 2 | 0 | 0 | 0 | 0 | 2 | 2 |
| No. of DLTs | 0 | 2 | 0 | 0 | 0 | 0 | 2 | 2 |

** One patient in Cohort 2 (1.2 mg/m$^2$ BT1718 twice weekly) was not included in DLT assessment population but was agreed to be evaluable for dose review decisions as received 5/6 doses of BT1718 during Cycle 1 (Cycle 1, Day 18 dose omitted due to public holiday).*
*\#There were two DLTs in Cohort 5A and this dose was declared non-tolerated, prompting expansion of Cohort 4A to an additional three patients. Although no DLTs had been observed in Cohort 4A during the initial dose escalation, two DLTs were observed in the three patients recruited to expand this cohort.*
*Abbreviations: DLT=dose limiting toxicity; N=number of patients; No.=number.*

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## ADVERSE EVENTS SUMMARIES: DOSE ESCALATION PHASE

### Frequency of Treatment Emergent Adverse Events Occurring in ≥5% Patients Overall, by Cohort (Dose Escalation Phase, Safety Population)

| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
| SYSTEM ORGAN CLASS<br>Preferred Term | All Dose Escalation (N=39) | Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4) | Cohort 5 (9.6 mg/m$^2$) (N=4) | Cohort 6 (7.2 mg/m$^2$) (N=7) | Cohort 1A (9.6 mg/m$^2$) (N=3) | Cohort 2A (15 mg/m$^2$) (N=3) | Cohort 3A (20 mg/m$^2$) (N=7) | Cohort 4A (25 mg/m$^2$) (N=6) | Cohort 5A (32 mg/m$^2$) (N=5) |
| **OVERALL TOTAL** | **38 (97.4) /546** | **3 (75.0) /17** | **4 (100) /61** | **7 (100) /73** | **3 (100) /33** | **3 (100) /86** | **7 (100) /114** | **6 (100) /75** | **5 (100) /87** |
| **BLOOD AND LYMPHATIC SYSTEM DISORDERS** | **16 (41.0) /21** | **1 (25.0) /1** | **2 (50.0) /2** | **1 (14.3) /1** | | **2 (66.7) /3** | **4 (57.1) /7** | **2 (33.3) /3** | **4 (80.0) /4** |
| Anaemia | 13 (33.3) /15 | 1 (25.0) /1 | 1 (25.0) /1 | 1 (14.3) /1 | | 2 (66.7) /2 | 3 (42.9) /4 | 2 (33.3) /3 | 3 (60.0) /3 |
| Lymphopenia | 2 (5.1) /2 | | | | | | 2 (28.6) /2 | | |
| Neutropenia | 2 (5.1) /2 | | 1 (25.0) /1 | | | | 1 (14.3) /1 | | |
| **GASTROINTESTINAL DISORDERS** | **37 (94.9) /168** | **3 (75.0) /5** | **4 (100) /18** | **6 (85.7) /21** | **3 (100) /19** | **3 (100) /23** | **7 (100) /29** | **6 (100) /22** | **5 (100) /31** |
| Abdominal discomfort | 2 (5.1) /2 | | | | 1 (33.3) /1 | | | | 1 (20.0) /1 |
| Abdominal distension | 3 (7.7) /3 | | 1 (25.0) /1 | 2 (28.6) /2 | | | | | |
| Abdominal pain | 9 (23.1) /14 | | 3 (75.0) /3 | | 1 (33.3) /4 | 2 (66.7) /3 | 1 (14.3) /2 | | 2 (40.0) /2 |
| Abdominal pain lower | 2 (5.1) /2 | | 1 (25.0) /1 | | | | | | 1 (20.0) /1 |
| Abdominal pain upper | 3 (7.7) /3 | | | 1 (14.3) /1 | | 1 (33.3) /1 | | | 1 (20.0) /1 |
| Anal incontinence | 2 (5.1) /2 | | | 1 (14.3) /1 | | | | 1 (16.7) /1 | |
| Constipation | 8 (20.5) /8 | | 1 (25.0) /1 | 2 (28.6) /2 | | | 1 (14.3) /1 | 2 (33.3) /2 | 2 (40.0) /2 |
| Diarrhoea | 19 (48.7) /40 | 1 (25.0) /1 | 1 (25.0) /2 | 1 (14.3) /2 | 2 (66.7) /8 | 2 (66.7) /4 | 4 (57.1) /7 | 4 (66.7) /5 | 4 (80.0) /11 |
| Dry mouth | 3 (7.7) /3 | | | 1 (14.3) /1 | | 1 (33.3) /1 | | | 1 (20.0) /1 |
| Dyspepsia | 2 (5.1) /2 | | 1 (25.0) /1 | 1 (14.3) /1 | | | | | |

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| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
| **SYSTEM ORGAN CLASS Preferred Term** | **All Dose Escalation (N=39)** | **Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4)** | **Cohort 5 (9.6 mg/m$^2$) (N=4)** | **Cohort 6 (7.2 mg/m$^2$) (N=7)** | **Cohort 1A (9.6 mg/m$^2$) (N=3)** | **Cohort 2A (15 mg/m$^2$) (N=3)** | **Cohort 3A (20 mg/m$^2$) (N=7)** | **Cohort 4A (25 mg/m$^2$) (N=6)** | **Cohort 5A (32 mg/m$^2$) (N=5)** |
| Gastrooesophageal reflux disease | 4 (10.3) /4 | 1 (25.0) /1 | | 1 (14.3) /1 | 1 (33.3) /1 | | 1 (14.3) /1 | | |
| Haematemesis | 2 (5.1) /2 | | 1 (25.0) /1 | 1 (14.3) /1 | | | | | |
| Nausea | 25 (64.1) /34 | 1 (25.0) /1 | 3 (75.0) /3 | 2 (28.6) /2 | 1 (33.3) /1 | 2 (66.7) /6 | 7 (100) /9 | 5 (83.3) /5 | 4 (80.0) /7 |
| Vomiting | 22 (56.4) /41 | | 2 (50.0) /4 | 2 (28.6) /6 | 1 (33.3) /4 | 3 (100) /7 | 6 (85.7) /8 | 5 (83.3) /8 | 3 (60.0) /4 |
| **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS** | **27 (69.2) /48** | **1 (25.0) /1** | **3 (75.0) /6** | **3 (42.9) /3** | **2 (66.7) /4** | **2 (66.7) /5** | **5 (71.4) /11** | **6 (100) /8** | **5 (100) /10** |
| Chest pain | 3 (7.7) /3 | | | | | 1 (33.3) /1 | | 1 (16.7) /1 | 1 (20.0) /1 |
| Fatigue | 21 (53.8) /32 | | 3 (75.0) /4 | 2 (28.6) /2 | 2 (66.7) /4 | 2 (66.7) /2 | 4 (57.1) /9 | 3 (50.0) /3 | 5 (100) /8 |
| Influenza like illness | 2 (5.1) /2 | | 1 (25.0) /1 | | | | 1 (14.3) /1 | | |
| Oedema peripheral | 2 (5.1) /2 | | | | | | | 2 (33.3) /2 | |
| Pyrexia | 7 (17.9) /7 | | 1 (25.0) /1 | 1 (14.3) /1 | | 1 (33.3) /1 | 1 (14.3) /1 | 2 (33.3) /2 | 1 (20.0) /1 |
| **INFECTIONS AND INFESTATIONS** | **16 (41.0) /24** | **1 (25.0) /1** | **1 (25.0) /1** | **3 (42.9) /3** | **2 (66.7) /2** | **2 (66.7) /5** | **4 (57.1) /8** | **1 (16.7) /1** | **2 (40.0) /3** |
| Influenza | 2 (5.1) /2 | | | 1 (14.3) /1 | | 1 (33.3) /1 | | | |
| Lower respiratory tract infection | 4 (10.3) /4 | | | | | 2 (66.7) /2 | 1 (14.3) /1 | | 1 (20.0) /1 |
| Upper respiratory tract infection | 2 (5.1) /2 | | | | 1 (33.3) /1 | | 1 (14.3) /1 | | |
| Urinary tract infection | 4 (10.3) /4 | 1 (25.0) /1 | 1 (25.0) /1 | 1 (14.3) /1 | | | 1 (14.3) /1 | | |
| **INVESTIGATIONS** | **25 (64.1) /77** | **2 (50.0) /3** | **4 (100) /15** | **4 (57.1) /11** | **1 (33.3) /1** | **3 (100) /14** | **5 (71.4) /13** | **3 (50.0) /12** | **3 (60.0) /8** |

