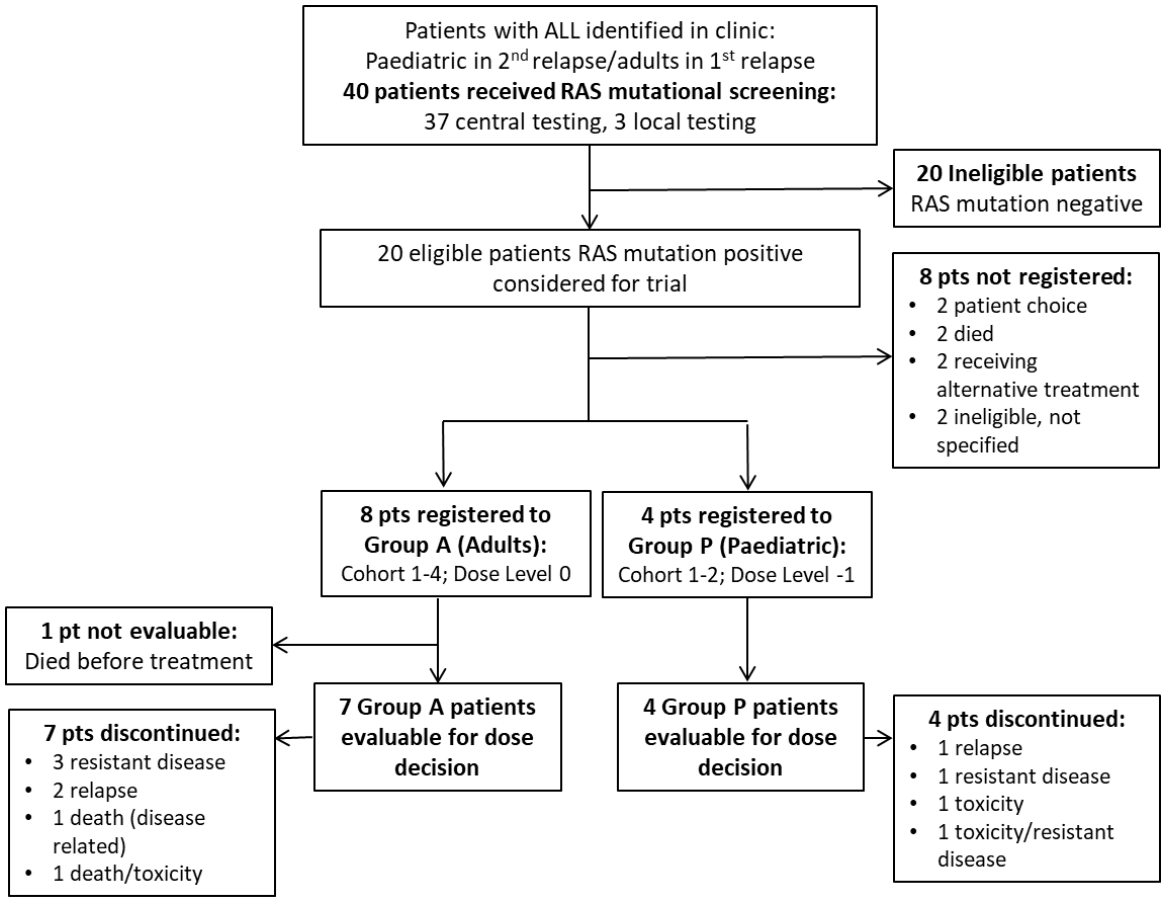
Participant Flow



# 1. Baseline Characteristics

**Table 1: Baseline Characteristics**

| Characteristic | | Number of Patients | | |
|---|---|---|---|---|
| | | Group A N=8 | Group P N=4 | Total N=12 |
| **Sex (%)** | | | | |
| | Male | 7 (88) | 1 (25) | 10 (83) |
| | Female | 1 (13) | 3 (75) | 2 (17) |
| **Age (years)** | | | | |
| | Mean (sd) | 50 (23) | 10 (3) | 36 (27) |
| | Median | 58 | 10 | 25 |
| | IQR | 25, 69 | 7, 12 | 12, 68 |
| | Range | 21, 73 | 5, 13 | 5, 73 |
| **Ethnicity (%)** | | | | |
| | Any other Asian background | 1 (13) | 0 | 1 (8.3) |
| | Any other ethnic group | 1 (13) | 0 | 1 (8.3) |
| | Arab | 0 | 1 (25) | 1 (8.3) |
| | Bangladeshi | 1 (13) | 0 | 1 (8.3) |
| | Caribbean | 0 | 1 (25) | 1 (8.3) |
| | English/Welsh/Scottish/Northern Irish/British | 5 (63) | 2 (50) | 7 (58) |
| **ECOG Performance Status (%)** | | | | |
| | 0 | 1 (17) | 0 | 1 (17) |
| | 1 | 4 (67) | 0 | 4 (67) |
| | 2 | 1 (17) | 0 | 1 (17) |
| | Unknown | 2 | 4 | 6 |
| **Current ALL disease status (%)** | | | | |
| | Progressive | 1 (13) | 0 | 1 (8.3) |
| | Refractory | 2 (25) | 0 | 2 (17) |
| | Relapsed | 5 (63) | 4 (100) | 9 (75) |
| | Total | 8 | 4 | 12 |
| **CNS disease status at diagnosis (%)** | | | | |
| | CNS1 | 4 (80) | 3 (75) | 7 (78) |
| | CNS2 | 1 (20) | 0 | 1 (11) |
| | CNS3 | 0 | 1 (25) | 1 (11) |
| | Unknown | 3 | 0 | 3 |
| **Previously received CAR T cell therapy (%)** | | | | |
| | No | 7 (88) | 2 (50) | 9 (75) |
