# Science Review: ERr 731®

ERr 731 is a nonhormonal therapy to alleviate the uncomfortable symptoms of menopause, including hot flashes.

With more than 30 years of safe, effective use in Europe (backed by decades of postmarketing surveillance data), ERr 731 has been clinically demonstrated, through extensive research, including randomized controlled trials, to safely and effectively reduce menopausal symptoms.

## ERr 731 Research Highlights

- ✓ In a 12-week randomized controlled trial, ERr 731 significantly reduced the number of hot flashes from a median of 12 to 2 daily
- ✓ In the same study, ERr 731 demonstrated an 83% reduction in hot flashes, as well as a significant decrease in anxiety
- ✓ No changes in gynecological findings (e.g., endometrial hyperplasia or abnormalities in breast tissue) and safety parameters were observed in a two-year observational study
- ✓ Postmarketing surveillance found that the incidence of ERr 731-associated adverse events was very low

## 12-week randomized controlled trial (RCT)

109 perimenopausal women
Heger M et al. *Menopause.* 2006[1]

- At 12 weeks, ERr 731 group had a significant reduction in total Menopause Rating Scale II (MRS II) score, as well as significant decreases in all 11 individual symptom scores compared with placebo ($p<0.001$)
- No abnormalities in safety parameters such as breast tissue, endometrium, hormones, liver enzymes, body weight, and blood pressure were noted

Kaszkin-Bettag M et al. *Menopause.* 2007[2]

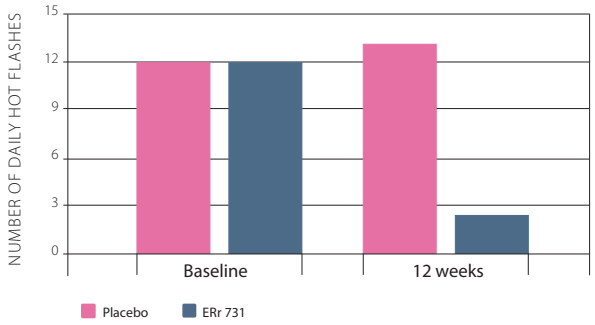
- The Hamilton Anxiety Scale (HAMA) total scores and HAMA factors scores for somatic and psychic anxiety were significantly reduced in ERr 731 group after just 4 weeks and even more pronounced after 12 weeks of treatment ($p<0.001$) but not placebo
- There were no differences in gynecological findings, including endometrial biopsies, bleeding, weight, blood pressure, pulse, and laboratory safety parameters, between the treatment groups, and no adverse events (AEs) related to ERr 731 were detected

## 12-week confirmatory RCT

112 perimenopausal women
Kaszkin-Bettag M et al. *Altern Ther Health Med.* 2009[3]

- At 12 weeks, ERr 731 group showed a significant reduction in the number of hot flashes compared to placebo, from a median of 12 to 2—an 83% reduction (**Figure 1**)
- The Hot-Flash-Weekly-Weighted-Score (HFWWS) was significantly decreased in ERr 731 group ($p<0.0001$) but not the placebo group

Figure 1

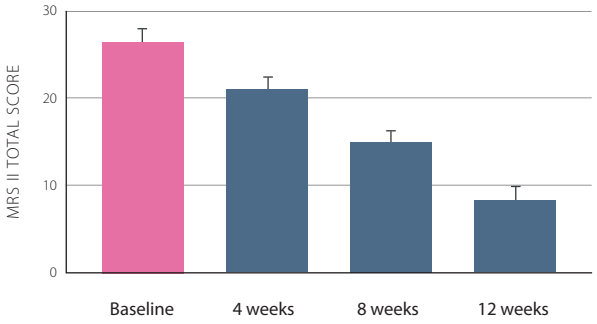



## 12-week efficacy and safety evaluation at 15 gynecology outpatient departments

108 Indian perimenopausal women
Shah J et al. *J Midlife Health.* 2021[4]

- Subjects showed a significant (68%) reduction in MRS II total score ($p<0.001$; **Figure 2**) as well as scores of somatic, urogenital, and psychological subscales
- ERr 731 was found to be safe and had no effect on endometrial thickness and cardiovascular risk factors

