**Supplemental Digital Content 3:** All treatment-emergent adverse events occurring during the first 3 days of IV therapy, while on IV therapy, and throughout the entire study duration (Safety population)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **First 3 days of IV therapy** | | **While on IV therapy** | | **Overall study duration\*** | |
| **Treatment-emergent adverse events,  n (%)** | **Ceftobiprole (n=94)** | **IV SoC cephalosporin (n=44)** | **Ceftobiprole (n=94)** | **IV SoC cephalosporin (n=44)** | **Ceftobiprole (n=94)** | **IV SoC cephalosporin (n=44)** |
| Vomiting | 3 (3.2) | 0 | 4 (4.3) | 1 (2.3) | 7 (7.4) | 1 (2.3) |
| Diarrhea | 1 (1.1) | 2 (4.5) | 1 (1.1) | 4 (9.1) | 2 (2.1) | 4 (9.1) |
| Viral infection | 0 | 1 (2.3) | 2 (2.1) | 1 (2.3) | 4 (4.3) | 1 (2.3) |
| Headache | 2 (2.1) | 0 | 3 (3.2) | 0 | 3 (3.2) | 0 |
| Pneumonia | 1 (1.1) | 0 | 1 (1.1) | 0 | 3 (3.2) | 0 |
| ALT increased | 0 | 0 | 0 | 0 | 2 (2.1) | 0 |
| Bronchitis | 0 | 0 | 0 | 0 | 0 | 2 (4.5) |
| Infusion site reaction | 1 (1.1) | 0 | 2 (2.1) | 0 | 2 (2.1) | 0 |
| Neutropenia | 0 | 0 | 0 | 0 | 1 (1.1) | 1 (2.3) |
| Phlebitis | 0 | 0 | 1 (1.1) | 0 | 2 (2.1) | 0 |
| Pyrexia | 0 | 0 | 1 (1.1) | 0 | 2 (2.1) | 0 |
| Urticaria | 1 (1.1) | 0 | 1 (1.1) | 0 | 1 (1.1) | 1 (2.3) |
| Abdominal pain | 0 | 0 | 0 | 1 (2.3) | 0 | 1 (2.3) |
| AST increased | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Aphthous ulcer | 1 (1.1) | 0 | 1 (1.1) | 0 | 1 (1.1) | 0 |
| Blood potassium increased | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Chromaturia | 1 (1.1) | 0 | 1 (1.1) | 0 | 1 (1.1) | 0 |
| Dehydration | 1 (1.1) | 0 | 1 (1.1) | 0 | 1 (1.1) | 0 |
| Dermatitis allergic | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Functional GI disorder | 1 (1.1) | 0 | 1 (1.1) | 0 | 1 (1.1) | 0 |
| Gastroenteritis | 0 | 1 (2.3) | 0 | 1 (2.3) | 0 | 1 (2.3) |
| Hypersensitivity | 0 | 0 | 1 (1.1) | 0 | 1 (1.1) | 0 |
| Laryngitis | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Nasopharyngitis | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Otitis media | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Pain in extremity | 0 | 1 (2.3) | 0 | 1 (2.3) | 0 | 1 (2.3) |
| Pharyngitis streptococcal | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Pleural effusion | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Pleurisy | 0 | 0 | 1 (1.1) | 0 | 1 (1.1) | 0 |
| Rhinitis | 0 | 0 | 0 | 0 | 0 | 1 (2.3) |
| Seizure-like phenomenon | 0 | 0 | 0 | 0 | 0 | 1 (2.3) |
| Tonsillitis streptococcal | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Thrombocytopenia | 0 | 0 | 0 | 0 | 0 | 1 (2.3) |
| Upper respiratory tract infection | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |
| Wheezing | 0 | 0 | 0 | 0 | 1 (1.1) | 0 |

\*Up to last follow-up visit.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GI, gastrointestinal; IV, intravenous; SoC, standard-of-care.