**Plasma ESR1 mutations and outcome to first-line chemotherapy with bevacizumab and paclitaxel in patients with advanced ER+/HER2- breast cancer**

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**BACKGROUND**
- ESR1 mutations are a mechanism of resistance to aromatase-inhibitors (AI)
- Optimal treatment for patients with ESR1 mutations (ESR1mut) after AI treatment has to be established

**OBJECTIVES**
- To assess whether paclitaxel/bevacizumab yields sufficient anti-tumor activity in ESR1mut patients to compare this treatment to fulvestrant

**POWER CALCULATION**
Assumptions
- 6-month PFR fulvestrant = 40%
- 6-month PFR of 75% is sufficient to further compare chemotherapy to fulvestrant

**Two-stage design:** α=0.05, β=0.20, P0=0.4 and P1=0.75

**RESULTS: ESR1 mutation detection at baseline and association with outcome**

- **Primary outcome:** 6-month PFR in ESR1mut patients treated with paclitaxel/bevacizumab = 86%
- **Results:** ESR1 variants in ESR1mut patients, N=21

**ESR1 Mutant prevalence at baseline**
- ESR1 Wild-type 8.7 months (6.2-9.2)
- ESR1 Mutant 20.7 months (7.7-33.7)

**Samples from 48 patients were analyzed**

**ESR1 MUTATION DETECTION**

- **Main inclusion criteria:**
  - No prior palliative chemotherapy
  - Prior treatment with aromatase-inhibitor in adjuvant and/or palliative setting

**STUDY SCHEME**

- **Randomized to receive taxane-beva-capacitabine (ATX)**
  - ATX consented
  - Randomized to receive taxane-beva (AT)
  - ATX N=312
  - N=156

- **Paclitaxel/bevacizumab**

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**CONCLUSIONS**

Treatment with bevacizumab/paclitaxel is worthwhile to start as treatment for patients with advanced ER+/HER2- breast cancer with plasma ESR1 mutations.

**FUTURE PERSPECTIVES**

Further studies comparing chemotherapy regimens with fulvestrant are necessary to determine the optimal treatment of patients with ESR1 mutations after AI treatment.