Supplemental Material

Methods

Blood samples to determine N-telopeptide were collected at screening and during treatment at the end of weeks 12 and 24 and during follow-up at the end of week 48 (or early termination). Samples were analyzed by a central laboratory (ICON laboratories, Farmingdale, NY) using an Enzyme-Linked Immunosorbent Assay. Change from baseline for observed values in N-telopeptide was analyzed by ANOVA.

The Visual Analog Scale for Pelvic Pain, with a horizontal line on which the left extreme was labeled “no pain” and the right extreme was labeled “worst pain ever felt” was used to monitor pain daily. The VAS was scored on a scale of 0 (no pain) to 100 (worst pain ever felt). Patients indicated the worst level of pain felt over a 24-hour period by “ticking” the horizontal line on their e-Diary at approximately the same time each day. Monthly mean VAS values were calculated from e-Diary data (a month was equal to the scheduled interval between visits, which was approximately 28 days). Descriptive statistics were calculated for the change from baseline in the monthly mean VAS.

Quality of life was assessed using the Endometriosis Health Profile-5 (EHP-5) core questionnaire with 5 categories. Responses were scored on a 0-100 scale (0=Never, 25=Rarely, 50=Sometimes, 75=Often, 100=Always). Descriptive statistics were calculated for the EHP-5 category scores.

Results

The mean change from baseline values for N-telopeptide were 0.2 ± 0.5, -0.3 ± 0.5, and -0.2 ± 0.5 nM BCE at week 24 and -1.3 ± 0.6, -1.5 ± 0.5, and -1.4 ± 0.5 nM BCE at Week 48 for the elagolix 150 mg q.d., elagolix 75 mg b.i.d, and DMPA-SC groups; respectively.

All treatment groups demonstrated improvement from baseline in the monthly mean VAS for pelvic pain throughout the treatment period. At week 24, the mean (SEM) change from baseline in monthly mean VAS for pelvic pain was -18.2 ± 3.2, -26.8 ± 3.0, and -22.8 ± 3.9 in the elagolix 150 mg q.d., elagolix 75 mg b.i.d., and DMPA-SC groups; respectively (***Supplemental Figure 2***)

Overall, there were improvements at week 24 in the core dimensions of the EHP-5 in all 3 treatment groups. The observed mean scores for the 5 core dimensions at baseline and week 24 are shown in ***Supplemental Table 1*****.**

