

LIBERTY: Long-term Extension Study Demonstrating One-Year Efficacy and Safety of Relugolix Combination Therapy in Women with Symptomatic Uterine Fibroids

A Al-Hendy¹; AS Lukes²; A Poindexter III³; R Venturella⁴; C Villarroel⁵;
RB Wagman⁶; Y Li⁶; L McKain⁶; EA Stewart⁷

University of Chicago, Chicago, Illinois, USA¹; Carolina Woman's Wellness Center, Durham, North Carolina, USA²; Baylor College of Medicine and St. Luke's Episcopal Hospital, Houston, Texas, USA³; University Magna Graecia, Catanzaro, Italy⁴; Instituto de Investigaciones Materno Infantil (IDIMI), University of Chile, Santiago, Chile⁵; Myovant Sciences Inc., Brisbane, California, USA⁶; Mayo Clinic, Rochester, Minnesota, USA⁷

Disclosures

- Ayman Al-Hendy, MD, PhD
 - Consultant: AbbVie, Bayer, Myovant Sciences
 - Research Support: National Institutes of Health (R01 ES 028615-01, R01HD 087417, R01 HD 094378, R01 HD 094380, R01 HD 10036701, U54 MD 007602)
 - Patent for methods for novel diagnostics and therapeutics for uterine sarcoma (US Pat No. 9,790,562 B2)
- Funding for this study was provided by Myovant Sciences GmbH

Introduction: LIBERTY Program

- Relugolix Combination Therapy (Relugolix CT; relugolix 40 mg, estradiol 1 mg and norethindrone acetate 0.5 mg) is being developed for the management of heavy menstrual bleeding (HMB) associated with uterine fibroids (UF)
- In the Phase 3, 24-week LIBERTY 1 and 2 studies, Relugolix CT:
 - significantly improved HMB compared with placebo
 - significantly reduced UF-associated pain compared with placebo
 - was generally well tolerated, with an overall incidence of adverse events similar to that observed with placebo

The Long-term Extension (LTE) study was conducted to assess the efficacy and safety of Relugolix Combination Therapy over 52 weeks of treatment in women with HMB associated with UF (NCT03412890)

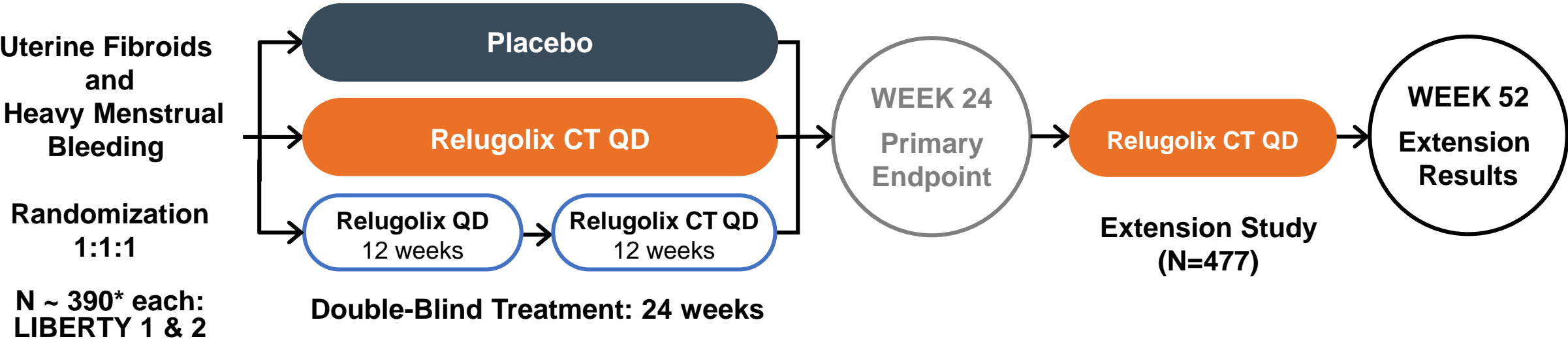
Study Design: LIBERTY 1 & 2 and Extension Study

Study Population: Pivotal Studies

- Premenopausal women 18 to 50 years of age
- Menstrual blood loss (MBL) ≥ 80 mL per cycle for 2 cycles or ≥ 160 mL during 1 cycle
- Ultrasound confirmation of uterine fibroids

Long-term Extension

- Patients who completed 24 weeks of treatment in LIBERTY 1 or 2
- Patients with a decrease of bone mineral density (BMD) Z-score $\geq 7\%$ from pivotal study baseline to Week 24 at lumbar spine, total hip or femoral neck were excluded



