PATRICIA II (SOLTI-1303): A phase II randomized trial of palbociclib in combination with trastuzumab and endocrine therapy in pretreated ER+ HER2+, PAM50 Luminal subtype, advanced breast cancer.

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BACKGROUND

- PATRICIA study (SOLTI-1303) began as a phase II trial to evaluate the combination of palbociclib, trastuzumab ± letrozole in heavily pretreated patients (up to 2–4 prior lines in the metastatic setting) with HER2-positive (HER2+) breast cancer (BC).
- 45 patients were included in 3 cohorts: **A**: estrogen receptor (ER)-negative; **B1**: ER+, received both trastuzumab and palbociclib and **B2**: ER+, received palbociclib, trastuzumab and letrozole. Palbociclib was administered at 200 mg/day for 14 days of 21-day cycles. Trastuzumab and letrozole were administered at usual doses.
- PAM50 was performed in Formalin-Fixed Paraffin-Embedded (FFPE) tissue samples (Fig. 1) and the resulting intrinsic subtypes were correlated with progression-free survival (PFS).

Figure 1. PAM50 subtype distribution in PATRICIA trial

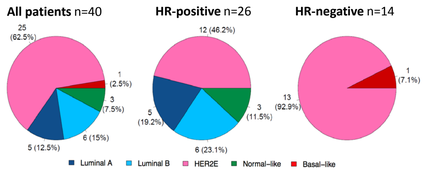
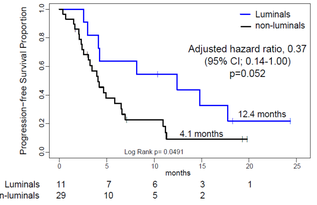
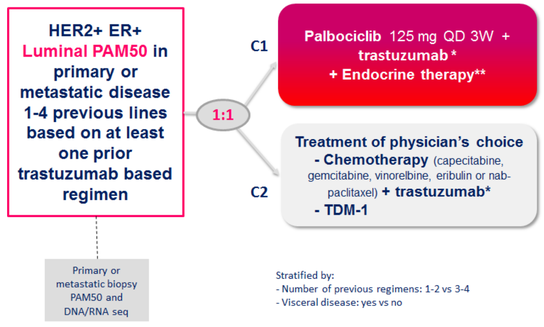


Figure 2. Efficacy data PATRICIA trial



- The results obtained showed that 19 of 45 patients in all 3 cohorts remained progression-free at 6 months with the combination, showing a higher median PFS in those with luminal versus non-luminal disease (12.4 vs. 4.1 months; adjusted HR=0.37; p-value=0.052) (Fig. 2). Clinical Benefit Rate (CBR6) also revealed better results in luminal tumors (73% vs. 31% (p=0.031)[1]
- **Based on these results, an amendment was presented, and PATRICIA II has started recruitment in August 2019 selecting patients based on PAM50 assay. Patients will be pre-screened and those with ER+/HER2+, PAM50 Luminal subtype pretreated with 1 to 4 prior therapies will be included in the study trying to confirm whether this subgroup will be more benefited from CDK4/6 inhibition when compared with standard therapy ; NCT02448420.**
- Translational Research: Gene expression and genetic analyses in FFPE samples to evaluate biomarkers are planned. Peripheral blood samples will be collected, and plasma extracted for circulating tumoral DNA (ctDNA) determination at C1D1, C2D1 and at disease progression to determine if changes in specific genetic alterations detected in the peripheral blood correlates with patient outcomes.

STUDY DESIGN



* Trastuzumab or biosimilar : loading dose 8mg/kg followed 6 mg/kg IV or trastuzumab 600 mg SC administration

** Endocrine therapy options are either an Aromatase Inhibitor ,Fulvestrant, tamoxifen.

OBJECTIVES

PRIMARY OBJECTIVE

- To demonstrate that the combination of palbociclib, trastuzumab and endocrine therapy is superior to treatment of physician's choice (TPC) in prolonging **PFS** in patients with pre-treated ER+/HER2+ and PAM50 Luminal intrinsic subtype advanced BC.

SECONDARY OBJECTIVES

- To evaluate **Disease Control Rate (DCR)** in both treatment arms.
- To evaluate **Overal Response rate (ORR)** in both treatment arms.
- To evaluate the **safety profile** in both treatment arms.
- To evaluate **12 months Overall Survival (OS)** in both treatment arms.
- To assess patient reported breast cancer specific **health related quality of life (HRQOL)** and general health status in both treatment arms.
- To investigate baseline **tumor and blood biomarkers** as predictors of response or resistance to the study treatment.

KEY ELIGIBILITY CRITERIA

Inclusion

- Pre and postmenopausal women, age ≥ 18 years.
- Histologically confirmed ER-positive and/or Progesterone Receptor (PgR) positive and HER2-positive tumor by locally assessed ASCO/CAP guidelines.
- Luminal subtype as per centrally assessed PAM50 analysis.
- At least one (maximum 4) previous lines of systemic treatment for metastatic, with at least one prior trastuzumab-based regimen. Prior pertuzumab and TDM-1 are allowed.

Exclusion

- Previous treatment with a cyclin-dependent kinase inhibitor.
- More than 4 previous lines of treatment (anti-HER2 agent +/- chemotherapy) for metastatic BC.

STATISTICS

- The study has an 80% power with two-sided alpha=0.05 to detect a hazard ratio of 0.62 in favor of the palbociclib arm.
- An adaptive design will be used to compare both treatment arms. An interim analysis (IA) adjusted for multiplicity from O'Brien-Fleming method and an estimation of the conditional power will be performed at 70% of the events.

CURRENT STATUS

A total of 516 patients will be pre-screened and 232 patients will be recruited. Recruitment is ongoing (15 sites in Spain). As of May 6th 14 patients have been recruited.

REFERENCES

1. Ciruelos et al. Abstract PD3-03. SABCS 2018.

ACKNOWLEDGEMENTS

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