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| **SYSTEM ORGAN CLASS Preferred Term** | **All Dose Escalation (N=39)** | **Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4)** | **Cohort 5 (9.6 mg/m$^2$) (N=4)** | **Cohort 6 (7.2 mg/m$^2$) (N=7)** | **Cohort 1A (9.6 mg/m$^2$) (N=3)** | **Cohort 2A (15 mg/m$^2$) (N=3)** | **Cohort 3A (20 mg/m$^2$) (N=7)** | **Cohort 4A (25 mg/m$^2$) (N=6)** | **Cohort 5A (32 mg/m$^2$) (N=5)** |
| Alanine aminotransferase increased | 15 (38.5) /20 | 1 (25.0) /1 | 3 (75.0) /4 | 3 (42.9) /3 | | 1 (33.3) /4 | 2 (28.6) /2 | 3 (50.0) /3 | 2 (40.0) /3 |
| Aspartate aminotransferase increased | 14 (35.9) /21 | 1 (25.0) /1 | 3 (75.0) /5 | 2 (28.6) /2 | | 2 (66.7) /4 | 2 (28.6) /3 | 2 (33.3) /4 | 2 (40.0) /2 |
| Blood alkaline phosphatase increased | 9 (23.1) /10 | | 3 (75.0) /3 | 1 (14.3) /1 | 1 (33.3) /1 | | 2 (28.6) /2 | 2 (33.3) /3 | |
| Blood bilirubin increased | 5 (12.8) /6 | | 1 (25.0) /1 | 1 (14.3) /2 | | 1 (33.3) /1 | | | 2 (40.0) /2 |
| Blood creatinine increased | 2 (5.1) /2 | 1 (25.0) /1 | | | | 1 (33.3) /1 | | | |
| Gamma-glutamyltransferase increased | 7 (17.9) /8 | | 1 (25.0) /1 | 2 (28.6) /2 | | 1 (33.3) /2 | 2 (28.6) /2 | 1 (16.7) /1 | |
| Weight decreased | 8 (20.5) /10 | | 1 (25.0) /1 | 1 (14.3) /1 | | 1 (33.3) /2 | 3 (42.9) /4 | 1 (16.7) /1 | 1 (20.0) /1 |
| **METABOLISM AND NUTRITION DISORDERS** | **25 (64.1) /43** | **1 (25.0) /1** | **2 (50.0) /4** | **5 (71.4) /8** | **1 (33.3) /3** | **3 (100) /8** | **5 (71.4) /9** | **4 (66.7) /5** | **4 (80.0) /5** |
| Decreased appetite | 20 (51.3) /27 | | 1 (25.0) /1 | 3 (42.9) /3 | 1 (33.3) /1 | 3 (100) /5 | 5 (71.4) /9 | 4 (66.7) /5 | 3 (60.0) /3 |
| Hypokalaemia | 4 (10.3) /6 | | 1 (25.0) /2 | 1 (14.3) /1 | 1 (33.3) /2 | | | | 1 (20.0) /1 |
| **MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS** | **18 (46.2) /26** | **2 (50.0) /2** | **3 (75.0) /4** | **3 (42.9) /4** | **1 (33.3) /1** | **1 (33.3) /6** | **4 (57.1) /4** | **1 (16.7) /2** | **3 (60.0) /3** |
| Arthralgia | 9 (23.1) /11 | 1 (25.0) /1 | 2 (50.0) /2 | | 1 (33.3) /1 | 1 (33.3) /3 | 2 (28.6) /2 | 1 (16.7) /1 | 1 (20.0) /1 |
| Muscular weakness | 2 (5.1) /2 | | | 1 (14.3) /1 | | | | | 1 (20.0) /1 |
| Myalgia | 6 (15.4) /8 | | 2 (50.0) /2 | | | 1 (33.3) /3 | 1 (14.3) /1 | 1 (16.7) /1 | 1 (20.0) /1 |
| **NERVOUS SYSTEM DISORDERS** | **25 (64.1) /62** | **1 (25.0) /1** | **3 (75.0) /5** | **3 (42.9) /11** | | **3 (100) /10** | **6 (85.7) /14** | **5 (83.3) /12** | **4 (80.0) /9** |

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| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
| **SYSTEM ORGAN CLASS Preferred Term** | **All Dose Escalation (N=39)** | **Cohort 1-4 (0.6-4.8 mg/m²) (N=4)** | **Cohort 5 (9.6 mg/m²) (N=4)** | **Cohort 6 (7.2 mg/m²) (N=7)** | **Cohort 1A (9.6 mg/m²) (N=3)** | **Cohort 2A (15 mg/m²) (N=3)** | **Cohort 3A (20 mg/m²) (N=7)** | **Cohort 4A (25 mg/m²) (N=6)** | **Cohort 5A (32 mg/m²) (N=5)** |
| Dizziness | 3 (7.7) /3 | | 1 (25.0) /1 | | | | 1 (14.3) /1 | 1 (16.7) /1 | |
| Dysgeusia | 2 (5.1) /2 | | | | | | 1 (14.3) /1 | | 1 (20.0) /1 |
| Headache | 4 (10.3) /4 | | 1 (25.0) /1 | | | 1 (33.3) /1 | 1 (14.3) /1 | 1 (16.7) /1 | |
| Lethargy | 7 (17.9) /14 | | 1 (25.0) /1 | 2 (28.6) /5 | | 1 (33.3) /4 | 1 (14.3) /2 | 2 (33.3) /2 | |
| Neuropathy peripheral | 17 (43.6) /19 | | 1 (25.0) /1 | 2 (28.6) /2 | | 3 (100) /4 | 3 (42.9) /3 | 4 (66.7) /4 | 4 (80.0) /5 |
| Paraesthesia | 5 (12.8) /5 | | 1 (25.0) /1 | 1 (14.3) /1 | | | 1 (14.3) /1 | 1 (16.7) /1 | 1 (20.0) /1 |
| Peripheral sensory neuropathy | 4 (10.3) /5 | | | | | | 2 (28.6) /3 | 1 (16.7) /1 | 1 (20.0) /1 |
| **PSYCHIATRIC DISORDERS** | **7 (17.9) /11** | | **1 (25.0) /1** | **1 (14.3) /1** | | | **2 (28.6) /5** | **1 (16.7) /1** | **2 (40.0) /3** |
| Depressed mood | 2 (5.1) /2 | | 1 (25.0) /1 | 1 (14.3) /1 | | | | | |
| Insomnia | 3 (7.7) /3 | | | | | | | 1 (16.7) /1 | 2 (40.0) /2 |
| **RENAL AND URINARY DISORDERS** | **4 (10.3) /7** | | | | | **1 (33.3) /3** | **2 (28.6) /3** | **1 (16.7) /1** | |
| Proteinuria | 4 (10.3) /5 | | | | | 1 (33.3) /2 | 2 (28.6) /2 | 1 (16.7) /1 | |
| **RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS** | **15 (38.5) /26** | | **2 (50.0) /4** | **1 (14.3) /1** | **2 (66.7) /2** | **2 (66.7) /6** | **3 (42.9) /7** | **2 (33.3) /2** | **3 (60.0) /4** |
| Cough | 5 (12.8) /6 | | 1 (25.0) /2 | | 1 (33.3) /1 | 1 (33.3) /1 | | 2 (33.3) /2 | |
| Dysphonia | 2 (5.1) /2 | | | | | | 1 (14.3) /1 | | 1 (20.0) /1 |
| Dyspnoea | 5 (12.8) /5 | | | | 1 (33.3) /1 | 1 (33.3) /1 | 3 (42.9) /3 | | |
| Oropharyngeal pain | 3 (7.7) /3 | | 1 (25.0) /1 | | | | | | 2 (40.0) /2 |
| Pneumothorax | 2 (5.1) /3 | | | | | | 1 (14.3) /2 | | 1 (20.0) /1 |
| Pulmonary embolism | 2 (5.1) /2 | | | 1 (14.3) /1 | | | 1 (14.3) /1 | | |

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|---|---|---|---|---|---|---|---|---|---|
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| **SYSTEM ORGAN CLASS<br>Preferred Term** | **All Dose Escalation (N=39)** | **Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4)** | **Cohort 5 (9.6 mg/m$^2$) (N=4)** | **Cohort 6 (7.2 mg/m$^2$) (N=7)** | **Cohort 1A (9.6 mg/m$^2$) (N=3)** | **Cohort 2A (15 mg/m$^2$) (N=3)** | **Cohort 3A (20 mg/m$^2$) (N=7)** | **Cohort 4A (25 mg/m$^2$) (N=6)** | **Cohort 5A (32 mg/m$^2$) (N=5)** |
| **SKIN AND SUBCUTANEOUS TISSUE DISORDERS** | **9 (23.1) /11** | | | **2 (28.6) /3** | | **2 (66.7) /2** | **2 (28.6) /2** | **1 (16.7) /1** | **2 (40.0) /3** |
| Pruritus | 4 (10.3) /4 | | | 1 (14.3) /1 | | 1 (33.3) /1 | 1 (14.3) /1 | | 1 (20.0) /1 |
| **VASCULAR DISORDERS** | **2 (5.1) /5** | **1 (25.0) /1** | | | | | | **1 (16.7) /4** | |
| Hypotension | 2 (5.1) /4 | 1 (25.0) /1 | | | | | | 1 (16.7) /3 | |

