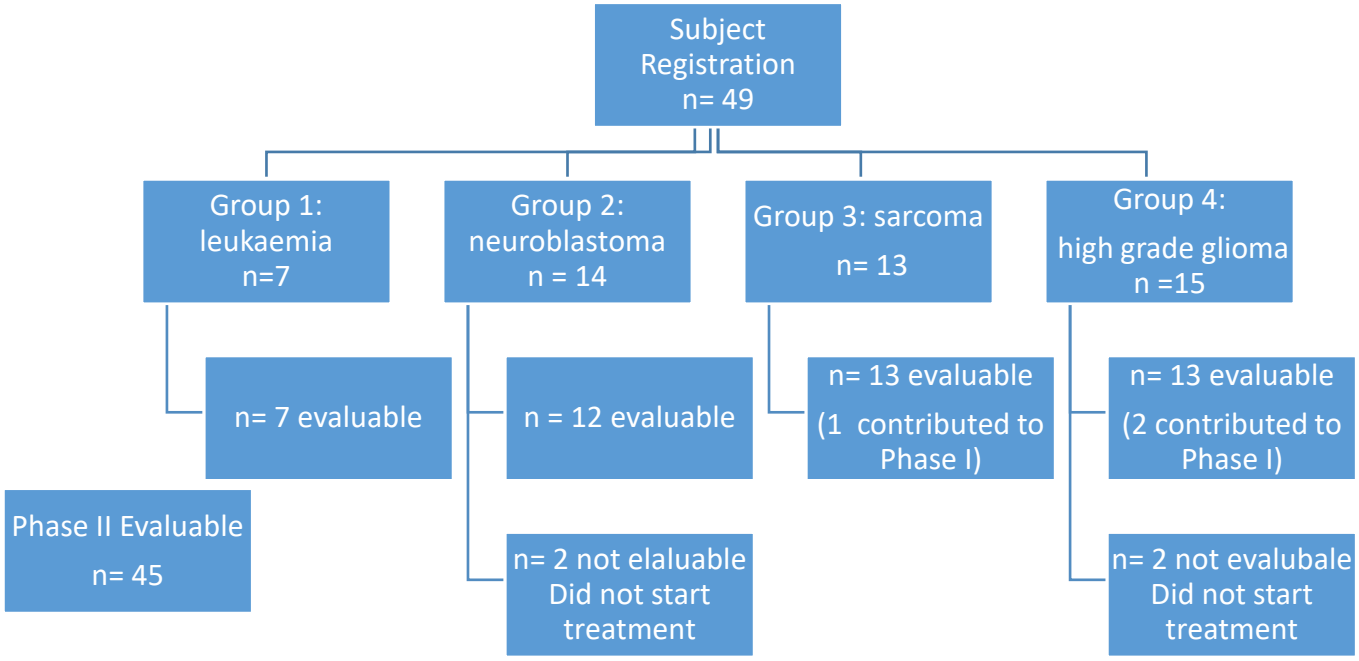
PARC Basic Results Summary

(ISRCTN21727048 https://doi.org/10.1186/ISRCTN21727048)

Participant Flow:



Baseline Characteristics:

Group 1: Baseline Characteristics (Leukaemia Patients)

Baseline Characteristics - Leukaemia Patients

Gender (N (%))	
Male	4 (57.1)
Female	3 (42.9)
Leukaemia Type (N (%))	
Acute Lymphoblastic Leukaemia (ALL)	3 (42.9)
Acute Myeloblastic Leukaemia (AML)	4 (57.1)
CNS Involvement (N (%))	
No	6 (85.7)
Yes	1 (14.3)
Relapse/Progressive (N (%))	
Relapsed	5 (71.4)
Progressive	2 (28.6)

CNS Involvement - Leukaemia Patients

Classification in CSF
CNS3 - > 5 x 106/L WCC in CSF with blasts (or clinically significant neurological deficits)

ALL Classification - Leukaemia Patients

ALL Classification	
B-cell Precursor ALL	1 (33.3)
T-ALL	2 (66.7)

AML Classification - Leukaemia Patients

FAB Classification	
M0 - Undifferentiated acute myeloblastic leukemia	1 (25.0)
M1 - Acute myeloblastic leukemia with minimal maturation	1 (25.0)
M7 - Acute megakaryocytic leukemia	2 (50.0)

