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GBG 93 - PADMA

A randomized, open-label, multi-center phase IV study evaluating palbociclib plus endocrine treatment versus a chemotherapy-based treatment strategy in patients with hormone receptor positive / HER2 negative breast cancer in a real world setting

EudraCT no.: 2016-004482-89

Priv. Doz. Dr. Marc Thill,
AGAPLESION MARKUS KRANKENHAUS,
Frankfurt / Main

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Study design

PATIENT POPULATION:
N=360
- HR+ / HER2- MBC
- No prior systemic anticancer treatment for advanced/ metastatic disease
- Male or female
- Pre-, peri-, post-menopausal
- Metastases (≥ 1 liver or ≥ 2 metastatic sites)
- CT deemed option by investigator

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1:1

Arm A: Endocrine Therapy* + Palbociclib

Arm B: Chemotherapy of physician´s choice** ± ET maintenance therapy

PRIMARY ENDPOINT:
Time-to-treatment Failure

KEY SECONDARY ENDPOINTS:
PFS, TFST, TSST, OS 36 months, patient-reported HR QoL (FACT-B), DMTI, safety, tolerability, compliance.

* AI, fulvestrant +/- GnRH analogue
** As defined in the study protocol

PFS = Progression-free survival
TFST = time to first subsequent therapy
TSST = time to second subsequent therapy
DMTI = Daily Monitoring Treatment Impact

STRATIFICATION FACTORS:
- hormone resistant (relapse on or within 12 months of end of adjuvant ET) versus hormone sensitive (relapse beyond 12 months after end of ET or *de novo* metastatic HR+ / HER2- breast cancer)
- symptomatic (defined as per investigator) versus asymptomatic (as defined by investigator)

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Rationale

Endocrine therapy is the recommended option for hormone-receptor-positive and HER2-negative breast cancer as first-line therapy, except those with rapidly progressing, life-threatening disease (visceral crisis).

CDK4/6 inhibitors in addition to either AI or fulvestrant are highly effective and change the treatment landscape rapidly

Data comparing endocrine treatment (ET) alone vs. chemotherapy is limited

Since palbociclib improved the efficacy of ET alone by about 50%, it is possible that ET + palbociclib is superior to mono-chemotherapy

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Primary objective

To compare the time-to-treatment failure (TTF) for patients randomized to receive pre-defined chemotherapy treatment strategy versus those randomized to receive palbociclib and endocrine therapy.

Time-to-treatment failure (TTF) is defined as time from randomization to discontinuation of treatment due to disease progression, treatment toxicity, patient's preference, or death.

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Secondary objectives (I)

- To compare time to first progression as assessed by investigator (PFS).
- To compare time to end of first-line MBC treatment regimen.
- To compare time to first subsequent treatment (TFST).
- To compare time to first subsequent chemotherapy (TFSCT).
- To compare duration of first subsequent treatment (DFST).
- To compare time to second subsequent treatment regimen (TSST).
- To compare the overall survival between treatment arms at 36 months.

Secondary objectives (II)

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- To compare patient well-being and health care utilization by daily monitoring treatment impact (DMTI) including sleep and activity levels, content with QoL and degree of bother by side-effects, number and duration of phone calls, and patient´s visits to medical facilities.
- To compare patient reported outcomes, measured by FACT-B.
- To compare time-to-deterioration in Trial Outcome Index-Physical/ Functional/Breast (TOI-PFB derived from FACT-B).

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Secondary endpoints (I)

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- Patient reported breast cancer specific quality of life.
- Time-to-deterioration (TTD) in TOI-PFB (FACT-B) is defined as an increase of 5 or more score points from baseline.
- Sleep and activity levels (DMTI) measured by:
  - Total sleep time (hours/day) defined as number of hours a sleep between time of sleep onset to morning awakening.
  - Minutes of interrupted sleep (minutes/day) defined as minutes awake after sleep onset.
  - Total nap time (NAPTIME) defined as >= 10 continuous minutes of inactivity during the out-of-bed time.

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Secondary endpoints (II)

- Activity counts per daytime hour defined as total number of activity counts during the day divided by total awake time of that day.
- Total daytime activity (counts/day) defined as total activity “counts” during the day.
- Percent sedentary defined as percent of daytime spent in sedentary activities as determined by the activity counts measured each minute.

