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Ospemifene's effects on lipids and coagulation factors: a post hoc analysis of phase 2 and 3 clinical trial data

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Abstract

Objective: To evaluate the effect of ospemifene 60 mg on the lipid and coagulation parameters of postmenopausal women using data from five phase 2 and 3 clinical trials.

Methods: Data for lipids and coagulation factors for 2,166 postmenopausal women were pooled from five randomized, placebo-controlled studies. Lipid and coagulation parameters included in this analysis were total cholesterol, high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglycerides, activated partial thromboplastin time (aPTT), fibrinogen, antithrombin antigen, protein C Ag, and protein S Ag free.

Results: Mean percent changes in HDL and LDL were significantly greater with ospemifene versus placebo at month 3 (HDL: 4.4% vs 0.2%; LDL: −5.2% vs 2.4%), month 6 (HDL: 5.1% vs 1.5%; LDL: −6.7% vs 2.4%), and month 12 (HDL: 2.3% vs −1.9%; LDL: −7.0% vs −2.1%; $P < 0.05$, for all comparisons). Ospemifene significantly reduced total cholesterol at 6 months (−1.8% vs 1.6%; $P = 0.0345$ versus placebo), and changes in triglycerides with ospemifene were similar to placebo at all three time points. In subgroup analyses based on age, body mass index, and baseline triglyceride level, ospemifene increased HDL and decreased LDL, but had no significant effect on total cholesterol and triglycerides relative to placebo. Ospemifene significantly improved fibrinogen and protein C antigen levels relative to placebo at months 3 (−8.7% vs −0.8% and −2.7% vs 0.5%, respectively), 6 (−6.0% vs 6.7% and −3.6 vs 8.0%), and 12 (−8.7% vs 7.3% and −4.5% vs 6.6%; $P < 0.01$, for all). The levels of all coagulation factors remained within the normal range throughout the studies.

Conclusion: Ospemifene 60 mg does not have a detrimental effect on lipid and coagulation parameters of postmenopausal women with up to 12 months of use.

Key Words: Coagulation factors – Dyspareunia – Fibrinogen – Lipids – Ospemifene – Vulvar and vaginal atrophy.

Estrogen decline at the onset of menopause can leave the vasculature vulnerable to cardiovascular disease, which is associated with changes in surrogate markers such as lipids and coagulation factors. Postmenopausal women have been shown to have significantly higher levels of total cholesterol, triglycerides, low-density lipoprotein (LDL) cholesterol, and very-LDL (VLDL) cholesterol, and a lower level of high-density lipoprotein (HDL) cholesterol than premenopausal women.[1] Hormone therapy (HT) has been shown to offset the detrimental effect of menopause on lipids by decreasing total cholesterol and LDL, and increasing HDL in postmenopausal women.[2-8]

Clinical studies have shown HT's effect on the risk of thrombotic diseases differs based on the route of administration. Oral HT has been shown to increase fibrinolysis and coagulation in postmenopausal women, with clinical studies showing an increased risk for venous thromboembolism (VTE), and increased fibrinolysis and coagulation with oral compared with transdermal HT.[9-12] Activated partial thromboplastin time (aPTT), fibrinogen, antithrombin antigen, protein C Ag, and protein S Ag free are regularly measured as surrogate markers for thrombophilia; however, the clinical impact of abnormal changes in these markers is not fully understood.[13-16]

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Ospemifene is an estrogen receptor agonist/antagonist (ERAA, also referred to as a selective estrogen receptor modulator [SERM]) approved by the US Food and Drug Administration (FDA) for the treatment of moderate-to-severe dyspareunia, a symptom of vulvar vaginal atrophy (VVA, which is also a component of genitourinary syndrome of menopause[17]) due to menopause.[18] Clinical and preclinical studies have shown that ospemifene can elicit tissue-specific estrogenic or antiestrogenic effects in the vagina,[19-25] bone,[26-30] and breast.[27,31,32] However, limited data are available characterizing ospemifene's effect on the surrogate markers for cardiovascular health of postmenopausal women. Two 3-month, phase 2 clinical studies have characterized the effect of ospemifene on lipids and coagulation factors relative to placebo and the SERM raloxifene (60 mg).[20,33] Data from both studies suggest that ospemifene may have a beneficial effect on levels of HDL, LDL, and fibrinogen.

