Cognitive function in postmenopausal women receiving adjuvant letrozole or tamoxifen as adjuvant endocrine treatment was compared during the fifth year of treatment in a substudy of the BIG 1-98 trial. In BIG 1-98 patients were randomized to receive adjuvant (A) 5-years tamoxifen, (B) 5-years letrozole, (C) 2-years tamoxifen followed by 3-years letrozole, or (D) 2-years letrozole followed by 3-years tamoxifen. The primary comparison was the difference in composite score for patients taking letrozole (B+C; N=65) vs. tamoxifen (A+D; N=55). The patients taking letrozole had better overall cognitive function than those taking tamoxifen (difference in mean composite z-scores=0.28, P=0.04, 95% CI: 0.02, 0.54, Cohen's D=0.40 indicating small to moderate effect). In this substudy, breast cancer patients taking adjuvant letrozole during the fifth year of treatment had better cognitive function than those taking tamoxifen, suggesting aromatase inhibitors do not adversely impact cognition compared with tamoxifen.