



A plain language summary of the long-term relugolix combination therapy study for uterine fibroids

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Summary

What is this summary about?

This is a summary of a research study (known as a clinical trial) called the LIBERTY extension study. The LIBERTY extension study is a long-term study looking at how well a medicine called relugolix combination therapy worked in reducing blood loss during menstrual periods in women with uterine fibroids with heavy menstrual periods. Women were included in the extension study if they finished the 24-week LIBERTY 1 or LIBERTY 2 studies. Heavy menstrual periods were considered to be menstrual blood loss of about one-third of a cup of blood (80 ml) per cycle for two cycles or about two-thirds of a cup of blood (160 ml) during one cycle. The LIBERTY extension study also looked at whether relugolix combination therapy was safe to take for up to 1 year.

What were the results?

Out of 770 total women with uterine fibroids with heavy menstrual bleeding who took part in the LIBERTY 1 and LIBERTY 2 studies, 476 took part in the LIBERTY extension study. From the start of the LIBERTY 1 and LIBERTY 2 studies through the end of the LIBERTY extension:

- 163 women took relugolix combination therapy for 52 weeks
- 149 women took relugolix alone for 12 weeks followed by relugolix combination therapy for 40 weeks
- 164 women took placebo for 24 weeks followed by relugolix combination therapy for 28 weeks

The LIBERTY extension study showed that most women in all three treatment groups responded to relugolix combination therapy by having less bleeding during their menstrual periods, having improved anemia symptoms, and having stable bone mineral loss. Side effects were similar across treatment groups, and the most common side effects were headaches and hot flushes.

What do the results mean?


Women with uterine fibroids with heavy menstrual bleeding taking relugolix combination therapy may have fewer uterine fibroid bleeding symptoms for up to 1 year of treatment.


Disclaimer

Relugolix combination therapy is approved to treat heavy menstrual bleeding associated with uterine fibroids in premenopausal women, the condition that is discussed in this summary. Approval varies by country; please check with your local provider for more details. This summary reports the results of more than one study. The results of these studies may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence.

How to say (double click on the sound icon to play the sound)


Estradiol: Est-RUH-Dy-Ole 


Leiomyoma: Lahy-Oh-Mahy-OH-Muh 

Placebo: Pluh-SEE-Bow 


Progesterone: PRO-Jest-UH-Rohn 

Norethindrone acetate:

NAWR-Eth-In-Drone As-Uh-Tate 

Relugolix: Reh-LU-Go-LIX 

Uterine fibroid:

YOU-Tuh-Ryne FY-Broyd 

Who is this article for?

This summary was written to help people with uterine fibroids, their families and caregivers, and healthcare professionals (such as doctors, nurses, nurse practitioners, and physician assistants) understand the results of the LIBERTY extension study.

Why were these studies done?

What are uterine fibroids?

Uterine fibroids are common non-cancerous (or benign) tumors that grow in the tissue of the uterus, a female reproductive organ also called the womb.



At least 1 out of 4 (or 25%) women with uterine fibroids have symptoms such as heavy bleeding during their menstrual periods and pain in the pelvis or groin.

- Women with mild symptoms from uterine fibroids can be treated with over-the-counter pain medication or birth control pills. Women with worse (moderate to severe) symptoms may need prescription oral (by mouth) medications, injections, or surgery to remove the fibroids.

What is relugolix and relugolix combination therapy?

- Relugolix is a medicine taken by mouth that can be used to lower levels of the hormones estrogen and progesterone in women with uterine fibroids. These hormones are chemical messengers in the body and are part of what controls how fibroids grow.
- Relugolix combination therapy is relugolix combined with two other hormones (estradiol, a type of estrogen, and norethindrone acetate). Together, these lessen potential side effects of too little estrogen and protect the lining of the uterus.

What did researchers find out in the LIBERTY 1 and LIBERTY 2 studies?

