A multicenter, open-label, single-dose study to evaluate the pharmacokinetics, safety, and tolerability of solifenacin succinate suspension in pediatric subjects from 5 to less than 18 years of age with neurogenic detrusor overactivity (NDO)

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INTRODUCTION

- Detrusor overactivity (DO) is a urodynamic observation characterized by involuntary detrusor contractions that are spontaneous or provoked during the filling phase involving a detrusor pressure increase of greater than 15 cm H2O above baseline
- Neurogenic detrusor overactivity (NDO) is defined by the International Children’s Continence Society as DO when there is a relevant neurological condition
- NDO is a manifestation of neurogenic bladder dysfunction; in children, the most prevalent cause is myelodysplasia, a group of developmental abnormalities that result from defects that occur during neural tube closure
- Neurogenic bladder (spasticity) dysfunction may lead to incontinence, urinary tract infections (UTIs), vesicoureteral reflux (VUR) and renal scarring
- Anticholinergics are first-line therapy for neurogenic bladder dysfunction. The main goal is to increase bladder compliance and store urine to prevent calcifications and renal damage

METHODS

Study design

- This was a multicenter, open-label, single-dose study to evaluate the pharmacokinetics, safety and tolerability of solifenacin succinate suspension in children and adolescents aged 5–17 years with NDO: Elefant study (W05 CL-075: NCT01593707)
- Patients received a single dose of solifenacin succinate on Day 1. Clinical assessments and laboratory investigations were undertaken throughout the seven-day follow-up period (Figure 1)
  - Blood samples were drawn for pharmacokinetic analysis at pre-dose (Day 1), and at time intervals up to 154 h post dose
  - The total number of pharmacokinetic blood samples taken depended on the age of the patient; 5–8 years, four samples; 9–11 years, six samples; 12–17 years, seven samples

RESULTS

Pharmacokinetic parameters

- Pharmacokinetic data are summarized in Table 3
- Mean values for Cmax (mg/L) and CL/F were similar for children aged 5–11 years and adolescents (aged 12–17 years)
- Total drug exposure (AUCinf) tended to be lower in children than adolescents (Figure 2), however, there was substantial overlap between the two age groups
- The half-life of solifenacin tended to be shorter in children than adolescents, with a mean t1/2 in children, compared with 52.9 h in adolescents, although median values were closer (10.7 versus 14.6 h)
- Pharmacokinetics in patients with NDO were similar to those observed in a previous study (W05 CL-075) in 42 children and adolescents aged 5–17 years with OAB (Figure 3)

Pharmacokinetic assessments

- Pharmacokinetic parameters included:
  - Maximum solifenacin concentration (Cmax)
  - Time to attain Cmax (Tmax)
  - Area under the curve extrapolated to infinity (AUC0∞)
- Apparent terminal elimination half-life (t1/2)
- Apparent total body clearance (CL/F)
- Apparent volume of distribution during the terminal phase (Vz/F)
- Safety assessments included:
  - Adverse events (AEs)
  - Vital signs
  - Clinical laboratory evaluations (hematology, biochemistry, electrolysis and drug-induced liver injury)
- Physical examination

Safety and tolerability

- Adverse events (AEs)
  - Five treatment-emergent adverse events (TEAEs) were reported in two patients, both in the adolescent group. None were considered to be related to study medication
  - No serious AEs were reported and no patients who received dosing discontinued the study
  - One patient reported micturition urgency, which was mild in severity, required no treatment and had not resolved at the end of study visit
  - One patient reported anxiety on one occasion; one pre-treatment and four treatment-emergent (at cut-off post baseline visit). The investigator assessed the cause of the anxiety AEs as being related to the symptom of pain

CONCLUSIONS

- In this study, solifenacin succinate suspension was well tolerated at a PE of 5 mg in children and adolescents with NDO

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REFERENCES


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