Climacteric

ISSN: 1369-7137 (Print) 1473-0804 (Online) Journal homepage: http://www.tandfonline.com/loi/icmt20

# A prospective study of DT56a (Femarelle®) for the treatment of menopause symptoms

R. Sánchez-Borrego, N. Mendoza & P. Llaneza

**To cite this article:** R. Sánchez-Borrego, N. Mendoza & P. Llaneza (2015): A prospective study of DT56a (Femarelle®) for the treatment of menopause symptoms, Climacteric, DOI: 10.3109/13697137.2015.1065247

**To link to this article:** http://dx.doi.org/10.3109/13697137.2015.1065247

Published online: 10 Oct 2015.

CLIMACTERIC 2015; Early Online: 1–4

# A prospective study of DT56a (Femarelle®) for the treatment of menopause symptoms

*R. Sánchez-Borrego, N. Mendoza* and P. Llaneza†*

DIATROS, Clínica de Atención a la Mujer, Barcelona; *Universidad de Granada, Departamento de Obstetricia y Ginecología, Granada; †Hospital Universitario Central de Asturias, Servicio de Ginecología y Obstetricia, Spain

Key words: PHYTOTHERAPY, PHYTOESTROGENS, MENOPAUSE, PHYTO-SERM, HOT FLUSHES



## ABSTRACT

*Background* DT56a (Femarelle®) is a natural medication that contains a variety of phytoestrogens derived from tofu. Treatment with DT56a affects bones, vascular tissues and the nervous system in a manner similar to that of estrogen but DT56a acts as an estrogen antagonist in breast and uterine tissues.

*Aim* The objective of this study was to analyze the efficacy of DT56a in the reduction of menopause symptoms in Spanish women who participated in the Post Marketing Menopausal Symptoms International Survey (POMMSIS).

*Patients and methods* A total of 631 Spanish menopausal or perimenopausal women with vasomotor symptoms who took DT56a for 4 weeks participated in this study. This study was an observational, questionnaire-based investigation that consisted of a baseline questionnaire, a hot flushes daily diary and a feedback questionnaire.

*Results* A statistically significant ($p < 0.01$) reduction in the number and intensity of hot flushes was experienced after 2 and 4 weeks of DT56a treatment. After 4 weeks of treatment with DT56a, 80.7% of the patients reported that their hot flushes were 'better' or 'much better'. The severity of hot flushes was also reduced by 38% in all study participants and by 36% in women who had experienced more than seven hot flushes per day initially, before treatment.

*Conclusion* Treatment with DT56a resulted in a significant reduction in the number and intensity of hot flushes in postmenopausal women, especially in those with frequent symptoms, and these effects were observed within the first month of treatment.

## INTRODUCTION

Postmenopausal estrogen deficiency causes vasomotor symptoms, vaginal dryness and an increased risk of osteoporosis. Estrogen- and progestogen-based hormone therapy is the first option for alleviating these ailments. However, the potential for side-effects makes these treatments less appealing and instead encourages the use of alternative treatments.

Estrogen-like natural substances (phytoestrogens) and estrogen-rich diets can provide gentle hormonal effects. Three main types of phytoestrogens can be obtained from dietary and pharmacological sources, including isoflavones, coumestans and lignans, and there is a growing interest in whether better results are obtained when two or more such compounds are consumed together rather than taken alone[1].

DT56a (Femarelle®) is a natural medication that contains a variety of phytoestrogens derived from tofu. Treatment with DT56a affects bones, vascular tissues and the nervous system in a manner similar to that of estrogen but DT56a acts as an estrogen antagonist in breast and uterine tissues. Due to these dual effects, DT56a is classified as a selective estrogen receptor modulator (SERM) and specifically a phyto-SERM[2]. The objective of this study was to analyze the efficacy of DT56a in the reduction of menopause symptoms.

## PATIENTS AND METHODS

A total of 631 Spanish menopausal or perimenopausal women participated in this study after written consent was obtained; the women were recruited through their gynecologists, general

Correspondence: Dr N. Mendoza, Maestro Montero 21, 18004 Granada, Spain; E-mail: nicomendoza@telefonica.net

ORIGINAL ARTICLE

DOI: 10.3109/13697137.2015.1065247

Received 22-02-2015
Revised 27-04-2015
Accepted 16-06-2015

practitioners or pharmacists. Eligible peri- or postmenopausal participants (who had irregular menstrual periods or who had stopped having menstrual periods) were not pregnant, were 45 years old or older, had not received hormone therapy in the past 6 months and were experiencing at least one hot flush per day.

The study consisted of observational, questionnaire-based investigations; in this study, three questionnaires were administered during two patient visits, and one questionnaire was given to be filled out by the patient at home between the two visits. At the first visit, which was the enrolment visit, participants received a baseline questionnaire and a hot flushes daily diary (to be completed at home). If a patient agreed to participate in the study and met the inclusion criteria, then she was given medication for 4 weeks. At the second visit, both the patients and the physician completed the feedback questionnaire.