*Abbreviations: INCL=including; N=number of patients; No.=number.*

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**Frequency of Treatment Emergent Serious Adverse Events Occurring in ≥5% Patients Overall, by Cohort (Dose Escalation Phase, Safety Population)**

| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
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| SYSTEM ORGAN CLASS<br>Preferred Term | All Dose Escalation (N=39) | Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4) | Cohort 5 (9.6 mg/m$^2$) (N=4) | Cohort 6 (7.2 mg/m$^2$) (N=7) | Cohort 1A (9.6 mg/m$^2$) (N=3) | Cohort 2A (15 mg/m$^2$) (N=3) | Cohort 3A (20 mg/m$^2$) (N=7) | Cohort 4A (25 mg/m$^2$) (N=6) | Cohort 5A (32 mg/m$^2$) (N=5) |
| **OVERALL TOTAL** | **18 (46.2) /43** | **2 (50.0) /3** | **3 (75.0) /6** | **3 (42.9) /5** | | **2 (66.7) /7** | **2 (28.6) /4** | **1 (16.7) /1** | **5 (100) /17** |
| **GASTROINTESTINAL DISORDERS** | **7 (17.9) /11** | **1 (25.0) /1** | **1 (25.0) /2** | **1 (14.3) /1** | | **2 (66.7) /2** | | | **2 (40.0) /5** |
| Abdominal pain | 2 (5.1) /2 | | 1 (25.0) /1 | | | | | | 1 (20.0) /1 |
| Vomiting | 4 (10.3) /4 | | 1 (25.0) /1 | | | 2 (66.7) /2 | | | 1 (20.0) /1 |
| **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS** | **6 (15.4) /6** | **1 (25.0) /1** | | | | **1 (33.3) /1** | **1 (14.3) /1** | **1 (16.7) /1** | **2 (40.0) /2** |
| Fatigue | 2 (5.1) /2 | | | | | | | | 2 (40.0) /2 |
| Pyrexia | 3 (7.7) /3 | | | | | 1 (33.3) /1 | 1 (14.3) /1 | 1 (16.7) /1 | |
| **INVESTIGATIONS** | **2 (5.1) /6** | | **1 (25.0) /3** | | | | | | **1 (20.0) /3** |
| Alanine aminotransferase increased | 2 (5.1) /2 | | 1 (25.0) /1 | | | | | | 1 (20.0) /1 |
| Aspartate aminotransferase increased | 2 (5.1) /2 | | 1 (25.0) /1 | | | | | | 1 (20.0) /1 |
| **RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS** | **4 (10.3) /6** | | | | | **1 (33.3) /1** | **1 (14.3) /3** | | **2 (40.0) /2** |
| Dyspnoea | 2 (5.1) /2 | | | | | 1 (33.3) /1 | 1 (14.3) /1 | | |
| Pneumothorax | 2 (5.1) /3 | | | | | | 1 (14.3) /2 | | 1 (20.0) /1 |

*Abbreviations: INCL=including; N=number of patients; No.=number.*

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**Frequency of Treatment Emergent Non Serious Adverse Events Occurring in ≥5% Patients Overall, by Cohort (Dose Escalation Phase, Safety Population)**

| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
| SYSTEM ORGAN CLASS<br>Preferred Term | All Dose Escalation (N=39) | Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4) | Cohort 5 (9.6 mg/m$^2$) (N=4) | Cohort 6 (7.2 mg/m$^2$) (N=7) | Cohort 1A (9.6 mg/m$^2$) (N=3) | Cohort 2A (15 mg/m$^2$) (N=3) | Cohort 3A (20 mg/m$^2$) (N=7) | Cohort 4A (25 mg/m$^2$) (N=6) | Cohort 5A (32 mg/m$^2$) (N=5) |
| **OVERALL TOTAL** | **38 (97.4) /503** | **3 (75.0) /14** | **4 (100) /55** | **7 (100) /68** | **3 (100) /33** | **3 (100) /79** | **7 (100) /110** | **6 (100) /74** | **5 (100) /70** |
| **BLOOD AND LYMPHATIC SYSTEM DISORDERS** | **16 (41.0) /21** | **1 (25.0) /1** | **2 (50.0) /2** | **1 (14.3) /1** | | **2 (66.7) /3** | **4 (57.1) /7** | **2 (33.3) /3** | **4 (80.0) /4** |
| Anaemia | 13 (33.3) /15 | 1 (25.0) /1 | 1 (25.0) /1 | 1 (14.3) /1 | | 2 (66.7) /2 | 3 (42.9) /4 | 2 (33.3) /3 | 3 (60.0) /3 |
| Lymphopenia | 2 (5.1) /2 | | | | | | 2 (28.6) /2 | | |
| Neutropenia | 2 (5.1) /2 | | 1 (25.0) /1 | | | | 1 (14.3) /1 | | |
| **GASTROINTESTINAL DISORDERS** | **37 (94.9) /157** | **3 (75.0) /4** | **4 (100) /16** | **6 (85.7) /20** | **3 (100) /19** | **3 (100) /21** | **7 (100) /29** | **6 (100) /22** | **5 (100) /26** |
| Abdominal discomfort | 2 (5.1) /2 | | | | 1 (33.3) /1 | | | | 1 (20.0) /1 |
| Abdominal distension | 3 (7.7) /3 | | 1 (25.0) /1 | 2 (28.6) /2 | | | | | |
| Abdominal pain | 7 (17.9) /12 | | 2 (50.0) /2 | | 1 (33.3) /4 | 2 (66.7) /3 | 1 (14.3) /2 | | 1 (20.0) /1 |
| Abdominal pain lower | 2 (5.1) /2 | | 1 (25.0) /1 | | | | | | 1 (20.0) /1 |
| Abdominal pain upper | 3 (7.7) /3 | | | 1 (14.3) /1 | | 1 (33.3) /1 | | | 1 (20.0) /1 |
| Constipation | 8 (20.5) /8 | | 1 (25.0) /1 | 2 (28.6) /2 | | | 1 (14.3) /1 | 2 (33.3) /2 | 2 (40.0) /2 |
| Diarrhoea | 18 (46.2) /39 | 1 (25.0) /1 | 1 (25.0) /2 | 1 (14.3) /2 | 2 (66.7) /8 | 2 (66.7) /4 | 4 (57.1) /7 | 4 (66.7) /5 | 3 (60.0) /10 |
| Dry mouth | 3 (7.7) /3 | | | 1 (14.3) /1 | | 1 (33.3) /1 | | | 1 (20.0) /1 |
| Dyspepsia | 2 (5.1) /2 | | 1 (25.0) /1 | 1 (14.3) /1 | | | | | |