A post hoc analysis of pooled data from 5 randomized, placebo-controlled clinical trials[16,21-25,33,34] was conducted to assess the effect of systemic ospemifene exposure on lipids and coagulation factors in postmenopausal women.

METHODS

Study design

The effect of once-daily oral ospemifene 60 mg on lipids and coagulation factors in postmenopausal women (40-80 years in age) was evaluated in a post hoc analysis using data from five randomized, double-blind, parallel-group, placebo-controlled, phase 2 and 3 clinical trials (15-50718,[25] 1506002,[16,33] 15-50615,[34] 15-50310,[21] and 15-50821[23,24]), including a 40-week extension of a phase 3 study (15-50310x[22]). Details of the study design and inclusion criteria for all five clinical trials have been previously reported.[16,21-25,33,34]

Briefly, the studies ranged from 6 weeks to 12 months in length and included healthy, postmenopausal women (1506002[16,33]), and also those with either at least seven moderate to very severe hot flushes per day or 50 per week (15-50615[34]), or VVA (15-50310[21]/15-50310x,[22] 15-50821,[23,24] and 15-50718[25]). Participants were randomized 6:1 to ospemifene 60 mg or placebo in the 52-week safety study (15-50718[25]) and 1:1 in the four remaining trials (1506002,[16,33] 15-50615,[34] 15-50310[21]/15-50310x,[22] and 15-50821[23,24]). Women who successfully completed a 12-week study (15-50310[21]) were allowed to continue the randomized therapy for an additional 40 weeks (15-50310x[22]). The 12-week studies, 15-50310[21] and 15-50821,[23,24] included women with and without an intact uterus, whereas studies 15-50718[25] and the 40-week extension study, 15-50310x,[22] were limited to postmenopausal women with an intact uterus.

Study assessments

Lipids evaluated included HDL, LDL, total cholesterol, and triglycerides, whereas coagulation parameters included antithrombin III antigen, aPTT, fibrinogen, protein C antigen, and free protein S antigen. The lipids and coagulation factors evaluated by each study are described in Table 1. The changes from baseline to 3, 6, and 12 months for each lipid and coagulation factor were evaluated in this post hoc analysis. For each parameter, the mean percent change from baseline was calculated and the Welch's t test was used to compare ospemifene 60 mg and placebo.

Additional subgroup analyses based on age, body mass index (BMI), and triglyceride levels were performed for the lipid parameters using the respective cut-off of 60 years, 32 kg/m^2, and 250 mg/dL. Subgroup analysis based on age was performed at 3, 6, and 12 months, whereas the analyses based on BMI and triglyceride levels were limited to 3 months due to small sample size. Statistical analyses were performed using SAS version 9.2 (Cary, NC).

RESULTS

Participant disposition, demographics, and baseline characteristics

Lipid and coagulation factor data were evaluated for 2,166 postmenopausal women participating in five placebo-controlled studies, ranging from 6 weeks to 12 months in length, with 1,242 randomized to ospemifene 60 mg and 924 to placebo (Fig. 1). Study completion rate was similar between the ospemifene (85.4%) and placebo (86.8%) groups. Discontinuation due to adverse events was 7.6% (n = 95) for ospemifene and 3.7% (n = 34) for placebo (Fig. 1).

Age, race, and BMI were comparable between the ospemifene and placebo groups (Table 2). The trial participants were predominantly white with a mean age of approximately 59 years and a mean BMI of approximately 26 kg/m^2. The percentage of postmenopausal women with an intact uterus was numerically higher for ospemifene (68.5%) versus placebo (58.8%), and a similar percentage of women had a prior history of HT use with ospemifene (21.1%) and placebo (18.8%).

Lipids

Mean percent increases in HDL from baseline were significantly greater with ospemifene versus placebo at 3 months (4.4% vs 0.2%; $P < 0.0001$), 6 months (5.1% vs 1.5%; $P = 0.0359$), and 12 months (2.3% vs −1.9%; $P = 0.0086$; Fig. 2A). Similarly, mean percent changes in LDL from baseline were significantly greater with ospemifene versus placebo at 3 months (−5.2% vs 2.4%; $P < 0.0001$), 6 months (−6.7% vs 2.4%; $P = 0.0002$), and 12 months (−7.0% vs −2.1%; $P = 0.0293$; Fig. 2A). Ospemifene significantly reduced total cholesterol at 6 months compared with placebo (−1.8% vs 1.6%; $P = 0.0345$; Fig. 2B). The increase in triglycerides with ospemifene use was similar to those found with placebo (Fig. 2B).

