|  |  |  |  |
| --- | --- | --- | --- |
| Disease Type | Phase I (5) | Phase II (44) | Overall (49) |
| Leukaemia | 1 (20) | 6 (13.6) | 7 (14.3) |
| Neuroblastoma | 0 | 14 (31.8) | 14 (28.6) |
| Sarcoma | 1 (20) | 12 (27.3) | 13 (26.5) |
| High Grade Glioma | 3 (60) | 12 (27.3) | 15 (30.6) |
| Total | 5 (100) | 44 (100) | 49 (100) |

Supplementary Table 1. Patients Recruited

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No. Weeks Treatment | Disease Type | | | |
| **Leukaemia (7)** | **Neuroblastoma (12)** | **Sarcoma (13)** | **High Grade Glioma (13)** |
| Mean (sd) | 4.1 (3.5) | 8.8 (10.6) | 12.7 (13.4) | 10.8 (17.5) |
| Median | 2 | 7 | 7 | 6 |
| Range | 1, 10 | 1, 40 | 2, 41 | 2, 68 |

Supplementary Table 2. Treatment Weeks: Summary Statistics by Group

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Disease Type | No. patients | Median Overall Survival in months (95%CI) | Estimated 6-month Overall Survival Probability (95%CI) | Estimated 12-month Overall Survival Probability (95%CI) |
| Leukaemia | 7 | 1.3 (0.5 – 4.5) | 0.14 (0.007 – 0.46) | N/A |
| Neuroblastoma | 12 | 2.9 (0.95 − ) | 0.50 (0.21 – 0.74) | 0.33 (0.10 – 0.59) |
| Sarcoma | 13 | 3.5 (1.6 – 6.8) | 0.31 (0.09 – 0.55) | 0.15 (0.02 – 0.39) |
| High Grade Glioma | 13 | 2.2 (1.3 – 4.5) | 0.15 (0.02 – 0.39) | N/A |
| Overall | 45 | 2.7 (2.2 – 4.5) | 0.29 (0.17 – 0.42) | 0.16 (0.07 – 0.28) |

Supplementary Table 3. Overall Survival: Estimates by Disease Group

Supplementary Table 4. Progression-Free Survival: Estimates by Disease Group

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Disease Type | No. patients | Median Progression-Free  Survival in months (95%CI) | Estimated 6-month Progression-Free Survival Probability (95%CI) | Estimated 12-month Progression-Free Survival Probability (95%CI) |
| Leukaemia | 7 | 1.1 (0.5 – 1.7) | N/A | N/A |
| Neuroblastoma | 12 | 1.8 (0.6 – 2.1) | 0.17 (0.03 – 0.41) | N/A |
| Sarcoma | 13 | 1.8 (0.9 – 1.9) | 0.15 (0.02 – 0.39) | N/A |
| High Grade  Glioma | 13 | 1.5 (0.7 – 2) | 0.15 (0.02 – 0.39) | 0.08 (0.005 – 0.29) |
| Overall | 45 | 1.6 (1 – 1.8) | 0.13 (0.05 – 0.25) | 0.03 (0.008 – 0.13) |

Supplementary Table 5. Number of Serious Adverse Events by Toxicity and Grade

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Grade | | | | | | | | |
| 1 | | 2 | | 3 | | 4 | | 5 |
| Toxicity (No. events (No. patients that experienced toxicity) | | | | | | | | | |
| Blood and lymphatic system disorders | | | | | | | | | |
| Cardiac arrest | 0 | | 0 | | 0 | | 0 | | 1 (1) |
| Cardiac disorders | | | | | | | | | |
| Atrial ectopics | 1 (1) | | 0 | | 0 | | 0 | | 0 |
| Sinus tachycardia | 0 | | 1 (1) | | 0 | | 0 | | 0 |
| Gastrointestinal disorders | | | | | | | | | |
| Diarrhoea | 1 (1) | | 0 | | 0 | | 0 | | 0 |
| Nausea | 1 (1) | | 0 | | 0 | | 0 | | 0 |
| Vomiting | 0 | | 1 (1) | | 1 (1) | | 0 | | 0 |
| General disorders and administration site conditions | | | | | | | | | |
| Fever | 11 (9) | 1 (1) | | 0 | | 0 | | 0 | |
| Infusion related reaction | 0 | 1 (1) | | 0 | | 0 | | 0 | |
| Immune system disorders | | | | | | | | | |
| Allergic reaction | 0 | 1 (1) | | 0 | | 0 | | 0 | |
| Infections and infestations | | | | | | | | | |
| Sepsis | 0 | 0 | | 0 | | 1 (1) | | 0 | |
| Upper respiratory infection | 0 | 0 | | 1 (1) | | 0 | | 0 | |
| Urinary tract infection | 0 | 0 | | 1 (1) | | 0 | | 0 | |
| Bacteraemia | 0 | 1 (1) | | 0 | | 0 | | 0 | |
| Musculoskeletal and connective tissue disorders | | | | | | | | | |
| Bone pain | 0 | 1 (1) | | 0 | | 0 | | 0 | |
| Neck pain | 0 | 1 (1) | | 0 | | 0 | | 0 | |
| Nervous system disorders | | | | | | | | | |
| Headache | 0 | 0 | | 1 (1) | | 0 | | 0 | |
| Seizure | 0 | 1 (1) | | 1 (1) | | 0 | | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | | | | | | | |
| Distress due to fluid overload | 0 | 0 | | 0 | | 1 (1) | | 0 | |
| Dyspnea | 0 | 0 | | 0 | | 5 (3) | | 0 | |
| Respiratory arrest | 0 | 0 | | 0 | | 1 (1) | | 0 | |