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| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
| SYSTEM ORGAN CLASS Preferred Term | All Dose Escalation (N=39) | Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4) | Cohort 5 (9.6 mg/m$^2$) (N=4) | Cohort 6 (7.2 mg/m$^2$) (N=7) | Cohort 1A (9.6 mg/m$^2$) (N=3) | Cohort 2A (15 mg/m$^2$) (N=3) | Cohort 3A (20 mg/m$^2$) (N=7) | Cohort 4A (25 mg/m$^2$) (N=6) | Cohort 5A (32 mg/m$^2$) (N=5) |
| Gastrooesophageal reflux disease | 4 (10.3) /4 | 1 (25.0) /1 | | 1 (14.3) /1 | 1 (33.3) /1 | | 1 (14.3) /1 | | |
| Haematemesis | 2 (5.1) /2 | | 1 (25.0) /1 | 1 (14.3) /1 | | | | | |
| Nausea | 25 (64.1) /33 | 1 (25.0) /1 | 3 (75.0) /3 | 2 (28.6) /2 | 1 (33.3) /1 | 2 (66.7) /6 | 7 (100) /9 | 5 (83.3) /5 | 4 (80.0) /6 |
| Vomiting | 21 (53.8) /37 | | 2 (50.0) /3 | 2 (28.6) /6 | 1 (33.3) /4 | 3 (100) /5 | 6 (85.7) /8 | 5 (83.3) /8 | 2 (40.0) /3 |
| **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS** | **25 (64.1) /42** | | **3 (75.0) /6** | **3 (42.9) /3** | **2 (66.7) /4** | **2 (66.7) /4** | **4 (57.1) /10** | **6 (100) /7** | **5 (100) /8** |
| Chest pain | 3 (7.7) /3 | | | | | 1 (33.3) /1 | | 1 (16.7) /1 | 1 (20.0) /1 |
| Fatigue | 20 (51.3) /30 | | 3 (75.0) /4 | 2 (28.6) /2 | 2 (66.7) /4 | 2 (66.7) /2 | 4 (57.1) /9 | 3 (50.0) /3 | 4 (80.0) /6 |
| Influenza like illness | 2 (5.1) /2 | | 1 (25.0) /1 | | | | 1 (14.3) /1 | | |
| Oedema peripheral | 2 (5.1) /2 | | | | | | | 2 (33.3) /2 | |
| Pyrexia | 4 (10.3) /4 | | 1 (25.0) /1 | 1 (14.3) /1 | | | | 1 (16.7) /1 | 1 (20.0) /1 |
| **INFECTIONS AND INFESTATIONS** | **14 (35.9) /21** | **1 (25.0) /1** | **1 (25.0) /1** | **2 (28.6) /2** | **2 (66.7) /2** | **2 (66.7) /4** | **4 (57.1) /8** | **1 (16.7) /1** | **1 (20.0) /2** |
| Lower respiratory tract infection | 3 (7.7) /3 | | | | | 2 (66.7) /2 | 1 (14.3) /1 | | |
| Upper respiratory tract infection | 2 (5.1) /2 | | | | 1 (33.3) /1 | | 1 (14.3) /1 | | |
| Urinary tract infection | 4 (10.3) /4 | 1 (25.0) /1 | 1 (25.0) /1 | 1 (14.3) /1 | | | 1 (14.3) /1 | | |
| **INVESTIGATIONS** | **24 (61.5) /71** | **2 (50.0) /3** | **4 (100) /12** | **4 (57.1) /11** | **1 (33.3) /1** | **3 (100) /14** | **5 (71.4) /13** | **3 (50.0) /12** | **2 (40.0) /5** |

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| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
| SYSTEM ORGAN CLASS<br>Preferred Term | All Dose Escalation (N=39) | Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4) | Cohort 5 (9.6 mg/m$^2$) (N=4) | Cohort 6 (7.2 mg/m$^2$) (N=7) | Cohort 1A (9.6 mg/m$^2$) (N=3) | Cohort 2A (15 mg/m$^2$) (N=3) | Cohort 3A (20 mg/m$^2$) (N=7) | Cohort 4A (25 mg/m$^2$) (N=6) | Cohort 5A (32 mg/m$^2$) (N=5) |
| Alanine aminotransferase increased | 14 (35.9) /18 | 1 (25.0) /1 | 3 (75.0) /3 | 3 (42.9) /3 | | 1 (33.3) /4 | 2 (28.6) /2 | 3 (50.0) /3 | 1 (20.0) /2 |
| Aspartate aminotransferase increased | 13 (33.3) /19 | 1 (25.0) /1 | 3 (75.0) /4 | 2 (28.6) /2 | | 2 (66.7) /4 | 2 (28.6) /3 | 2 (33.3) /4 | 1 (20.0) /1 |
| Blood alkaline phosphatase increased | 9 (23.1) /10 | | 3 (75.0) /3 | 1 (14.3) /1 | 1 (33.3) /1 | | 2 (28.6) /2 | 2 (33.3) /3 | |
| Blood bilirubin increased | 4 (10.3) /5 | | 1 (25.0) /1 | 1 (14.3) /2 | | 1 (33.3) /1 | | | 1 (20.0) /1 |
| Blood creatinine increased | 2 (5.1) /2 | 1 (25.0) /1 | | | | 1 (33.3) /1 | | | |
| Gamma-glutamyltransferase increased | 6 (15.4) /7 | | | 2 (28.6) /2 | | 1 (33.3) /2 | 2 (28.6) /2 | 1 (16.7) /1 | |
| Weight decreased | 8 (20.5) /10 | | 1 (25.0) /1 | 1 (14.3) /1 | | 1 (33.3) /2 | 3 (42.9) /4 | 1 (16.7) /1 | 1 (20.0) /1 |
| **METABOLISM AND NUTRITION DISORDERS** | **25 (64.1) /42** | **1 (25.0) /1** | **2 (50.0) /4** | **5 (71.4) /8** | **1 (33.3) /3** | **3 (100) /7** | **5 (71.4) /9** | **4 (66.7) /5** | **4 (80.0) /5** |
| Decreased appetite | 20 (51.3) /27 | | 1 (25.0) /1 | 3 (42.9) /3 | 1 (33.3) /1 | 3 (100) /5 | 5 (71.4) /9 | 4 (66.7) /5 | 3 (60.0) /3 |
| Hypokalaemia | 4 (10.3) /6 | | 1 (25.0) /2 | 1 (14.3) /1 | 1 (33.3) /2 | | | | 1 (20.0) /1 |
| **MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS** | **15 (38.5) /23** | **2 (50.0) /2** | **3 (75.0) /4** | **3 (42.9) /4** | **1 (33.3) /1** | **1 (33.3) /6** | **4 (57.1) /4** | **1 (16.7) /2** | |
| Arthralgia | 8 (20.5) /10 | 1 (25.0) /1 | 2 (50.0) /2 | | 1 (33.3) /1 | 1 (33.3) /3 | 2 (28.6) /2 | 1 (16.7) /1 | |
| Myalgia | 5 (12.8) /7 | | 2 (50.0) /2 | | | 1 (33.3) /3 | 1 (14.3) /1 | 1 (16.7) /1 | |
| **NERVOUS SYSTEM DISORDERS** | **25 (64.1) /60** | **1 (25.0) /1** | **3 (75.0) /5** | **3 (42.9) /9** | | **3 (100) /10** | **6 (85.7) /14** | **5 (83.3) /12** | **4 (80.0) /9** |
| Dizziness | 3 (7.7) /3 | | 1 (25.0) /1 | | | | 1 (14.3) /1 | 1 (16.7) /1 | |

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| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
| SYSTEM ORGAN CLASS<br>Preferred Term | All Dose Escalation (N=39) | Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4) | Cohort 5 (9.6 mg/m$^2$) (N=4) | Cohort 6 (7.2 mg/m$^2$) (N=7) | Cohort 1A (9.6 mg/m$^2$) (N=3) | Cohort 2A (15 mg/m$^2$) (N=3) | Cohort 3A (20 mg/m$^2$) (N=7) | Cohort 4A (25 mg/m$^2$) (N=6) | Cohort 5A (32 mg/m$^2$) (N=5) |
| Dysgeusia | 2 (5.1) /2 | | | | | | 1 (14.3) /1 | | 1 (20.0) /1 |
| Headache | 4 (10.3) /4 | | 1 (25.0) /1 | | | 1 (33.3) /1 | 1 (14.3) /1 | 1 (16.7) /1 | |
| Lethargy | 7 (17.9) /14 | | 1 (25.0) /1 | 2 (28.6) /5 | | 1 (33.3) /4 | 1 (14.3) /2 | 2 (33.3) /2 | |
| Neuropathy peripheral | 17 (43.6) /19 | | 1 (25.0) /1 | 2 (28.6) /2 | | 3 (100) /4 | 3 (42.9) /3 | 4 (66.7) /4 | 4 (80.0) /5 |
| Paraesthesia | 5 (12.8) /5 | | 1 (25.0) /1 | 1 (14.3) /1 | | | 1 (14.3) /1 | 1 (16.7) /1 | 1 (20.0) /1 |
| Peripheral sensory neuropathy | 4 (10.3) /5 | | | | | | 2 (28.6) /3 | 1 (16.7) /1 | 1 (20.0) /1 |
| **PSYCHIATRIC DISORDERS** | **7 (17.9) /11** | | **1 (25.0) /1** | **1 (14.3) /1** | | | **2 (28.6) /5** | **1 (16.7) /1** | **2 (40.0) /3** |
| Depressed mood | 2 (5.1) /2 | | 1 (25.0) /1 | 1 (14.3) /1 | | | | | |
| Insomnia | 3 (7.7) /3 | | | | | | | 1 (16.7) /1 | 2 (40.0) /2 |
| **RENAL AND URINARY DISORDERS** | **4 (10.3) /6** | | | | | **1 (33.3) /2** | **2 (28.6) /3** | **1 (16.7) /1** | |
| Proteinuria | 4 (10.3) /5 | | | | | 1 (33.3) /2 | 2 (28.6) /2 | 1 (16.7) /1 | |
| **RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS** | **12 (30.8) /20** | | **2 (50.0) /4** | **1 (14.3) /1** | **2 (66.7) /2** | **2 (66.7) /5** | **2 (28.6) /4** | **2 (33.3) /2** | **1 (20.0) /2** |
| Cough | 5 (12.8) /6 | | 1 (25.0) /2 | | 1 (33.3) /1 | 1 (33.3) /1 | | 2 (33.3) /2 | |
| Dysphonia | 2 (5.1) /2 | | | | | | 1 (14.3) /1 | | 1 (20.0) /1 |
| Dyspnoea | 3 (7.7) /3 | | | | 1 (33.3) /1 | | 2 (28.6) /2 | | |
| Oropharyngeal pain | 2 (5.1) /2 | | 1 (25.0) /1 | | | | | | 1 (20.0) /1 |
| Pulmonary embolism | 2 (5.1) /2 | | | 1 (14.3) /1 | | | 1 (14.3) /1 | | |

