In overweight/obese women with PCOS, plasma PAI-1 levels at baseline correlated in univariate analysis with the BMI (r=0.300, p=0.034), the W (r=0.319, p=0.024), serum LH levels (r=0.348, p=0.013), the LH/FSH ratio (r=0.386, p=0.006), the FAI (r=0.347, p=0.013), the mean ovarian volume (r=0.533, p <0.001) and the mean number of follicles in the ovaries (r=0.340, p=0.016). In multivariate regression analysis, plasma PAI-1 levels were independently correlated with the BMI, serum LH levels and the mean ovarian volume (p=0.007, p=0.002 and p <0.001, respectively), after adjusting for W, LH/FSH ratio, FAI and the mean number of follicles in the ovaries.

At baseline, overweight/obese women randomized to receive sibutramine had higher serum LH, T and 17α-OHP levels as well as greater FAI than women randomized to receive orlistat (p=0.009, p=0.020, p=0.011 and p=0.037, respectively). Other parameters did not differ at baseline between these two groups.

Changes in overweight/obese women with PCOS after 6 months of sibutramine or orlistat treatment are shown in Table 2. Both sibutramine and orlistat reduced the BMI, the W and the waist/hip ratio (WHR); these reductions did not differ between the two agents. In contrast, the effects of sibutramine and orlistat on the FAI were significantly different (p=0.027); sibutramine reduced the FAI (p=0.005), whereas orlistat had no significant effect. The effects of the two agents on the other circulating androgens were not significant. Both sibutramine and orlistat improved markers of IR (serum insulin levels, the glucose/insulin ratio and the indices HOMA-IR and QUICKI); this improvement did not differ between the two agents. However, the effects of sibutramine and orlistat on plasma PAI-1 levels were significantly different (p=0.042): sibutramine reduced plasma PAI-1 levels (p <0.001), whereas orlistat had no significant effect.

In the total study population (n=73), the reduction in plasma PAI-1 levels was greater in women with PCOS treated with metformin than in women treated with sibutramine or orlistat after adjusting for the change in BMI (p=0.007).

**DISCUSSION**

To our knowledge, this is the first study that assessed the effects of metformin on circulating PAI-1 levels in normal weight women with PCOS. Three previous studies in overweight/obese women with PCOS reported a decline in circulating PAI-1 levels after treatment with metformin for 6 months,20-22 but two others did not show a significant change after treatment for 1.5 to 24 months.23,24 In normal weight women with PCOS, we observed a significant reduction in plasma PAI-1 antigen levels after treatment with metformin for 6 months. This decrease might be attributed to the reduction in IR and in the BMI, which are associated with elevated PAI-1 levels.6 Interestingly, in the three studies that reported a decline in PAI-1 levels after treatment with metformin there was no change in BMI, whereas markers of IR improved.20-22 In contrast, IR did not change despite a reduction in BMI in a study that did not detect a change in PAI-1 levels after treatment with metformin.23 Therefore, the improvement of IR appears to contribute more