- Two previous studies, LIBERTY 1 and LIBERTY 2, looked at menstrual blood loss, pain, and symptoms of anemia (having low iron or low blood count) in women with uterine fibroids with heavy menstrual bleeding.
- Women receiving relugolix combination therapy for up to 24 weeks, or about 6 months, had much less bleeding during their menstrual periods, pain, and anemia symptoms compared with women receiving a placebo (a pill with no medication).
- Women who took relugolix combination therapy had few side effects and steady bone mineral density (a measure of bone strength) for up to 24 weeks (or 6 months) after starting treatment.

What did researchers want to find out in the LIBERTY extension study?

- Researchers continued the LIBERTY 1 and LIBERTY 2 studies for up to 1 year to look at the long-term efficacy (how well someone responds to treatment) and safety of relugolix combination therapy.
- In this long-term study, researchers looked at how well relugolix combination therapy helped reduce blood loss during menstrual periods, helped keep bone mineral density stable, and helped improve anemia symptoms for up to 1 year.



Researchers wanted to know

In women with uterine fibroids with heavy menstrual bleeding:

- Does 1 year of relugolix combination therapy lower the amount of menstrual blood lost during their menstrual periods?
- Is it safe to take relugolix combination therapy for up to 1 year?

- Researchers also looked at other outcomes of treatment, which are not covered in this summary. If you would like more information on the other outcomes they investigated, see the web links provided at the end of this plain language summary in a section titled: **“Where can readers find more information on these studies?”**.

Who took part in the LIBERTY 1, LIBERTY 2, and LIBERTY extension studies?



All the women who took part in the LIBERTY studies were:

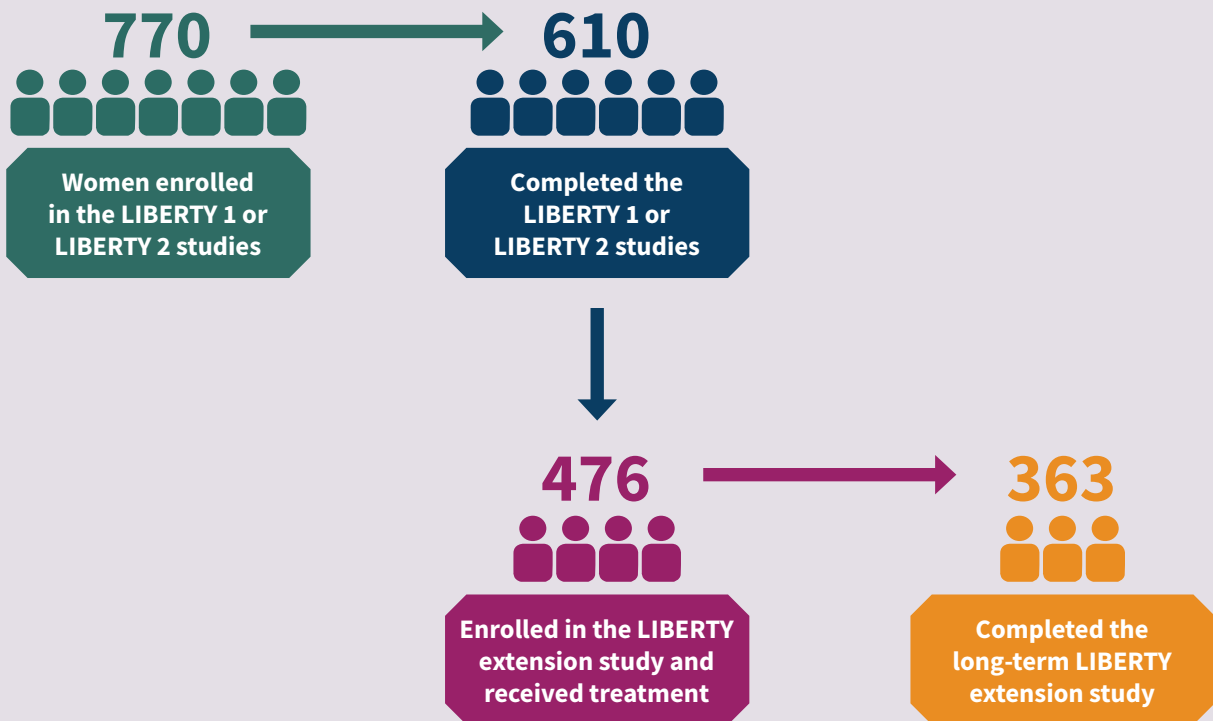
- ✓ 18 to 50 years old
- ✓ Premenopausal (still having menstrual periods)
- ✓ Diagnosed with uterine fibroids and had heavy bleeding during their menstrual periods