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| | No. of Patients (%)/No. of Episodes | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Twice Weekly Dosing | | | Once Weekly Dosing | | | | |
| SYSTEM ORGAN CLASS<br>Preferred Term | All Dose Escalation (N=39) | Cohort 1-4 (0.6-4.8 mg/m$^2$) (N=4) | Cohort 5 (9.6 mg/m$^2$) (N=4) | Cohort 6 (7.2 mg/m$^2$) (N=7) | Cohort 1A (9.6 mg/m$^2$) (N=3) | Cohort 2A (15 mg/m$^2$) (N=3) | Cohort 3A (20 mg/m$^2$) (N=7) | Cohort 4A (25 mg/m$^2$) (N=6) | Cohort 5A (32 mg/m$^2$) (N=5) |
| **SKIN AND SUBCUTANEOUS TISSUE DISORDERS** | **9 (23.1) /10** | | | **2 (28.6) /3** | | **2 (66.7) /2** | **2 (28.6) /2** | **1 (16.7) /1** | **2 (40.0) /2** |
| Pruritus | 4 (10.3) /4 | | | 1 (14.3) /1 | | 1 (33.3) /1 | 1 (14.3) /1 | | 1 (20.0) /1 |
| **VASCULAR DISORDERS** | **2 (5.1) /5** | **1 (25.0) /1** | | | | | | **1 (16.7) /4** | |
| Hypotension | 2 (5.1) /4 | 1 (25.0) /1 | | | | | | 1 (16.7) /3 | |

*Abbreviations: N=number of patients; No.=number.*

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## ADVERSE EVENTS SUMMARIES: DOSE EXPANSION PHASE

### Frequency of Treatment Emergent Adverse Events Occurring in ≥5% Patients Overall, by Cohort (Expansion Phase, Safety Population)

| | No. of Patients (%)/No. of Episodes | | | | |
|---|---|---|---|---|---|
| **SYSTEM ORGAN CLASS<br>Preferred Term** | **All Expansion<br>(N=27)** | **sqNSCLC Cohort<br>(N=11)** | **Basket Cohort<br>(N=16)** | **15 mg/m$^2$ starting dose<br>(N=21)** | **20 mg/m$^2$ starting dose<br>(N=6)** |
| **OVERALL TOTAL** | **27 (100) /352** | **11 (100) /150** | **16 (100) /202** | **21 (100) /242** | **6 (100) /110** |
| **BLOOD AND LYMPHATIC SYSTEM DISORDERS** | **10 (37.0) /11** | **4 (36.4) /4** | **6 (37.5) /7** | **6 (28.6) /7** | **4 (66.7) /4** |
| Anaemia | 9 (33.3) /9 | 3 (27.3) /3 | 6 (37.5) /6 | 6 (28.6) /6 | 3 (50.0) /3 |
| **GASTROINTESTINAL DISORDERS** | **26 (96.3) /100** | **10 (90.9) /41** | **16 (100) /59** | **20 (95.2) /60** | **6 (100) /40** |
| Abdominal pain | 10 (37.0) /10 | 4 (36.4) /4 | 6 (37.5) /6 | 6 (28.6) /6 | 4 (66.7) /4 |
| Constipation | 13 (48.1) /16 | 6 (54.5) /6 | 7 (43.8) /10 | 10 (47.6) /13 | 3 (50.0) /3 |
| Diarrhoea | 11 (40.7) /20 | 4 (36.4) /8 | 7 (43.8) /12 | 6 (28.6) /8 | 5 (83.3) /12 |
| Dry mouth | 4 (14.8) /4 | 2 (18.2) /2 | 2 (12.5) /2 | 4 (19.0) /4 | |
| Dyspepsia | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| Gastrooesophageal reflux disease | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 2 (9.5) /2 | |
| Nausea | 14 (51.9) /23 | 6 (54.5) /9 | 8 (50.0) /14 | 10 (47.6) /16 | 4 (66.7) /7 |
| Vomiting | 9 (33.3) /16 | 3 (27.3) /7 | 6 (37.5) /9 | 3 (14.3) /5 | 6 (100) /11 |
| **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS** | **18 (66.7) /32** | **6 (54.5) /8** | **12 (75.0) /24** | **13 (61.9) /21** | **5 (83.3) /11** |
| Chest pain | 2 (7.4) /2 | | 2 (12.5) /2 | 1 (4.8) /1 | 1 (16.7) /1 |
| Fatigue | 16 (59.3) /20 | 6 (54.5) /6 | 10 (62.5) /14 | 11 (52.4) /14 | 5 (83.3) /6 |
| Mucosal inflammation | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| Non-cardiac chest pain | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| Pyrexia | 4 (14.8) /4 | | 4 (25.0) /4 | 3 (14.3) /3 | 1 (16.7) /1 |

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| | No. of Patients (%)/No. of Episodes | | | | |
|---|---|---|---|---|---|
| **SYSTEM ORGAN CLASS<br>Preferred Term** | **All Expansion<br>(N=27)** | **sqNSCLC Cohort<br>(N=11)** | **Basket Cohort<br>(N=16)** | **15 mg/m$^2$ starting dose<br>(N=21)** | **20 mg/m$^2$ starting dose<br>(N=6)** |
| **INFECTIONS AND INFESTATIONS** | **17 (63.0) /24** | **7 (63.6) /8** | **10 (62.5) /16** | **14 (66.7) /20** | **3 (50.0) /4** |
| COVID-19 | 2 (7.4) /2 | 2 (18.2) /2 | | 2 (9.5) /2 | |
| Lower respiratory tract infection | 4 (14.8) /4 | 2 (18.2) /2 | 2 (12.5) /2 | 4 (19.0) /4 | |
| Pneumonia | 2 (7.4) /3 | 1 (9.1) /1 | 1 (6.3) /2 | 1 (4.8) /2 | 1 (16.7) /1 |
| Urinary tract infection | 4 (14.8) /5 | 1 (9.1) /1 | 3 (18.8) /4 | 3 (14.3) /4 | 1 (16.7) /1 |
| **INVESTIGATIONS** | **15 (55.6) /58** | **6 (54.5) /21** | **9 (56.3) /37** | **12 (57.1) /38** | **3 (50.0) /20** |
| Alanine aminotransferase increased | 9 (33.3) /13 | 5 (45.5) /8 | 4 (25.0) /5 | 6 (28.6) /8 | 3 (50.0) /5 |
| Aspartate aminotransferase increased | 7 (25.9) /9 | 3 (27.3) /4 | 4 (25.0) /5 | 4 (19.0) /4 | 3 (50.0) /5 |
| Blood albumin decreased | 2 (7.4) /2 | | 2 (12.5) /2 | 2 (9.5) /2 | |
| Blood alkaline phosphatase increased | 6 (22.2) /8 | 3 (27.3) /5 | 3 (18.8) /3 | 6 (28.6) /8 | |
| Blood bilirubin increased | 2 (7.4) /4 | | 2 (12.5) /4 | 1 (4.8) /1 | 1 (16.7) /3 |
| Blood potassium decreased | 2 (7.4) /4 | | 2 (12.5) /4 | 1 (4.8) /1 | 1 (16.7) /3 |
| Gamma-glutamyltransferase increased | 4 (14.8) /4 | 1 (9.1) /1 | 3 (18.8) /3 | 4 (19.0) /4 | |
| Weight decreased | 4 (14.8) /4 | 1 (9.1) /1 | 3 (18.8) /3 | 3 (14.3) /3 | 1 (16.7) /1 |
| **METABOLISM AND NUTRITION DISORDERS** | **11 (40.7) /28** | **5 (45.5) /9** | **6 (37.5) /19** | **8 (38.1) /16** | **3 (50.0) /12** |
| Decreased appetite | 8 (29.6) /8 | 4 (36.4) /4 | 4 (25.0) /4 | 5 (23.8) /5 | 3 (50.0) /3 |
| Dehydration | 4 (14.8) /5 | 2 (18.2) /2 | 2 (12.5) /3 | 1 (4.8) /1 | 3 (50.0) /4 |
| Hypoalbuminaemia | 2 (7.4) /2 | | 2 (12.5) /2 | 1 (4.8) /1 | 1 (16.7) /1 |
| Hypokalaemia | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| Hypomagnesaemia | 3 (11.1) /5 | | 3 (18.8) /5 | 2 (9.5) /2 | 1 (16.7) /3 |
| Hyponatraemia | 3 (11.1) /4 | 1 (9.1) /2 | 2 (12.5) /2 | 3 (14.3) /4 | |