Relugolix CT = relugolix 40 mg + estradiol 1 mg and norethindrone acetate 0.5 mg

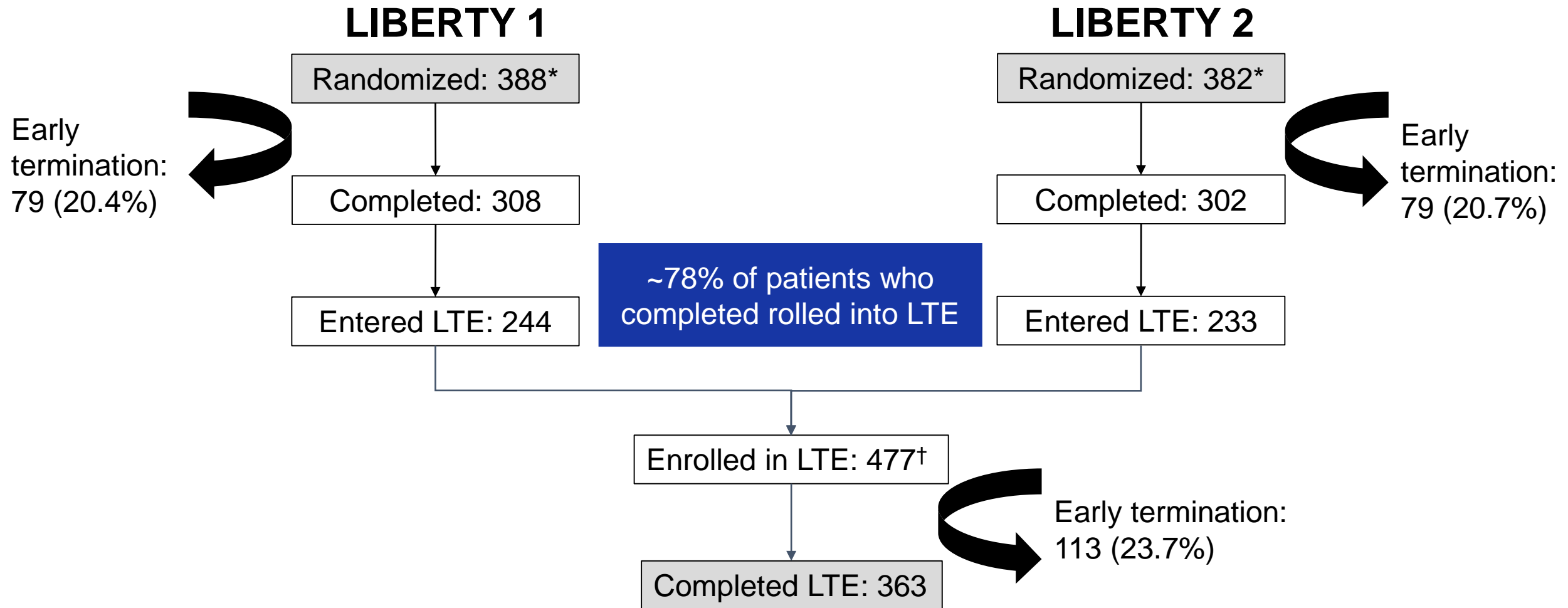
CT = Combination Therapy; QD = once daily.
*388 and 382 women were randomized in LIBERTY 1 (NCT03049735) and LIBERTY 2 (NCT03103087).

Long-term Extension Study: Endpoints and Analyses

Primary Efficacy Endpoint	Selected Secondary Endpoints
Treatment responders: Proportion of women who achieved or maintained <ul style="list-style-type: none">• MBL volume < 80 mL and a• $\geq 50\%$ reduction from parent study baseline to the last 35 days of treatment in MBL volume, as measured by the alkaline hematin method	Mean percentage change in menstrual blood volume
	Amenorrhea rate
	Improvements in anemia
	Adverse events
	Change from baseline BMD assessed by dual-energy x-ray absorptiometry
<hr/> <ul style="list-style-type: none">• Outcomes were analyzed by baseline treatment assignment in the 24-week LIBERTY studies using descriptive statistics without statistical comparisons between groups*:<ul style="list-style-type: none">• Placebo → Relugolix CT• Relugolix CT• Delayed Relugolix CT	

*Mixed-effect model was used with visit, region, baseline MBL volume (<225 mL, ≥ 225 mL), age/BMI/BMD at baseline, and race included as fixed effects.
BMI = body mass index; BMD = bone mineral density; CT = Combination Therapy; MBL = menstrual blood loss.

Patient Flow



Baseline Demographics in the Extension Safety Population Were Balanced Between Treatment Groups

Baseline Characteristic		Placebo → Relugolix CT (N = 164)	Relugolix CT (N = 163)	Delayed Relugolix CT (N = 149)
Age, Mean years (SD)		41.9 (5.43)	42.6 (5.08)	42.1 (5.58)
Race n (%)	Black or African American	88 (53.7%)	69 (42.3%)	81 (54.4%)
	White	71 (43.3%)	85 (52.1%)	51 (34.2%)
	Other*	5 (3.0%)	9 (5.5%)	17 (11.4%)
Region n (%)	North America	117 (71.3%)	113 (69.3%)	104 (69.8%)
	Rest of World†	47 (28.7%)	50 (30.7%)	45 (30.2%)