Heavy bleeding during menstrual periods was defined as menstrual blood loss of about one-third of a cup of blood (80 ml) per cycle for two cycles or about two-thirds of a cup of blood (160 ml) during one cycle. The normal amount of menstrual blood loss is a quarter of a cup (60 ml).

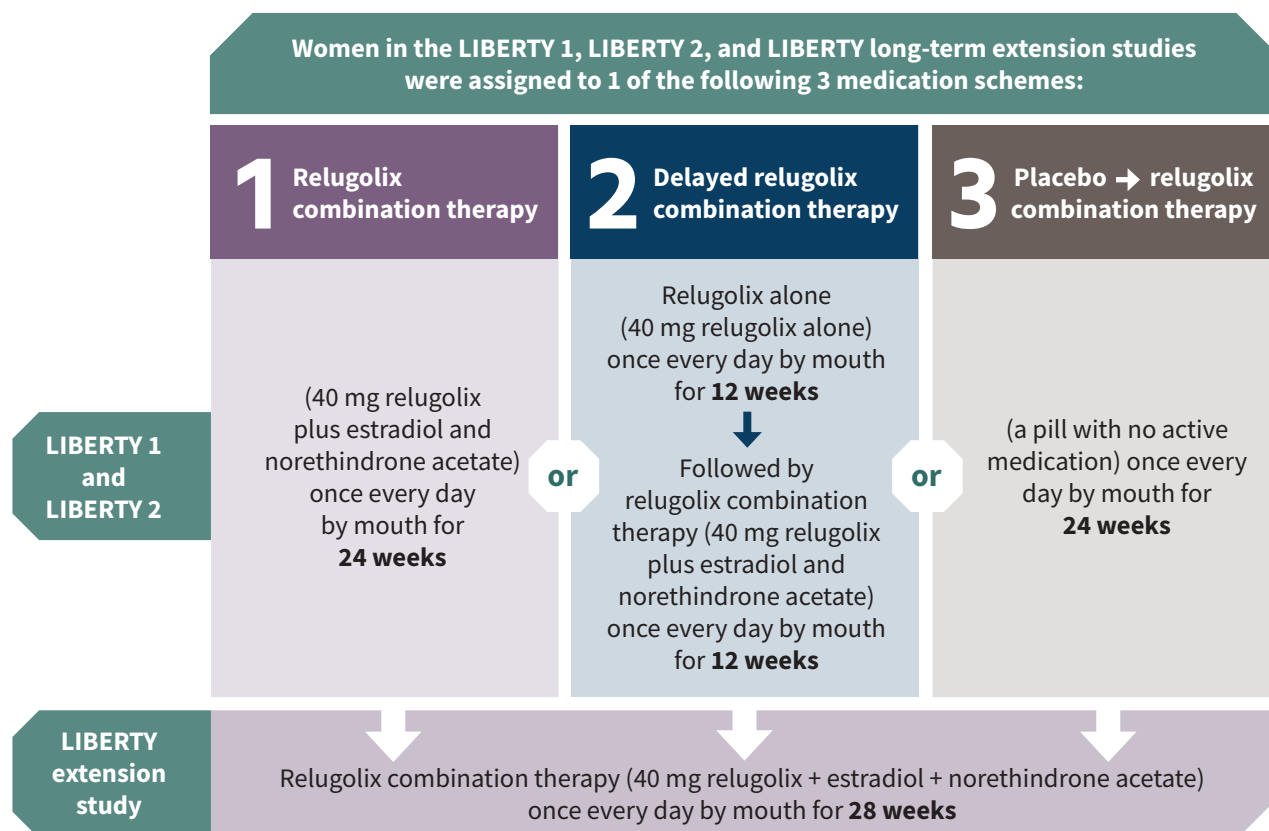
- To participate in the LIBERTY extension study, women had to have finished either the LIBERTY 1 or LIBERTY 2 studies.
- Women could not take part in the LIBERTY studies if they had other causes of heavy menstrual bleeding, were taking other hormone therapies (such as birth control pills), could not take estradiol or norethindrone acetate because of past medical conditions such as blood clots or breast cancer, or had low bone mineral density.