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| SYSTEM ORGAN CLASS<br>Preferred Term | No. of Patients (%)/No. of Episodes<br>All Expansion (N=27) | sqNSCLC Cohort (N=11) | Basket Cohort (N=16) | 15 mg/m$^2$ starting dose (N=21) | 20 mg/m$^2$ starting dose (N=6) |
|---|---|---|---|---|---|
| **MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS** | **15 (55.6) /20** | **8 (72.7) /13** | **7 (43.8) /7** | **12 (57.1) /17** | **3 (50.0) /3** |
| Arthralgia | 4 (14.8) /4 | 3 (27.3) /3 | 1 (6.3) /1 | 4 (19.0) /4 | |
| Back pain | 5 (18.5) /5 | 3 (27.3) /3 | 2 (12.5) /2 | 4 (19.0) /4 | 1 (16.7) /1 |
| Myalgia | 2 (7.4) /3 | 2 (18.2) /3 | | 2 (9.5) /3 | |
| Pain in extremity | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 2 (9.5) /2 | |
| **NERVOUS SYSTEM DISORDERS** | **21 (77.8) /32** | **9 (81.8) /19** | **12 (75.0) /13** | **17 (81.0) /28** | **4 (66.7) /4** |
| Dizziness | 2 (7.4) /2 | 2 (18.2) /2 | | 1 (4.8) /1 | 1 (16.7) /1 |
| Headache | 3 (11.1) /3 | 3 (27.3) /3 | | 3 (14.3) /3 | |
| Lethargy | 2 (7.4) /2 | 2 (18.2) /2 | | 2 (9.5) /2 | |
| Neuropathy peripheral | 11 (40.7) /13 | 3 (27.3) /5 | 8 (50.0) /8 | 10 (47.6) /12 | 1 (16.7) /1 |
| Paraesthesia | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 2 (9.5) /2 | |
| Peripheral sensory neuropathy | 4 (14.8) /5 | 3 (27.3) /4 | 1 (6.3) /1 | 2 (9.5) /3 | 2 (33.3) /2 |
| **PSYCHIATRIC DISORDERS** | **4 (14.8) /6** | **3 (27.3) /4** | **1 (6.3) /2** | **3 (14.3) /5** | **1 (16.7) /1** |
| Insomnia | 3 (11.1) /3 | 2 (18.2) /2 | 1 (6.3) /1 | 2 (9.5) /2 | 1 (16.7) /1 |
| **RENAL AND URINARY DISORDERS** | **4 (14.8) /4** | **1 (9.1) /1** | **3 (18.8) /3** | **1 (4.8) /1** | **3 (50.0) /3** |
| Dysuria | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| **RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS** | **14 (51.9) /24** | **7 (63.6) /16** | **7 (43.8) /8** | **12 (57.1) /20** | **2 (33.3) /4** |
| Cough | 4 (14.8) /4 | 3 (27.3) /3 | 1 (6.3) /1 | 4 (19.0) /4 | |
| Dyspnoea | 4 (14.8) /6 | 3 (27.3) /5 | 1 (6.3) /1 | 2 (9.5) /4 | 2 (33.3) /2 |
| Haemoptysis | 2 (7.4) /2 | 2 (18.2) /2 | | 2 (9.5) /2 | |
| Pulmonary embolism | 3 (11.1) /3 | | 3 (18.8) /3 | 2 (9.5) /2 | 1 (16.7) /1 |

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| | No. of Patients (%)/No. of Episodes | | | | |
|---|---|---|---|---|---|
| **SYSTEM ORGAN CLASS<br>Preferred Term** | **All Expansion<br>(N=27)** | **sqNSCLC Cohort<br>(N=11)** | **Basket Cohort<br>(N=16)** | **15 mg/m$^2$ starting dose<br>(N=21)** | **20 mg/m$^2$ starting dose<br>(N=6)** |
| Pulmonary oedema | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 2 (9.5) /2 | |

*Abbreviations: COVID-19=coronavirus disease 2019; INCL=including; N=number of patients; No.=number; SARS-CoV-2=Severe Acute Respiratory Syndrome CoronaVirus 2; sqNSCLC=squamous non-small cell lung cancer.*

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**Frequency of Treatment Emergent Serious Adverse Events Occurring in ≥5% Patients Overall, by Cohort (Expansion Phase, Safety Population)**

| | No. of Patients (%)/No. of Episodes | | | | |
|---|---|---|---|---|---|
| **SYSTEM ORGAN CLASS Preferred Term** | **All Expansion (N=27)** | **sqNSCLC Cohort (N=11)** | **Basket Cohort (N=16)** | **15 mg/m$^2$ starting dose (N=21)** | **20 mg/m$^2$ starting dose (N=6)** |
| **OVERALL TOTAL** | **14 (51.9) /33** | **6 (54.5) /9** | **8 (50.0) /24** | **10 (47.6) /15** | **4 (66.7) /18** |
| **GASTROINTESTINAL DISORDERS** | **5 (18.5) /10** | **2 (18.2) /3** | **3 (18.8) /7** | **1 (4.8) /2** | **4 (66.7) /8** |
| Abdominal pain | 2 (7.4) /2 | | 2 (12.5) /2 | 1 (4.8) /1 | 1 (16.7) /1 |
| Diarrhoea | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | | 2 (33.3) /2 |
| Nausea | 2 (7.4) /2 | | 2 (12.5) /2 | | 2 (33.3) /2 |
| Vomiting | 4 (14.8) /4 | 2 (18.2) /2 | 2 (12.5) /2 | 1 (4.8) /1 | 3 (50.0) /3 |
| **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS** | **3 (11.1) /4** | | **3 (18.8) /4** | **1 (4.8) /1** | **2 (33.3) /3** |
| Pyrexia | 2 (7.4) /2 | | 2 (12.5) /2 | 1 (4.8) /1 | 1 (16.7) /1 |
| **INFECTIONS AND INFESTATIONS** | **5 (18.5) /5** | **1 (9.1) /1** | **4 (25.0) /4** | **4 (19.0) /4** | **1 (16.7) /1** |
| Lower respiratory tract infection | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 2 (9.5) /2 | |

*Abbreviations: N=number of patients; No.=number; sqNSCLC=squamous non-small cell lung cancer.*

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**Frequency of Treatment Emergent Non Serious Adverse Events Occurring in ≥5% Patients Overall, by Cohort (Expansion Phase, Safety Population)**