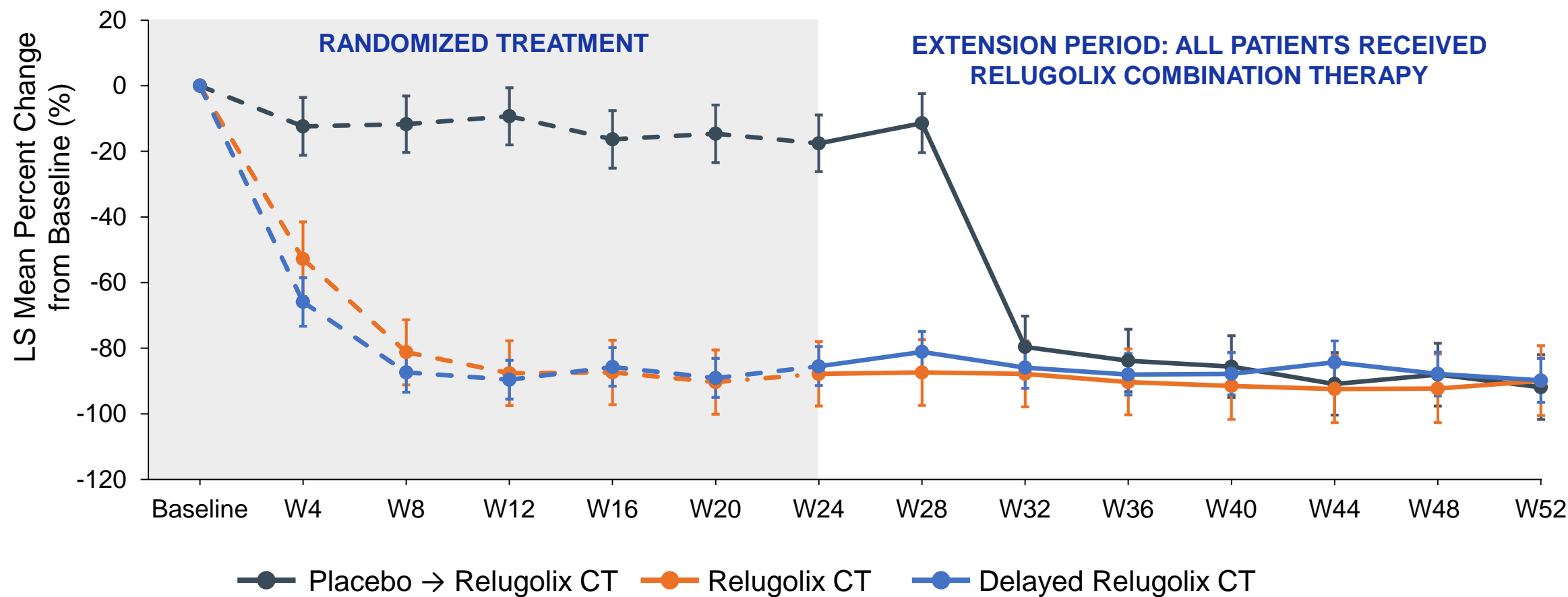
Baseline Clinical Characteristics in the Extension Safety Population Were Balanced Between Treatment Groups

Baseline Characteristic	Placebo → Relugolix CT (N = 164)	Relugolix CT (N = 163)	Delayed Relugolix CT (N = 149)
Body Mass Index, Mean kg/m ² (SD)	32.6 (7.5)	31.4 (7.0)	31.0 (6.4)
MBL Volume, Mean mL (SD)	216.0 (123.8)	248.7 (196.7)	238.8 (155.3)
Uterine Volume, Mean cm ³ (SD)	401.5 (351.5)	386.7 (320.5)	442.4 (370.9)
Index Fibroid Volume, Mean cm ³ (SD)	74.2 (128.1)	80.0 (145.1)	91.5 (137.8)
Hemoglobin, Mean g/dL (SD)	11.2 (1.5)	11.4 (1.5)	11.0 (1.6)

Data shown by randomization treatment assignment.
CT = Combination Therapy; MBL = menstrual blood loss; SD = standard deviation.

