GBG 94 – PATINA

A Randomized, Open Label, Phase III Trial to Evaluate the Efficacy and Safety of Palbociclib + Anti-HER2 Therapy + Endocrine Therapy vs. Anti-HER2 Therapy + Endocrine Therapy after Induction Treatment for Hormone Receptor Positive (HR+)/HER2-Positive Metastatic Breast Cancer

GBG Jahrestreffen 2017

Jana Barinoff

Triple positive Mammakarzinome profitieren weniger durch die endokrine Therapie als Her2neu-negatives HR-positives Mammakarzinom

M. Dowsett *et al.*

Relationship between quantitative estrogen and progesterone receptor expression and human epidermal growth factor receptor 2 (HER-2) status with recurrence in the arimidex, tamoxifen, alone or in combination trial

J Clin Oncol, 26 (2008), pp. 1059–1065

M. De Laurentiis *et al.*

A meta-analysis on the interaction between HER-2 expression and response to endocrine treatment in advanced breast cancer

Clin Cancer Res, 11 (2005), pp. 4741–4748

A. Lipton *et al.*

Elevated serum Her-2/neu level predicts decreased response to hormone therapy in metastatic breast cancer

J Clin Oncol, 20 (2002), pp. 1467–1472

Der cross-talk zwischen dem Her2neu- und ER/PR-Rezeptoren bedingt eine endokrine Resistenz der triple positiven Mammakarzinome

C.K. Osborne et al

Mechanisms of endocrine resistance in breast cancer

Annu Rev Med, 62 (2011), pp. 233–247

J. Shou *et al.*

Mechanisms of tamoxifen resistance: increased estrogen receptor-HER2/neu cross-talk in ER/HER2-positive breast cancer

J Natl Cancer Inst, 96 (2004), pp. 926–935

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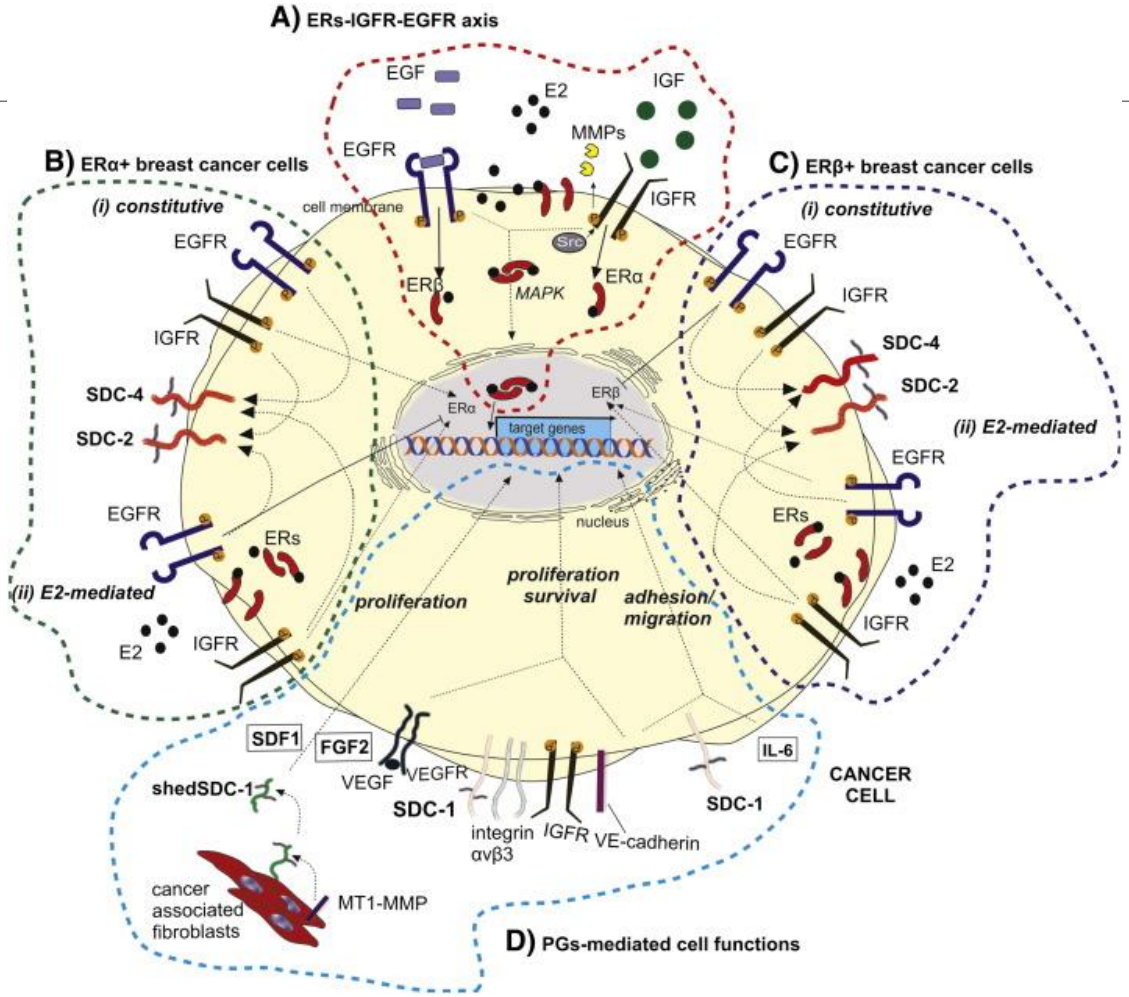

S. Skandalis et al. Cross-talk between estradiol receptor and EGFR/IGF-IR signaling pathways
in estrogen-responsive breast cancers: Focus on the role and impact of proteoglycans. Matrix Biology. Volumen 35. April 2014. 182-193.

