

# GENESIS

GYNECOLOGIE - OBSTETRIQUE - ENDOCRINOLOGIE

No. 183 Monthly  
March/April 2015

ISSN 1275-9589



Interview with Professor  
Patrice Lopès

p. 4

Vulvovaginal  
Atrophy and  
Fractional CO2  
Laser

p. 6

Assessment of the  
quality of life,  
effectiveness, and  
tolerance of  
Sérélys® in women  
during  
peri-menopause  
and menopause

p. 10

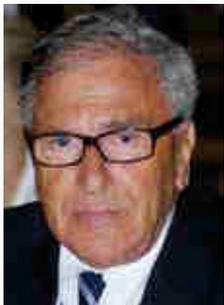
Can breast surgery  
be performed on  
an outpatient  
basis?

p. 16

Updates on HPV  
Vaccination in  
France

p. 20

# Assessment of Quality of Life, Effectiveness, and Tolerance of Sérélys® for women in perimenopause and menopause



DR René Druckmann  
Nice



DR Michèle Lachowsky  
Paris



DR David Elia  
Paris

With life expectancy on the rise, quality of life becomes a crucial health factor in an aging population. As the age of menopause onset remains unchanged, each woman spends about a third of her life in a state of hormonal deficiency. The functional symptoms linked to this deficiency significantly impact the quality of life for menopausal women (1). Therefore, it is essential to manage this unique phase of a woman's life effectively, relieving her of estrogen deficiency symptoms so she can fully enjoy this new stage of life.

In France, six and a half million women are menopausal and aged 50 to 65, and approximately 400,000 new women enter menopause every year. About 70% of them will experience menopausal symptoms (2,3). The severity of these symptoms and the degree to which they interfere with their activity and quality of life varies from woman to woman. About 20% of these women report severe symptoms, and 10 to 15% seek treatment (4). These menopausal symptoms can be transient (one or two years) but can also last longer in some women, thus profoundly affecting women's personal and social lives and quality of life (6).

In this context, a clinical study was conducted to investigate a beneficial effect of Sérélys® in improving the quality of life associated with this vasomotor symptomatology in patients in perimenopause or in confirmed menopause

#### •Product

Sérélys® contains purified cytoplasmic extracts of pollens whose patented cytoplasmic extraction process is carried out according to Good Manufacturing Practices, allowing the extraction of the active part of the pollen grain (the cytoplasm) from its shell. An additional step

allows the removal of pollen envelopes, eliminating the potentially allergenic fraction and ensuring perfect safety of use (no contraindication for patients allergic to pollen).

Sérélys® has been used in Europe since 1998 and has already received marketing authorization as a medicine in Sweden and Norway.

#### •Method

##### Study Objective:

To assess the tolerance and effectiveness of Sérélys® tablets in women during peri-menopause and menopause by studying the progression of climacteric disturbances (hot flashes, irritability, fatigue, sleep quality) and its impact on the patients' quality of life after 3 months of treatment with Sérélys®. To confirm the effectiveness of Sérélys® in both peri-menopause and menopause.

##### Study Group:

324 women, monitored by 90 gynecologists, participated in this open, multicenter clinical study in France.

##### •Treatment Under Study

The treatment involved taking 2 Sérélys® tablets daily, administered orally for 90 days.

## •Study Procedure

The women participating in the trial had two consultations, one at the beginning of the study (Day 0): C1, and the other at the end of evaluation after 3 months of treatment with Séréllys® (Day 90): C2. Visual analog scales (VAS) and a questionnaire related to specific menopause items were completed and analyzed to characterize and rate the intensity and frequency of symptoms experienced by the patient: hot flashes, irritability, fatigue, sleep quality, and their impact on quality of life.

## •Evaluation Criteria

**Effectiveness was assessed using a questionnaire and visual analog scales (VAS) for the following items: hot flashes (frequency, intensity, and occurrence); irritability; fatigue; sleep; quality of life.**

**Tolerance was evaluated using a four-level rating scale employed by the investigating physician based on complaints reported by patients and clinical examination data.**

- 1 = Excellent tolerance
- 2 = Good
- 3 = Average
- 4 = Poor

## Overall Appreciation by Patients and Investigators

The data resulting from patient evaluations using VAS were subject to statistical analysis.

## •Statistical Methods

### - Description of Patients

The demographic characteristics of patients and the evaluation of their symptoms were described using means, standard deviations, medians, and quartiles for quantitative variables, and counts and frequencies for qualitative variables.

### - Evaluation of Main Criteria

The progression of climacteric issues was measured using Chi-square tests, and intensity through repeated series variance analysis based on groups of patients in peri-menopause or menopause.

