

CombiPatch® Significantly Improves Women's Sexual Quality of Life Compared to Prempro™ in a Randomized Trial

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ABSTRACT

OBJECTIVE: While transdermal hormone therapy (HT) is absorbed directly into the bloodstream, oral HT undergoes first-pass metabolism by the liver. These distinct metabolic routes have differential effects on several hormones, which may result in different effects on female sexual function. Specifically, this study analyzed differences in sexual quality of life (QOL) in postmenopausal women treated with transdermal patch HT using CombiPatch® (17β-estradiol [E₂]/norethindrone acetate [NETA]) or with oral HT using Prempro™ (conjugated equine estrogens [CEE]/medroxyprogesterone acetate [MPA]).

DESIGN: This randomized, double-blind, double-dummy, parallel treatment-group, multicenter trial involved 186 women, 1 to 6 years postmenopausal. After a 4-week placebo run-in phase, patients were randomized to 1 of 2 treatment arms for 20 weeks: CombiPatch (50 μg E₂/140 μg NETA) + placebo capsule or Prempro capsule (0.625 mg CEE/2.5 mg MPA) + placebo patch. The Menopause-specific Quality of Life (MENQOL) questionnaire was administered by phone every 4 weeks, beginning at week 0 (minimum level for clinical significance was set at ≥ 1 unit change from baseline). In the sexual domain of the MENQOL questionnaire, patients rated themselves on a scale of 0 to 6 (0=not bothered at all; 6=extremely bothered) on 3 sexual QOL parameters: change in sexual desire, vaginal dryness during intercourse, and avoiding intimacy.

RESULTS: After 20 weeks, one third of the CombiPatch-treated women (33% [27/81]) reported improvement in sexual QOL scores, nearly twice that of Prempro-treated women (17% [14/84]), and fewer CombiPatch-treated women (2.5% [2/81]) reported poorer sexual QOL than Prempro-treated women (4.8% [4/84]), $P=0.045$, 2-tailed Fisher's Exact Test. Sexual ($P=0.0075$) and psychosocial ($P=0.0094$) domain scores showed statistically significant improvements from baseline with CombiPatch compared to Prempro. Each sexual domain question, analyzed separately, showed similar trends, although the results were not significant.

CONCLUSION: Transdermal delivery of HT with CombiPatch resulted in improvements in sexual QOL scores, as measured by the sexual domain of MENQOL, in a significantly greater proportion of postmenopausal women compared to oral delivery with Prempro.

INTRODUCTION

Sexual activity is one of the most important QOL issues among postmenopausal women. An estimated 25% to 63% of postmenopausal women suffer from some form of female sexual dysfunction,¹ ranging from dyspareunia to a

decline in sexual desire and decreased sexual activity. Several studies have suggested that some decreases in libido and sexual response that occur after menopause may be related to changes in the levels of circulating ovarian and adrenal hormones.^{2,3}

- While transdermal HT is absorbed directly into the bloodstream, oral HT undergoes first-pass metabolism by the liver. These distinct metabolic routes have differential effects on several hormones, which may result in different effects on female sexual function.
- Data previously presented from the present study showed that sex hormone binding globulin (SHBG) levels were significantly higher with Prempro than with CombiPatch and, in addition, testosterone, free testosterone, dehydroepiandrosterone sulfate, and 3α-androstaneol glucuronide were significantly lower with Prempro than CombiPatch.⁴ This observation suggests that patients on transdermal HT may have improved sexual QOL compared with those on oral HT.
- This is the first randomized trial comparing the effects of CombiPatch and Prempro on sexual QOL.

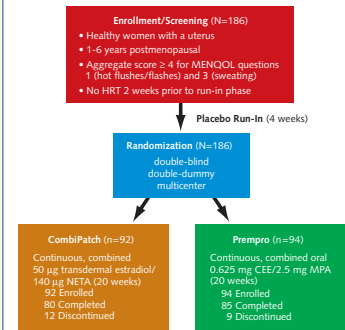
OBJECTIVE

To compare changes in sexual quality of life (QOL) of women treated with transdermal E₂/NETA (CombiPatch) and oral CEE/MPA (Prempro).

PATIENTS & METHODS

Study Design

FIGURE 1. Study Design



CombiPatch is a registered trademark of Novogyne Pharmaceuticals. Prempro is a trademark of Wyeth Pharmaceuticals.