Women enrolled in the LIBERTY 1, LIBERTY 2, and long-term LIBERTY extension studies:



What happened during the LIBERTY 1, LIBERTY 2, and LIBERTY extension studies?

- Information about the LIBERTY 1 and LIBERTY 2 studies can also be found in the plain language summary which is available to read here: www.futuremedicine.com/doi/10.2217/pmt-2022-0085.
- Women with uterine fibroids received relugolix combination therapy for 28 weeks in the LIBERTY extension study after completing the 24-week LIBERTY 1 or LIBERTY 2 studies.



Women in the long-term LIBERTY extension study were:

	Number of women	Average age (years)	Black/ African-American	White	Other*
Relugolix combination therapy	163	43	42%	52%	6%
Delayed relugolix combination therapy	149	42	54%	34%	11%
Placebo → relugolix combination therapy	164	42	54%	43%	3%

*Other refers to Asian, American-Indian, Alaska Native, other race/ethnic group, and multiple races/ethnic groups

Where and when did these studies take place?



What were the main findings of the LIBERTY studies?

After 1 year, women were considered to have responded to treatment if they had both:

<80 ml

Menstrual blood loss less than one-third of a cup (80 ml)

+



Reduction of at least half (or 50%) the amount of menstrual period blood loss compared with what it was at the start of the study

1 Most women in all three treatment groups had good responses to relugolix combination therapy, with most women having less menstrual blood loss after treatment.