The questionnaires were available in both paper and electronic form and were used to collect demographic data, health data, including self-reported menopausal status, and information about medication use.

The study was conducted in routine clinical settings, in the outpatient clinics of gynecology departments and in family planning centers of public and private institutions in Spain, as part of the Post Marketing Menopausal Symptoms International Survey (POMMSIS).

The statistical software IBM SPSS Statistic Base version 22.0 was used to analyze the data. The data are expressed as absolute numbers and percentages or as means and standard deviations (SDs). Normally distributed continuous data were compared with Student's *t*-test or an analysis of variance (ANOVA). When data distributions departed from normality, the Mann–Whitney *U*-test or the Kruskal–Wallis test was used. The $\chi^2$ test was used to compare categorical variable data. A value of $p < 0.05$ was considered statistically significant for all statistical tests performed.

## RESULTS

The descriptive characteristics of the study sample are shown in Table 1. Hot flushes were the symptoms most frequently experienced by these patients, and most hot flushes were experienced with great intensity (see Table 2). Forty-one percent of the patients suffered seven or more hot flushes daily, with an average of 6.92 (SD = 4.49) hot flushes daily.

Patients experienced a statistically significant ($p < 0.01$) reduction in the number and intensity of hot flushes after 2 and 4 weeks of DT56a treatment (see Table 3). In addition, the number of hot flushes was reduced by 50%, on average, after 4 weeks of treatment in all study participants and by 48% in women who had experienced more than seven hot flushes per day before treatment. The severity of hot flushes was also reduced by 38% in all study participants and by 36% in women who had experienced more than seven hot flushes per day before treatment.

**Table 1** Characteristics of the Spanish women participating in the study. Data are given as mean ± standard deviation or *n* (%)

| | *n* = 631 |
|---|---|
| Age (years) | 52 ± 4.83 |
| Weight (kg) | 66 ± 10.02 |
| Height (cm) | 161 ± 5.93 |
| Smokers (%) | 33.80 |
| Age at menopause (years) | 49 ± 3.92 |
| *Last menstrual period* | |
| More than 1 year ago | 66.2 |
| A few months ago | 33.3 |
| Within the last month | 0.5 |
| *Cause of cessation* | |
| Natural | 90 |
| Surgical | 10 |

After 4 weeks of treatment with DT56a, 80.7% of the patients reported that their hot flush symptoms were 'better' or 'much better'. Table 4 analyzes in detail patients' feedback with respect to this improvement and the proportion of patients who were referred for other symptoms. With respect to how the patients felt overall, 79.3% of the participants reported one or more positive effects after 4 weeks of treatment with DT56a; the most common responses were 'General improvement in quality of life' and 'Brought back the vitality I had lost'.

## DISCUSSION

The primary findings of this study are that treatment with DT56a resulted in a significant reduction in the number and intensity of hot flushes in Spanish postmenopausal women, especially in those with frequent symptoms (> seven hot flushes/day). These effects were observed within the first month of treatment. The present study was a part of a multi-country survey that provides physicians and pharmacists with exposure to DT56a and studies patient satisfaction. Hot flushes and night sweats were the prominent symptoms experienced in all five countries, although there was some difference in how women experienced hot flushes between the countries. Thus, a 'feeling of suffocation' was reported much more frequently in Spain than in the other countries in which the survey was conducted. However, 84.4% of the study participants, especially those with the most frequent symptoms, reported that their hot flush symptoms were 'better' or 'much better' after 4 weeks of treatment.

The main limitations of this study are related to the study procedure itself. This study consisted of an observational, questionnaire-based investigation but, to our knowledge, this is the first study that investigated the effects of DT56a in a large cohort (631 subjects) and that lasted long enough to show a reduction in vasomotor symptoms, primarily in patients who experienced more than seven hot flushes/day. Two previous observational studies have analyzed the efficacy of DT56a in terms of improvements in menopausal symptoms;

**Table 2** Intensity of symptoms

| | *% Hot flushes* ($n = 621$) | *% Night sweats* ($n = 597$) | *% Headaches* ($n = 459$) | *% Joint and muscle pain* ($n = 509$) |
|---|---|---|---|---|
| Insignificant | 1 | 3.7 | 19.8 | 14.5 |
| Mild | 11.4 | 14.6 | 33.8 | 30.3 |
| Moderate | 40.9 | 34.7 | 27.7 | 29.1 |
| Frequent | 36.6 | 35.5 | 13.5 | 20 |
| Very frequent | 10.1 | 11.6 | 5.2 | 6.1 |
| Mean ± standard deviation | 3.43 ± 0.85 | 3.37 ± 0.98 | 2.51 ± 1.11 | 2.73 ± 1.12 |