| | Yes | 1 (13) | 2 (50) | 3 (25) |

| Characteristic | | Number of Patients | | |
|---|---|---|---|---|
| | | Group A N=8 | Group P N=4 | Total N=12 |
| **Previously received HSCT (%)** | | | | |
| | No | 7 (88) | 0 | 7 (58) |
| | Yes | 1 (13) | 4 (100) | 5 (42) |
| **ALL classification (%)** | | | | |
| | B-cell precursor ALL | 2 (25) | 4 (100) | 6 (50) |
| | T-ALL | 6 (75) | 0 | 6 (50) |
| **Bone marrow blast score (%)** | | | | |
| | M2 | 1 (14) | 1 (25) | 2 (18) |
| | M3 | 6 (86) | 3 (75) | 9 (82) |
| | Unknown | 1 | 0 | 1 |
| **Cellularity (%)** | | | | |
| | Hypercellular | 3 (50) | 2 (50) | 5 (50) |
| | Hypocellular | 0 | 2 (50) | 2 (20) |
| | Normocellular | 3 (50) | 0 | 3 (30) |
| | Unknown | 2 | 0 | 2 |
| **CNS disease classification in CSF (%)** | | | | |
| | CNS1 | 7 (100) | 3 (75) | 10 (91) |
| | CNS3 | 0 | 1 (25) | 1 (9.1) |
| | Unknown | 1 | 0 | 0 |
| **Weight (kg)** | | | | |
| | Mean (sd) | 84 (22) | 38 (14) | 69 (29) |
| | Median | 81 | 35 | 67 |
| | IQR | 67, 94 | 28, 49 | 49, 87 |
| | Range | 56, 128 | 27, 57 | 27, 128 |
| **Height (metre)** | | | | |
| | Mean (sd) | 1.75 (0.09) | 1.41 (0.17) | 1.64 (0.20) |
| | Median | 1.74 | 1.45 | 1.71 |
| | IQR | 1.71, 1.82 | 1.30, 1.52 | 1.52, 1.77 |
| | Range | 1.60, 1.89 | 1.17, 1.57 | 1.17, 1.89 |
| **Body Surface Area** | | | | |
| | Mean (sd) | 2.00 (0.30) | 1.24 (0.28) | 1.75 (0.47) |
| | Median | 1.97 | 1.19 | 1.79 |
| | IQR | 1.79, 2.13 | 1.02, 1.45 | 1.45, 2.01 |
| | Range | 1.65, 2.60 | 0.96, 1.60 | 0.96, 2.60 |