The subgroup analyses based on age found that ospemifene significantly increased HDL in postmenopausal women 60 years of age or older at 3, 6, and 12 months, but only at 3 months in women less than 60 years of age (Table 3). LDL levels in contrast were significantly decreased by ospemifene at 3 and 6 months in both age groups. Ospemifene

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TABLE 1. *Descriptions of the five phase 2 and 3 clinical trials included in this report*

Study number	Study design	Study duration	Treatment administered	Lipid and coagulation factors measured
15-50615[34]	Phase 2, placebo-controlled	6 wks	Once-daily oral dose of ospemifene 60 mg (n = 100) Placebo (n = 98)	Coagulation factors: Factor V Leiden[b] and thromboplastin time Evaluated at screening and wk 6
1506002[16,33]	Phase 2, placebo-controlled	12 wks	Once-daily oral doses of ospemifene 30 mg (n = 40) 60 mg (n = 40) 90 mg (n = 40) Placebo (n = 40)	Lipids: HDL, HDL-2, LDL, LDL-BCD, Lp (a), total cholesterol, and triglycerides Coagulation factors: Endothelin-1, plasma nitric oxide, prostacyclin, fibrinogen, prothrombin fragments 1 + 2, thrombin-antithrombin III complex, D-dimer, tissue-type plasminogen activator, plasminogen activator inhibitor-1, and homocysteine in plasma Evaluated at screening and wks 12 and 14 to 16 (after treatment discontinuation)
15-50821[23,24]	Phase 3, placebo-controlled	12 wks	Once-daily oral dose of ospemifene 60 mg (n = 463) Placebo (n = 456)	Lipids: HDL, LDL, total cholesterol, and triglycerides Coagulation factors: Factor V Leiden,[b] antithrombin III, fibrinogen, protein C, protein S, and thromboplastin time Evaluated at screening and wk 12
15-50310[21]/ 15-50310x[22 a]	15-50310: Phase 3, placebo-controlled	12 wks	Once-daily oral dose of ospemifene 30 mg (n = 282) 60 mg (n = 276) Placebo (n = 268)	Lipids: HDL, LDL, total cholesterol, and triglycerides Coagulation factors: Factor V Leiden,[b] thromboplastin time, fibrinogen, antithrombin III antigen, protein C antigen, and free protein S antigen Evaluated at screening (coagulation factors) or at randomization (lipids) and at wk 12
	15-50310x: Phase 3, placebo-controlled, safety study	40-wk extension	Once-daily oral dose of ospemifene 30 mg (n = 62) 60 mg (n = 69) Placebo (n = 49)	Lipids: HDL, LDL, total cholesterol, and triglycerides Coagulation factors: aPTT, fibrinogen, antithrombin III antigen, protein C antigen, and free protein S antigen Evaluated at wks 26 and 52
15-50718[25]	Phase 3, placebo-controlled safety study	52 wks	Once-daily oral dose of ospemifene 60 mg (n = 363) Placebo (n = 63)	Lipids: HDL, LDL, total cholesterol, and triglycerides Coagulation factors: Factor V Leiden,[b] antithrombin III, protein C, and protein S Evaluated at screening and wks 12, 26, and 52.

aPTT, activated partial thromboplastin time; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LDL-BCD, baseline conjugated dienes of low-density lipoprotein; Lp (a), lipoprotein a.
[a]15-50310 and 15-50310x are considered to be one clinical study.
[b]Evaluated only at screening.

significantly decreased total cholesterol relative to placebo in women less than 60 years of age only at 6 months and had no effect among women aged 60 years or older. Ospemifene had no significant effects, compared with placebo, on the triglyceride levels of postmenopausal women, regardless of their age (Table 3).

Ospemifene also significantly increased HDL and decreased LDL levels from baseline to 3 months in women with BMI less than 32 kg/m^2 and those with triglyceride levels less than 250 mg/dL ($P < 0.0001$ vs placebo for all; data not shown). In contrast, ospemifene had no significant effect on HDL or LDL among women with high BMI or triglyceride levels. Total cholesterol and triglyceride levels at 3 months remained unchanged, regardless of the BMI or triglyceride level.