- Content with QoL and degree of bother by side-effects measured by two daily FACT-derived questions on a 5-point scale for level of agreement
- Number and duration of phone calls, and patient´s visits to medical facilities.

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Inclusion criteria

- Histologically confirmed locally advanced or metastatic invasive hormone receptor positive and HER2 negative breast cancer.
- Patients who are candidates suitable for randomization for mono-chemotherapy treatment.
- One or more liver metastases or ≥ 2 metastatic sites involved.
- Life-expectancy > 6 months.
- Female or male.
- Age ≥ 18 years.

Real world!

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Exclusion criteria

- Indication for poly-chemotherapy or single-agent endocrine therapy only or bevacizumab.
- Asymptomatic bone metastases as the only site of metastatic disease.
- Uncontrolled/untreated central nervous system lesions.

Real world!

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Study timelines and key variables

- Enrollment period: 18 months (Q-II 2017 - Q-III 2018)
- First Patient In: Q-II 2017
- Study duration: 36 months
- Follow-up period: 18 months after Last Patient In

- Number of sites: 130
  - Germany: 72 (invited in JAN-2017)
  - Canada: 10
  - France: 10
  - Italy: 10
  - Poland: 10
  - Spain: 10
  - UK: 10

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Participating countries

- **Canada (CCTG)**
- **France (GINECO)**
- **Germany (GBG)**
  Co-ordinating investigator:
  PD Dr. Marc Thill (Agaplesion Markus Krankenhaus Frankfurt am Main)
- **Italy (GIM)**
- **Poland (CECOG)**
- **Spain (GEICAM / MedSIR)**
- **UK (study group)**

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Drug supply

- Palbociclib (125mg / 100mg / 75mg) will be provided.
- All other drugs are standard of care.

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Patient-reported Outcome via PADMA phone (Android Smart Phone)

(1) FACT-B:

- Time-points:

  at randomisation,

  on day 7 of each cycle until month 6,

  thereafter on day 7 of every second cycle.

(2) Quality-of-Life:

- Two questions with 5-point scale for level of agreement:

  “I am bothered by the side effects of treatment.”

  “I am content with the quality of my life right now.”

- Time-point: daily.

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Daily Monitoring Treatment Impact
ActiWatch™ Spectrum PRO

Sleep and activity levels via ActiWatch™ (non-dominant wrist):

(1) System software and logistics

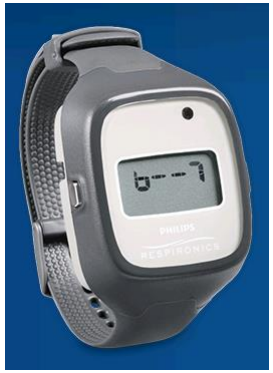
- **Storage and configuration of watches by AMS.**
- **Site shipping dates: sending of 3 watches after site activation (depot) and thereafter tbd.**

(2) Recording

- **Starting during screening phase (baseline) and thereafter on days 2-4 of every cycle.**

(3) Data handling

- **Data read-out at AMS and forwarded to Philips for scoring (ActiGraphs).**



Daily Monitoring Treatment Impact
Health Care Utilization - Geofencing

Geofencing - recording of patient´s presence in the site:

- Participation via PADMA phone: optional (otherwise documented via GBG EDC System MedCODES).
- CRA and SN will set mobile markings on all accessible entrances/exits of the site at the initiation visit.
- Collection of patient´s presence with time stamps.
- Data transfer to AMS server in real time.
- Weekly reporting to PM (duration of patient´s presence > 24h: SAE?).

Daily Monitoring Treatment Impact
Health Care Utilization - Call Tracking

Call Tracking - Recording of phone calls patient-site (number and duration):

- Participation via PADMA phone: optional (otherwise documented via GBG EDC System MedCODES).
- Covers all participating countries.
- One unique tracking number per patient.

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Investigator Meeting

Heute 18.00 Uhr
Raum ARA II

(nur für PADMA Zentren)

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Contacts

- International Study Chair

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- Projektmanagement / Randomisierung / SAE-Meldungen

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