# 2. Outcome Measures

## 2.1 Primary Outcome

### 2.1.1 Dose Limiting Toxicities and Continual Reassessment Model (CRM) Dose Decision

**Table 2: Patient dose allocations and outcome.**

| Group | Cohort | Dose Level | Selumetinib Dose | DLT |
|---|---|---|---|---|
| A | 1 | 0 | 75mg | No |
| A | 1 | 0 | 75mg | No |
| A | 2 | 0 | 75mg | No |
| A | 2 | 0 | 75mg | Yes |
| A | 3 | 0 | 75mg | No |
| A | 3 | 0 | 75mg | No |
| A | 4 | 0 | 75mg | No |
| P | 1 | -1 | 20mg/m$^2$ | No |
| P | 1 | -1 | 20mg/m$^2$ | Yes |
| P | 2 | -1 | 20mg/m$^2$ | No |
| P | 2 | -1 | 20mg/m$^2$ | No |

Each row of the table represents an individual patient.

**Table 3: Prior and final posterior probabilities of DLTs in Groups A and P.**

| Group | Dose Level | Prior Prob (DLT) | Number of Evaluable Patients | Number of DLTS | Posterior Prob (DLT) |
|---|---|---|---|---|---|
| A | -1 | 0.03 | 0 | 0 | 0.031 (0.001, 0.192) |
| A | 0 | 0.15 | 7 | 1 | 0.154 (0.02, 0.41) |
| A | 1 | 0.27 | 0 | 0 | 0.275 (0.067, 0.54) |
| P | -1 | 0.03 | 4 | 1 | 0.207 (0.022, 0.52) |
| P | 0 | 0.15 | 0 | 0 | 0.426 (0.128, 0.702) |
| P | 1 | 0.27 | 0 | 0 | 0.555 (0.242, 0.784) |

## 2.2 Secondary Outcomes

### 2.2.1 Pharmacokinetics (PK)

**Table 4: Pharmacokinetic results by Group for selumetinib in combination with dexamethasone at Cycle 1 Day 4.**

| | Group A<br>N=7 | Group P<br>N=4 | Overall<br>N=11 |
|---|---|---|---|
| **AUC** | | | |
| Median (Q1, Q3) | 4,514 (3,586, 5,270) | 1,407 (588, 2,226) | 4,017 (2,666, 4,925) |
| Mean (SD) | 4,418 (936) | 1,407 (1,158) | 3,665 (1,662) |
| Min, Max | 3,105, 5,520 | 588, 2,226 | 588, 5,520 |
| Unknown | 1 | 2 | 3 |
| **Cmax** | | | |
| Median (Q1, Q3) | 1,470 (1,000, 2,080) | 474 (237, 711) | 1,450 (711, 1,632) |
| Mean (SD) | 1,512 (577) | 474 (335) | 1,281 (688) |
| Min, Max | 642, 2,310 | 237, 711 | 237, 2,310 |
| Unknown | 0 | 2 | 2 |
| **Tmax** | | | |
| Median (Q1, Q3) | 1.00 (1.00, 1.10) | 1.95 (1.90, 2.00) | 1.00 (1.00, 1.80) |
| Mean (SD) | 1.11 (0.31) | 1.95 (0.07) | 1.30 (0.46) |
| Min, Max | 0.90, 1.80 | 1.90, 2.00 | 0.90, 2.00 |
| Unknown | 0 | 2 | 2 |
| **THalf** | | | |
| Median (Q1, Q3) | 1.95 (1.70, 2.10) | 1.30 (1.20, 1.40) | 1.80 (1.35, 2.05) |
| Mean (SD) | 1.85 (0.31) | 1.30 (0.14) | 1.71 (0.37) |
| Min, Max | 1.30, 2.10 | 1.20, 1.40 | 1.20, 2.10 |
| Unknown | 1 | 2 | 3 |