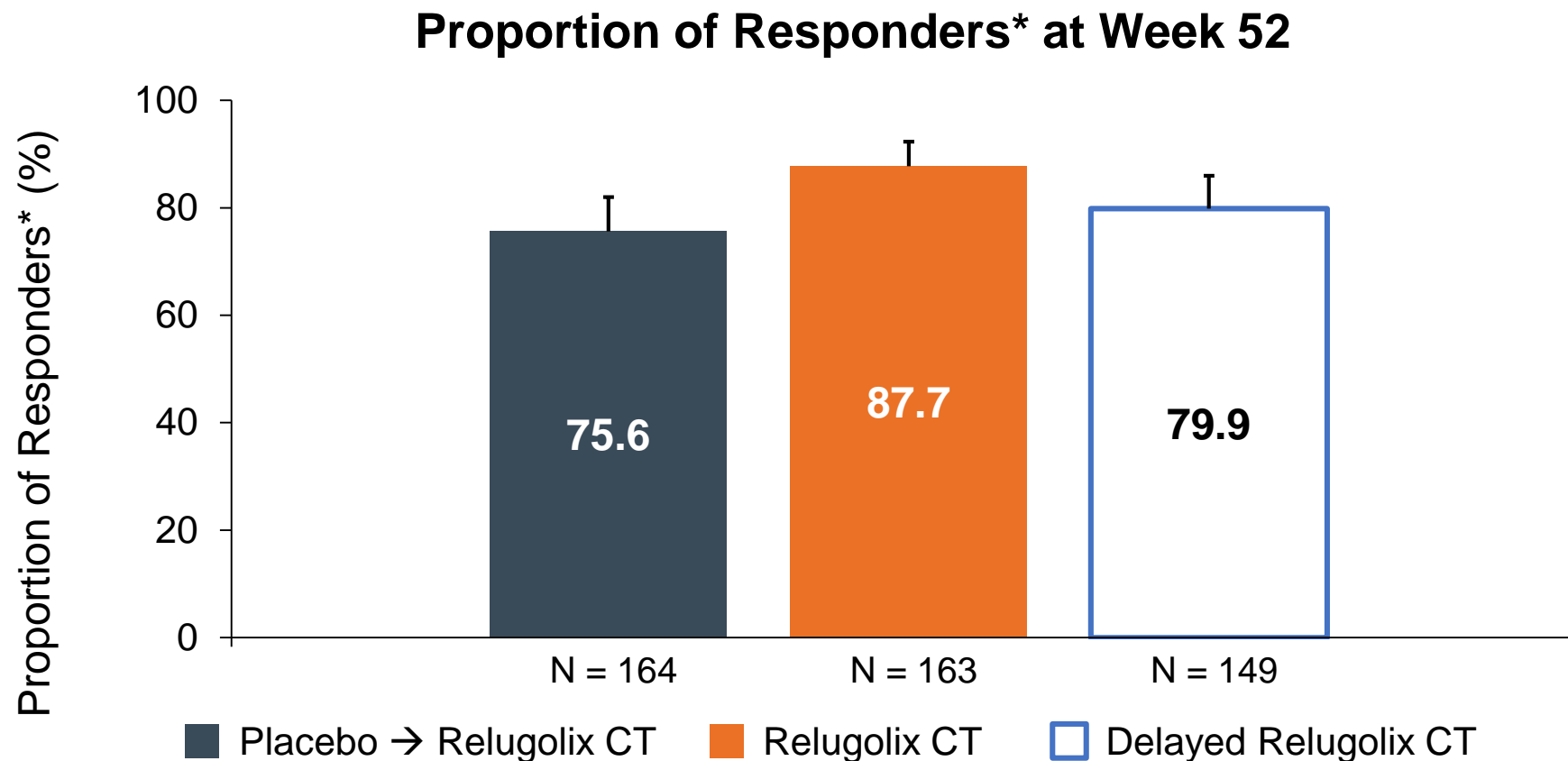
Mean MBL Volume was Reduced by 90% from Baseline to Week 52 in the Relugolix Combination Therapy Group

Percent Change in MBL Volume from Baseline to Week 52



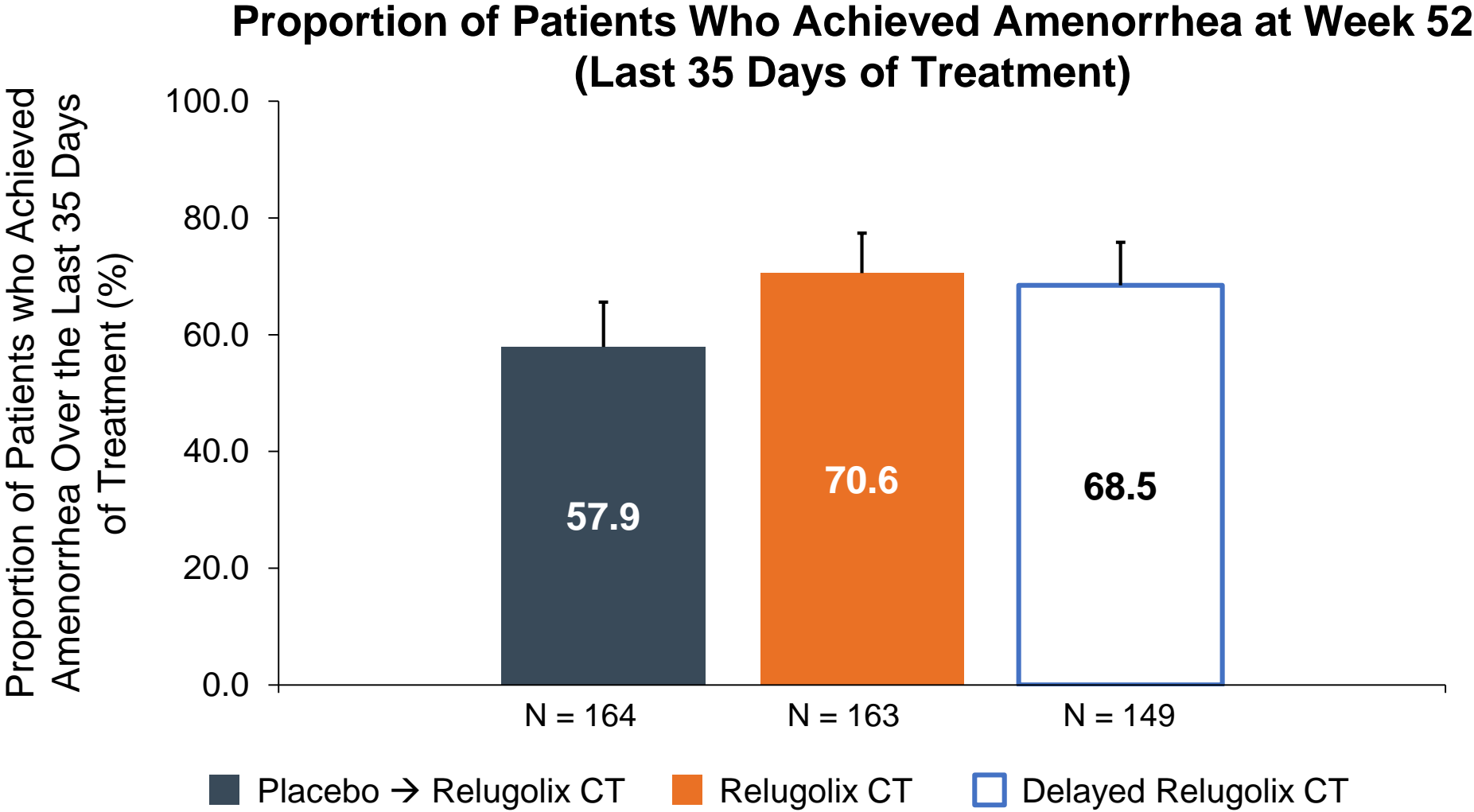
Error bars show 95% confidence intervals.
CT = Combination Therapy; MBL = menstrual blood loss; LS = least squares; W = Week.