Baseline Characteristics - Leukaemia Patients

Diagnosis: Time to Registration (Months)	
N	7
Mean (sd)	22.6 (28.3)
Median	10.1
Range	1.8, 80.5
Age (Years)	
N	7
Mean (sd)	9.0 (6.3)
Median	7.9
Range	1.2, 17.4
Weight (Kg)	
N	7
Mean (sd)	34.1 (23.9)
Median	26.9
Range	9.9, 70.5
Bilirubin (umol/L)	
N	7
Mean (sd)	7.4 (4.9)
Median	6.0
Range	3.0, 17.0
ALT (U/L)	
N	7
Mean (sd)	50.0 (35.4)
Median	40.0
Range	12.0, 110.0

Relapse Details - Leukaemia Patients

Latest Relapse: Time to Registration (Days)	
N	5
Mean (sd)	15.4 (10.4)
Median	15.0
Range	5.0, 31.0
Number of Relapses	
N	5
Mean (sd)	2.4 (0.9)
Median	3.0
Range	1.0, 3.0

Progression Details - Leukaemia Patients

Progression: Time to Registration (Days)	
N	2
Mean (sd)	2.5 (3.5)
Median	2.5
Range	0.0, 5.0

Group 2: Baseline Characteristics (Neuroblastoma Patients)

Baseline Characteristics - Neuroblastoma Patients

Gender (N (%))	
Male	7 (50.0)
Female	7 (50.0)
MYCN Status (N (%))	
Amplified	3 (21.4)
Not amplified	11 (78.6)
Chromosomal Aberration: Diagnosis (N (%))	
No	2 (14.3)
Yes	8 (57.1)
Not Known	4 (28.6)
INRGSS: Diagnosis (N (%))	
M	13 (92.9)
.	1 (7.1)
INSS: Diagnosis (N (%))	
4	14 (100.0)
Relapse/Progressive (N (%))	
Relapsed	11 (78.6)
Progressive	3 (21.4)
Disease Confirmed by Biopsy (N (%))	
No	9 (64.3)
Yes	5 (35.7)

Baseline Characteristics - Neuroblastoma Patients

Diagnosis: Time to Registration (Months)	
N	14
Mean (sd)	49.8 (49.8)
Median	27.5
Range	4.1, 186.0
Age (Years)	
N	14
Mean (sd)	9.9 (5.5)
Median	10.3
Range	2.0, 18.8
Weight (Kg)	
N	14
Mean (sd)	35.5 (22.9)
Median	25.7
Range	12.0, 86.1
Bilirubin (umol/L)	
N	14
Mean (sd)	5.4 (2.3)
Median	5.0
Range	3.0, 11.0
ALT (U/L)	
N	14
Mean (sd)	39.9 (32.8)
Median	24.0
Range	13.0, 115.0

Neuroblastoma Patients

Latest Relapse: Time to Registration (Days)	
N	11
Mean (sd)	65.7 (106.1)
Median	26.0
Range	7.0, 370.0
Number of Relapses	
N	11
Mean (sd)	3.0 (1.4)
Median	3.0
Range	1.0, 6.0

Progression Details - Neuroblastoma Patients

Progression: Time to Registration (Days)	
N	3
Mean (sd)	65.3 (70.6)
Median	35.0
Range	15.0, 146.0

Group 3: Baseline Characteristics (Sarcoma Patients)

Baseline Characteristics - Sarcoma Patients

Gender (N (%))	
Male	8 (61.5)
Female	5 (38.5)
Sarcoma Type (N (%))	
Osteosarcoma	1 (7.7)
Ewing's	6 (46.2)
RMS	3 (23.1)
NRSTS	2 (15.4)
.	1 (7.7)
Tumour Site (N (%))	
Bone	6 (46.2)
Soft Tissue	7 (53.8)
Stage: Diagnosis (N (%))	
Localised	5 (38.5)
Metastatic	8 (61.5)
Metastatic Disease (N (%))	
No	1 (7.7)
Yes	12 (92.3)
Relapse/Progressive (N (%))	
Relapsed	8 (61.5)
Progressive	5 (38.5)
Disease Confirmed by Biopsy (N (%))	
No	10 (76.9)
Yes	2 (15.4)
.	1 (7.7)

NRSTS Specify - Sarcoma Patients

NRSTS Specify	
Synovial Sarcoma	1 (50.0)
.	1 (50.0)