**Table 5: Pharmacokinetic results by Group for selumetinib in combination with dexamethasone at Cycle 2 Day 1.**

| | Group A<br>N=5 | Group P<br>N=3 | Overall<br>N=8 |
|---|---|---|---|
| **AUC** | | | |
| Median (Q1, Q3) | 5,265 (2,962, 5,576) | 1,426 (720, 2,801) | 2,882 (1,799, 5,421) |
| Mean (SD) | 4,872 (2,447) | 1,649 (1,058) | 3,664 (2,554) |
| Min, Max | 2,171, 8,387 | 720, 2,801 | 720, 8,387 |
| **Cmax** | | | |
| Median (Q1, Q3) | 1,020 (777, 1,130) | 610 (137, 798) | 788 (670, 1,075) |
| Mean (SD) | 1,097 (442) | 515 (341) | 879 (485) |
| Min, Max | 730, 1,830 | 137, 798 | 137, 1,830 |
| **Tmax** | | | |
| Median (Q1, Q3) | 1.00 (1.00, 2.00) | 1.90 (0.90, 2.00) | 1.45 (1.00, 2.00) |
| Mean (SD) | 1.80 (1.30) | 1.60 (0.61) | 1.73 (1.04) |
| Min, Max | 1.00, 4.00 | 0.90, 2.00 | 0.90, 4.00 |
| **THalf** | | | |

| | | | |
|---|---|---|---|
| Median (Q1, Q3) | 2.30 (2.00, 2.90) | 2.60 (1.40, 3.10) | 2.45 (1.90, 3.00) |
| Mean (SD) | 2.50 (0.70) | 2.37 (0.87) | 2.45 (0.71) |
| Min, Max | 1.80, 3.50 | 1.40, 3.10 | 1.40, 3.50 |

**Table 6: Pharmacokinetic results by Group for selumetinib alone at Cycle 1 Day 1.**

| | **Group A** | **Group P** | **Overall** |
|---|---|---|---|
| | N=7 | N=4 | N=11 |
| **AUC** | | | |
| Median (Q1, Q3) | 4,698 (2,933, 6,843) | 1,199 (645, 1,257) | 3,192 (1,257, 5,335) |
| Mean (SD) | 4,786 (1,854) | 1,034 (338) | 3,661 (2,367) |
| Min, Max | 2,815, 7,429 | 645, 1,257 | 645, 7,429 |
| Unknown | 0 | 1 | 1 |
| **Cmax** | | | |
| Median (Q1, Q3) | 891 (763, 1,430) | 308 (214, 487) | 802 (487, 977) |
| Mean (SD) | 1,020 (331) | 336 (139) | 815 (432) |
| Min, Max | 699, 1,540 | 214, 487 | 214, 1,540 |
| Unknown | 0 | 1 | 1 |
| **Tmax** | | | |
| Median (Q1, Q3) | 1.10 (1.00, 2.00) | 1.00 (0.90, 1.80) | 1.05 (1.00, 2.00) |
| Mean (SD) | 1.44 (0.52) | 1.23 (0.49) | 1.38 (0.50) |
| Min, Max | 1.00, 2.00 | 0.90, 1.80 | 0.90, 2.00 |
| Unknown | 0 | 1 | 1 |
| **THalf** | | | |
| Median (Q1, Q3) | 6.50 (4.50, 6.80) | 4.00 (1.40, 7.60) | 6.40 (4.00, 6.80) |
| Mean (SD) | 6.04 (1.33) | 4.33 (3.11) | 5.53 (2.01) |
| Min, Max | 3.90, 7.60 | 1.40, 7.60 | 1.40, 7.60 |
| Unknown | 0 | 1 | 1 |