Relugolix Combination Therapy Consistently Achieved and Maintained Improvement in MBL at Week 52



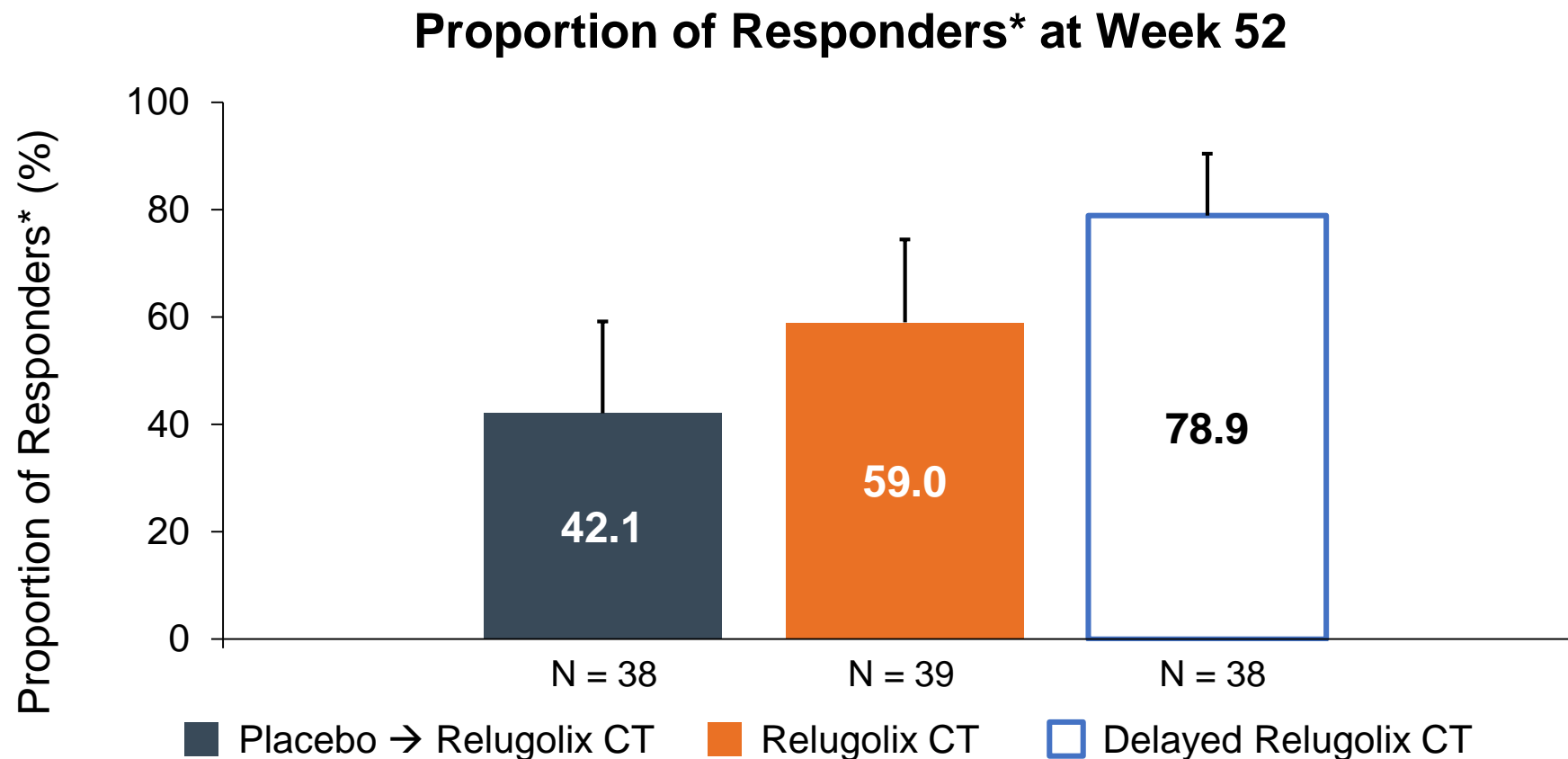
***Treatment responder (MBL)** – proportion of women who achieved or maintained an MBL volume < 80 mL and a ≥ 50% reduction from pivotal study baseline to the last 35 days of treatment in MBL volume

Most Patients Achieved Amenorrhea at Week 52 in all Treatment Groups



Error bars show upper 95% confidence intervals.
CT = Combination Therapy.

