ENDOMETRIAL SAFETY ASSESSMENT OF A SPECIFIC AND STANDARDIZED SOY EXTRAC

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INTRODUCTION AND OBJECTIVES:

As isoflavones extracts are taken to alleviate post menopausal symptoms, the question of their endometrial safety is raised. Some clinical studies on the effects of isoflavones on the endometrium in post menopausal women have been carried out but their results are discordant mainly due to the difference in assessment method and also to the type and quantity of isoflavones used. This study was designed to assess the endometrial safety of a standardized soy extract (Phyto Soya®) according to the EMEA Guidelines (EMEA/CHMP/021/97).

METHODS:

Study design:
This is an international open study with centres located in Australia, Belgium, France and Spain. 499 post menopausal women have been selected and 395 have been included.

Treatment:
2 capsules in the morning and 2 capsules in the evening of Phyto Soya® corresponding to a daily dose of 70 mg of isoflavone (35 mg daidzin, 21 mg glycitin and 14 mg genistin).
Patients were treated for 1 year and they had the possibility to continue the treatment 2 additional years.

Main inclusion criteria:
- non hysterectomised women, 45-65 years old, post menopaused since at least 2 years
- women presenting hot flushes or climacteric symptoms
- wash out of 3 months for HRT, DHEA, tibolone, raloxifene, 2 months for isoflavones
- BMI < 30 Kg/m

Main non inclusion criteria:
- thromboembolic disease, uncontrolled arterial hypertension.
- history of hormonodependent malignant tumurs
- cervical stenosis, active endometriosis, endometrial hyperplasia, endometrial polyp, ovarian cyst > 30 mm, sub mucous myoma, endometrial thickness > 4mm

Method:
Endometrial biopsy and transvaginal ultrasounds were performed at inclusion and after 12 months and 36 months of treatment according to the European guidelines.
Biopsies were assessed by 2 independent pathologists (Dr Bergeron and Pr Nogales) blinded to time of biopsy.
300 patients treated for 1 year are necessary to estimate the incidence rate of hyperplasia with the required precision.

RESULTS AND CONCLUSIONS:

CLASSIFICATION	INCLUSION	1 YEAR	3 YEARS
No tissue	1	2	3
Tissue insufficient for diagnosis	39	47	21
Atrophic/inactive	348	255	127
Proliferative	6	1	0
Secretory/menstrual	0	0	0
Hyperplasia	0	0	0
Cancer	0	0	0
Total of biopsy	394	305	151*

** results after 3 years for all patients will be available in October 2008.*

Endometrial thickness:
No increase has been observed after 12 months of treatment: 2.2 ± 0.98 mm at inclusion and 2.12 ± 1.1 mm at the end of the study.

Monitoring of vaginal bleeding:
The vaginal bleeding were monitored daily by using an electronic patient diary. We collected a total of more than 89000 days with answer during treatment period.
The percentage of days without any bleeding represented 99.2% of days with answers during the treatment period whereas they were 95% during selection period.

Biopsy results:
No case of hyperplasia or cancer was diagnosed for the 305 biopsies of women who completed the 1 year of treatment. For all results "no endometrial tissue" or "tissue insufficient for diagnosis", the endometrial thickness was ≤ 4 mm. At 1 year, the calculated incidence rate of hyperplasia outcome was 0% with an upper limit of 95% Confidence Interval of 0.012.
Among the 235 patients who wished to continue the study, **151** have already completed their 3 years of treatment (biopsy results below).

Conclusions:

On the basis of our results, we can conclude that this specific and standardized soy extract doesn't exert a mitogenic effect on the endometrium. It represents a safe alternative among the various treatments proposed to post menopausal women.

Référence : 227.00 Thematic Area: Complementary and alternative medicine