We identified infants exposed to Pip in the Pediatric Trials Network (PTN) database. We analyzed data from 747 infants with a total of 5901 infant days of exposure to Pip. The safety of Pip was evaluated by identifying adverse events (AEs) from the second day until the end of the study. AEs were captured from the second day until the end of the study, for a total of 5901 infant days of exposure. Our results showed a favorable safety profile in infants, which was consistent with previous reports. In the cohort studied, the incidence of seizures (1.3%) and elevated ALT (0.1%) were uncommon but both were associated with piperacillin exposure. Additional studies to further assess this relationship are warranted. Combining PK modeling with EHR data is a feasible and novel method to evaluate drug safety in infants.

### Methods

We identified infants exposed to Pip-Tazo discharged from 339 neonatal intensive care units managed by the PTN Medical Group between 1997 and 2012. Typical values for CL and V were simulated according to the following relationships: CL (L/h) = 0.080·WT (kg)/PMA (postmenstrual age) and V (L) = 0.42·WT, respectively, where WT is body weight (kg) and PMA is postmenstrual age (weeks). The coefficient of variation for the CL interindividual variability was 37%, whereas no interindividual variability in volume was assumed.

The safety of Pip-Tazo was evaluated by identifying adverse events listed in the FDA product label including: seizure, rash, hypernatremia (>155 mEq/L), hypokalemia (<3.5 meq/L), prolonged prothrombin time (>15 seconds) and partial thromboplastin time (>50 seconds), low hematocrit (<37%), leukopenia (<5000/mm²), thrombocytopenia (<100,000/mm²), elevated creatinine (>1.7 mg/dL), and elevated AST (>600 U/L) and ALT (>225 U/L).

### Results

This study included 747 infants who received 839 courses of Pip-Tazo for a total of 5901 infant days. Table 1 shows the demographics of the study population. The safety data is a feasible and novel method to evaluate drug safety in infants. Clinical AE’s (Patients, %) are shown in Table 2. Seizures (1.3%), rash (0.8%), serum electrolytes (Infant days, %), hyponatremia (0.4%), hypokalemia (0.8%), renal dysfunction (Infant days, %), elevated creatinine (0.5%), complete blood count (Infant days, %), thrombocytopenia (13.5%), leukopenia (1.5%), low hematocrit (5.4%), and coagulation (Infant days, %) were reported. The safety data is a feasible and novel method to evaluate drug safety in infants. Additional studies to further assess this relationship are warranted. Combining PK modeling with EHR data is a feasible and novel method to evaluate drug safety in infants.

### References