**Table 7: Pharmacokinetic results by Group for dexamethasone at Cycle 1 Day 4.**

| | **Group A** | **Group P** | **Overall** |
|---|---|---|---|
| | N=7 | N=3 | N=10 |
| **AUC** | | | |
| Median (Q1, Q3) | 1,187 (663, 1,379) | 389 (388, 389) | 663 (389, 1,379) |
| Mean (SD) | 1,055 (454) | 389 (1) | 865 (493) |
| Min, Max | 500, 1,546 | 388, 389 | 388, 1,546 |
| Unknown | 2 | 1 | 3 |
| **Cmax** | | | |
| Median (Q1, Q3) | 114 (94, 151) | 94 (78, 110) | 110 (94, 133) |
| Mean (SD) | 116 (41) | 94 (23) | 111 (38) |
| Min, Max | 47, 174 | 78, 110 | 47, 174 |
| Unknown | 0 | 1 | 1 |
| **Tmax** | | | |
| Median (Q1, Q3) | 2.50 (0.90, 4.10) | 1.50 (1.10, 1.90) | 2.00 (1.10, 3.80) |
| Mean (SD) | 3.11 (2.54) | 1.50 (0.57) | 2.76 (2.32) |

| | | | |
|---|---|---|---|
| Min, Max | 0.50, 8.00 | 1.10, 1.90 | 0.50, 8.00 |
| Unknown | 0 | 1 | 1 |
| **THalf** | | | |
| Median (Q1, Q3) | 6.80 (4.50, 7.00) | 2.45 (2.30, 2.60) | 4.50 (2.30, 7.00) |
| Mean (SD) | 6.08 (3.09) | 2.45 (0.21) | 5.04 (3.09) |
| Min, Max | 1.90, 10.20 | 2.30, 2.60 | 1.90, 10.20 |
| Unknown | 2 | 1 | 3 |

**Table 8: Pharmacokinetic results by Group for dexamethasone at Cycle 2 Day 1.**

| | **Group A** | **Group P** | **Overall** |
|---|---|---|---|
| | N=5 | N=3 | N=8 |
| **AUC** | | | |
| Median (Q1, Q3) | 286 (286, 286) | 291 (239, 342) | 286 (239, 342) |
| Mean (SD) | 286 (NA) | 291 (73) | 289 (52) |
| Min, Max | 286, 286 | 239, 342 | 239, 342 |
| Unknown | 4 | 1 | 5 |
| **Cmax** | | | |
| Median (Q1, Q3) | 42 (34, 46) | 67 (22, 74) | 44 (28, 64) |
| Mean (SD) | 40 (17) | 54 (29) | 45 (21) |
| Min, Max | 16, 62 | 22, 74 | 16, 74 |
| **Tmax** | | | |
| Median (Q1, Q3) | 2.00 (1.00, 7.70) | 1.00 (0.90, 1.00) | 1.00 (1.00, 4.85) |
| Mean (SD) | 3.94 (3.59) | 0.97 (0.06) | 2.83 (3.12) |
| Min, Max | 1.00, 8.00 | 0.90, 1.00 | 0.90, 8.00 |
| **THalf** | | | |
| Median (Q1, Q3) | 2.50 (2.50, 2.50) | 2.60 (2.30, 2.90) | 2.50 (2.30, 2.90) |
| Mean (SD) | 2.50 (NA) | 2.60 (0.42) | 2.57 (0.31) |
| Min, Max | 2.50, 2.50 | 2.30, 2.90 | 2.30, 2.90 |
| Unknown | 4 | 1 | 5 |

**Table 9: Absolute and percentage difference in AUC for selumetinib single agent and in combination with dexamethasone.**

| Group | AUC - single agent | AUC | Difference | % Difference | AUC | Difference | % Difference |
|---|---|---|---|---|---|---|---|
| A | 7429 | 4447 | -2982 | 60 | 5576 | -1853 | 75 |
| A | 2815 | 3105 | 290 | 110 | 2171 | -644 | 77 |
| A | 2933 | 3586 | 653 | 122 | 2962 | 29 | 101 |
| A | 4698 | 4580 | -118 | 97 | | | |
| P | 645 | | | | 720 | 75 | 112 |
| P | | 2226 | | | | | |
| A | 6843 | 5270 | -1573 | 77 | 5265 | -1578 | 77 |
| A | 3451 | 5520 | 2069 | 160 | 8387 | 4936 | 243 |
| A | 5335 | | | | | | |
| P | 1199 | 588 | -611 | 49 | 2801 | 1602 | 234 |
| P | 1257 | | | | 1426 | 169 | 113 |

Each row of the table represents an individual patient.