88% Relugolix combination therapy

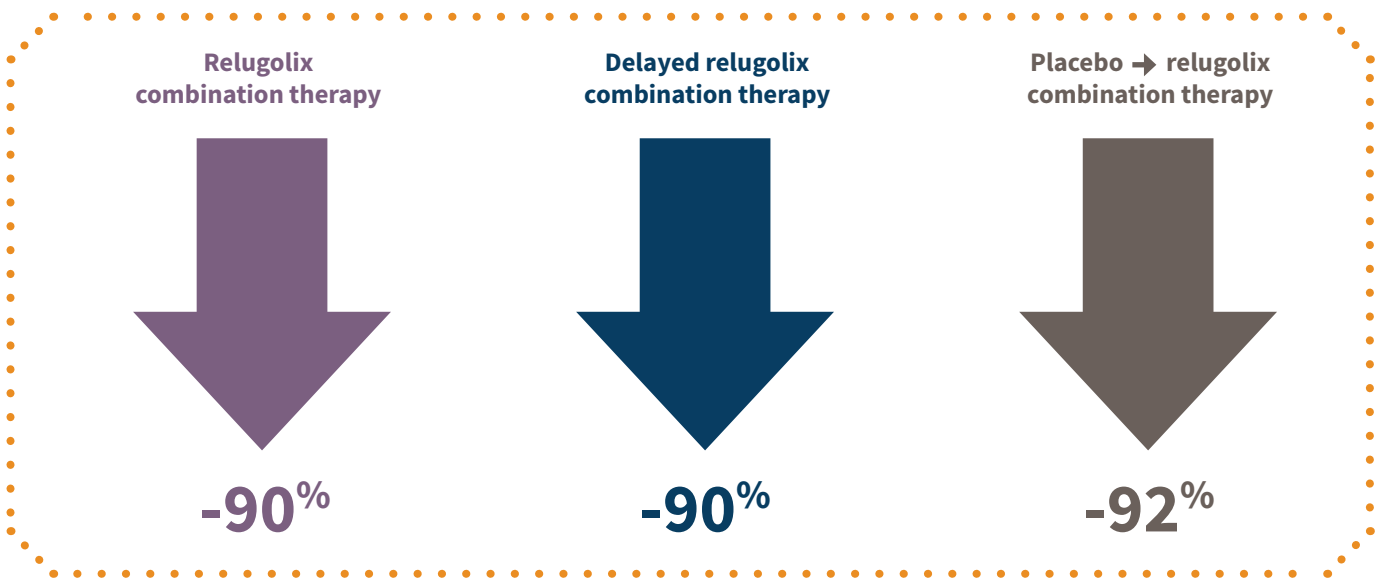


80% Delayed relugolix combination therapy

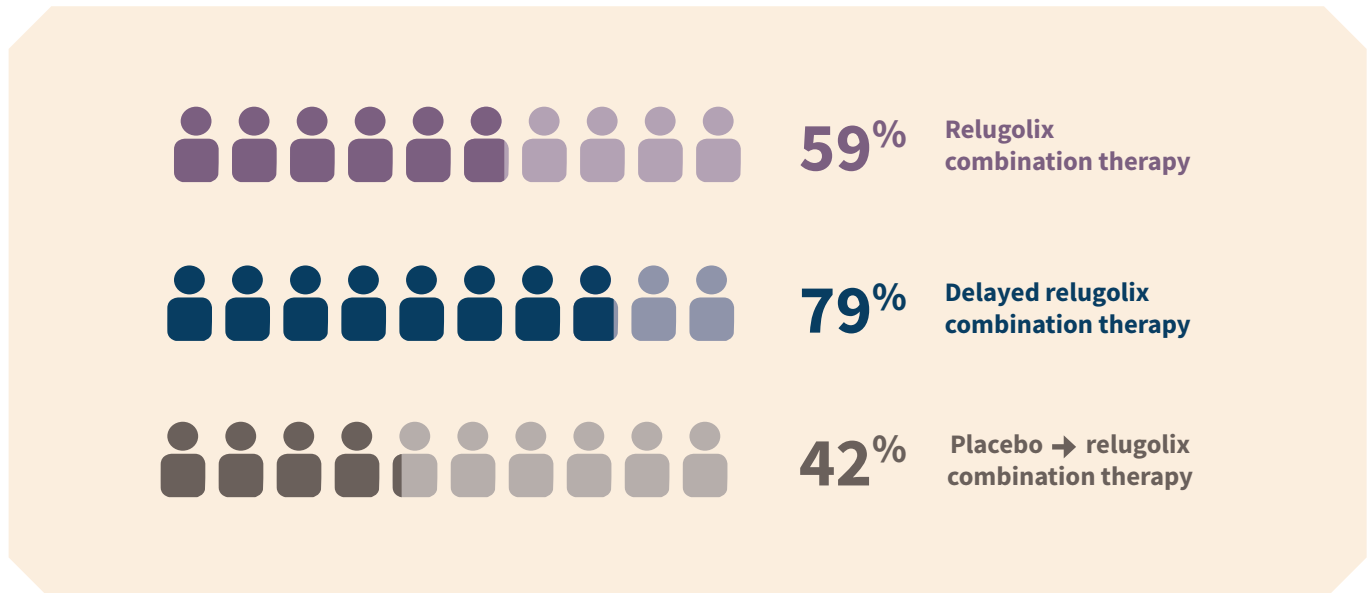


76% Placebo → relugolix combination therapy

2 Women in all three treatment groups had less menstrual blood loss during their menstrual periods with relugolix combination therapy.