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Frischer Bronzeguss und antikes Original

DESIGN

n=496

HER2+ HR+ Metastatic Breast Cancer; after 1-st line CHT (Taxan or Navalbine)+ Trastuzumab

1:1

Palbociclib (D1-21 of 28d cycle)
Anti-HER2 Therapy (every 3w)*
Endocrine Therapy**

Until disease progression

Anti-HER2 Therapy (every 3w)*
Endocrine Therapy**

Until disease progression

***Clinical FU q12w until tumor progression

Survival FU q6m for 5y

*Anti-HER2 treatment options are Trastuzumab plus Pertuzumab or Trastuzumab only (limited to 20% of the study population). The same anti-HER2-regimen should be used before and post randomization.

**Endocrine therapy options are either an Aromatase Inhibitor or Fulvestrant

*** for patients who discontinue treatment prior to disease progression

ClinicalTrials.gov Identifier: NCT02947685

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Primary Objective / Endpoint

- **The primary objective of this study is to demonstrate that the combination of palbociclib with anti-HER2 therapy plus endocrine therapy is superior to anti-HER2-based therapy plus endocrine therapy in prolonging PFS in participants with hormone receptor-positive, HER2+ metastatic breast cancer who have not received any prior treatment beyond induction treatment in this setting.**

- **Endpoint:**

  Progression-free survival (PFS) as assessed by the Investigator

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Secondary Objectives

- To compare measures of tumor control (including PFS, OR, CBR, DOR) between the treatment arms
- To compare median overall survival and overall survival probabilities at 3-years and 5-years between the treatment groups
- To compare safety and tolerability between the treatment arms
- To compare the incidence of CNS metastasis between the treatment arms
- To compare patient reported time to symptom progression as assessed by the FACT-B TOI-PFB
- To compare patient reported breast cancer specific health related quality of life (HRQOL) and general health status

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Main Screening criteria

- Signed informed consent
- Participants must have histologically confirmed invasive breast cancer that is metastatic or not amenable for resection or radiation therapy with curative intent.
- Patients must have histologically confirmed HER2+ and hormone receptor positive (ER+ and/or PR+), metastatic breast cancer.
- Representative formalin-fixed paraffin-embedded (FFPE) tumor tissue block (preferred) or at least 15 unstained slides along with a pathology report documenting HER2 positivity and hormone receptor positivity
- Representative tumor specimen obtained from metastatic disease if clinically feasible.

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Main inclusion criteria for randomization (1)

- ECOG performance status 0-1
- Patients must be able and willing to swallow and retain oral medication
- Serum or urine pregnancy test must be negative within 7 days of randomization in women of childbearing potential
- Resolution of all acute toxic effects of prior induction anti-HER2-based chemotherapy regimen
- Willingness and ability to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures

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Main inclusion criteria for randomization (2)

- Patients may or may not have received neo/adjuvant therapy, but must have a disease-free interval from completion of anti-HER2 therapy to metastatic diagnosis ≥6 months.
- For this study, chemotherapy is limited to a taxane or vinorelbine (only for trastuzumab-based regimen). Eligible patients are expected to have completed 6 cycles of chemotherapy containing anti-HER2-therapy treatment.
- Anti-HER2 treatment options are Trastuzumab plus Pertuzumab or Trastuzumab only (limited to 20% of the study population).
- Endocrine therapy options are either an Aromatase Inhibitor or Fulvestrant
- No evidence of disease progression by local assessment

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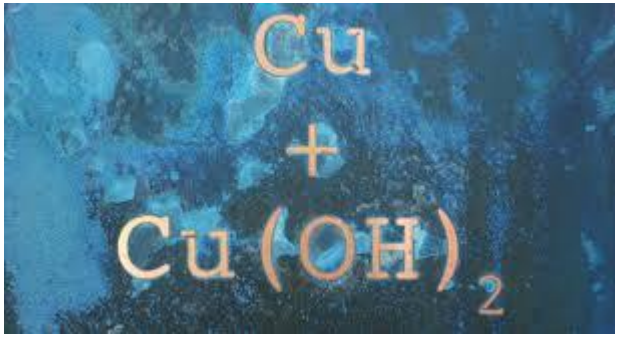
Main exclusion criteria (1)

- Concurrent therapy with other Investigational Products.
- Prior therapy with any CDK inhibitor.
- Patients receiving any medications or substances that are strong inhibitors or inducers of CYP3A isoenzymes within 7 days of randomization.
- Patients on combination antiretroviral therapy
- QTc interval >480 msec, Brugada syndrome or known history of QTc prolongation or Torsade de Pointes.
- Patients with clinically significant history of liver disease, including viral or other known hepatitis, current alcohol abuse, or cirrhosis

Administrative

- Global Sponsor: Alliance Foundation Trials USA
- Number of patients (global): 496
- Global Study Start: QI 2017
- Estimated enrollment time period: 2 years
- Study Start Germany: QIII 2017
- LKP Germany: Dr. Jana Barinoff



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