### 2.2.2 Response

**Table 10: Response at Cycle 1 Day 28 for each patient.**

| Group | Cohort | Dose Level | Response |
|---|---|---|---|
| A | 1 | 0 | NR |
| A | 1 | 0 | NR |
| A | 2 | 0 | CRi |
| A | 3 | 0 | CRi |
| A | 3 | 0 | CR |
| A | 4 | 0 | NR |
| P | 1 | -1 | NR |
| P | 2 | -1 | CR |
| P | 2 | -1 | NR |

Each row of the table represents an individual patient.

Complete remission (CR); Complete remission with incomplete platelet recovery (CRi); Partial remission (PR); No response (NR)

**Table 11: Summary of response at Cycle 1 Day 28.**

| Response | Group A (%) | Group P (%) | Total (%) |
|---|---|---|---|
| n | 6 | 3 | 9 |
| NR | 3 (50) | 2 (67) | 5 (56) |
| PR | 0 | 0 | 0 |
| CRi | 2 (33) | 0 | 2 (22) |
| CR | 1 (17) | 1 (33) | 2 (22) |

## 2.3 Tertiary Outcomes

- **Exploratory pharmacodynamic (PD) biomarker studies will be undertaken if clinical responses are observed.**
  Due to the early stopping of the trial and a lack of patient samples, the data required for assessing the pharmacodynamic effects was unavailable.

## 3. Adverse Events

**Table 12: Adverse events by group according to CTCAE v4.0 category and term**

| | | Number of Events (Patients Affected) | | |
|---|---|---|---|---|
| **Category** | **Term** | **Group A** | **Group P** | **Total** |
| Blood and lymphatic system disorders | Alt increase | 4 (1) | 0 (0) | 4 (1) |
| | Anemia | 28 (4) | 14 (3) | 42 (7) |
| | Cytopenia | 1 (1) | 0 (0) | 1 (1) |
| | Deranged clotting | 0 (0) | 2 (1) | 2 (1) |
| | Febrile neutropenia | 5 (2) | 12 (2) | 17 (4) |
| | Ggt | 4 (1) | 0 (0) | 4 (1) |
| | Thrombotic thrombocytopenic purpura | 0 (0) | 1 (1) | 1 (1) |
| Cardiac disorders | Heart failure | 1 (1) | 0 (0) | 1 (1) |
| | Pericardial effusion | 0 (0) | 1 (1) | 1 (1) |
| | Sinus bradycardia | 0 (0) | 1 (1) | 1 (1) |
| | Sinus tachycardia | 0 (0) | 1 (1) | 1 (1) |
| Endocrine disorders | Cushingoid | 11 (1) | 0 (0) | 11 (1) |
| Eye disorders | Conjunctivitis | 4 (1) | 0 (0) | 4 (1) |
| | Papilledema | 0 (0) | 1 (1) | 1 (1) |
| Gastrointestinal disorders | Abdominal pain | 2 (2) | 3 (2) | 5 (4) |
| | Anal pain | 6 (1) | 0 (0) | 6 (1) |
| | Bloating | 1 (1) | 0 (0) | 1 (1) |
| | Constipation | 12 (1) | 1 (1) | 13 (2) |
| | Diarrhea | 5 (2) | 3 (2) | 8 (4) |
| | Dyspepsia | 0 (0) | 3 (2) | 3 (2) |
| | Esophagitis | 0 (0) | 1 (1) | 1 (1) |
| | Hard stool | 1 (1) | 0 (0) | 1 (1) |
| | Increased appetite | 0 (0) | 1 (1) | 1 (1) |
| | Malabsorption | 0 (0) | 10 (1) | 10 (1) |
| | Mucositis oral | 0 (0) | 9 (1) | 9 (1) |
| | Nausea | 1 (1) | 2 (1) | 3 (2) |
| | Stomach pain | 0 (0) | 1 (1) | 1 (1) |
| | Vomiting | 3 (3) | 2 (1) | 5 (4) |
| General disorders and administration site conditions | Edema face | 1 (1) | 0 (0) | 1 (1) |
| | Edema limbs | 7 (3) | 0 (0) | 7 (3) |
| | Fatigue | 15 (4) | 0 (0) | 15 (4) |
| | Fever | 10 (3) | 6 (2) | 16 (5) |
| | Irritability | 0 (0) | 1 (1) | 1 (1) |
| | Pain | 0 (0) | 10 (2) | 10 (2) |
| Hepatobiliary disorders | Jaundice | 0 (0) | 1 (1) | 1 (1) |
| | Liver dysfunction | 0 (0) | 2 (1) | 2 (1) |
| Infections and infestations | Bacteremia | 0 (0) | 1 (1) | 1 (1) |
| | Buttock abscess | 6 (1) | 0 (0) | 6 (1) |