High Proportion of Patients with Anemia at Baseline Experienced Anemia Improvement Over 52 Weeks

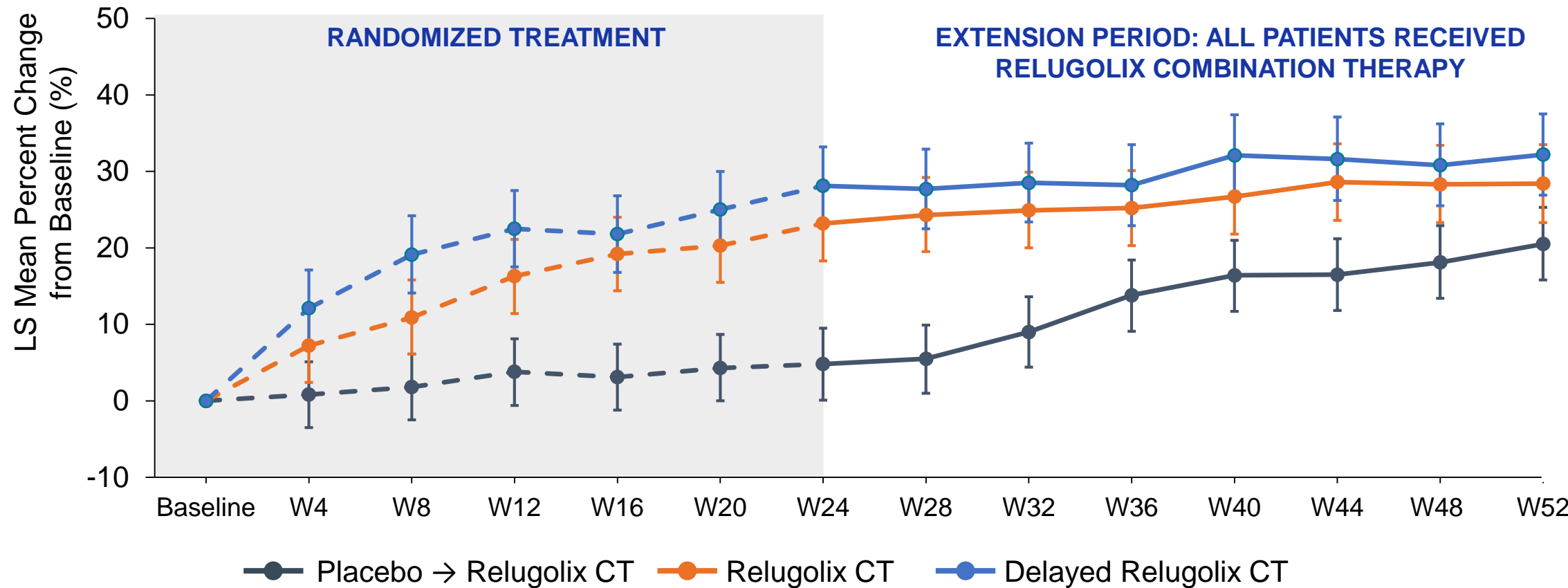


Anemia-evaluable population: patients with hemoglobin ≤ 10.5 g/dL at baseline and have a hemoglobin value at Week 24

***Treatment responder (hemoglobin)** – proportion of women with hemoglobin ≤ 10.5 g/dL at pivotal study baseline who achieve an increase of > 2 g/dL at Week 52