Baseline Characteristics - Sarcoma Patients

Diagnosis: Time to Registration (Months)	
N	13
Mean (sd)	25.7 (11.1)
Median	26.3
Range	8.4, 40.6
Age (Years)	
N	13
Mean (sd)	10.5 (4.4)
Median	12.2
Range	1.3, 15.4
Weight (Kg)	
N	13
Mean (sd)	33.0 (16.2)
Median	31.5
Range	10.7, 58.0
Bilirubin (umol/L)	
N	13
Mean (sd)	7.2 (2.5)
Median	7.0
Range	4.0, 12.0
ALT (U/L)	
N	13
Mean (sd)	15.3 (5.2)
Median	14.0
Range	9.0, 25.0

Relapse Details - Sarcoma Patients

Latest Relapse: Time to Registration (Days)	
N	8
Mean (sd)	71.8 (145.9)
Median	17.0
Range	-41.0, 419.0
Number of Relapses	
N	8
Mean (sd)	3.1 (2.3)
Median	2.5
Range	1.0, 8.0

Progression Details - Sarcoma Patients

Progression: Time to Registration (Days)	
N	5
Mean (sd)	137.0 (127.3)
Median	200.0
Range	0.0, 273.0

Group 4: Baseline Characteristics (High Grade Glioma Patients)

Baseline Characteristics - HGG Patients

Gender (N (%))	
Male	7 (46.7)
Female	8 (53.3)
WHO Grade (N (%))	
III	1 (6.7)
IV	12 (80.0)
.	2 (13.3)
Disease Subtype (N (%))	
01: Anaplastic Astrocytoma, IDH-Mutant	1 (6.7)
02: Glioblastoma, IDH Wildtype	4 (26.7)
04: Diffuse Midline Glioma H3 K27M -mutant	9 (60.0)
.	1 (6.7)
Tumour Localisation (N (%))	
Brain	12 (80.0)
Spine	3 (20.0)
Metastases: Diagnosis (N (%))	
No	13 (86.7)
Yes	2 (13.3)
Relapse/Progressive (N (%))	
Relapsed	4 (26.7)
Progressive	11 (73.3)
Metastatic Disease (N (%))	
No	9 (60.0)
Yes	6 (40.0)
Disease Confirmed by Biopsy (N (%))	
No	11 (73.3)
Yes	3 (20.0)
.	1 (6.7)

Diagnosis Metastases - HGG Patients

Brain Metastases	Spine Metastases	Diffuse Lepto Metastases
Yes	No	No
Yes	No	No

Baseline Characteristics - HGG Patients

Diagnosis: Time to Registration (Months)	
N	15
Mean (sd)	22.0 (38.7)
Median	10.9
Range	3.5, 158.5
Age (Years)	
N	15
Mean (sd)	11.6 (4.5)
Median	12.0
Range	4.8, 20.0
Weight (Kg)	
N	15
Mean (sd)	41.0 (22.0)
Median	33.3
Range	19.4, 94.4
Bilirubin (umol/L)	
N	15
Mean (sd)	5.6 (2.4)
Median	6.0
Range	3.0, 10.0
ALT (U/L)	
N	15
Mean (sd)	23.8 (16.9)
Median	17.0
Range	7.0, 64.0

Relapse Details - HGG Patients

Latest Relapse: Time to Registration (Days)	
N	4
Mean (sd)	12.3 (4.6)
Median	12.0
Range	7.0, 18.0
Number of Relapses	
N	4
Mean (sd)	1.8 (0.5)
Median	2.0
Range	1.0, 2.0

Progression Details - HGG Patients

Progression: Time to Registration (Days)	
N	10
Mean (sd)	47.4 (87.4)
Median	13.5
Range	0.0, 284.0

Outcome Measures:

Primary outcome measure:

Phase I	
Phase I: the safe and optimal (in terms of arginine depletion) Recommended Phase 2 Dose (RP2D) of BCT-100 as determined by: 1. Safety profile as measured by the occurrence/non-occurrence of DLT within 28 days of treatment with BCT-100 2. Optimal dose as measured by the complete depletion of arginine. This is defined as AAD <8μM arginine in the blood after 3 doses of BCT-100	1600U/kg BCT-100
Phase II	
Disease response (Complete Response (CR) or Partial Response (PR)) after 8 weeks of treatment with BCT-100 as defined by:	
Group 1 (Leukaemia): CR, Complete response with incomplete count recovery (CRi), Complete response without platelet recovery (CRp; Acute Lymphoblastic Leukaemia (ALL) only), or PR determined by bone marrow, peripheral blood count/blasts and extramedullary disease (AML criteria based on Cheson et al 2003)	Non-responder 7 (100.0)
Group 2 (Neuroblastoma): CR/PR determined by cross-sectional imaging by CT or MRI, MIBG scan and bone marrow evaluation using the International Neuroblastoma Response Criteria (INRC)	Non-responder 12 (100.0)
Group 3 (Sarcoma): CR/PR determined by cross-sectional imaging by CT or MRI using RECIST version 1.1	Non-responder 13 (100.0)
Group 4 (High grade glioma): CR/PR determined by cross-sectional imaging by MRI using RANO criteria	Non-responder 13 (100.0)

