# Safety Analysis

The frequency of adverse events was summarized as the proportion of patients with at least one day with an event. The proportions were compared between the treatment groups for IT-ITT, IT-PP, IM-ITT, IM-PP and IM-ALL.

## Any adverse event

### IT-ITT population

Adverse Events.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Intrathecal treatment (N=136)** | | **Sham procedure (N=135)** | |  |
| **Characteristic** | n | Summary statistic | n | Summary statistic | P-value |
| GradeI | 136 | 25/136 (18%) | 135 | 23/135 (17%) | 0.772 |
| GradeII | 136 | 55/136 (40%) | 135 | 55/135 (41%) | 0.96 |
| GradeIII | 136 | 17/136 (12%) | 135 | 23/135 (17%) | 0.292 |
| GradeIV | 136 | 5/136 (4%) | 135 | 5/135 (4%) | 0.991 |
| Rel | 136 | 2/136 (1%) | 135 | 2/135 (1%) | 0.994 |
| PosRel\* | 136 | 20/136 (15%) | 135 | 13/135 (10%) | 0.201 |
| UnRel | 136 | 72/136 (53%) | 135 | 84/135 (62%) | 0.122 |
| NumAE | 136 |  | 135 |  | 0.0759 |
| - 0 |  | 52/136 (38%) |  | 47/135 (35%) |  |
| - 1 |  | 27/136 (20%) |  | 27/135 (20%) |  |
| - 2 |  | 17/136 (12%) |  | 21/135 (16%) |  |
| - 3 |  | 6/136 (4%) |  | 13/135 (10%) |  |
| - 4 |  | 14/136 (10%) |  | 9/135 (7%) |  |
| - 5 |  | 13/136 (10%) |  | 4/135 (3%) |  |
| - >5 |  | 7/136 (5%) |  | 14/135 (10%) |  |