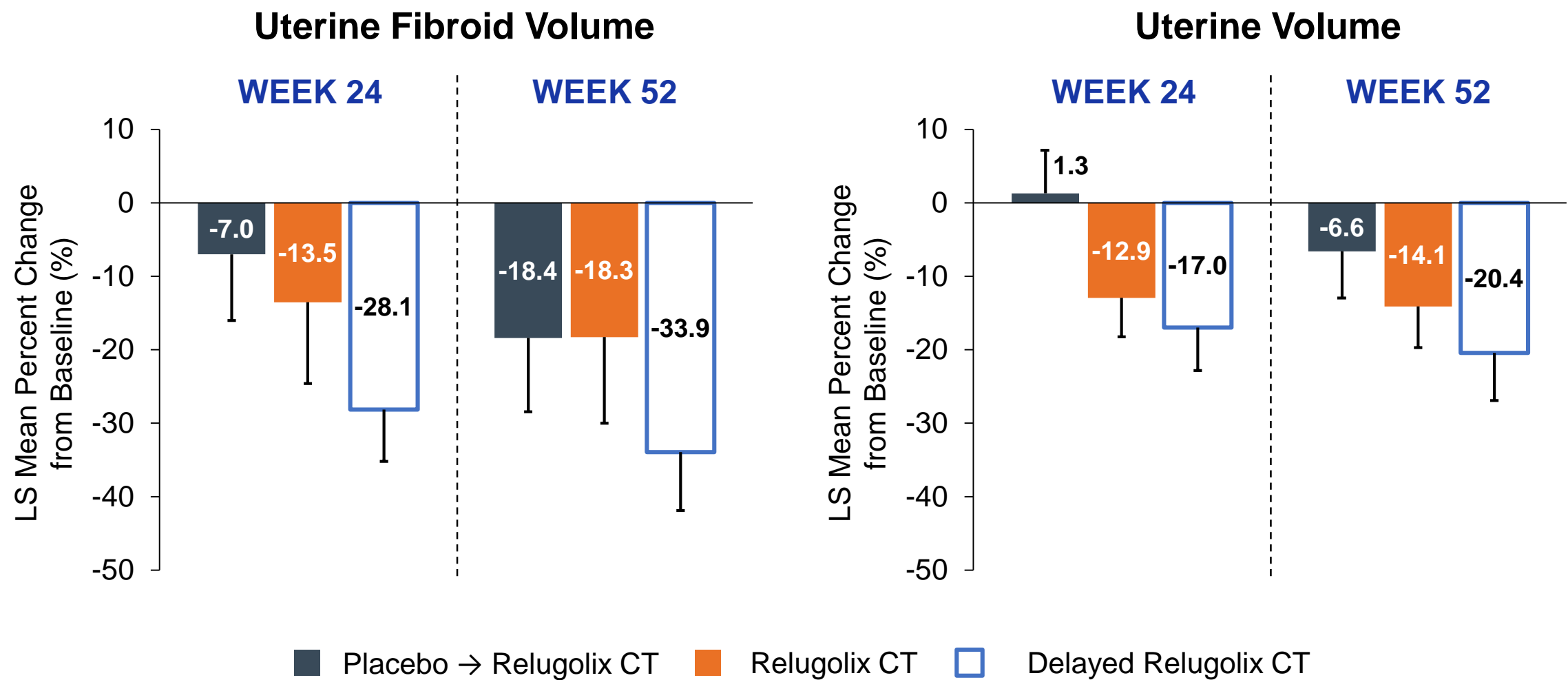
Clinically Meaningful Increase in Hgb Concentrations with Relugolix CT in Women with Anemia at Baseline

Percent Change in Hemoglobin from Baseline to Week 52 in Anemia-Evaluable Population



Error bars show 95% confidence intervals.
CT = Combination Therapy; Hgb = hemoglobin; LS = least squares, W = Week.

Reductions in Uterine and Uterine Fibroid Volume were Maintained from Week 24 to Week 52 with Relugolix CT



Error bars show upper and lower 95% confidence intervals.
CT = Combination Therapy; LS = least squares.

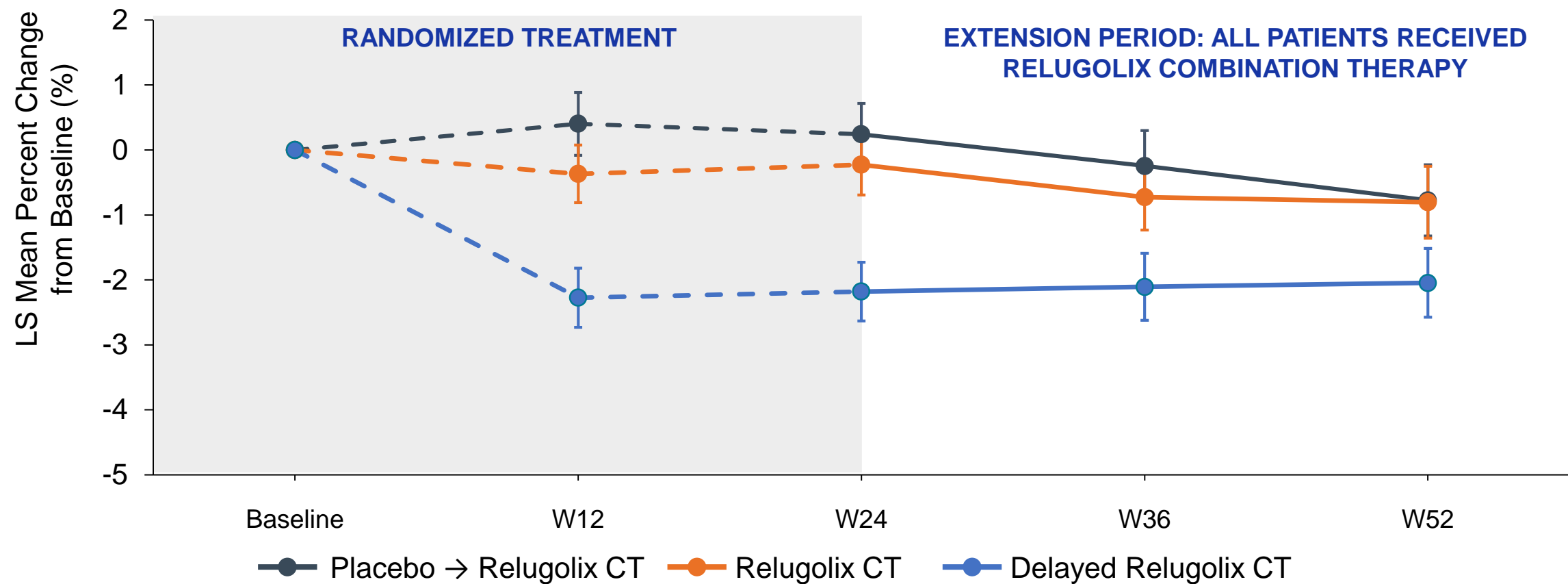
Summary of Adverse Events Reported over 52 Weeks of Treatment