Secondary outcome measures:

Incidence and severity of Adverse Events (AEs) defined by National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v4 as measured from the date of commencement of protocol defined treatment until 28 days after the administration of the last dose of trial treatment	See Adverse Event section
Disease response (CR / PR) at any time during treatment with BCT-100	
Group 1 (Leukaemia): CR, Complete response with incomplete count recovery (CRi), Complete response without platelet recovery (CRp; Acute Lymphoblastic Leukaemia (ALL) only), or PR determined by bone marrow, peripheral blood count/blasts and extramedullary disease (AML criteria based on Cheson et al 2003)	Non-responder 7 (100.0)
Group 2 (Neuroblastoma): CR/PR determined by cross-sectional imaging by CT or MRI, MIBG scan and bone	Non-responder 12 (100.0)

marrow evaluation using the International Neuroblastoma Response Criteria (INRC)	
Group 3 (Sarcoma): CR/PR determined by cross-sectional imaging by CT or MRI using RECIST version 1.1	Non-responder 13 (100.0)
Group 4 (High grade glioma): CR/PR determined by cross-sectional imaging by MRI using RANO criteria	Responder (PR) at week 16 : 1(7.7) Non-responder 12 (92.3)

Progression free survival, measured using follow up data (patients followed up for at least 1 year)	Presented below

Progression-Free survival - Estimates by disease group

Disease Type	Number of 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)	0.15 (0.02 – 0.39)	0.08 (0.005 – 0.29)
Overall	45	1.6 (1.0 – 1.8)	0.13 (0.05 – 0.25)	0.03 (0.008 – 0.13)

Overall survival, measured using follow up data (patients followed up for at least 1 year)	Presented below

Overall survival - Estimates by disease group

Disease Type	Number of 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)

PK profile of BCT-100 concentration in blood, bone marrow, and CSF	Not reportable. Unsolvable technical issues with the bespoke PK assay kit provided, PK profiles were not assessed.

Adverse Events:

In total, 46 patients experienced 222 types of toxicities amounting to 1,098 adverse events from grade 1 to 5

	Grade				
	1	**2**	**3**	**4**	**5**
Toxicity (No. events (No. patients that experienced toxicity))					
Blood and lymphatic system disorders					
Anemia	40 (21)	20 (12)	15 (10)	1 (1)	0 (0)
Platelet Count Decreased	17 (9)	8 (3)	18 (7)	17 (9)	0 (0)
White Blood Cell Count Decreased	34 (15)	12 (8)	9 (5)	2 (2)	0 (0)
Neutrophil Count Decreased	6 (4)	11 (7)	15 (7)	6 (4)	0 (0)
Hematocrit Decreased	22 (14)	0 (0)	0 (0)	0 (0)	0 (0)
Neutrophil Count Increased	16 (8)	0 (0)	1 (1)	0 (0)	0 (0)
Red Blood Cell Count Decreased	15 (9)	0 (0)	0 (0)	0 (0)	0 (0)
Platelet Count Increased	8 (5)	0 (0)	0 (0)	0 (0)	0 (0)
White Blood Cell Count Increased	6 (3)	0 (0)	0 (0)	0 (0)	0 (0)
Febrile Neutropenia	1 (1)	0 (0)	4 (4)	0 (0)	0 (0)
Red Blood Cell Count Increase	2 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Hypertension	0 (0)	2 (1)	0 (0)	0 (0)	0 (0)
Leukocytosis	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)
Enlarged Lymph Node	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Hematocrit Increased	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Cardiac disorders					
Tachycardia	5 (2)	1 (1)	0 (0)	0 (0)	0 (0)
Sinus Tachycardia	3 (3)	2 (2)	0 (0)	0 (0)	0 (0)
Cardiac Arrest	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Ear and labyrinth disorders					
Ear Pain	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Buzzing In Left Ear	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Endocrine disorders					
Cushingoid	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
TSH Level Decreased	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
FSH Level Decreased	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Adrenal Insufficiency	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)
LH Level Decreased	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Hypoparathyroidism	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Eye disorders					
Optic Nerve Disorder	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Blurred Vision	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Papilledema	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)