3 Relugolix combination therapy improved anemia symptoms in women in all three treatment groups.



- Women taking relugolix combination therapy had less menstrual blood loss during their menstrual periods and less anemia symptoms because of uterine fibroids for up to 1 year of treatment.
- The results for the placebo → relugolix combination therapy group in the LIBERTY extension study were similar to results in the LIBERTY 1 and LIBERTY 2 studies. This supports the clinical benefits of relugolix combination therapy for heavy menstrual bleeding.
- Efficacy was similar for each of the 3 treatment groups regardless of the woman's age, race, or where she lived.

What were the most common side effects in the LIBERTY studies?



Hot flushes (also known as a hot flashes) are a sudden feeling of warmth in the upper body usually in the face, neck and chest.

Women experiencing hot flushes during treatment:

During the long-term extension (weeks 25 to 52)



Across all 52 weeks



Women experiencing headaches during treatment:

During the long-term extension (weeks 25 to 52)



Across all 52 weeks



How did treatment affect bone mineral density?

- Bone mineral density at the start of the LIBERTY studies was compared with bone mineral density at the end of the studies.
- Women had similar bone mineral density after taking relugolix combination therapy as they did before.
- Women who took delayed relugolix combination therapy lost more bone mineral density while taking relugolix alone. Once they started taking relugolix combination therapy, they stopped losing bone mineral density.
- Women who took placebo → relugolix combination therapy lost a small amount of bone mineral density while taking relugolix combination therapy.

What do the results of the LIBERTY studies mean?

- Women with uterine fibroids with heavy menstrual bleeding who took relugolix combination therapy had less heavy menstrual bleeding during their menstrual periods, had improvements in their anemia symptoms, and had steady bone mineral density over long-term treatment of 1 year.
- Side effects were similar across all treatment groups in women with uterine fibroids with heavy menstrual bleeding.
- The most common side effects were headaches and hot flushes over 1 year of relugolix combination therapy.
- Relugolix combination therapy may help women with uterine fibroids with heavy menstrual bleeding have fewer uterine fibroid symptoms over long-term treatment.

Who sponsored these studies?

These studies were sponsored by Myovant Sciences GmbH.

This summary was funded by Pfizer and Myovant Sciences GmbH. Myfembree (a tablet containing relugolix, estradiol, and norethindrone acetate) is jointly developed by Myovant Sciences and Pfizer Inc.

Where can readers find more information on these studies?

Original article

The original article 'Long-term Relugolix Combination Therapy for Symptomatic Uterine Leiomyomas' was published in *Obstetrics & Gynecology*. The full citation for the original article is: Al-Hendy A, et al. *Obstet Gynecol.* 2022;140:920-930.

You can read the full article at:

https://journals.lww.com/greenjournal/Fulltext/2022/12000/Long_term_Relugolix_Combination_Therapy_for.4.aspx

Trial registration site:

You can read more about the LIBERTY 1, LIBERTY 2, and LIBERTY extension studies at the following trial registration websites:

LIBERTY 1 study: <https://clinicaltrials.gov/ct2/show/NCT03049735>

LIBERTY 2 study: <https://clinicaltrials.gov/ct2/show/NCT03103087>

LIBERTY extension study: <https://clinicaltrials.gov/ct2/show/NCT03412890>

For more information on clinical trials in general, please visit: <https://www.clinicaltrials.gov/ct2/about-studies/learn>

Disclosures and Acknowledgments

Disclosure forms provided by the authors are available with the full text in the *Obstetrics & Gynecology* article.

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