Adverse Events n (%)		Placebo → Relugolix CT (N = 164)	Relugolix CT (N = 163)	Delayed Relugolix CT (N = 149)
Any		138 (84.1%)	127 (77.9%)	125 (83.9%)
Leading to Discontinuation		9 (5.5%)	5 (3.1%)	5 (3.4%)
Grade 3 or Higher		27 (16.5%)	12 (7.4%)	21 (14.1%)
Serious		15 (9.1%)	6 (3.7%)	8 (5.4%)
Fatal Outcome		0 (0%)	0 (0%)	0 (0%)
Most Common Adverse Events (>10%)	Headache	29 (17.7%)	21 (12.9%)	36 (24.2%)
	Hot flush	24 (14.6%)	18 (11.0%)	58 (38.9%)

There were no safety signals reported for Relugolix Combination Therapy over 52 weeks of treatment

Lumbar Spine BMD was Maintained with Relugolix Combination Therapy over 52 Weeks

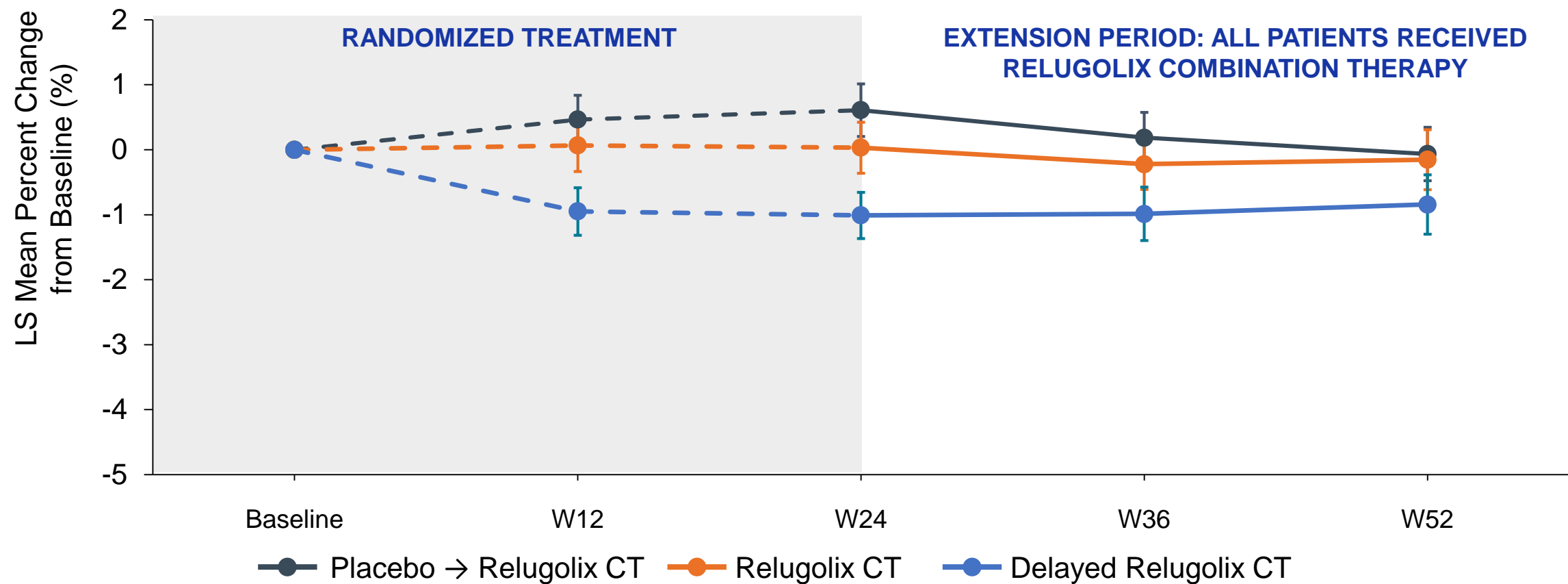
Percent Change in Lumbar Spine BMD to Week 52



Error bars show 95% confidence intervals.
BMD = bone mineral density; CT = Combination Therapy; LS = least squares; W = Week.

Total Hip BMD was Maintained with Relugolix Combination Therapy over 52 Weeks

Percent Change in Hip BMD to Week 52



Error bars show 95% confidence intervals.
BMD = bone mineral density; CT = Combination Therapy; LS = least squares; W = Week.

Conclusions

- Relugolix Combination Therapy in women with heavy menstrual bleeding associated with uterine fibroids led to
 - Rapid reduction in menstrual blood loss volume,
 - Improvement of anemia, and
 - Reduction of uterine volume, which were maintained over 52 weeks of treatment
- No safety concerns were identified with long-term treatment, and bone mass was maintained
- Relugolix Combination Therapy represents a potential long-term treatment for women with heavy menstrual bleeding associated with uterine fibroids