### - Evaluation of Secondary Criteria

The evaluation of the product by the patient and the gynecologist was described using frequencies and counts for qualitative variables and compared between groups using a Chi-square test.

### - Evaluation of Tolerance

The product's tolerance was described using a 4-point Likert scale by frequencies and counts.

### - Analysis Software

The analyses were conducted using SAS software version 9.3 by CEN Nutriment and the significance level HVW IL[p j

## •Results

### Symptom Progression after 3 Months of Séréllys® Treatment

The progression of symptoms was measured by the difference between the baseline and end-of-study values, then categorized as 'worsening,' 'stable,' or 'improvement.' Globally, 85.5% and 91% of women showed improvement in the frequency and intensity of hot flashes. No significant differences were observed between women in perimenopause and those postmenopausal.

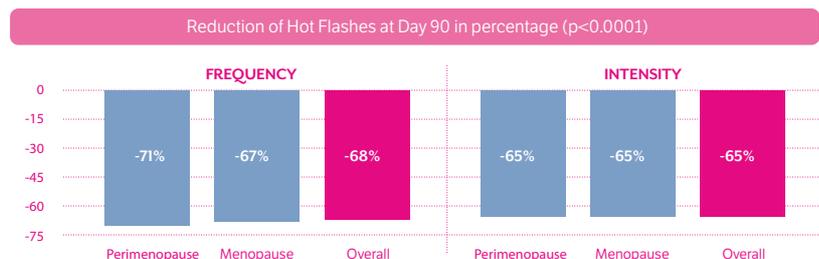
Figure 1 presents the results concerning the intensity and frequency of hot flashes in both patient groups and the overall treated population.



**Figure 1.** In the global population, respectively 85.5 % and 91% of the patients have experienced improvement in frequency, intensity of the hot flashes without significant discrepancy between the pre and post-menopause group

The intensity of symptoms was measured on a visual analog scale from 0 to 100.

A significant average decrease ( $p < 0.0001$ ) of  $41.7 \pm 23.6$  is observed for the frequency of hot flashes and  $45.8 \pm 23.0$  for the intensity of these hot flashes (Figure 2).



**Figure 2. Significant reduction ( $p < 0.0001$ ), equivalent in both groups for frequency and intensity of hot flashes.**

An improvement in irritability is noted in 62.0% of women.

The intensity of this irritability drops from  $41.8 \pm 31.5$  to  $16.5 \pm 20.0$ , a very significant statistical decrease of  $25.1 \pm 26.8$  ( $p < 0.0001$ ). No significant differences are observed between women in perimenopause and those postmenopausal.

An improvement in fatigue is noted in 60.8% of women, with an average intensity decreasing from  $45.5 \pm 31.2$  to  $19.8 \pm 22.4$ , also a statistically significant decrease of  $25.5 \pm 25.7$  ( $p < 0.0001$ ). No significant differences are observed between women in perimenopause and those postmenopausal (Figure 3).

## •Menopause

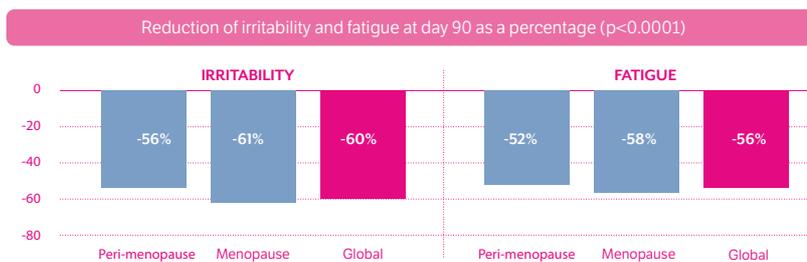


Figure 3. Significant reduction ( $p < 0.0001$ ) in irritability and fatigue, consistent across both groups.

The quality of sleep also improved for 47.8% of women, with intensity changing from  $57.5 \pm 28.6$  to  $32.1 \pm 25.7$ , showing a decrease of  $25.5 \pm 34.8$  ( $p < 0.0001$ ). No significant difference was noted between peri-menopausal and menopausal women.

Finally, 71.9% of women also perceived an improvement in their quality of life, with intensity moving from  $55.8 \pm 23.3$  to  $25.9 \pm 18.1$ , showing a change of  $29.8 \pm 23.7$  ( $p < 0.0001$ ). No significant difference was observed between peri-menopausal and menopausal women (Figure 4).