Coagulation factors

Mean percent changes in fibrinogen and protein C antigen levels from baseline were significantly greater with ospemifene versus placebo at 3 months (−8.7% vs −0.8%; $P < 0.0001$, and −2.7% vs 0.5%; $P = 0.0008$, respectively), 6 months (−6.0% vs 6.7%; $P = 0.0019$, and −3.6% vs 8.0%; $P < 0.0001$), and 12 months (−8.7% vs 7.3%; $P = 0.0029$, and −4.5% vs 6.6%; $P < 0.0001$) were significantly greater with ospemifene versus placebo (Fig. 3). Ospemifene numerically lowered aPTT levels from baseline to 3 and 6 months, with the change being significantly greater than that for placebo at 3 months (−1.9% vs 0.7%; $P = 0.0009$). Antithrombin III antigen levels also decreased from baseline to 3 months with ospemifene, with the change being greater than that with placebo (−2.9% vs −0.8%; $P = 0.0004$). Ospemifene numerically increased free protein S antigen levels at all measured time points (Fig. 3B), with the change being significantly greater than placebo at 3 months (5.8% vs 1.6%; $P < 0.0001$). None of these changes were outside the range of normal values for each parameter.

DISCUSSION

This post hoc analysis of pooled data from five placebo-controlled clinical studies found ospemifene 60 mg increased HDL and decreased LDL levels in postmenopausal women with no adverse effects on total cholesterol and triglycerides. Ospemifene 60 mg also decreased the levels of fibrinogen (a risk factor for coronary heart disease[35]) from baseline, with a significant difference from placebo; however, the postbaseline fibrinogen level remained within the normal range for the

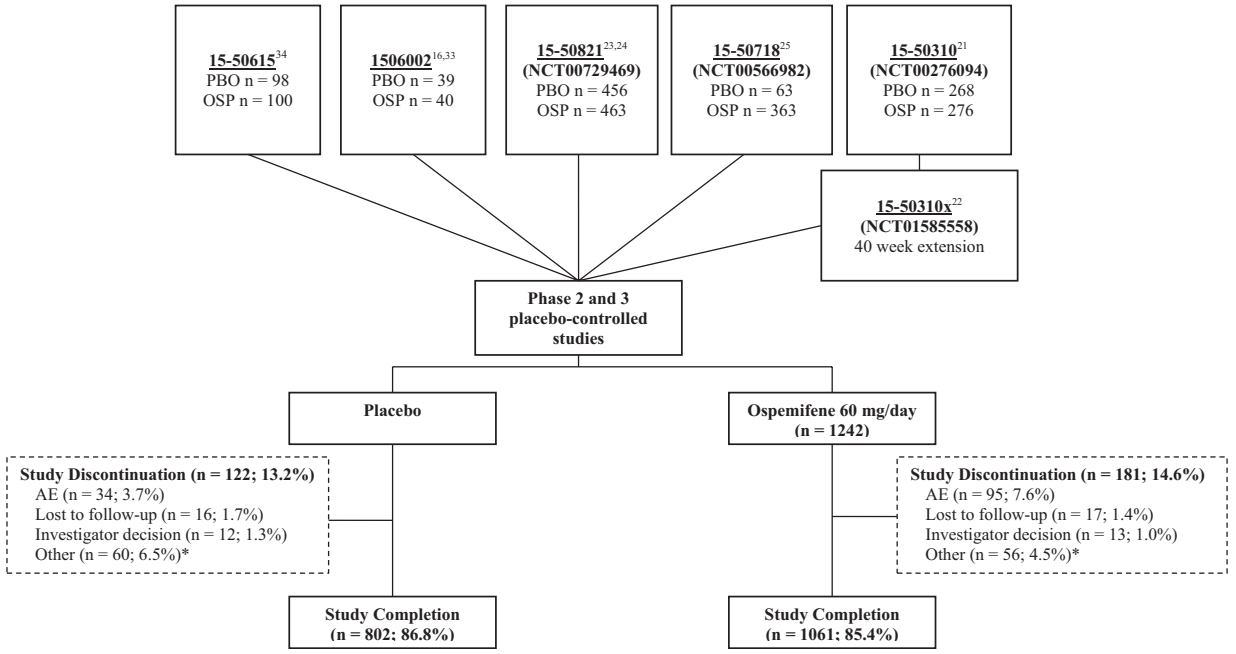

FIG. 1. Disposition of participants from the five placebo-controlled phase 2 and 3 clinical studies used to evaluate the effect of ospemifene on the lipid and coagulation factors. *Other included withdrew consent, lack of efficacy, and noncompliance. AE, adverse event; OSP, ospemifene; PBO, placebo.

majority of the participants and would not be expected to have any clinical consequences. Collectively, we found that once-daily ospemifene 60 mg for up to 12 months did not have a negative effect on lipid and coagulation factors in postmenopausal women.