Table 6: Number of Serious Adverse Events related to treatment

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Grade | | | | | | | | |
| 1 | | 2 | | 3 | | 4 | | 5 |
| Toxicity (No. events (No. patients that experienced toxicity) | | | | | | | | | |
| Immune system disorders | | | | | | | | | |
| Allergic reaction | 0 | 1 (1) | | 0 | | 0 | | 0 | |
| Nervous system disorders | | | | | | | | | |
| Seizure | 0 | 1 (1) | | 0 | | 0 | | 0 | |

Supplementary Table 7: Number of Adverse Events by Toxicity and Grade

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Grade | | | | | | | |
| 1 | | 2 | 3 | | | 4 | 5 |
| Toxicity (No. events (No. patients that experienced toxicity) | | | | | | | | |
| Blood and lymphatic system disorders | | | | | | | | |
| Anaemia | 40 (21) | | 20 (12) | 15 (10) | | | 1 (1) | 0 |
| Platelet count decreased | 17 (9) | | 8 (3) | 18 (7) | | | 17 (9) | 0 |
| White blood cell count decreased | 34 (15) | | 12 (8) | 9 (5) | | | 2 (2) | 0 |
| Neutrophil count decreased | 6 (4) | | 11 (7) | 15 (7) | | | 6 (4) | 0 |
| Haematocrit decreased | 22 (14) | | 0 | 0 | | | 0 | 0 |
| Neutrophil count increased | 16 (8) | | 0 | 1 (1) | | | 0 | 0 |
| Red blood cell count decreased | 15 (9) | | 0 | 0 | | | 0 | 0 |
| Platelet count increased | 8 (5) | | 0 | 0 | | | 0 | 0 |
| White blood cell count increased | 6 (3) | | 0 | 0 | | | 0 | 0 |
| Febrile neutropenia | 1 (1) | | 0 | 4 (4) | | | 0 | 0 |
| Red blood cell count increased | 2 (1) | | 0 | 0 | | | 0 | 0 |
| Hypertension | 0 | | 2 (1) | 0 | | | 0 | 0 |
| Leukocytosis | 0 | | 0 | 1 (1) | | | 0 | 0 |
| Enlarged lymph node | 0 | | 1 (1) | 0 | | | 0 | 0 |
| Haematocrit increased | 1 (1) | | 0 | 0 | | | 0 | 0 |
| Cardiac disorders | | | | | | | | |
| Tachycardia | 5 (2) | | 1 (1) | 0 | | | 0 | 0 |
| Sinus tachycardia | 3 (3) | | 2 (2) | 0 | | | 0 | 0 |
| Cardiac arrest | 0 | | 0 | 0 | | | 0 | 1 (1) |
| Ear and labyrinth disorders | | | | | | | | |
| Ear pain | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Buzzing in left ear | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Endrocrine disorders | | | | | | | | |
| Cushingoid | 1 (1) | | 0 | 0 | | 0 | | 0 |
| TSH level decreased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| FSH level decreased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Adrenal insufficiency | 0 | | 0 | 1 (1) | | 0 | | 0 |
| LH level decreased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Hypoparathyroidism | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Eye disorders | | | | | | | | |
| Optic nerve disorder | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Blurred vision | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Papilledema | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Gastrointestinal disorders | | | | | | | | |
| Vomiting | 27 (13) | | 5 (5) | 1 (1) | | | 0 | 0 |
| Constipation | 9 (7) | | 10 (8) | 0 | | | 0 | 0 |
| Nausea | 10 (5) | | 7 (6) | 0 | | | 0 | 0 |
| Diarrhoea | 4 (4) | | 4 (3) | 0 | | | 0 | 0 |
| Dysphagia | 0 | | 2 (1) | 4 (4) | | | 0 | 0 |
| Abdominal pain | 3 (2) | | 0 | 2 (2) | | | 0 | 0 |
| Stomach pain | 3 (3) | | 0 | 0 | | | 0 | 0 |
| Oral pain | 0 (0) | | 2 (1) | 0 | | | 0 | 0 |
| Dyspepsia | 1 (1) | | 1 (1) | 0 | | | 0 | 0 |
| Dry mouth | 1 (1) | | 0 | 0 | | | 0 | 0 |
| Blood in stool | 0 (0) | | 1 (1) | 0 | | | 0 | 0 |
| Dental caries | 1 (1) | | 0 | 0 | | | 0 | 0 |
| Bloating | 1 (1) | | 0 | 0 | | | 0 | 0 |
| Enterocolitis | 0 | | 1 (1) | 0 | | | 0 | 0 |
| Soft stool | 1 (1) | | 0 | 0 | | | 0 | 0 |
| Crohn’s disease | 0 | | 1 (1) | 0 | | | 0 | 0 |
| Hypersalivation | 0 | | 1 (1) | 0 | | | 0 | 0 |
| General disorders and administration site conditions | | | | | | | | |
| Fever | 30 (16) | | 2 (2) | 1 (1) | | 0 | | 0 |
| Pain | 7 (6) | | 8 (6) | 8 (8) | | 0 | | 0 |
| Fatigue | 7 (6) | | 2 (2) | 0 | | 0 | | 0 |
| Runny nose | 4 (2) | | 0 | 0 | | 0 | | 0 |
