SOLTI-1710 PROMETEO II study: Palbociclib in combination with letrozole in Hormone Receptor-positive (HR+)/HER2-negative residual disease after standard neoadjuvant chemotherapy

112TiP

Eva Ciruelos[1,2,3], Xavier González Farré[2,4], Antonia Perelló[5] , Emilio Alba[6] , Patricia Palacios[7] , Salvador Bofil[8], María Merino[9], Patricia Villagrasa[2], Pamela Celiz[2], Tomás Pascual[2] ,Aleix Prat[2,10] and Sonia Pernas[2,11]

[1] Hospital 12 de octubre, Madrid, Spain; [2] SOLTI Breast Cancer Research Group, Barcelona, Spain; [3] HM CIOCC, Madrid, Spain ; [4] Hospital General de Catalunya, Barcelona, Spain; [5] Hospital Universitari Son Espases, Palma de Mallorca, Spain; [6] Hospital Virgen de la Victoria, Málaga, Spain; [7] Hospital Clínico Universitario de Santiago-CHUS, Santiago de Compostela, Spain; [8] Hospital Virgen del Rocío, Sevilla, Spain ; [9] Hospital Universitario Infanta Sofía, Madrid, Spain; [10] Hospital Clinic de Barcelona, Barcelona, Spain ; [11] Institut Catala d'Oncologia, L'Hospitalet- Barcelona, Spain.

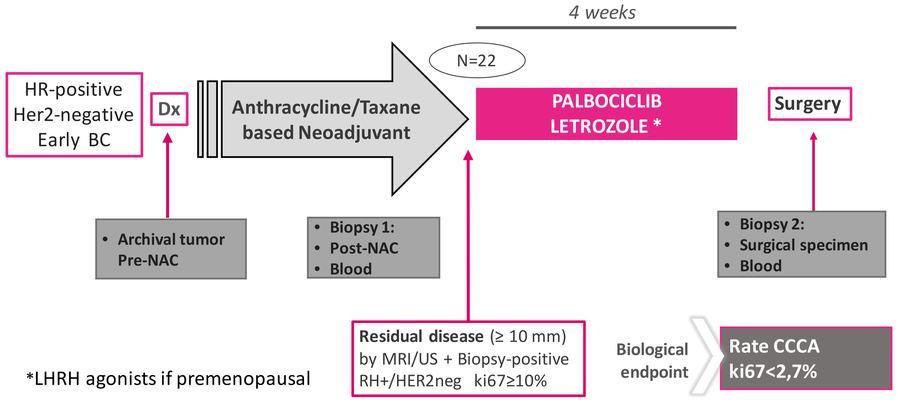
BACKGROUND

- Despite the improvement in the treatment of early-stage breast cancer (BC) with chemotherapy, many patients have residual disease with a higher risk of metastatic recurrence and poorer outcome than those who achieve a pathological complete response (pCR), particularly in highly proliferative tumors[1].
- In HR+ BC, the pCR rates after NAC are around 10-15%. Thereby additional strategies are necessary to eradicate these residual tumor cells.
- The post-neoadjuvant setting represents the best scenario to select a population with a high recurrence risk.
- The combination of cyclin-dependent kinase inhibitors with first or second-line endocrine therapy are options for advanced BC[2-3] and its role in the early-setting is being evaluated in several studies.
- Posttreatment Ki67 levels provide prognostic information for patients with HR+ BC and residual disease[4], but the prospective validation of this biomarker is necessary.

HYPOTHESIS

We hypothesize that the combination of palbociclib with letrozole offers clinical benefit in the preoperative setting for HR+ Her2-negative early breast cancer patients, with high risk of recurrence with residual disease after NAC.

STUDY DESIGN



*LHRH agonists if premenopausal

KEY ELEGIBILITY CRITERIA

Inclusion

- Pre and postmenopausal patients.
- Have completed ≥80% total dose of an anthracycline/ taxane-based NAC.
- Histologically confirmed HR+/HER2- BC:
  - Eligible for surgery.
  - A residual lesion ≥ 10 mm by MRI after neoadjuvant chemotherapy.
  - Ki67% ≥ 10% after neoadjuvant chemotherapy locally assessed.

Exclusion

- Inoperable , locally advanced after NAC.
- Prior therapy with palbociclib or any CDK inhibitor.

PRIMARY ENDPOINT

- To analyse **Complete Cell Cycle Arrest (CCCA)** determined by Ki67< 2.7% at surgery, by central assessment.

SECONDARY ENDPOINTS

- To assess the residual cancer burden (RCB), after neoadjuvant treatment, as per local assessment.
- To determine the pCR (ypT0/TisypN0) rate after neoadjuvant treatment.

EXPLORATORY ENDPOINTS

- Changes in gene expression (752 genes) and PAM50 intrinsic subtype between pre and post-treatment paired samples.
- Rate of cell cycle suppression according to BC subtype.
- Changes in TILs and in PDL1 expression by IHQ pre and posttreatment.
- celTIL score increase at surgery.
- ctDNA determination postNAC and at surgery.

CURRENT STATUS

The recruitment is ongoing in 8 sites across Spain.

REFERENCES

1. Cortazar P. et al . Lancet 2014.
2. Finn RS et al. N Engl J Med 2016.
3. Turner NC. Et al. N Engl J Med 2018.
4. MA C.X et al . Clin. Cancer Research 2017.
5. W.F. Symmans. JCO 2007

ACKNOWLEDGEMENTS

We thank Pfizer for their provision of palbociclib and their financial contribution.