**Table 2.**  Adverse events that either occurred in >10% of patients at any grade, or occurred at grade ≥3 in patients with relapsed or refractory Ewing sarcoma and osteosarcoma treated with the combination of cabozantinib, topotecan and cyclophosphamide (n=12). Adverse events considered unrelated or unlikely related to protocol therapy are excluded.

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| --- | --- | --- | --- |
|  |  | **Any grade**  **(n=12)** | **Grade 3 or 4\***  **(n=12)** |
| Category | Toxicity | n (%) | n (%) |
| Blood and lymphatic system disorders | Anemia | 12 (100) | 9 (75) |
| Febrile neutropenia | 3 (25) | 3 (25) |
| Cardiac disorders | Sinus tachycardia | 10 (83.3) | 0 (0) |
| Gastrointestinal disorders | Constipation | 6 (50) | 0 (0) |
| Diarrhea | 6 (50) | 0 (0) |
| Dyspepsia | 2 (16.7) | 0 (0) |
| Nausea | 12 (100) | 0 (0) |
| Vomiting | 8 (66.7) | 0 (0) |
| Abdominal pain | 5 (41.7) | 0 (0) |
| Mucositis oral | 3 (25) | 0 (0) |
| Typhlitis | 1 (8.3) | 1 (8.3) |
| Oral pain | 2 (16.7) | 0 (0) |
| General disorders and administration site conditions | Fatigue | 10 (83.3) | 0 (0) |
| Pain | 5 (41.7) | 0 (0) |
| Edema limbs | 3 (25) | 0 (0) |
| Fever | 3 (25) | 0 (0) |
| Injury, poisoning and procedural complications | Bruising | 4 (33.3) | 0 (0) |
| Investigations | Alanine aminotransferase increased | 9 (75) | 0 (0) |
| Alkaline phosphatase increased | 8 (66.7) | 0 (0) |
| Lymphocyte count decreased | 12 (100) | 11 (91.7) |
| Neutrophil count decreased | 12 (100) | 11 (91.7) |
| Platelet count decreased | 12 (100) | 11 (91.7) |
| Weight loss | 3 (25) | 0 (0) |
| White blood cell decreased | 12 (100) | 11 (91.7) |
| EKG QT corrected interval prolonged | 3 (25) | 0 (0) |
| Activated partial thromboplastin time prolonged | 3 (25) | 0 (0) |
| Aspartate aminotransferase increased | 5 (41.7) | 0 (0) |
| Blood lactate dehydrogenase increased | 3 (25) | 0 (0) |
| Thyroid stimulating hormone increased | 3 (25) | 0 (0) |
| Blood bicarbonate decreased | 5 (41.7) | 0 (0) |
| Metabolism and nutrition disorders | Anorexia | 9 (75) | 0 (0) |
| Hypocalcemia | 4 (33.3) | 0 (0) |
| Hypokalemia | 2 (16.7) | 0 (0) |
| Hyponatremia | 5 (41.7) | 0 (0) |
| Hyperglycemia | 2 (16.7) | 0 (0) |
| Hypoalbuminemia | 3 (25) | 0 (0) |
| Hypophosphatemia | 3 (25) | 0 (0) |
| Hypermagnesemia | 2 (16.7) | 0 (0) |
| Hyperkalemia | 3 (25) | 0 (0) |
| Hyperphosphatemia | 2 (16.7) | 0 (0) |
| Musculoskeletal and connective tissue disorders | Pain in extremity | 2 (16.7) | 0 (0) |
| Back pain | 2 (16.7) | 0 (0) |
| Muscle cramp | 3 (25) | 0 (0) |
| Muscle weakness lower limb | 2 (16.7) | 0 (0) |
| Nervous system disorders | Peripheral sensory neuropathy | 2 (16.7) | 0 (0) |
| Headache | 4 (33.3) | 0 (0) |
| Paresthesia | 2 (16.7) | 0 (0) |
| Dizziness | 3 (25) | 0 (0) |
| Syncope | 1 (8.3) | 1 (8.3) |
| Renal and urinary disorders | Hematuria | 7 (58.3) | 1 (8.3) |
| Proteinuria | 7 (58.3) | 0 (0) |
| Glucosuria | 2 (16.7) | 0 (0) |
| Respiratory, thoracic and mediastinal disorders | Epistaxis | 5 (41.7) | 1 (8.3) |
| Pleural effusion | 2 (16.7) | 0 (0) |
| Cough | 2 (16.7) | 0 (0) |
| Dyspnea | 3 (25) | 0 (0) |
| Hypoxia | 1 (8.3) | 1 (8.3) |
| Pneumothorax | 1 (8.3) | 1 (8.3) |
| Skin and subcutaneous tissue disorders | Alopecia | 7 (58.3) | 0 (0) |
| Skin and subcutaneous tissue disorders | 2 (16.7) | 0 (0) |
| Rash maculo-papular | 2 (16.7) | 0 (0) |
| Vascular disorders | Hypertension | 8 (66.7) | 0 (0) |

**\***There wereno grade 5 AEs (toxic deaths).