- The MENQOL questionnaire is a self-administered instrument validated to measure physical, vasomotor, psychosocial, and sexual aspects of quality of life (QOL) in menopausal women.⁵
- The MENQOL questionnaire was administered by phone every 4 weeks, beginning at week 0. The minimum level for clinical significance was set at ≥ 1 unit change from baseline.
- For the MENQOL sexual domain, patients were asked whether they had experienced in the past month a change in sexual desire, vaginal dryness during intercourse, or avoiding intimacy. If so, they were asked to rate how much they were bothered by the problem on a scale of 0 to 6 (0=not bothered at all; 6=extremely bothered).⁵
- For the MENQOL psychosocial domain, patients were asked if they had experienced dissatisfaction with personal life; feeling anxious or nervous; poor memory; accomplishing less than they used to; feeling depressed, down, or blue; being impatient with other people; and feelings of wanting to be alone. If so, they were asked to rate how much they were bothered by each symptom on a scale of 0 to 6 (0=not bothered at all; 6=extremely bothered).⁵

RESULTS

Patient Demographics

TABLE 1: Demographic Characteristics

Demographic Characteristics	CombiPatch (n=92)	Prempro (n=94)	P-value
Age (y; mean ± SD)	51.9 ± 4.2	52.5 ± 4.7	0.340
Race [n (%)]			
Caucasian	81 (88)	83 (88)	0.760
African American	3 (3.2)	6 (6.4)	
Asian	2 (2.2)	1 (1.1)	
Hispanic	5 (5.4)	4 (4.3)	
Other	1 (1.1)	0 (0.0)	
Weight (lbs; mean ± SD)	162.9 ± 32.8	159.5 ± 29.4	0.467
Height (in.; mean ± SD)	64.4 ± 2.2	64.3 ± 2.5	0.848
Time since menopause (y; mean ± SD)	3.1 ± 2.4	3.2 ± 3.0	0.834

Demographic characteristics were analyzed by a 2-sample t-test, except for race, which was analyzed by a 2-tailed Fisher's Exact Test.

- Demographic characteristics, including age, race, weight, height and time since menopause, as well as baseline MENQOL scores were similar between the treatment groups.

MENQOL Questionnaire Domain Scores

TABLE 2: MENQOL Domain Score Improvements From Baseline to End of Treatment

Domain	% Improvement from Baseline		P-value
	CombiPatch	Prempro	
Sexual	38.4	15.1	0.0075
Psychosocial	32.3	19.3	0.0094
Physical	21.7	19.6	0.5237
Vasomotor	65.0	64.0	0.8120

- The CombiPatch group had significantly greater improvement from baseline to end of treatment than the Prempro group in the sexual and psychosocial domains ($P<0.01$).

TABLE 3: Proportion of Patients Who Improved, Did Not Change, or Worsened for the MENQOL Sexual Domain

n (%)	Treatment		P-value
	CombiPatch (n=81)	Prempro (n=84)	
Sexual domain			
Improved	27 (33.3)	14 (16.7)	0.045
No change	52 (64.2)	66 (78.6)	
Worse	2 (2.5)	4 (4.8)	
Change in sexual desire			
Improved	16 (19.8)	12 (14.3)	0.201
No change	63 (77.8)	65 (77.4)	
Worse	2 (2.5)	7 (8.3)	
Vaginal dryness during intercourse			
Improved	28 (34.6)	19 (22.6)	0.199
No change	49 (60.5)	58 (69.0)	
Worse	4 (4.9)	7 (8.3)	
Avoiding intimacy			
Improved	17 (21.0)	12 (14.3)	0.068
No change	63 (77.8)	65 (77.4)	
Worse	1 (1.2)	7 (8.3)	

- After 20 weeks, one third of the CombiPatch-treated women (33%) reported improvement in sexual QOL scores, nearly twice the proportion of Prempro-treated women (17%) ($P=0.045$).
- Fewer CombiPatch-treated women (2.5%) reported poorer sexual QOL than Prempro-treated women (4.8%) ($P=0.045$).

- Patient proportions for each sexual domain question (change in sexual desire, vaginal dryness during intercourse, and avoiding intimacy) independently showed similar trends, although the results were not statistically significant. The psychosocial domain questions were not analyzed individually.

CONCLUSIONS

- Scores for the MENQOL sexual and psychosocial domains improved significantly more with transdermal CombiPatch than oral Prempro in postmenopausal women.
- A significantly greater proportion of postmenopausal women had improved QOL in some MENQOL domains after transdermal delivery with CombiPatch than after oral delivery with Prempro.
- Transdermal patch HT may be a better choice than oral HT for postmenopausal women who report diminished sexual desire.

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