| | | | | |
|---|---|---|---|---|
| | Catheter related infection | 0 (0) | 1 (1) | 1 (1) |
| | Lung infection | 1 (1) | 1 (1) | 2 (2) |
| | Mouth ulcer | 0 (0) | 1 (1) | 1 (1) |
| | Mouth ulcers - possible viral | 1 (1) | 0 (0) | 1 (1) |
| | Mucosal infection | 0 (0) | 1 (1) | 1 (1) |
| | Oral infection: candidiasis | 0 (0) | 1 (1) | 1 (1) |
| | Oropharyngeal candidiasis | 1 (1) | 0 (0) | 1 (1) |
| | Papulopustular rash | 1 (1) | 0 (0) | 1 (1) |
| | Paronychia | 6 (1) | 0 (0) | 6 (1) |
| | Sepsis | 1 (1) | 3 (2) | 4 (3) |
| | Sepsis due to relapsed all | 1 (1) | 0 (0) | 1 (1) |
| | Upper respiratory infection | 0 (0) | 1 (1) | 1 (1) |
| | Urinary tract infection | 7 (1) | 0 (0) | 7 (1) |
| Injury, poisoning and procedural complications | Bruising | 0 (0) | 5 (2) | 5 (2) |
| Investigations | Alanine aminotransferase increased | 8 (2) | 16 (1) | 24 (3) |
| | Aspartate aminotransferase increased | 1 (1) | 11 (1) | 12 (2) |
| | Blood bilirubin increased | 1 (1) | 8 (2) | 9 (3) |
| | Electrolyte disturbance | 0 (0) | 1 (1) | 1 (1) |
| | GGT increased | 6 (1) | 0 (0) | 6 (1) |
| | Ldh increased | 2 (1) | 0 (0) | 2 (1) |
| | Lymphocyte count decreased | 0 (0) | 13 (1) | 13 (1) |
| | Neutrophil count decreased | 4 (1) | 10 (1) | 14 (2) |
| | Platelet count decreased | 18 (3) | 11 (2) | 29 (5) |
| | Weight gain | 1 (1) | 0 (0) | 1 (1) |
| | White blood cell decreased | 5 (1) | 10 (1) | 15 (2) |
| | White cell count increased | 2 (1) | 0 (0) | 2 (1) |
| Metabolism and nutrition disorders | Hyperglycemia | 19 (1) | 0 (0) | 19 (1) |
| | Hypoalbuminemia | 0 (0) | 6 (1) | 6 (1) |
| | Hypokalemia | 0 (0) | 7 (1) | 7 (1) |
| | Hypomagnesemia | 0 (0) | 7 (1) | 7 (1) |
| | Hyponatremia | 14 (2) | 2 (1) | 16 (3) |
| | Hypophosphatemia | 0 (0) | 10 (1) | 10 (1) |
| | Reduced oral intake | 0 (0) | 1 (1) | 1 (1) |
| Musculoskeletal and connective tissue disorders | Back pain | 1 (1) | 0 (0) | 1 (1) |
| | Bone pain | 0 (0) | 2 (1) | 2 (1) |
| | Generalized muscle weakness | 1 (1) | 0 (0) | 1 (1) |
| | Mild cramps in hand | 3 (1) | 0 (0) | 3 (1) |
| | Muscle weakness lower limb | 11 (1) | 0 (0) | 11 (1) |
| | Myalgia | 0 (0) | 1 (1) | 1 (1) |
| | Proximal myopathy | 5 (1) | 0 (0) | 5 (1) |
| | Shoulder pain | 3 (1) | 0 (0) | 3 (1) |
| | Headache | 3 (1) | 1 (1) | 4 (2) |