| | No. of Patients (%)/No. of Episodes | | | | |
|---|---|---|---|---|---|
| **SYSTEM ORGAN CLASS Preferred Term** | **All Expansion (N=27)** | **sqNSCLC Cohort (N=11)** | **Basket Cohort (N=16)** | **15 mg/m$^2$ starting dose (N=21)** | **20 mg/m$^2$ starting dose (N=6)** |
| **OVERALL TOTAL** | **27 (100) /319** | **11 (100) /141** | **16 (100) /178** | **21 (100) /227** | **6 (100) /92** |
| **BLOOD AND LYMPHATIC SYSTEM DISORDERS** | **10 (37.0) /11** | **4 (36.4) /4** | **6 (37.5) /7** | **6 (28.6) /7** | **4 (66.7) /4** |
| Anaemia | 9 (33.3) /9 | 3 (27.3) /3 | 6 (37.5) /6 | 6 (28.6) /6 | 3 (50.0) /3 |
| **GASTROINTESTINAL DISORDERS** | **26 (96.3) /90** | **10 (90.9) /38** | **16 (100) /52** | **20 (95.2) /58** | **6 (100) /32** |
| Abdominal pain | 8 (29.6) /8 | 4 (36.4) /4 | 4 (25.0) /4 | 5 (23.8) /5 | 3 (50.0) /3 |
| Constipation | 13 (48.1) /16 | 6 (54.5) /6 | 7 (43.8) /10 | 10 (47.6) /13 | 3 (50.0) /3 |
| Diarrhoea | 11 (40.7) /18 | 4 (36.4) /7 | 7 (43.8) /11 | 6 (28.6) /8 | 5 (83.3) /10 |
| Dry mouth | 4 (14.8) /4 | 2 (18.2) /2 | 2 (12.5) /2 | 4 (19.0) /4 | |
| Dyspepsia | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| Gastrooesophageal reflux disease | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 2 (9.5) /2 | |
| Nausea | 13 (48.1) /21 | 6 (54.5) /9 | 7 (43.8) /12 | 10 (47.6) /16 | 3 (50.0) /5 |
| Vomiting | 7 (25.9) /12 | 2 (18.2) /5 | 5 (31.3) /7 | 2 (9.5) /4 | 5 (83.3) /8 |
| **GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS** | **17 (63.0) /28** | **6 (54.5) /8** | **11 (68.8) /20** | **12 (57.1) /20** | **5 (83.3) /8** |
| Fatigue | 16 (59.3) /19 | 6 (54.5) /6 | 10 (62.5) /13 | 11 (52.4) /14 | 5 (83.3) /5 |
| Mucosal inflammation | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| Non-cardiac chest pain | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| Pyrexia | 2 (7.4) /2 | | 2 (12.5) /2 | 2 (9.5) /2 | |
| **INFECTIONS AND INFESTATIONS** | **13 (48.1) /19** | **6 (54.5) /7** | **7 (43.8) /12** | **10 (47.6) /16** | **3 (50.0) /3** |
| COVID-19 | 2 (7.4) /2 | 2 (18.2) /2 | | 2 (9.5) /2 | |
| Lower respiratory tract infection | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 2 (9.5) /2 | |
| Pneumonia | 2 (7.4) /3 | 1 (9.1) /1 | 1 (6.3) /2 | 1 (4.8) /2 | 1 (16.7) /1 |
| Urinary tract infection | 4 (14.8) /5 | 1 (9.1) /1 | 3 (18.8) /4 | 3 (14.3) /4 | 1 (16.7) /1 |
| **INVESTIGATIONS** | **15 (55.6) /57** | **6 (54.5) /21** | **9 (56.3) /36** | **12 (57.1) /37** | **3 (50.0) /20** |
| Alanine aminotransferase increased | 9 (33.3) /13 | 5 (45.5) /8 | 4 (25.0) /5 | 6 (28.6) /8 | 3 (50.0) /5 |
| Aspartate aminotransferase increased | 7 (25.9) /9 | 3 (27.3) /4 | 4 (25.0) /5 | 4 (19.0) /4 | 3 (50.0) /5 |
| Blood albumin decreased | 2 (7.4) /2 | | 2 (12.5) /2 | 2 (9.5) /2 | |
| Blood alkaline phosphatase increased | 6 (22.2) /8 | 3 (27.3) /5 | 3 (18.8) /3 | 6 (28.6) /8 | |

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| SYSTEM ORGAN CLASS<br>Preferred Term | No. of Patients (%)/No. of Episodes<br>All Expansion (N=27) | sqNSCLC Cohort (N=11) | Basket Cohort (N=16) | 15 mg/m$^2$ starting dose (N=21) | 20 mg/m$^2$ starting dose (N=6) |
|---|---|---|---|---|---|
| Blood bilirubin increased | 2 (7.4) /4 | | 2 (12.5) /4 | 1 (4.8) /1 | 1 (16.7) /3 |
| Blood potassium decreased | 2 (7.4) /4 | | 2 (12.5) /4 | 1 (4.8) /1 | 1 (16.7) /3 |
| Gamma-glutamyltransferase increased | 4 (14.8) /4 | 1 (9.1) /1 | 3 (18.8) /3 | 4 (19.0) /4 | |
| Weight decreased | 4 (14.8) /4 | 1 (9.1) /1 | 3 (18.8) /3 | 3 (14.3) /3 | 1 (16.7) /1 |
| **METABOLISM AND NUTRITION DISORDERS** | **11 (40.7) /25** | **5 (45.5) /9** | **6 (37.5) /16** | **8 (38.1) /16** | **3 (50.0) /9** |
| Decreased appetite | 7 (25.9) /7 | 4 (36.4) /4 | 3 (18.8) /3 | 5 (23.8) /5 | 2 (33.3) /2 |
| Dehydration | 3 (11.1) /3 | 2 (18.2) /2 | 1 (6.3) /1 | 1 (4.8) /1 | 2 (33.3) /2 |
| Hypoalbuminaemia | 2 (7.4) /2 | | 2 (12.5) /2 | 1 (4.8) /1 | 1 (16.7) /1 |
| Hypokalaemia | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| Hypomagnesaemia | 3 (11.1) /5 | | 3 (18.8) /5 | 2 (9.5) /2 | 1 (16.7) /3 |
| Hyponatraemia | 3 (11.1) /4 | 1 (9.1) /2 | 2 (12.5) /2 | 3 (14.3) /4 | |
| **MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS** | **14 (51.9) /19** | **8 (72.7) /13** | **6 (37.5) /6** | **11 (52.4) /16** | **3 (50.0) /3** |
| Arthralgia | 4 (14.8) /4 | 3 (27.3) /3 | 1 (6.3) /1 | 4 (19.0) /4 | |
| Back pain | 5 (18.5) /5 | 3 (27.3) /3 | 2 (12.5) /2 | 4 (19.0) /4 | 1 (16.7) /1 |
| Myalgia | 2 (7.4) /3 | 2 (18.2) /3 | | 2 (9.5) /3 | |
| **NERVOUS SYSTEM DISORDERS** | **19 (70.4) /30** | **8 (72.7) /18** | **11 (68.8) /12** | **15 (71.4) /26** | **4 (66.7) /4** |
| Dizziness | 2 (7.4) /2 | 2 (18.2) /2 | | 1 (4.8) /1 | 1 (16.7) /1 |
| Headache | 3 (11.1) /3 | 3 (27.3) /3 | | 3 (14.3) /3 | |
| Lethargy | 2 (7.4) /2 | 2 (18.2) /2 | | 2 (9.5) /2 | |
| Neuropathy peripheral | 11 (40.7) /13 | 3 (27.3) /5 | 8 (50.0) /8 | 10 (47.6) /12 | 1 (16.7) /1 |
| Paraesthesia | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 2 (9.5) /2 | |
| Peripheral sensory neuropathy | 4 (14.8) /5 | 3 (27.3) /4 | 1 (6.3) /1 | 2 (9.5) /3 | 2 (33.3) /2 |
| **PSYCHIATRIC DISORDERS** | **4 (14.8) /6** | **3 (27.3) /4** | **1 (6.3) /2** | **3 (14.3) /5** | **1 (16.7) /1** |
| Insomnia | 3 (11.1) /3 | 2 (18.2) /2 | 1 (6.3) /1 | 2 (9.5) /2 | 1 (16.7) /1 |
| **RENAL AND URINARY DISORDERS** | **4 (14.8) /4** | **1 (9.1) /1** | **3 (18.8) /3** | **1 (4.8) /1** | **3 (50.0) /3** |
| Dysuria | 2 (7.4) /2 | 1 (9.1) /1 | 1 (6.3) /1 | 1 (4.8) /1 | 1 (16.7) /1 |
| **RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS** | **12 (44.4) /19** | **6 (54.5) /13** | **6 (37.5) /6** | **10 (47.6) /16** | **2 (33.3) /3** |
| Cough | 4 (14.8) /4 | 3 (27.3) /3 | 1 (6.3) /1 | 4 (19.0) /4 | |
| Dyspnoea | 3 (11.1) /5 | 3 (27.3) /5 | | 2 (9.5) /4 | 1 (16.7) /1 |
| Haemoptysis | 2 (7.4) /2 | 2 (18.2) /2 | | 2 (9.5) /2 | |

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| | No. of Patients (%)/No. of Episodes | | | | |
|---|---|---|---|---|---|
| **SYSTEM ORGAN CLASS<br>Preferred Term** | **All Expansion (N=27)** | **sqNSCLC Cohort (N=11)** | **Basket Cohort (N=16)** | **15 mg/m$^2$ starting dose (N=21)** | **20 mg/m$^2$ starting dose (N=6)** |
| Pulmonary embolism | 2 (7.4) /2 | | 2 (12.5) /2 | 1 (4.8) /1 | 1 (16.7) /1 |

*Abbreviations: COVID-19=coronavirus disease 2019; INCL=including; N=number of patients; No.=number; SARS-CoV-2=Severe Acute Respiratory Syndrome CoronaVirus 2; sqNSCLC=squamous non-small cell lung cancer.*