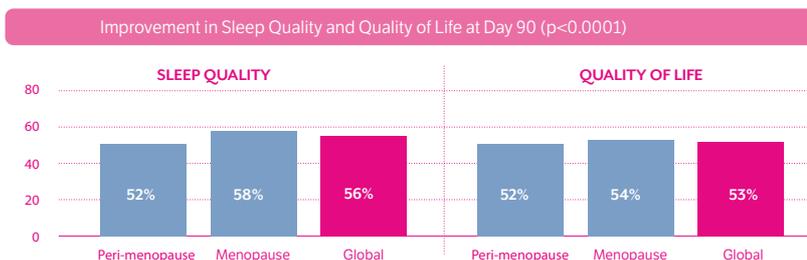


Figure 4. Improvement in Sleep Quality and Quality of Life at Day 90

### •Analysis by Groups

Regarding symptom progression, no differences were found between the groups (peri-menopause/menopause) in the frequency of hot flashes, their intensity, changes in irritability, fatigue, sleep quality, and overall quality of life.

### •Overall Patient Evaluation

Patients rated the product with an average score of  $14.9 \pm 2.5$  out of 20, indicating very positive feedback.

The product under study was rated as very effective or quite effective by 93.5% of patients for improving issues related to peri-menopause or menopause. Its acceptability, in terms of intake constraints and possible taste of tablets, was considered very good or quite good by 96.6% of patients. 93.2% of patients believe Séréllys® is very or quite effective in enhancing their quality of life related to symptoms experienced during peri-menopause or menopause.

Out of 170 patients, 149 (87.6%) who had used another

product, found Séréllys® to be noticeably or somewhat better than the other product.

### •Overall Gynecologist Evaluation

From the gynecologist's perspective, the product under study was rated as very effective or quite effective by 93.5% of gynecologists. 92.5% of gynecologists who prescribed other products found Séréllys® to be noticeably or somewhat better than the other product.

### •Tolerance

The tolerance of Séréllys® is very good, with 92.1% judging it as excellent and 6.6% as good, totaling 98.7%.

Only 3 side effects were reported by patients. No link with Séréllys® treatment could be demonstrated. They included: nausea in the first few days (1), nighttime nausea and pressure (1), and occasional pelvic heaviness (1). These effects did not lead to an early discontinuation of the treatment.

### •Analysis by Groups

No difference between groups was found in the ratings on Séréllys® effectiveness for improving issues, acceptability, enhancing quality of life, and in comparison to previously used products.

The assessments made by gynecologists are similar for both peri-menopausal and menopausal women, whether it's regarding the overall effectiveness of Séréllys® or its perceived effectiveness compared to other previously prescribed products.

•Séréllys® has proven its effectiveness in reducing the frequency and intensity of hot flashes in menopausal women. It has been the subject of numerous clinical studies, including three double-blind placebo-controlled trials, demonstrating its benefits in treating climacteric symptoms and premenstrual syndrome (7, 8, 12). In a randomized double-blind placebo-controlled study conducted with 64 menopausal women over a period of months, a statistically significant difference ( $p < 0.006$ ) of 20 to 30% was observed between the two groups in favor of Séréllys® concerning the frequency and intensity of hot flashes. A significant improvement ( $p < 0.031$ ) in all quality of life parameters for treated women was also shown. The product was found to be perfectly well-tolerated (7). In treating premenstrual symptoms, Séréllys® significantly reduced sleep disturbances compared to placebo ( $p < 0.05$ ), as well as premenstrual weight gain (50%, compared to placebo), and all quality of life parameters in two randomized placebo-controlled studies conducted with 32 and 101 women, respectively (8, 12). The safety of Séréllys® was demonstrated in these two studies, where no significant difference between the treated and placebo groups was reported. An open clinical study, spanning 12 weeks,

was also conducted by 102 French doctors on a total of 417 menopausal women experiencing functional symptoms such as hot flashes, night sweats, sleep disturbances, and mood swings related to menopause (9). The treatment was effective according to both the investigators and the women treated, improving menopause-related issues (reducing the frequency and intensity of hot flashes and sweating episodes) and enhancing quality of life associated with these symptoms. Tolerance was excellent for more than 98% of the treated women. A statistically significant reduction in all menopause-related symptoms, particularly hot flashes (-57.3%), night sweats (-62.6%), and sleep disturbances (-54.7%), was observed in 80 women in an open-label pilot study over 3 months (10). No adverse effects, especially no allergic reactions, were reported.

Sérélys® is free of estrogenic activity and uterotrophic effects. The search for phytoestrogens in its composition was negative. Therefore, a hormonal action is excluded (9). An exhaustive bibliographic review demonstrated that Sérélys® is a non-estrogenic alternative to hormone therapy for women who are prematurely menopausal due to breast cancer or are survivors of such cancer (11).