| | | | | |
|---|---|---|---|---|
| Nervous system disorders | Hydrocephalus | 0 (0) | 1 (1) | 1 (1) |
| | Lethargy | 0 (0) | 1 (1) | 1 (1) |
| | Peripheral motor neuropathy | 1 (1) | 0 (0) | 1 (1) |
| | Peripheral sensory neuropathy | 15 (1) | 0 (0) | 15 (1) |
| | Proximal myopathy | 1 (1) | 0 (0) | 1 (1) |
| | Syncope | 1 (1) | 0 (0) | 1 (1) |
| | Tremor | 1 (1) | 0 (0) | 1 (1) |
| Psychiatric disorders | Anxiety | 0 (0) | 1 (1) | 1 (1) |
| | Euphoria | 1 (1) | 0 (0) | 1 (1) |
| | Insomnia | 1 (1) | 0 (0) | 1 (1) |
| | Low mood | 1 (1) | 0 (0) | 1 (1) |
| Renal and urinary disorders | Jaundice | 0 (0) | 1 (1) | 1 (1) |
| | Proteinuria | 0 (0) | 2 (1) | 2 (1) |
| | Renal dysfunction | 0 (0) | 2 (1) | 2 (1) |
| | Urinary tract pain | 3 (1) | 0 (0) | 3 (1) |
| Respiratory, thoracic and mediastinal disorders | Cough | 5 (1) | 0 (0) | 5 (1) |
| | Dyspnea | 4 (3) | 0 (0) | 4 (3) |
| | Epistaxis | 0 (0) | 2 (2) | 2 (2) |
| | Oesophagitis | 0 (0) | 1 (1) | 1 (1) |
| | Right sided pneumonia | 2 (1) | 0 (0) | 2 (1) |
| Skin and subcutaneous tissue disorders | Acne | 4 (1) | 0 (0) | 4 (1) |
| | Alopecia | 6 (2) | 0 (0) | 6 (2) |
| | Buccal mucosa erythema | 0 (0) | 1 (1) | 1 (1) |
| | Dry ski | 0 (0) | 1 (1) | 1 (1) |
| | Face and neck red | 1 (1) | 0 (0) | 1 (1) |
| | Folliculitis | 4 (1) | 0 (0) | 4 (1) |
| | Petechial rash | 1 (1) | 0 (0) | 1 (1) |
| | Pressure sore | 0 (0) | 1 (1) | 1 (1) |
| | Pruritus | 1 (1) | 1 (1) | 2 (2) |
| | Rash maculo-papular | 10 (3) | 1 (1) | 11 (4) |
| Vascular disorders | Hypertension | 2 (1) | 0 (0) | 2 (1) |
| | Hypotension | 0 (0) | 3 (1) | 3 (1) |
| | Vascular access complication | 1 (1) | 0 (0) | 1 (1) |

**Table 13: Serious Adverse Events category, outcome and expectedness information by treatment group**

| | Number of Events (%) | | |
|---|---|---|---|
| | **Group A** | **Group P** | **Total** |
| **Serious Adverse Event Category** | | | |
| Unrelated SAE | 3 (30) | 2 (33) | 5 (31) |
| SAR | 2 (20) | 2 (33) | 4 (25) |
| Non-fatal/life-threatening SUSAR | 4 (40) | 0 | 4 (25) |
| Fatal/life-threatening SUSAR | 1 (10) | 2 (33) | 3 (19) |
| **Total** | **10** | **6** | **16** |
| **Outcome** | | | |
| Unresolved | 2 (29) | 0 | 2 (17) |
| Resolved – no sequelae | 4 (57) | 3 (60) | 7 (58) |
| Resolved – with sequelae | 1 (14) | 2 (40) | 3 (25) |
| Unknown | 3 | 1 | 4 |
| **Total** | **10** | **6** | **16** |