## All adverse events

### IT-ITT population

Adverse Events.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Intrathecal treatment (N=303)** | | **Sham procedure (N=330)** | |  |
| **Characteristic** | n | Summary statistic | n | Summary statistic | P-value |
| Adverse Event | 251 |  | 283 |  | 0.004 |
| - Acute renal failure |  | 1/251 (0%) |  | 3/283 (1%) |  |
| - Adrenal insufficiency |  | 1/251 (0%) |  | 2/283 (1%) |  |
| - Allergy |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Anemia |  | 2/251 (1%) |  | 9/283 (3%) |  |
| - Appendicitis |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Arterial thromboembolism |  | 2/251 (1%) |  | 0/283 (0%) |  |
| - arthralgia |  | 2/251 (1%) |  | 1/283 (0%) |  |
| - Arthralgia |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Arthritis |  | 4/251 (2%) |  | 1/283 (0%) |  |
| - Aspiration pneumonia\* |  | 2/251 (1%) |  | 6/283 (2%) |  |
| - Atrial fibrillation |  | 0/251 (0%) |  | 2/283 (1%) |  |
| - Atrial thrombosis |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Back pain |  | 1/251 (0%) |  | 1/283 (0%) |  |
| - Blood stream infection |  | 9/251 (4%) |  | 8/283 (3%) |  |
| - Bruising |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Cardiac arrest |  | 0/251 (0%) |  | 3/283 (1%) |  |
| - Cellulitis |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Cerbral infarction |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Cerebral hemorrhage |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Chills |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Cholangitis |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Chronic venous insufficiency |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Conjunctivitis |  | 2/251 (1%) |  | 3/283 (1%) |  |
| - Constipation |  | 19/251 (8%) |  | 19/283 (7%) |  |
| - Creatinine increase |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Deep vein thrombosis |  | 1/251 (0%) |  | 3/283 (1%) |  |
| - Dizziness |  | 3/251 (1%) |  | 1/283 (0%) |  |
| - Dysphagia |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - facial nerve disorder |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Failed extubation |  | 2/251 (1%) |  | 0/283 (0%) |  |
| - Fever |  | 5/251 (2%) |  | 0/283 (0%) |  |
| - Gastritis |  | 4/251 (2%) |  | 1/283 (0%) |  |
| - Gastrointestinal disorder |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Headache |  | 8/251 (3%) |  | 0/283 (0%) |  |
| - Heat stroke |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Hematuria |  | 1/251 (0%) |  | 2/283 (1%) |  |
| - Hemorrhoids |  | 2/251 (1%) |  | 1/283 (0%) |  |
| - Hiccup |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Hospital acquired pneumonia |  | 2/251 (1%) |  | 2/283 (1%) |  |
| - Hyperglycaemia |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Hypernatremia |  | 0/251 (0%) |  | 2/283 (1%) |  |
| - Hyperpyrexia |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Hypertension |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Hypoalbuminemia |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Hypocalcemia |  | 15/251 (6%) |  | 17/283 (6%) |  |
| - Hypokalemia |  | 21/251 (8%) |  | 30/283 (11%) |  |
| - Hypomagnesemia |  | 4/251 (2%) |  | 4/283 (1%) |  |
| - Hyponatremia |  | 14/251 (6%) |  | 13/283 (5%) |  |
| - Hypotension |  | 1/251 (0%) |  | 6/283 (2%) |  |
| - Insomnia |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Low weight, muscle wasting |  | 1/251 (0%) |  | 2/283 (1%) |  |
| - Myalgia |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Myocardial ischaemia |  | 2/251 (1%) |  | 1/283 (0%) |  |
| - Myocarditis |  | 1/251 (0%) |  | 1/283 (0%) |  |
| - Nausea |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Necrotic wound |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Neuralgia |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Nose bleed |  | 5/251 (2%) |  | 2/283 (1%) |  |
| - Oral infection |  | 3/251 (1%) |  | 1/283 (0%) |  |
| - Otitis |  | 1/251 (0%) |  | 2/283 (1%) |  |
| - pharyngitis |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Phlebitis |  | 2/251 (1%) |  | 6/283 (2%) |  |
| - Platelet count decreased |  | 0/251 (0%) |  | 2/283 (1%) |  |
| - Pleural abscess |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Pneumothorax |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Postoperative hemorrage |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Pressure ulcer |  | 1/251 (0%) |  | 4/283 (1%) |  |
| - Pruritus |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Pyloric stenosis |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Recurrent tetanus |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Rhabdomyolysis |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Sinus bradycardia |  | 0/251 (0%) |  | 2/283 (1%) |  |
| - Sinusitis |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Skin allergy |  | 6/251 (2%) |  | 9/283 (3%) |  |
| - Spinal disc herniation |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Subcutaneous emphysema |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Torticolis |  | 1/251 (0%) |  | 0/283 (0%) |  |
| - Tracheal hemorrhage |  | 13/251 (5%) |  | 3/283 (1%) |  |
| - Tracheal stenosis |  | 0/251 (0%) |  | 1/283 (0%) |  |
| - Upper gastrointestinal hemorrhage |  | 11/251 (4%) |  | 11/283 (4%) |  |
| - Upper respiratory infection |  | 3/251 (1%) |  | 1/283 (0%) |  |
| - Urinary retention |  | 2/251 (1%) |  | 1/283 (0%) |  |
| - UTI |  | 20/251 (8%) |  | 34/283 (12%) |  |
| - Ventilator associated pneumonia |  | 28/251 (11%) |  | 36/283 (13%) |  |
| - Viral infection |  | 0/251 (0%) |  | 2/283 (1%) |  |
| - Voice alteration |  | 0/251 (0%) |  | 3/283 (1%) |  |
| - Wound bleed |  | 2/251 (1%) |  | 0/283 (0%) |  |
| - Wound infection |  | 2/251 (1%) |  | 1/283 (0%) |  |

## 

## Severe adverse events

The frequency of severe adverse events was summarized. The proportions were compared between the treatment groups for IT-ITT, IT-PP, IM-ITT, IM-PP and IM-ALL.

### IT-ITT population

Adverse Events.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Intrathecal treatment (N=136)** | | **Sham procedure (N=135)** | |  |
| **Characteristic** | n | Summary statistic | n | Summary statistic | P-value |
| Adverse Event | 8 |  | 13 |  | 0.812 |
| - Hypotension/Cardiac arrest |  | 1/8 (12%) |  | 5/13 (38%) |  |
| - OTHER |  | 3/8 (38%) |  | 4/13 (31%) |  |
| - Respiratory complication |  | 3/8 (38%) |  | 3/13 (23%) |  |
| - Venous Thromboembolism |  | 1/8 (12%) |  | 1/13 (8%) |  |
|  |  |  |  |  |  |