| Gait disturbance | 1 (1) | | 1 (1) | 0 | | 0 | | 0 |
| Weakness | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Common cold | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Hypothermia | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Non-cardiac chest pain | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Chills | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Coryzal symptoms | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Night sweats | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Excess transpiration | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Localised oedema | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Oedema trunk | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Immune system disorders | | | | | | | | |
| Allergic reaction | 1 (1) | | 1 (1) | 1 (1) | | 0 | | 0 |
| Infections and infestations | | | | | | | | |
| Urinary tract infection | 0 | | 0 | 4 (1) | | 0 | | 0 |
| Upper respiratory infection | 2 (2) | | 1 (1) | 1 (1) | | 0 | | 0 |
| Sepsis | 0 | | 0 | 3 (1) | | 0 | | 0 |
| COVID-19 | 2 (2) | | 0 | 0 | | 0 | | 0 |
| Oral fungal infection | 1 (1) | | 1 (1) | 0 | | 0 | | 0 |
| Common cold | 1 (1) | | 1 (1) | 0 | | 0 | | 0 |
| Rhinovirus | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Blood – staphylococcus epidermis | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Unknown viral cough | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Bacteraemia | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Nail infection | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Bacillus cereus | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Conjunctivitis | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Hand foot and mouth | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Herpetic lip lesions | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Injury, poisoning and procedural complications | | | | | | | | |
| Bruising | 2 (2) | | 1 (1) | 0 | | 0 | | 0 |
| Investigations | | | | | | | | |
| Lymphocyte count decreased | 28 (15) | | 16 (13) | 7 (7) | | 2 (2) | | 0 |
| Alanine aminotransferase increased | 22 (15) | | 2 (2) | 1 (1) | | 1 (1) | | 0 |
| Aspartate aminotransferase increased | 16 (11) | | 2 (1) | 3 (1) | | 0 | | 0 |
| Creatinine decreased | 19 (8) | | 0 | 0 | | 0 | | 0 |
| Chloride high | 13 (2) | | 0 | 0 | | 0 | | 0 |
| Bicarbonate low | 8 (2) | | 0 | 0 | | 0 | | 0 |
| Creatinine increased | 7 (4) | | 1 (1) | 0 | | 0 | | 0 |
| GGT increased | 3 (3) | | 3 (2) | 1 (1) | | 0 | | 0 |
| Monocyte count increased | 7 (5) | | 0 | 0 | | 0 | | 0 |
| MCV decrease | 6 (5) | | 0 | 0 | | 0 | | 0 |
| MCV increase | 6 (4) | | 0 | 0 | | 0 | | 0 |
| CRP increased | 4 (2) | | 0 | 0 | | 0 | | 0 |
| Eosinophils decreased | 4 (2) | | 0 | 0 | | 0 | | 0 |
| Alkaline phosphatase increased | 4 (4) | | 0 | 0 | | 0 | | 0 |
| Lymphocyte count increased | 0 | | 2 (2) | 1 (1) | | 0 | | 0 |
| Phosphate high | 3 (2) | | 0 | 0 | | 0 | | 0 |
| ALT decreased | 3 (2) | | 0 | 0 | | 0 | | 0 |
| Creatinine decreased | 3 (1) | | 0 | 0 | | 0 | | 0 |
| Weight loss | 2 (2) | | 1 (1) | 0 | | 0 | | 0 |
| Elevated bicarbonate levels | 2 (1) | | 0 | 0 | | 0 | | 0 |
| Mean corpuscular volume decreased | 2 (1) | | 0 | 0 | | 0 | | 0 |
| Monocytes low | 2 (1) | | 0 | 0 | | 0 | | 0 |
| Haemoglobin increased | 2 (1) | | 0 | 0 | | 0 | | 0 |
| MCHC high | 2 (1) | | 0 | 0 | | 0 | | 0 |
| C-Reactive protein increase | 1 (1) | | 1 (1) | 0 | | 0 | | 0 |
| Alkaline phosphatase decrease | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Cholesterol high | 0 | | 1 (1) | 0 | | 0 | | 0 |