	Grade		
	1	2	3
Gastrointestinal disorders			
Vomiting	27 (13)	5 (5)	1 (1)
Constipation	9 (7)	10 (8)	0 (0)
Nausea	10 (5)	7 (6)	0 (0)
Diarrhoea	4 (4)	4 (3)	0 (0)
Dysphagia	0 (0)	2 (1)	4 (4)
Abdominal Pain	3 (2)	0 (0)	2 (2)
Stomach Pain	3 (3)	0 (0)	0 (0)
Oral Pain	0 (0)	2 (1)	0 (0)
Dyspepsia	1 (1)	1 (1)	0 (0)
Dry Mouth	1 (1)	0 (0)	0 (0)
Blood In Stool	0 (0)	1 (1)	0 (0)
Dental Caries	1 (1)	0 (0)	0 (0)
Bloating	1 (1)	0 (0)	0 (1)
Enterocolitis	0 (0)	1 (1)	0 (0)
Soft Stool	1 (1)	0 (0)	0 (0)
Crohn's Disease	0 (0)	1 (1)	0 (0)
Hypersalivation	0 (0)	1 (1)	0 (0)
General disorders and administration site conditions			
Fever	30 (16)	2 (2)	1 (1)
Pain	7 (6)	8 (6)	8 (8)
Fatigue	7 (6)	2 (2)	0 (0)
Runny Nose	4 (2)	0 (0)	0 (0)
Gait Disturbance	1 (1)	1 (1)	0 (0)
Weakness	0 (0)	1 (1)	0 (0)
Common Cold	1 (1)	0 (0)	0 (0)
Hypothermia	0 (0)	1 (1)	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)
Localized Edema	1 (1)	0 (0)	0 (0)
Edema Trunk	0 (0)	1 (1)	0 (0)
Immune system disorders			
Allergic Reaction	1 (1)	1 (1)	1 (1)

	Grade		
	1	2	3
Infections and infestations			
Urinary Tract Infection	0 (0)	0 (0)	4 (1)
Upper Respiratory Infection	2 (2)	1 (1)	1 (1)
Sepsis	0 (0)	0 (0)	3 (1)
COVID-19	2 (2)	0 (0)	0 (0)
Oral Fungal Infection	1 (1)	1 (1)	0 (0)
Common Cold? Virus Unknown	1 (1)	0 (0)	0 (0)
Rhinovirus	0 (0)	0 (0)	1 (1)
Blood - Staphylococcus Epidermidis	0 (0)	0 (0)	1 (1)
Unknown Viral Cough	1 (1)	0 (0)	0 (0)
Bacteremia	0 (0)	0 (0)	1 (1)
Nail Infection	0 (0)	1 (1)	0 (0)
Bacillus Cereus	0 (0)	0 (0)	1 (1)
Conjunctivitis	1 (1)	0 (0)	0 (0)
Hand Foot And Mouth	0 (0)	1 (1)	0 (0)
Herpetic Lip Lesions	0 (0)	1 (1)	0 (0)
Common Cold? No Virology Done	0 (0)	1 (1)	0 (0)
Injury, poisoning and procedural complications			
Bruising	2 (2)	1 (1)	0 (0)