Figure 2

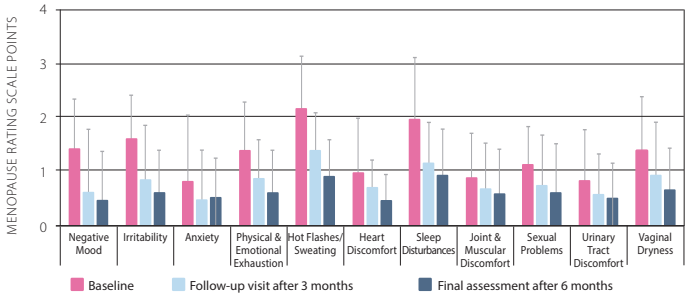


## 6-month observational study (OS) at 70 gynecological practices

252 peri- and postmenopausal women
Kaszkin-Bettag M et al. *Altern Ther Health Med.* 2008[6]

- Subjects showed a significant decrease in MRS total score from a mean of 14.5 points at baseline to 6.5 at 6 months ($p<0.0001$); all 11 individual symptom scores were improved (**Figure 3**)
- 90% of women rated the tolerability of ERr 731 "very good" or "good," and there were no ERr 731-related AEs

Figure 3

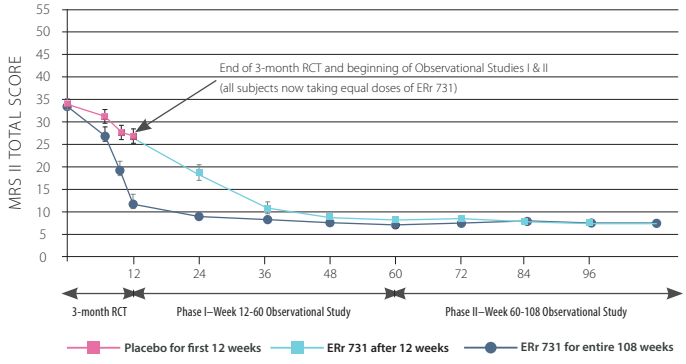



## Two-year post-RCT observational study (OS)

OS I (48 weeks) consisted of 80 menopausal women; OS II (additional 48 weeks) consisted of 51 women from OS I
Hasper I et al. *Menopause.* 2009[6]

- The mean MRS II total score was reduced from 34.0 at baseline to 5.7 at end of OS II—an 83% reduction (**Figure 4**)
- ERr 731 demonstrated a sustained alleviation of menopausal symptoms, and no changes in safety parameters were observed over two years
- By the end of two years, the endometrial thickness showed a slight decrease in all women
- No increases in serum progesterone or 17β-estradiol levels were observed, suggesting a lack of a potential hyperproliferative activity of ERr 731 in endometrium or breast

Figure 4




## Postmarketing surveillance since 1993

Chang J et al. *Integr Med (Encinitas).* 2016[6]

- Postmarketing surveillance began in Germany (in 1993) and expanded to USA (in 2009), South Africa (in 2011), and Canada (in 2012)
- Published postmarketing surveillance data, from approximately 153 million doses sold since 1993, suggest ERr731 is generally safe for consumption

## ERr 731 inclusion in *JAMA* review

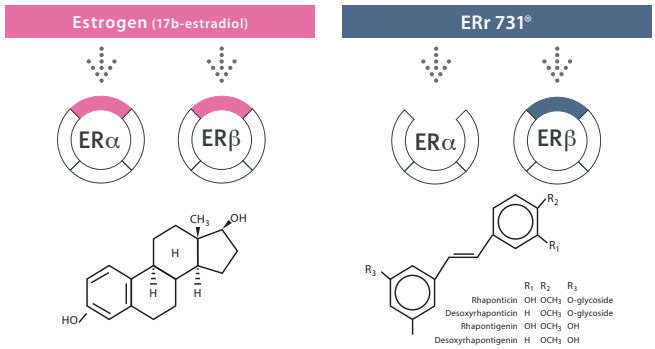
Franco OH et al. *JAMA*. 2016[8]

- *The Journal of the American Medical Association* (*JAMA*) published a systematic review article based on published RCTs of plant-based therapies and reported remedies such as ERr 731 to be associated with improvements in the number of hot flashes

## ERr 731: selective binding of Estrogen Receptor β (ERβ)

- The clinical benefits of ERr 731 appear to be related to selective binding of ERβ and lack of affinity for ERα (**Figure 5**)[9-12]
- In an animal model mimicking human menopause, ERr 731 dose-dependently reduced the increase in skin temperature, suggesting an improvement in hot flashes[12]
- In tissues where both ERα and ERβ are expressed, ERβ may function as a negative regulator of ERα, offering relief of menopausal symptoms as well as protection against inflammation and hyperproliferation[13,14]

Figure 5




## Conclusion

With extensive preclinical and clinical research demonstrating efficacy and safety as well as a decades-long postmarketing surveillance safety record, ERr 731 is a thoroughly tested plant-derived extract that offers an innovative approach to relieving menopausal symptoms, including hot flashes.

**References:**

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