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AN EVALUATION OF TREATMENT EFFECT IN RESPONDER AND NON-RESPONDER PATIENTS WITH NOCTURIA RECEIVING SER120 NASAL SPRAY IN 2 PHASE III CLINICAL STUDIES

Hypothesis / aims of study

SER120 nasal spray was evaluated in 2 Phase III clinical studies (DB3 and DB4) for nocturia. The objective of these investigations was to explore the treatment effect size for patients on active drug for each of the efficacy endpoints between responder and non-responder patients receiving either the 1.5 or 0.75 mcg dose of SER120 nasal spray.

Study design, materials and methods

The design of the DB3 and DB4 studies were identical except for 1) the DB3 study had 1 more dose level (1.0 mcg) of SER120 and 2) the DB4 study used a validated QOL instrument (Impact of Night-time Urination – INTU questionnaire) in compliance with current FDA guidelines. The data from the 1.0 mcg will not be presented here.

Eligible patients at least 50 years old with a history of 2 or more nocturic voids per night were enrolled on Day 1 into a 2-week double-blind placebo lead-in period. On Day 15, all patients were randomized to one of the SER120 groups or placebo for a 12-week treatment period. Patients completed a 3-day voiding diaries weekly during Screening and the 2-week placebo lead-in period and at Weeks 1, 2, 4, 6, 8, 10 and 12. For the DB4 study, patients also completed an INTU questionnaire corresponding to each voiding diary completed during Screening and at Weeks 6 and 12.

Treatment responders were defined as patients with 50% or more reduction in nocturic voids between screening and the treatment period and treatment non-responders were those patients that did not meet this criterion. The percentage of treatment responders and treatment non-responders in the ITT population were calculated for each study (DB3 and DB4). The treatment effect size was assessed for mean change in nocturic voids (primary endpoint) and the secondary endpoints of change in time from bedtime to first nocturic void, change in the percentage of patients with 0 or 1 or less nocturic voids and reduction in nocturnal urine volume. The reduction from baseline in INTU total and night-time domain scores in the DB4 study was evaluated. All analyses were based on all available data.

Results

The percentage of treatment responders and treatment non-responders in the DB3 and DB4 studies are shown in Table 1.

Table 1: Number (Percentage) of Treatment Responders and Treatment Non-Responders

Dose (mcg)	DB3			DB4		
	N	Responders [Number (%)]	Non-Responders [Number (%)]	N	Responders [Number (%)]	Non-Responders [Number (%)]
1.5	179	93 (52.0%)	86 (48.0%)	260	121 (46.5%)	139 (53.5%)
0.75	186	77 (41.4%)	109 (58.6%)	262	93 (35.5%)	169 (64.5%)

The treatment effect size for the primary and secondary endpoints is summarized in Table 2.

Table 2: Treatment Effect Size of Efficacy Endpoints between Treatment Responders and Treatment Non-Responders

Efficacy Endpoints	Dose (mcg)	DB3		DB4	
		Responders (N = 93 [1.5 mcg]) (N = 77 [0.75 mcg])	Non-Responders (N = 86 [1.5 mcg]) (N =109 [0.75 mcg])	Responders (N = 121 [1.5 mcg]) (N =93 [0.75 mcg])	Non-Responders (N = 139 [1.5 mcg]) (N =169 [0.75 mcg])
Reduction in Mean Nocturic Voids (LSM)	1.5	-2.1	-0.9	-2.1	-0.8
	0.75	-2.1	-0.9	-2.1	-1.0
Mean Time (Change) from Bedtime to First Void (min.) (LSM)	1.5	306 (+156)	198 (+54)	312 (+168)	192 (+48)
	0.75	294 (+150)	186 (+48)	312 (+168)	198 (+54)
Change in % of Nights with 0 Nocturic Voids (LSM)	1.5	+17.4	+0.9	+18.21	+1.80
	0.75	+16.1	+0.3	+19.02	+1.23
Change in % of Nights with 1 or Less Void (LSM)	1.5	+72.0	+18.5	+76.07	+15.37
	0.75	+72.0	+15.8	+74.34	+20.02
Change in Mean Nocturnal Urine Volume (mL) (LSM)	1.5	-256.0	-145.6	-357.1	-217.0
	0.75	-239.0	-130.3	-328.2	-146.8

LSM = Least Square Mean

The treatment effect size of the reduction of INTU total and night time domain scores (QOL instrument) between treatment responders and treatment non-responders in the DB4 study is summarized in Table 3.

Table 3: Treatment Effect Size of INTU Scores (QOL Instrument) between Treatment Responders and Treatment Non-Responders (DB4)

INTU Score	Dose (mcg)	Responders (N = 119 [1.5 mcg]) (N = 84 [0.75 mcg])	Non-Responders (N = 124 [1.5 mcg]) (N =163 [0.75 mcg])
Reduction in Mean Total Score (LS Mean)	1.5	-21.3	-8.2
	0.75	-19.0	-8.4
Reduction in Mean Night Time Domain Score (LS Mean)	1.5	-26.1	-11.0
	0.75	-23.5	-11.3

LSM = Least Square Mean

There were no meaningful correlations between low serum sodium (less than 130 mmol/L) and responders/non-responders.

Interpretation of results

As shown in Table 1, the number of patients responding to SER120 treatment was dose dependent with a higher number and percentage of patients showing response at the 1.5 mcg than at the 0.75 mcg. This effect was seen in both DB3 and DB4 studies. Both doses of SER120 were statistically superior to placebo for most efficacy endpoints.

There was a greater reduction of more than 1 nocturic void per night in the treatment responders compared to the non-responders as shown in Table 2. The other efficacy endpoints including the INTU questionnaire (Table 3) showed up to 10-fold greater improvement for the responders compared to the non-responders. Among responding patients, both doses of SER120 (1.5 mcg and 0.75 mcg) resulted in similar improvement.

Concluding message

SER120 was effective and produced a dose dependent response in terms of the percentage of responders at doses of 1.5 and 0.75 mcg. However, among the responders, the magnitude of the treatment effect was independent of dose. These results indicate that responding patients will benefit in similar fashion from both the 1.5 mcg and 0.75 mcg doses of SER120.

Disclosures

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