	Grade			
	1	2	3	4
Investigations				
Lymphocyte Count Decreased	28 (15)	16 (13)	7 (7)	2 (2)
Alanine Aminotransferase Increased	22 (15)	2 (2)	1 (1)	1 (1)
Aspartate Aminotransferase Increased	16 (11)	2 (1)	3 (1)	0 (0)
Creatinine Decreased	19 (8)	0 (0)	0 (0)	0 (0)
Chloride High	13 (2)	0 (0)	0 (0)	0 (0)
Bicarbonate Low	8 (2)	0 (0)	0 (0)	0 (0)
Creatinine Increased	7 (4)	1 (1)	0 (0)	0 (0)
GGT Increased	3 (3)	3 (2)	1 (1)	0 (0)
Monocyte Count Increased	7 (5)	0 (0)	0 (0)	0 (0)
MCV Decrease	6 (5)	0 (0)	0 (0)	0 (0)
MCV Increase	6 (4)	0 (0)	0 (0)	0 (0)
CRP Increased	4 (2)	0 (0)	0 (0)	0 (0)
Eosinophils Decreased	4 (2)	0 (0)	0 (0)	0 (0)
Alkaline Phosphatase Increased	4 (4)	0 (0)	0 (0)	0 (0)
Lymphocyte Count Increased	0 (0)	2 (2)	1 (1)	0 (0)
Phosphate High	3 (2)	0 (0)	0 (0)	0 (0)
ALT Decreased	3 (2)	0 (0)	0 (0)	0 (0)
Creatinine Decrease	3 (1)	0 (0)	0 (0)	0 (0)
Weight Loss	2 (2)	1 (1)	0 (0)	0 (0)
Elevated Bicarbonate Levels	2 (1)	0 (0)	0 (0)	0 (0)
Mean Corpuscular Volume Decrease	2 (1)	0 (0)	0 (0)	0 (0)
Monocytes Low	2 (1)	0 (0)	0 (0)	0 (0)
Haemoglobin Increased	2 (1)	0 (0)	0 (0)	0 (0)
MCHC High	2 (1)	0 (0)	0 (0)	0 (0)
C-Reactive Protein Increase	1 (1)	1 (1)	0 (0)	0 (0)
Alkaline Phosphatase Decrease	1 (1)	0 (0)	0 (0)	0 (0)
Cholesterol High	0 (0)	1 (1)	0 (0)	0 (0)
INR Increased	0 (0)	0 (0)	1 (1)	0 (0)
Basophils High	1 (1)	0 (0)	0 (0)	0 (0)
Urine Output Decreased	0 (0)	0 (0)	1 (1)	0 (0)
Lactate Dehydrogenase Increase	1 (1)	0 (0)	0 (0)	0 (0)
Haemoglobin Low	1 (1)	0 (0)	0 (0)	0 (0)
Weight Gain	1 (1)	0 (0)	0 (0)	0 (0)
Mean Cell Haemoglobin Decrease	1 (1)	0 (0)	0 (0)	0 (0)
Activated Partial Thromboplastin Time Prolonged	0 (0)	1 (1)	0 (0)	0 (0)
Mean Cell Haemoglobin Increase	1 (1)	0 (0)	0 (0)	0 (0)
Chloride Increased	1 (1)	0 (0)	0 (0)	0 (0)
High Ferritine	0 (0)	1 (1)	0 (0)	0 (0)
Thrombin Time Increased	1 (1)	0 (0)	0 (0)	0 (0)
Increased Urine Output	0 (0)	1 (1)	0 (0)	0 (0)
Blood Prolactin Abnormal	1 (1)	0 (0)	0 (0)	0 (0)

	Grade		
	1	2	3
Metabolism and nutrition disorders			
Hypokalemia	23 (9)	2 (2)	5 (5)
Hypoalbuminemia	11 (8)	4 (4)	1 (1)
Hyponatremia	9 (7)	0 (0)	2 (2)
Hypomagnesemia	14 (8)	0 (0)	0 (0)
Hypophosphatemia	3 (2)	4 (4)	1 (1)
Hypernatremia	5 (5)	2 (2)	0 (0)
Anorexia	3 (2)	0 (0)	0 (0)
Blood Glucose Increased	2 (1)	0 (0)	0 (0)
Hypocalcemia	2 (2)	0 (0)	0 (0)
Hyperphosphatemia	2 (1)	0 (0)	0 (0)
Hyperuricemia	2 (2)	0 (0)	0 (0)
Dehydration	0 (0)	0 (0)	2 (2)
Chloride Levels Decreased	1 (1)	0 (0)	0 (0)
Increased Thirst	0 (0)	0 (0)	1 (1)
Hyperglycemia	0 (0)	1 (1)	0 (0)
Weight Gain	0 (0)	1 (1)	0 (0)
Hyperkalemia	1 (1)	0 (0)	0 (0)
Hypertriglyceridemia	0 (0)	0 (0)	1 (1)
Musculoskeletal and connective tissue disorders			
Muscle Weakness Left-Sided	1 (1)	2 (2)	2 (2)
Pain In Extremity	1 (1)	2 (2)	1 (1)
Generalized Muscle Weakness	0 (0)	1 (1)	2 (2)
Back Pain	2 (2)	0 (0)	1 (1)
Neck Pain	0 (0)	1 (1)	1 (1)
Muscle Weakness Lower Limb	0 (0)	0 (0)	1 (1)
Flank Pain	0 (0)	1 (1)	0 (0)
Pain In Right Shoulder	0 (0)	1 (1)	0 (0)
Myalgia	0 (0)	1 (1)	0 (0)
Muscle Weakness Right-Sided	0 (0)	0 (0)	1 (1)
Muscle Weakness Trunk	0 (0)	1 (1)	0 (0)
Joint Range Of Motion Decreased	1 (1)	0 (0)	0 (0)