TABLE 2. *Demographics and baseline characteristics of women receiving ospemifene 60 mg/d or placebo in five placebo-controlled trials (15-50718,[25] 1506002,[16,33] 15-50615,[34] 15-50310[21]/15-50310x,[22] and 15-50821[23,24])*

	Ospemifene 60 mg (n = 1,242)	Placebo (n = 924)
Age, y		
Mean ± SD	59.4 ± 6.49	58.9 ± 6.24
Ethnic origin, n (%)		
White	1,159 (93.3)	837 (90.8)
Black or African American	47 (3.8)	49 (5.1)
Asian	12 (1.0)	9 (0.9)
Other	24 (1.9)	29 (2.9)
BMI, kg/m^2		
Mean ± SD	25.7 ± 4.03	26.0 ± 4.20
Intact uterus		
n (%)	851 (68.5)	543 (58.8)
Prior HT use within 6 mos of study entry		
n (%)	262 (21.1)	174 (18.8)
Lipid parameters, mean ± SD		
HDL, mmol/L	1.76 ± 0.44	1.72 ± 0.45
LDL, mmol/L	3.32 ± 0.91	3.26 ± 0.88
Total cholesterol, mmol/L	5.68 ± 0.10	5.64 ± 1.00
Triglycerides, mmol/L	1.27 ± 0.65	1.32 ± 0.75
Coagulation parameters, mean ± SD		
aPTT, s	27.5 ± 3.80	27.7 ± 4.11
Fibrinogen, μmol/L	10.2 ± 2.0	10.1 ± 2.0
Antithrombin antigen, %	99.4 ± 12.9	100.1 ± 11.8
Protein C Ag, %	104.7 ± 19.0	103.2 ± 22.2
Protein S Ag, free, %	111.0 ± 21.8	111.7 ± 21.1

aPTT, activated partial thromboplastin time; BMI, body mass index; HDL, high-density lipoprotein; HT, hormone therapy; LDL, low-density lipoprotein; SD, standard deviation.

Data characterizing ospemifene's effect on lipid and coagulation factors relative to placebo was previously limited to a 3-month, phase 2 clinical trial (study 1506002, included in this pooled dataset) of 160 healthy, postmenopausal women randomized to either ospemifene at doses of 30, 60, and 90 mg or placebo.[33] Ospemifene increased HDL and decreased total cholesterol and LDL from baseline to 3 months, but the changes were not significant versus placebo and vanished within 2 to 4 weeks of treatment cessation.[33] Triglycerides increased significantly with ospemifene 90 mg relative to placebo ($P = 0.017$).[33] Ospemifene also decreased plasma fibrinogen levels ($P < 0.05$), which returned to baseline levels upon treatment cessation.[33] More specifically, fibrinogen levels significantly decreased with ospemifene 60 mg ($P = 0.0145$) and 90 mg ($P = 0.0232$) relative to placebo at 3 months.[33] The results from our post hoc analysis further extend initial data from study 1506002[33] and demonstrate that ospemifene 60 mg, the clinical US FDA-approved dose, does not negatively influence lipids and coagulation factors in postmenopausal women either in good health or diagnosed with VVA.

The significant improvement in HDL and LDL with ospemifene observed in this post hoc analysis is consistent with the majority of the clinical literature for estrogen therapies and other ERAAs/SERMs, including raloxifene and bazedoxifene.[2-5,7,36-38] However, ospemifene has no significant effect on triglycerides, which is in contrast with the increase in triglycerides typically seen with oral estrogens,[2,4,6,39] but is consistent with clinical data for bazedoxifene.[36,38] A 3-month