Supplemental Table 1. Summary of EHP-5 Core Dimension Scores

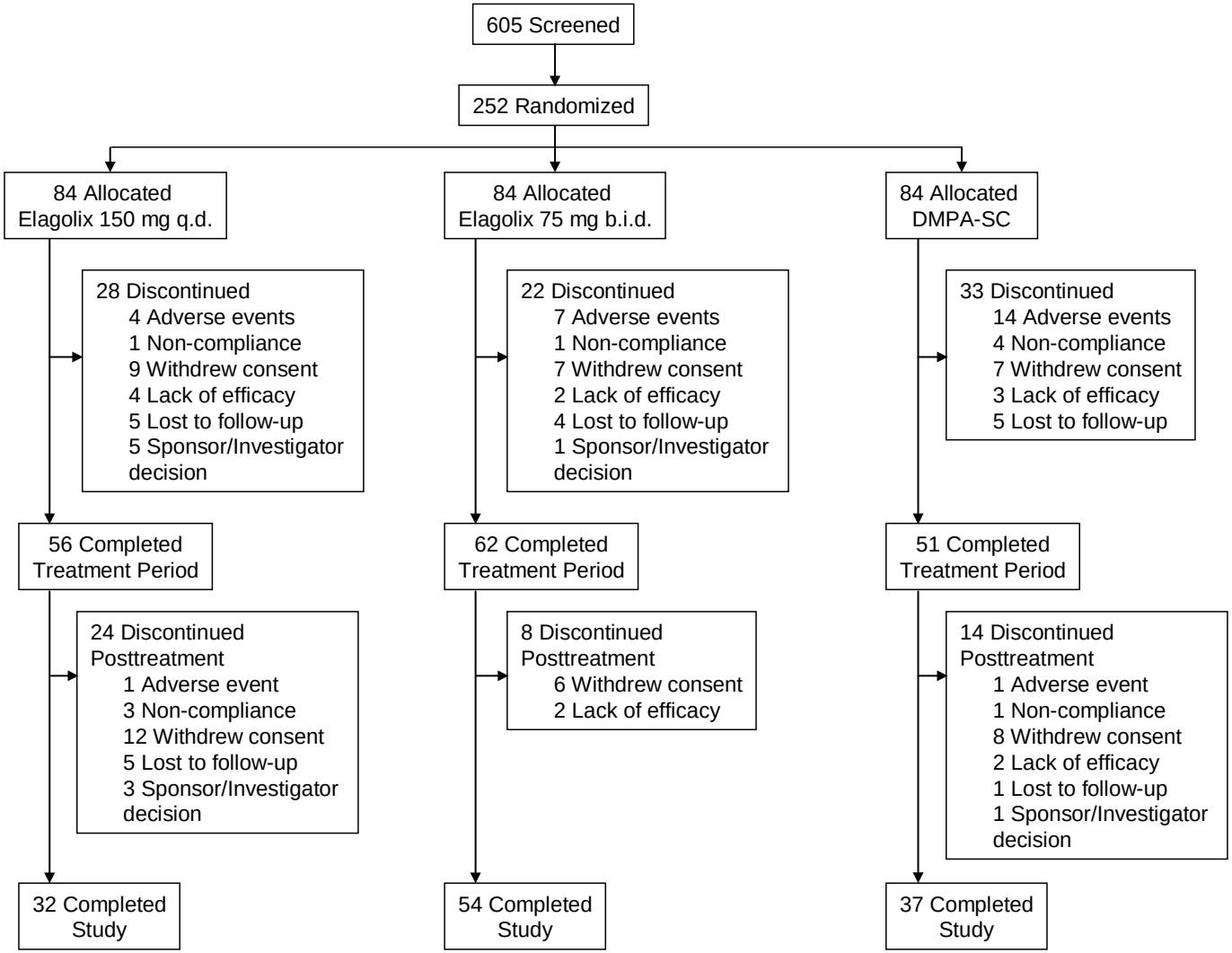
Core Dimension	Elagolix 150 mg q.d. (N=84)	Elagolix 75 mg b.i.d. (N=84)	DMPA-SC (N=83)
Pain, Mean (SEM)			
Baseline	47.0 (2.4)	50.6 (2.2)	48.5 (2.4)
Week 24	15.4 (2.6)	21.5 (2.8)	22.1 (3.5)
Control and Powerlessness, Mean (SEM)			
Baseline	56.3 (2.3)	61.3 (2.8)	63.0 (2.4)
Week 24	15.8 (3.1)	26.2 (3.6)	27.5 (4.3)
Emotional Well-Being			
Baseline	59.8 (2.3)	61.3 (2.4)	61.4 (2.3)
Week 24	34.6 (3.7)	37.7 (3.0)	36.8 (3.9)
Social Support			
Baseline	67.0 (2.9)	69.9 (2.7)	68.4 (2.8)
Week 24	21.5 (3.6)	28.8 (3.8)	34.8 (4.8)
Self-image			
Baseline	47.9 (3.1)	52.7 (3.3)	48.8 (3.0)
Week 24	21.1 (3.7)	21.9 (3.6)	24.0 (4.1)

Supplemental Table 2. Serious Adverse Events During the Study

Dose	Event	Study Period	Intensity	Investigator Assessment of Causality
Elagolix				
150 mg q.d.	Dehydration	Treatment	Severe	Unlikely related
150 mg q.d.	Ovarian Dysgerminoma	Posttreatment	Severe	Not related
150 mg q.d.	Pelvic Pain	Posttreatment	Severe	Not related
150 mg q.d.	Aspiration Pneumonia[a]	Posttreatment	Severe	Not related
150 mg q.d.	Cleft Palate[a]	Posttreatment	Moderate	Unlikely related
75 mg b.i.d.	Suicidal ideation	Treatment	Moderate	Not related
75 mg b.i.d.	Migraine	Treatment	Severe	Unlikely related
75 mg b.i.d.	Pneumonia	Posttreatment	Moderate	Unlikely related
75 mg b.i.d.	Hyperemesis gravidarum	Posttreatment	Moderate	Not related
DMPA-SC				
DMPA-SC	Appendicitis	Treatment	Severe	Not related
DMPA-SC	Food Poisoning	Treatment	Moderate	Not related
DMPA-SC	Chest Pain	Treatment	Moderate	Not related
DMPA-SC	Pelvic Congestion	Posttreatment	Severe	Not related
DMPA-SC	Pneumothorax	Posttreatment	Moderate	Not related
DMPA-SC	Pelvic Pain[b]	Posttreatment	Severe	Not related

[a]Serious adverse event occurred in an infant of a patient enrolled in the study
[b]Chronic pelvic pain resulting in elective total abdominal hysterectomy/bilateral salpingo-oophorectomy

Supplemental Figure 1.



Supplemental Figure 2