	Grade			
	1	2	3	4
Nervous system disorders				
Headache	9 (6)	4 (3)	4 (4)	0 (0)
Lethargy	5 (4)	6 (5)	0 (0)	0 (0)
Dysarthria	2 (2)	2 (2)	3 (3)	0 (0)
Seizure	0 (0)	4 (4)	2 (1)	0 (0)
Hydrocephalus	0 (0)	1 (1)	1 (1)	1 (1)
Ataxia	1 (1)	1 (1)	1 (1)	0 (0)
Facial Muscle Weakness	1 (1)	1 (1)	0 (0)	0 (0)
Paresthesia	2 (2)	0 (0)	0 (0)	0 (0)
Left Sided Weakness - Hemiplegia	0 (0)	0 (0)	1 (1)	0 (0)
Spasticity	0 (0)	1 (1)	0 (0)	0 (0)
Sleep Disturbance - Wakes Early	1 (1)	0 (0)	0 (0)	0 (0)
Paraplegia	0 (0)	0 (0)	1 (1)	0 (0)
Bladder Emptying Disorder	0 (0)	0 (0)	1 (1)	0 (0)
Memory Impairment	0 (0)	1 (1)	0 (0)	0 (0)
Dysesthesia	1 (1)	0 (0)	0 (0)	0 (0)
Tremor	0 (0)	0 (0)	1 (1)	0 (0)
Imbalance	1 (1)	0 (0)	0 (0)	0 (0)
Somnolence	0 (0)	0 (0)	1 (1)	0 (0)
Spinal Cord Injury	0 (0)	0 (0)	1 (1)	0 (0)
Polydipsia	0 (0)	0 (0)	1 (1)	0 (0)
Dysphagia	0 (0)	1 (1)	0 (0)	0 (0)
Hypersomnia	1 (1)	0 (0)	0 (0)	0 (0)
Bowel Emptying Disorder	0 (0)	0 (0)	1 (1)	0 (0)
Dysgeusia	1 (1)	0 (0)	0 (0)	0 (0)
Intratumoural Haemorrage And Surrounding Cerebral Oedema	0 (0)	0 (0)	0 (0)	1 (1)
Dizziness	1 (1)	0 (0)	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 (0)	1 (1)	2 (2)	0 (0)
Libido Decreased	1 (1)	0 (0)	0 (0)	0 (0)
Low Mood	1 (1)	0 (0)	0 (0)	0 (0)
Euphoria	0 (0)	1 (1)	0 (0)	0 (0)
Restlessness	0 (0)	1 (1)	0 (0)	0 (0)

	Grade			
	1	2	3	4
Renal and urinary disorders				
Urea Increased	15 (8)	0 (0)	0 (0)	0 (0)
Urea Decreased	13 (7)	0 (0)	0 (0)	0 (0)
Urea Low	2 (1)	0 (0)	0 (0)	0 (0)
Acute Kidney Injury	1 (1)	0 (0)	1 (1)	0 (0)
Urinary Retention	0 (0)	1 (1)	0 (0)	0 (0)
Urea High	1 (1)	0 (0)	0 (0)	0 (0)
Urinary Incontinence	0 (0)	1 (1)	0 (0)	0 (0)
Cystitis Non-infective	1 (1)	0 (0)	0 (0)	0 (0)
Polyuria	0 (0)	0 (0)	1 (1)	0 (0)
Bladder Spasm	0 (0)	1 (1)	0 (0)	0 (0)
Bladder Perforation	0 (0)	0 (0)	1 (1)	0 (0)
Reproductive system and breast disorders				
Vaginal Pain	1 (1)	0 (0)	0 (0)	0 (0)
Respiratory, thoracic and mediastinal disorders				
Dyspnea	3 (3)	1 (1)	7 (5)	1 (1)
Cough	8 (6)	0 (0)	0 (0)	0 (0)
Hypoxia	0 (0)	1 (1)	3 (3)	0 (0)
Pleural Effusion	0 (0)	1 (1)	2 (2)	0 (0)
Sore Throat	2 (2)	0 (0)	0 (0)	0 (0)
Epistaxis	0 (0)	2 (2)	0 (0)	0 (0)
Respiratory Failure	0 (0)	0 (0)	0 (0)	1 (1)
Respiratory Distress	0 (0)	0 (0)	0 (0)	1 (1)
Pulmonary Edema	0 (0)	0 (0)	1 (1)	0 (0)
Runny Nose	1 (1)	0 (0)	0 (0)	0 (0)
Apnea	0 (0)	1 (1)	0 (0)	0 (0)
Skin and subcutaneous tissue disorders				
Rash Maculo-Papular	4 (4)	0 (0)	1 (1)	0 (0)
Alopecia	1 (1)	3 (3)	0 (0)	0 (0)
Pruritus	2 (2)	0 (0)	0 (0)	0 (0)
Itching	1 (1)	0 (0)	0 (0)	0 (0)
Photosensitivity	1 (1)	0 (0)	0 (0)	0 (0)
Skin Atrophy	0 (0)	1 (1)	0 (0)	0 (0)
Skin Ulceration	0 (0)	1 (1)	0 (0)	0 (0)
Blister On Abdomen	1 (1)	0 (0)	0 (0)	0 (0)
Rash-Graft Versus Host Disease	0 (0)	1 (1)	0 (0)	0 (0)
Shingles	0 (0)	1 (1)	0 (0)	0 (0)
Urticaria	1 (1)	0 (0)	0 (0)	0 (0)
Dry Skin	1 (1)	0 (0)	0 (0)	0 (0)