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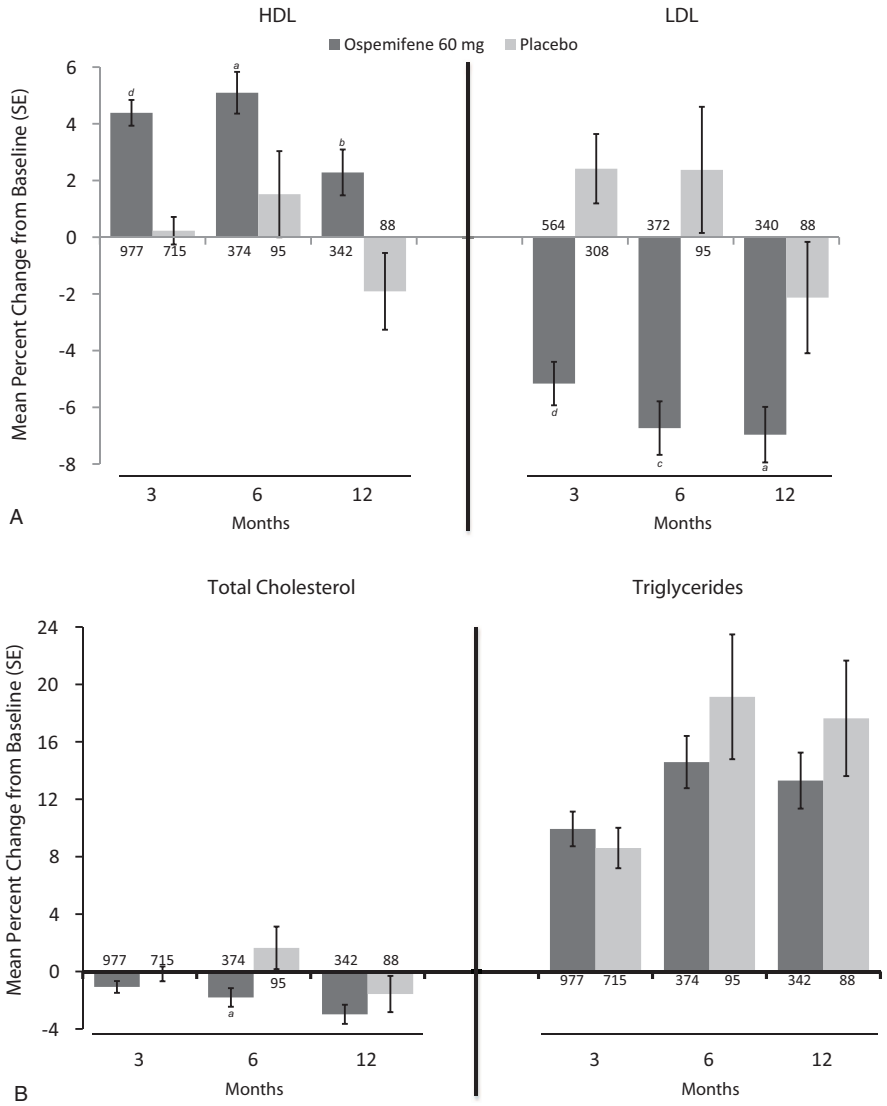

FIG. 2. Mean percent change in serum lipid levels (**A**: HDL- and LDL- Cholesterol; **B**: Total Cholesterol and Triglycerides) of postmenopausal women treated with ospemifene 60 mg for up to12 months in five placebo-controlled studies (15-50718,[25] 1506002,[16,33] 15-50615,[34] 15-50310[21]/15-50310x,[22] and 15-50821[23,24]). The values of n for each group appear at the base of each bar. [a]$P < 0.05$; [b]$P < 0.01$; [c]$P < 0.001$; [d]$P < 0.0001$. HDL, high-density lipoproteins; LDL, low-density lipoproteins.

TABLE 3. *The effect of age on the mean percent change in serum lipid levels of postmenopausal women treated with ospemifene 60 mg from studies 15-50718,[25] 1506002,[16,33] 15-50615,[34] 15-50310[21]/15-50310x,[22] and 15-50821[23,24]*