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## SECONDARY OUTCOME MEASURES

### BT1718 Pharmacokinetics Stratified by Cohort (Pharmacokinetic Population)

| Cohort | Normalised Dose ($mg/m^2$) | N | $T_{max}$ (h) | $C_{max}$ (µg/L) | Terminal elimination $T_{½}$ (h) | AUC (µg·h/L) |
|---|---|---|---|---|---|---|
| **Twice weekly dosing** | | | | | | |
| 1 | 0.6 | 1 | 0.67 (-) | 11.30 (-) | 0.55 (-) | 14.60 (-) |
| 2 | 1.2 | 1 | 1.02 (-) | 50.40 (-) | 0.16 (-) | 41.73 (-) |
| 3 | 2.4 | 1 | 1.10 (-) | 47.10 (-) | 0.08 (-) | 50.37 (-) |
| 4 | 4.8 | 1 | 0.67 (-) | 163.00 (-) | 0.17 (-) | 154.65 (-) |
| 6 | 7.2 | 8 | 1.01±0.2 | 643.13±908 | 0.18±0.02 | 499.42±546 |
| 5 | 9.6 | 4 | 0.80±0.35 | 2724.75±4323 | 0.26±0.06 | 1666.29±2212 |
| **Once weekly dosing** | | | | | | |
| 1A | 9.6 | 3 | 1.04±0.22 | 570.00±417 | 0.24±0.06 | 546.81±386 |
| 2A | 15 | 5 | 1.13±0.17 | 1048.20±383 | 0.33±0.11 | 1189.83±472 |
| Expansion | 15 | 23 | 1.01±0.24 | 1066.04±310 | 0.28±0.08 | 1136.21±330 |
| 3A | 20 | 13 | 1.00±0.24 | 2311.69±2000 | 0.36±0.06 | 2215.19±1537 |
| Expansion | 20 | 9 | 1.06±0.23 | 1796.67±591 | 0.36±0.15 | 1760.29±496 |
| 4A | 25 | 11 | 0.96±0.17 | 2069.09±478 | 0.41±0.07 | 2399.12±567 |
| 5A | 32 | 8 | 0.99±0.23 | 2662.50±428 | 0.43±0.07 | 3324.15±516 |

*All data shown as mean ±standard deviation. N=total number of cycles assessed by NCA for each dosing cohort (Cycles 1 and 2). Later cycles in the expansion phase were not included as they did not have enough datapoints to assess using NCA. Samples were available for pharmacokinetic analysis for 38 patients in the dose escalation phase and 27 patients in the expansion phase.*
*Abbreviations: AUC=area under the plasma concentration-time curve; $C_{max}$=maximum observed plasma concentration; h=hour; NCA=non-compartmental analysis; $T_{½}$=half-life; $T_{max}$=time to reach $C_{max}$.*

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### Summary of Pharmacokinetic Data Generated for Total DM1 From Samples Collected on Cycle 1, Day 1 (Dose Escalation Phase, Pharmacokinetic Population)

| Cohort | Dose Level ($mg/m^2$) | $C_{max}$ (nM) | $T_{½}$ (h) | AUC (nM.h) |
|---|---|---|---|---|
| 1 (N=1) | 0.6 | BLLOQ | ND | ND |
| 2 (N=1) | 1.2 | 153 | 0.8 | 209 |
| 3 (N=1) | 2.4 | 153 | 0.6 | 250 |
| 4 (N=1) | 4.8 | 222 | 1.1 | 513 |
| 5 (N=4) | 9.6 | 697 ±243 | 3.4 ±1.6 | 1714 ±86 |
| 6 (N=6) | 7.2 | 615 ±390 | 4.1 ±1.6 | 1603 ±608 |
| 1A (N=3) | 9.6 | 643 ±204 | 3.1 ±0.6 | 1932 ±806 |
| 2A (N=3) | 15 | 1133 ±201 | 4.7 ±3.7 | 3712 ±1509 |
| 3A (N=7) | 20 | 1264 ±482 | 4.4 ±3.1 | 4150 ±1868 |
| 4A (N=6) | 25 | 1312 ±321 | 8.5 ±8.2 | 7425 ±5247 |
| 5A (N=5) | 32 | 1869 ±532 | 8.3 ±0.8 | 8967 ±2100 |

*Patients in Cohorts 1 to 6 received BT1718 twice weekly; patients in Cohorts 1A to 5A received BT1718 once weekly.*
*All data shown as mean ±standard deviation for cohorts with multiple patients.*
*Abbreviations: AUC=area under the plasma concentration-time curve; BLLOQ=below the limit of quantification for the assay; $C_{max}$=maximum observed plasma concentration; DM1=N2'-deacetyl-N2'-(3-mercapto-1-oxopropyl)-maytansine; h=hour; N=number of patients in the cohort; ND=no data; $T_{½}$=terminal elimination half-life.*

### Summary of Pharmacokinetic Data Generated for Total DM1 From Samples Collected on Cycle 1, Day 1 (Expansion Phase, Pharmacokinetic Population)

| Cohort | Dose Level ($mg/m^2$) | $C_{max}$ (nM) | $T_{½}$ (h) | AUC (nM.h) |
|---|---|---|---|---|
| Exp 1 (N=6) | 20 | 1556 ±254 | 4.7 ±2.7 | 4818 ±1534 |
| Exp 2 (N=21) | 15 | 848 ±156 | 3.3 ±1.9 | 2489 ±791 |

*Exp 1 includes patients in the expansion phase who started dosing at 20 $mg/m^2$ BT1718 and Exp 2 includes patients in the expansion phase who started dosing at 15 $mg/m^2$ BT1718.*
*All data shown as mean ±standard deviation.*
*Abbreviations: AUC=area under the plasma concentration-time curve; $C_{max}$=maximum observed plasma concentration; DM1=N2'-deacetyl-N2'-(3-mercapto-1-oxopropyl)-maytansine; h=hour; N=number of patients in the cohort; $T_{½}$=terminal elimination half-life.*

### Best Overall Response (Response Population)

| Best Tumour Response | Overall No. of Patients (N=48) | Dose Escalation Phase No. of Patients (N=27) | Expansion Phase sqNSCLC Cohort No. of Patients (N=7) | Expansion Phase Basket Cohort No. of Patients (N=14) |
|---|---|---|---|---|
| SD (Stable Disease)* | 28 (58.3%) | 17 (63.0%) | 5 (71.4%) | 6 (42.9%) |
| PD (Progressive Disease) | 20 (41.7%) | 10 (37.0%) | 2 (28.6%) | 8 (57.1%) |

** Two patients had a partial response at one timepoint each that was not confirmed by a subsequent scan (one patient in the Dose Escalation Phase and one patient in the Expansion Phase Basket Cohort). The best overall response for these patients was categorised as stable disease per protocol.*
*Abbreviations: N=number of patients in the cohort; No.=number; sqNSCLC=squamous non-small cell lung cancer.*

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### Progression Free Survival Summary (Survival Population)

| | Overall No. of Patients (N=54) | Escalation Phase No. of Patients (N=31) | Expansion Phase sqNSCLC Cohort No. of Patients (N=7) | Expansion Phase Basket Cohort No. of Patients (N=16) |
|---|---|---|---|---|
| Median (days) | 67 | 71 | 113 | 56.5 |
| Min (days) | 14 | 22 | 49 | 14 |
| Max (days) | 761 | 380 | 761 | 273 |
| PFS rate at 6 months | 8 of 54 | 5 of 31 | 2 of 7 | 1 of 16 |

*Abbreviations: max=maximum; min=minimum; N=number of patients in the cohort; No.=number; PFS=progression free survival; sqNSCLC=squamous non-small cell lung cancer.*

### Overall Survival Summary (Survival Population)

| | Overall No. of Patients (N=54) | Escalation Phase No. of Patients (N=31) | Expansion Phase sqNSCLC Cohort No. of Patients (N=7) | Expansion Phase Basket Cohort No. of Patients (N=16) |
|---|---|---|---|---|
| Median (days) | 202.5 | 209 | 170 | 185.5 |
| Min (days) | 32 | 63 | 137 | 32 |
| Max (days) | 1962 | 1962 | 768 | 611 |
| OS rate at 6 months | 32 of 54 | 20 of 31 | 3 of 7 | 9 of 16 |

*Abbreviations: max=maximum; min=minimum; N=number of patients in the cohort; No.=number; OS=overall survival; sqNSCLC=squamous non-small cell lung cancer.*

### Duration of Response (Response Population)

Duration of response was not analysed as there were no confirmed responses.