**Supplemental Digital Content 6.**

**Supplemental Table 3. All-causality and treatment-related adverse events and their severity**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Infants | Toddlers | Preschoolers | Schoolchildren | Total |
|  | (*n* = 13) | (*n* = 18) | (*n* = 18) | (*n* = 12) | (*n* = 61) |
| TEAEa | Any  | Mi | Mo | Se | Any | Mi | Mo | Se | Any | Mi | Mo | Se | Any | Mi | Mo | Se | Any | Mi | Mo | Se |
| Bradycardia |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Allb | 5 | 5 | 0 | 0 | 7  | 7 | 0 | 0 | 5  | 5 | 0 | 0 | 2  | 2 | 0 | 0 | 19  | 19 | 0 | 0 |
|  | (38.5) |  |  |  | (38.9) |  |  |  | (27.8) |  |  |  | (16.7) |  |  |  | (31.1) |  |  |  |
| Relatedc | 3 | 3 | 0 | 0 | 1 | 1 | 0 | 0 | 2 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 7 | 7 | 0 | 0 |
|  | (23.1) |  |  |  | (5.6) |  |  |  | (11.1) |  |  |  | (8.3) |  |  |  | (11.5) |  |  |  |
| Nausea |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Allb | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 5 | 4 | 1 | 0 | 7 | 6 | 1 | 0 |
|  | (0.0) |  |  |  | (0.0) |  |  |  | (11.1) |  |  |  | (41.7) |  |  |  | (11.5) |  |  |  |
| Relatedc | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
|  | (0.0) |  |  |  | (0.0) |  |  |  | (0.0) |  |  |  | (8.3) |  |  |  | (1.6) |  |  |  |
| Vomiting |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Allb | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 2 | 1 | 1 | 0 | 5 | 3 | 2 | 0 | 9 | 6 | 3 | 0 |
|  | (7.7) |  |  |  | (5.6) |  |  |  | (11.1) |  |  |  | (41.7) |  |  |  | (14.8) |  |  |  |
| Relatedc | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 2 | 1 | 1 | 0 | 4 | 3 | 1 | 0 |
|  | (7.7) |  |  |  | (0.0) |  |  |  | (5.6) |  |  |  | (16.7) |  |  |  | (6.6) |  |  |  |
| Agitation |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Allb | 4 | 0 | 4 | 0 | 2 | 0 | 2 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 7 | 0 | 7 | 0 |
|  | (30.8) |  |  |  | (11.1) |  |  |  | (5.6) |  |  |  | (0.0) |  |  |  | (11.5) |  |  |  |
| Relatedc | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 |
|  | (7.7) |  |  |  | (0.0) |  |  |  | (0.0) |  |  |  | (0.0) |  |  |  | (1.6) |  |  |  |
| Respiratory depression |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Allb | 2 | 2 | 0 | 0 | 7 | 6 | 1 | 0 | 2 | 2 | 0 | 0 | 5 | 4 | 1 | 0 | 16 | 14 | 2 | 0 |
|  | (15.4) |  |  |  | (38.9) |  |  |  | (11.1) |  |  |  | (41.7) |  |  |  | (26.2) |  |  |  |
| Relatedc | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 0 | 2 | 1 | 1 | 0 |
|  | (0.0) |  |  |  | (0.0) |  |  |  | (0.0) |  |  |  | (16.7) |  |  |  | (3.3) |  |  |  |
| Hypotension |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Allb | 2 | 2 | 0 | 0 | 8 | 7 | 1 | 0 | 10 | 9 | 1 | 0 | 9 | 9 | 0 | 0 | 29 | 27 | 2 | 0 |
|  | (15.4) |  |  |  | (44.4) |  |  |  | (55.6) |  |  |  | (75.0) |  |  |  | (47.5) |  |  |  |
| Relatedc | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 3 | 3 | 0 | 0 |
|  | (0.0) |  |  |  | (0.0) |  |  |  | (11.1) |  |  |  | (8.3) |  |  |  | (4.9) |  |  |  |

Any = any grade, Mi = mild, Mo = moderate, Se = severe, TEAE = treatment-emergent adverse event.

Data are *n* (%).

aTEAEs reported in ≥10% of all the patients are presented.

bAll-causality TEAEs.

cTreatment-related TEAEs.