| INR increased | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Basophils high | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Urine output decreased | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Lactate dehydrogenase increased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Haemoglobin low | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Mean cell haemoglobin decrease | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Chloride increased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| High ferritin | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Thrombin time increased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Increased urine output | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Blood prolactin abnormal | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Metabolism and nutrition disorders | | | | | | | | |
| Hypokalaemia | 23 (9) | | 2 (2) | 5 (5) | | 0 | | 0 |
| Hypoalbuminemia | 11 (8) | | 4 (4) | 1 (1) | | 0 | | 0 |
| Hyponatremia | 9 (7) | | 0 | 2 (2) | | 0 | | 0 |
| Hypomagnesemia | 14 (8) | | 0 | 0 | | 0 | | 0 |
| Hypophosphatemia | 3 (2) | | 4 (4) | 1 (1) | | 0 | | 0 |
| Hypernatremia | 5 (5) | | 2 (2) | 0 | | 0 | | 0 |
| Anorexia | 3 (2) | | 0 | 0 | | 0 | | 0 |
| Blood glucose increased | 2 (1) | | 0 | 0 | | 0 | | 0 |
| Hypocalcaemia | 2 (2) | | 0 | 0 | | 0 | | 0 |
| Hyperphosphatemia | 2 (1) | | 0 | 0 | | 0 | | 0 |
| Hyperuricemia | 2 (2) | | 0 | 0 | | 0 | | 0 |
| Dehydration | 0 | | 0 | 2 (2) | | 0 | | 0 |
| Chloride levels decreased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Increased thirst | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Hyperglycaemia | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Weight gain | 1 (1) | | 1(1) | 0 | | 0 | | 0 |
| Hyperkalaemia | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Hypertriglyceridemia | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Musculoskeletal and connective tissue disorders | | | | | | | | |
| Muscle weakness left-sided | 1 (1) | | 2 (2) | 2 (2) | | 0 | | 0 |
| Pain in extremity | 1 (1) | | 2 (2) | 1 (1) | | 0 | | 0 |
| Generalised muscle weakness | 0 | | 1 (1) | 2 (2) | | 0 | | 0 |
| Back pain | 2 (2) | | 0 | 1 (1) | | 0 | | 0 |
| Neck pain | 0 | | 1 (1) | 1 (1) | | 0 | | 0 |
| Muscle weakness lower limb | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Flank pain | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Pain in right shoulder | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Myalgia | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Muscle weakness right-sided | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Muscle weakness trunk | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Joint range of motion decreased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Nervous system disorders | | | | | | | | |
| Headache | 9 (6) | | 4 (3) | 4 (4) | | 0 | | 0 |
| Lethargy | 5 (4) | | 6 (5) | 0 | | 0 | | 0 |
| Dysarthria | 2 (2) | | 2 (2) | 3 (3) | | 0 | | 0 |
| Seizure | 0 | | 4 (4) | 2 (1) | | 0 | | 0 |
| Hydrocephalus | 0 | | 1 (1) | 1 (1) | | 1 (1) | | 0 |
| Ataxia | 1 (1) | | 1 (1) | 1 (1) | | 0 | | 0 |
| Facial muscle weakness | 1 (1) | | 1 (1) | 0 | | 0 | | 0 |
| Paraesthesia | 2 (2) | | 0 | 0 | | 0 | | 0 |
| Hemiplegia | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Spasticity | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Sleep disturbance – wakes early | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Paraplegia | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Bladder emptying disorder | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Memory impairment | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Dysesthesia | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Tremor | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Imbalance | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Somnolence | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Spinal cord injury | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Polydipsia | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Dysphagia | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Hypersomnia | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Bowel emptying disorder | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Dysgeusia | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Intra-tumoral haemorrhage and surrounding cerebral oedema | 0 | | 0 | 0 | | 1 (1) | | 0 |