**Table 3** Weekly mean scores showing reduction in hot flushes

| *Week* | *Number of hot flushes (all responders, n = 497)* | *Number of hot flushes (7+ hot flushes at baseline, n = 171)* | *Intensity level of hot flushes (all respondents, n = 462)* | *Intensity level of hot flushes (7+ hot flushes at baseline, n = 157)* |
|---|---|---|---|---|
| 0 | 6.56 | 11.62 | 3.47 | 3.98 |
| 2 | 4.98 | 9.03 | 2.78 | 3.28 |
| 4 | 3.27 | 5.99 | 2.14 | 2.53 |

$p < 0.01$

**Table 4** Feedback from patients at the end of the study. Data are given as % of patients

| *Post treatment* | *Hot flushes* | *Quality of sleep* | *Quality of life* | *Night sweats* | *Headaches* | *Joint and muscle pain* |
|---|---|---|---|---|---|---|
| Much worse | 0.5 | 0 | 0.2 | 0.5 | 0.4 | 0.2 |
| Worse | 0.8 | 1 | 0.5 | 0.7 | 0.6 | 1 |
| The same | 18 | 36.2 | 25.1 | 25.6 | 55.9 | 62 |
| Better | 55.9 | 45.6 | 58.7 | 52.1 | 35.1 | 31.6 |
| Much better | 24.8 | 17.2 | 15.6 | 21.1 | 7.9 | 5.2 |



both studies investigated approximately 80–90 subjects. These studies found that vasomotor symptoms decreased rapidly with DT56a treatment, albeit not to the same extent as that observed with hormone treatment (HT)[3,4].

Another limitation of this study is related to the composition of DT56a, which has not been described in sufficient detail. It is generally agreed that HT is the first option for menopausal symptom relief, although the side-effects, or the fear of side-effects, have decreased its use; thus, alternative therapies have been developed that involve the pharmacological and dietary intake of phytoestrogens[5]. DT56a contains more than 11 types of phytoestrogens and has been classified as a phyto-SERM[6]. However, a lack of understanding of the composition of this substance makes the management of its use confusing and has led to studies that have analyzed the isolated or combined effects of individual components of this medication. Studies that have directly analyzed the effects of DT56a on vasomotor symptoms have reported a time scale for relief (2–4 weeks) similar to those observed in studies that have analyzed the effects of isoflavones alone, highlighting the rapid action of DT56a[7]. Differences in the effects of DT56a and those of single phytoestrogens is likely due to the combined effects of the different phytoestrogens in DT56a, all of which exhibit different pharmacokinetics[8].

Adverse effects of DT56a were not reported in this study. In general, information about the safety of DT56a can only be inferred from safety data previously published for other phytoestrogens; thus, studies should be conducted over longer time periods to address the lack of safety data specific to DT56a[2,3]. Taken together, these limitations highlight a need for further investigation of DT56a, primarily in the areas of drug design, safety and efficacy. In particular, it would be useful for future studies to consist primarily of randomized, controlled trials and for efficacy analyses to focus on concerns of postmenopausal women other than hot flushes, such as vaginal atrophy, specific psychological symptoms and the prevention of osteoporosis.

In conclusion, treatment with DT56a resulted in a significant reduction in the number and intensity of hot flushes in postmenopausal women, especially in those with frequent symptoms, and these effects were observed within the first month of treatment.

*Conflict of interest* The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper.

*Source of funding* Nil.

## References


1. Sánchez-Borrego R, Coronado P, Pérez-López FR. Responding to menopause. Answer to emergent controversies. The Spanish Menopause Society and Women's Health. *Climacteric* 2011;14(Suppl 1):44
2. Yoles I, Yogev Y, Frenkel Y, Nahum R, Hirsch M. Kaplan B. Tofupill/Femarell (DT56a) – a new phyto-selective estrogen receptor modulator like substance for the treatment of post-menopausal bone loss. *Menopause* 2003;10:522–5
3. Yoles I, Yogev Y, Frenkel Y, Hirsch M, Nahum R, Kaplan B. Efficacy and safety of standard versus low-dose Femarelle (DT56a) for the treatment of menopausal symptoms. *Clin Exp Obstet Gynecol* 2004;31:123–6
4. Labos G, Trakakis E, Pliatsika P, *et al*. Efficacy and safety of DT56a (Femarelle) compared to hormone therapy in Greek postmenopausal women. *J Endocrinol Invest* 2013;36:521–6
5. de Villiers TJ, Gass ML, Haines CJ, *et al*. Global Consensus Statement on menopausal hormone therapy. *Climacteric* 2013;16:203–4
6. Somjen D, Katzburg S, Knoll E, *et al*. DT56a (Femarelle): a natural selective estrogen receptor modulator (SERM). *J Steroid Biochem Mol Biol* 2007;104:252–8
7. Sánchez-Borrego R, Navarro MC, Llaneza P, Hormigo A, Duran M, Mendoza N. Efficacy and safety of a phyto-SERM as an alternative for hormone therapy. *Climacteric* 2015;18:350–7
8. Nachtigall M, Naftolin F, Nachtigall R, Yoles I, Nachtigall L. A prospective study of DT56a (Femarelle®) for the treatment of postmenopausal vaginal atrophy. *Menopause* 2011;18:285–8