	Grade	
	1	2
Vascular disorders		
Hypertension	2 (2)	2 (2)
Hypotension	1 (1)	1 (1)
Flushing	1 (1)	0 (0)
Thromboembolic Event	0 (0)	1 (1)

Serious Adverse Events:

37 Serious Adverse Events (SAEs) were reported from patients on treatment

Disease Type	Toxicity	Grade	Reason	Category	Outcome	Sequel
High Grade Glioma	Upper respiratory infection	3	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
High Grade Glioma	Seizure	2	Hospitalisation	Non fatal/life-threatening SUSAR	Resolved - no sequelae	
Sarcoma	Headache	3	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Neuroblastoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Diarrhea	1	Hospitalisation	Unrelated SAE	Unresolved	
Sarcoma	Urinary tract infection	3	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Dyspnea	4	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Sarcoma	Dyspnea	4	Hospitalisation	Unrelated SAE	Resolved - with sequelae	Effusions still present and continued dyspnea
Leukaemia	Distress due to fluid overload	4	Hospitalisation	Unrelated SAE	Death	
Leukaemia	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
High Grade Glioma	Sinus tachycardia	2	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Leukaemia	Infusion related reaction	2	Medically significant, immediate action required	Unrelated SAE	Resolved - no sequelae	
Leukaemia	bacterienie	2	Antibiotics given, no admittance to hospital on inpatient basis	Unrelated SAE	Unresolved	
High Grade Glioma	Dyspnea	4	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
High Grade Glioma	Dyspnea	4	Hospitalisation	Unrelated SAE	Unresolved	
High Grade Glioma	Dyspnea	4	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
High Grade Glioma	Seizure	3	Deemed to be significant medical event - ?seizure followed by apnea requiring some resuscitation	Unrelated SAE	Resolved - no sequelae	
High Grade Glioma	Vomiting	2	Hospitalisation	Unrelated SAE	Unresolved	
High Grade Glioma	Vomiting	3	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Leukaemia	Sepsis	4	Hospitalisation	Unrelated SAE	Unresolved	
Neuroblastoma	respiratory arrest	4	Life-threatening	Unrelated SAE	Resolved - no sequelae	
High Grade Glioma	Fever	2	Hospitalisation	Unrelated SAE	Unresolved	
Neuroblastoma	Allergic reaction	2	Hospitalisation	Non fatal/life-threatening SUSAR	Resolved - no sequelae	
Leukaemia	Cardiac Arrest	5	Death	Unrelated SAE	Death	
Neuroblastoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Neuroblastoma	Bone pain	2	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Neuroblastoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Neuroblastoma	neck pain	2	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Neuroblastoma	Nausea	1	Hospitalisation	Unrelated SAE	Unresolved	
Neuroblastoma	Fever	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	
Neuroblastoma	Atrial ectopics	1	Hospitalisation	Unrelated SAE	Resolved - no sequelae	

One patient experienced an SAE prior to staring treatment

Disease Type	Category	Toxicity	Grade
High Grade Glioma	Renal and urinary disorders	Polyuria Polydispsia	3