| Dizziness | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Psychiatric disorders | | | | | | | | |
| Anxiety | 2 (2) | | 2 (2) | 1 (1) | | 0 | | 0 |
| Insomnia | 1 (1) | | 1 (1) | 2 (1) | | 0 | | 0 |
| Confusion | 0 | | 1 (1) | 2 (2) | | 0 | | 0 |
| Libido decreased | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Low mood | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Euphoria | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Restlessness | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Renal and urinary disorders | | | | | | | | |
| Urea increased | 15 (8) | | 0 | 0 | | 0 | | 0 |
| Urea decreased | 13 (7) | | 0 | 0 | | 0 | | 0 |
| Urea low | 2 (1) | | 0 | 0 | | 0 | | 0 |
| Acute kidney injury | 1 (1) | | 0 | 1 (1) | | 0 | | 0 |
| Urinary retention | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Urea high | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Urinary incontinence | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Cystitis non-infective | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Polyuria | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Bladder spasm | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Bladder perforation | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Reproductive system and breast disorders | | | | | | | | |
| Vaginal pain | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Respiratory, thoracic and mediastinal disorders | | | | | | | | |
| Dyspnoea | 3 (3) | | 1 (1) | 7 (5) | | 1 (1) | | 0 |
| Cough | 8 (6) | | 0 | 0 | | 0 | | 0 |
| Hypoxia | 0 | | 1 (1) | 3 (3) | | 0 | | 0 |
| Pleural effusion | 0 | | 1 (1) | 2 (2) | | 0 | | 0 |
| Sore throat | 2 (2) | | 0 | 0 | | 0 | | 0 |
| Epistaxis | 0 | | 2 (2) | 0 | | 0 | | 0 |
| Respiratory failure | 0 | | 0 | 0 | | 1 (1) | | 0 |
| Respiratory distress | 0 | | 0 | 0 | | 1 (1) | | 0 |
| Pulmonary oedema | 0 | | 0 | 1 (1) | | 0 | | 0 |
| Runny nose | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Apnoea | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Skin and subcutaneous tissue disorders |  | |  |  | |  | |  |
| Rash maculo-papular | 4 (4) | | 0 | 1 (1) | | 0 | | 0 |
| Alopecia | 1 (1) | | 3 (3) | 0 | | 0 | | 0 |
| Pruritus | 2 (2) | | 0 | 0 | | 0 | | 0 |
| Itching | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Photosensitivity | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Skin atrophy | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Skin ulceration | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Blister on abdomen | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Rash-graft versus host disease | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Shingles | 0 | | 1 (1) | 0 | | 0 | | 0 |
| Urticaria | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Dry skin | 1 (1) | | 0 | 0 | | 0 | | 0 |
| Vascular disorders | | | | | | | | |
| Hypertension | 2 (2) | 2 (2) | | | 0 | 0 | | 0 |
| Hypotension | 1 (1) | 1 (1) | | | 0 | 0 | | 0 |
| Flushing | 1 (1) | 0 | | | 0 | 0 | | 0 |
| Thromboembolic event | 0 | 1 (1) | | | 0 | 0 | | 0 |

Supplementary Table 8. Number of Adverse Events related to treatment

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Grade | | | | | | | | |
| 1 | 2 | | 3 | | 4 | | | 5 |
| Toxicity (No. events (No. patients that experienced toxicity) | | | | | | | | | |
| Gastrointestinal disorders | | | | | | | | | |
| Vomiting | 1 (1) | | 0 | | 0 | | 0 | 0 | |
| Abdominal pain | 1 (1) | | 0 | | 0 | | 0 | 0 | |
| Immune system disorders | | | | | | | | | |
| Allergic reaction | 0 | | 1 (1) | | 0 | | 0 | 0 | |
| Skin and subcutaneous tissue disorders | | | | | | | | | |
| Urticaria | 1 (1) | | 0 | | 0 | | 0 | 0 | |