		Mean percent change from baseline (n)					
		Age < 60 y			Age ≥60 y		
	Time point, mos	Ospemifene 60 mg (n = 664)	Placebo (n = 545)	*P*	Ospemifene 60 mg (n = 578)	Placebo (n = 379)	*P*
HDL	3	3.5608 (498)	0.4212 (418)	0.0005	5.2473 (479)	−0.0429 (297)	<0.0001
	6	3.7713 (162)	4.4413 (43)	0.7886	6.1076 (212)	−0.9000 (52)	0.0027
	12	2.4799 (150)	−1.0935 (40)	0.1614	2.1321 (192)	−2.5890 (48)	0.0204
LDL	3	−4.5125 (263)	2.9522 (163)	<0.0001	−5.7298 (301)	1.8122 (145)	0.0010
	6	−5.2666 (160)	3.3872 (43)	0.0144	−7.8387 (212)	1.5365 (52)	0.0075
	12	−6.4397 (148)	−3.3896 (40)	0.3080	−7.3690 (192)	−1.0783 (48)	0.0525
Triglycerides	3	10.7017 (498)	8.0056 (418)	0.2944	9.1318 (479)	9.4436 (297)	0.9086
	6	17.0465 (162)	19.8375 (43)	0.6828	12.7093 (212)	18.5546 (52)	0.3768
	12	12.6197 (150)	15.7714 (40)	0.6416	13.8306 (192)	19.1875 (48)	0.3778
Total cholesterol	3	−0.655 (498)	0.0740 (418)	0.3649	−1.5039 (479)	−0.4904 (297)	0.3652
	6	−1.2853 (162)	3.4364 (43)	0.0473	−2.2008 (212)	0.1701 (52)	0.2919
	12	−2.7399 (150)	−2.0868 (40)	0.7407	−3.1654 (192)	−1.1288 (48)	0.325