The results of the present study show that all studied parameters: hot flashes, irritability, fatigue, sleep quality, and quality of life improved statistically significantly between the first consultation at day 0 and the second at day 90 after 3 months of treatment with Sérélys®. Regular intake of Sérélys® provides statistically significant improvements

across all the women, in a manner

comparable between post-menopausal and peri-menopausal women, significantly enhancing their quality of life

Sérélys® is also very well tolerated by both post-menopausal and peri-menopausal women. Considering the large number of investigating doctors and included patients, the observed results seem to be a good reflection of the benefits to be expected from this product in everyday practice, starting with the first functional symptoms of menopausal transition. The results of the present study confirm those already observed previously.

#### •Conclusion

Based on this clinical study and previous ones, the cytoplasmic pollen extract in Sérélys® shows notable effectiveness on climacteric symptoms. It significantly improves the quality of life for women who are menopausal or in the peri-menopausal period and serves as a non-estrogenic alternative to hormone therapy.

The product's good tolerance, the absence of phytoestrogens in its composition, and its non-hormonal mechanism of action allow it to be safely offered to women from the peri-menopausal phase through menopause.

Sérélys® thus finds its place in the therapeutic arsenal offered to gynecologists in response to a demand for non-hormonal, safe strategies capable of relieving climacteric symptoms and their impact on the quality of life of women in peri-menopause or menopause. ●●●●

#### RÉFÉRENCES

- Hunter M., Battersby R., Whitehead M. 1986. Relationships between psychological symptoms, somatic complaints and menopausal status. *Maturitas* 8, 217-228.
- Letombe B. Le syndrome climatérique et la qualité de vie : balance bénéfiques/risques du THM et des traitements symptomatiques. *Mises à jour en gynécologie médicale*. 2010 ;2010;513-542
- Afssaps. Informations générales sur le traitement hormonal substitutif de la ménopause. Juillet 2006.
- Guthrie J, Dennerstein L, Taffe J, Donnelly V. Health care-seeking for menopausal problems. *Climacteric* 2003;6:112-7.
- Politi MC, Schleinitz MD, Col NF. Revisiting the duration of vasomotor symptoms of menopause: a meta-analysis. *J Gen Intern Med* 2008;23:1507-13.
- Anderson E, Hamburger S, Liu JH, Rebar RW. Characteristics of menopausal women seeking assistance. *Am J Obstet Gynecol* 1987;156:428-33.
- Winther K, Rein E, Hedman C. Femal®, a herbal remedy made from pollen extracts, reduces hot flashes and improves quality of life in menopausal women: a randomized, placebo-controlled, parallel study. *CLIMACTERIC* 2005;8:162-170.
- Gerhardsen G, Hansen AV, Killi M, Fornitz GG, Pedersen F, Roos SB. The efficacy of Femal® in women with premenstrual syndrome: a randomized, double-blind, parallel-group, placebo-controlled, multicentre study. *Adv Ther*. 2008;25(6):595-607.
- Elia D, Mares P. Évaluation de la tolérance et de l'efficacité d'un complément alimentaire Sérélys® (Femal®) chez les femmes en période de ménopause. *Génésis*.2008 ;135:12-15.
- Kimura H, Gruber P. Perimenopausal symptoms such as hot flashes and mood swings are reduced by a standardised pollen and pistil extracts. Poster. 2008.
- Espié M. Bouffées de chaleur et cancer du sein : Quelle prise en charge efficace et sans risque ? *Cancers au féminin*. 2013 ; 1-16.
- Winther K, Hedman C. Assessment of the effects of the herbal remedy Femal® on the symptoms of premenstrual syndrome: a randomized, double-blind, placebo-controlled study. *Current Therapeutic Research* 2002; 63 (5): 344-353.
- Espié M, Druckmann R. : How can hot flashes be managed effectively and without without risk for menopausal women with breast cancer or a history of breast cancer - World congress on Menopause, Cancun 2014.
- Goldstein S, Espié M, Druckmann R. : Does Relizen®, a non-hormonal treatment for vasomotor symptoms, inhibit the CYP2D6 enzyme system? National American Menopause society congress Washington 2014.
- Espié M, Druckmann R. : How can hot flashes be managed for breast cancer patients and survivors without risk? National American Menopause society congress Washington 2014.
- Druckmann R, Lachowsky M., Elia D. : A non-hormonal treatment, efficient and save on climacteric symptoms during pre-menopause and menopause, improve women's quality of life, World congress on reproduction - Berlin 2015