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

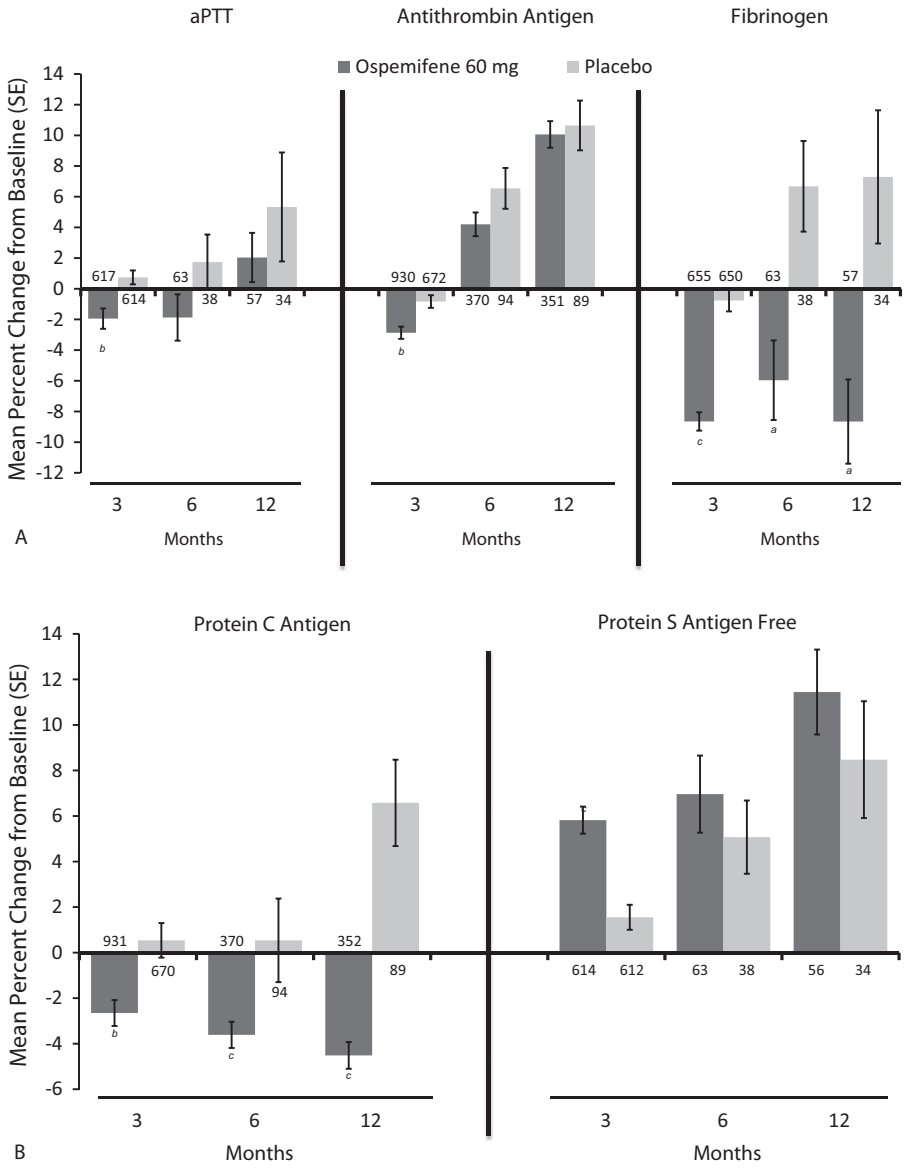

FIG. 3. Mean percent change from baseline to 3, 6, and 12 months in the coagulation parameters (**A**: aPTT, Antithrombin Antigen, and Fibrinogen; **B**: Protein C Antigen and Protein S Antigen Free) of postmenopausal women treated with ospemifene 60 mg or placebo in five placebo-controlled studies (15-50718,[25] 1506002,[16,33] 15-50615,[34] 15-50310[21]/15-50310x,[22] and 15-50821[23,24]). The values of n for each group appear at the base of each bar. [a]$P < 0.01$; [b]$P < 0.001$; [c]$P < 0.0001$. aPTT, activated partial thromboplastin time.

phase 2 clinical study comparing ospemifene (30, 60, and 90 mg) with raloxifene 60 mg showed no significant differences in the triglyceride levels between the four treatment groups (changes from baseline were not reported).[20] However, raloxifene's effect on triglycerides varies from no change reported by several studies[38,40,41] to a significant increase ($P < 0.05$) at 4 years in the Multiple Outcomes of Raloxifene Evaluation (MORE) study.[42] Additional longer-term, placebo, and active-controlled clinical trials are needed to fully confirm the initial results from this analysis, which suggest ospemifene is likely to improve HDL and LDL levels in postmenopausal women with no detrimental effect on their triglyceride levels.

Ospemifene, like HT[4,6,43] and raloxifene,[37,41] also does not have a negative effect on fibrinogen levels of postmenopausal women. The significant decrease in fibrinogen levels with ospemifene 60 mg (mean percent change of 8.7%; $P = 0.0145$) initially observed at 3 months in study 1506002[33] extends for up to 12 months of treatment (mean percent change of 8.7%) in this post hoc analysis. A 6-month, placebo-controlled study, which compared the effect of raloxifene (60 and 120 mg) with placebo and HT (0.625 mg conjugated equine estrogen and 2.5 mg medroxyprogesterone acetate [CE/MPA]) in 390 healthy, postmenopausal women, reported a 10% to 12% decrease compared with baseline fibrinogen levels with the two raloxifene doses ($P < 0.001$ vs placebo), whereas CE/MPA

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did not.[41] Assuming a 0.5% reduction in the cardiovascular risk for every 0.01 g/L decrease in fibrinogen level, raloxifene was estimated to reduce the risk of cardiovascular events by 21%.[41] Because the decrease in fibrinogen with ospemifene 60 mg was still within the normal range of 1.5 to 4.0 g/L,[44] these initial data suggest that ospemifene will not have a negative effect on the fibrinogen levels of postmenopausal women. More rigorous clinical trials are needed to further evaluate ospemifene's effect on coagulation factors in postmenopausal women, and also any potential association between ospemifene use and possible reduction in risk for cardiovascular events.

This post hoc analysis of pooled data is limited by the variations in the duration of treatment and study population across the five trials. Women participating in the trials were predominantly white (90%-93%), with an average BMI of 26 kg/m^2, therefore limiting the generalization of the findings. In addition, the individual studies were not designed to evaluate ospemifene's effect on lipids and coagulation factors as primary or secondary endpoints. The lack of statistical significance observed between ospemifene and placebo in the subgroup analyses could also be attributed to the small sample size, particularly at the time point of 12 months and women with high BMI or triglyceride level. The strength of this post hoc analysis lies in the pooling of data from multiple, randomized, placebo-controlled clinical trials. The results of this trial also demonstrate the consistency of ospemifene's effect since they support previously published studies comparing ospemifene's effects on lipids and coagulation factors with placebo or raloxifene.

CONCLUSIONS

Post hoc analysis of pooled data from five randomized, placebo-controlled studies found ospemifene 60 mg to significantly increase HDL and decrease LDL, while having little effect on triglycerides relative to placebo. Significant decreases in fibrinogen were also reported with 12 months of ospemifene treatment; however, this was not considered to be of clinical significance as the values remained within the normal range for both parameters. Taken together, ospemifene 60 mg, when prescribed for postmenopausal symptoms of VVA or GSM, does not have adverse effects on lipid levels and coagulation factors.

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