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HOTEL EXCELSIOR SAN MARCO

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SPARK - Study

Impact of gonadotropin-releasing hormone agonist (GnRHa) on ovarian function suppression in premenopausal advanced HER2-negative/Hormone Receptor-positive breast cancer patients treated with Aromatase inhibitors and CDK4/6 inhibitors

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Background

- In the adjuvant setting, a series of studies reported variable incidence (from 15% to 30%) of suboptimal ovarian function suppression (OFS) with the combination of an aromatase inhibitor (AI) plus GnRHa. Moreover, an incomplete estrogen suppression with GnRHa seems to reduce the clinical efficacy of AI.
- In the metastatic setting, few evidence regarding the incidence and the impact on outcome of a potential inadequate OFS throughout the treatment period with GnRHa in combination with AI and CDK4/6 inhibitor are available, even if international guidelines suggest to analytically confirm the adequate OFS through serial evaluations of serum estradiol.
- The SPARK study will be a **prospective observational multicentric study** to collect serial evaluations of serum estradiol and follicle-stimulating hormone (FSH) in order to evaluate the OF during 1st-line treatment with Triptorelin in combination with a CDK4/6 inhibitor and AI in pre/perimenopausal patients with HER-negative/HR-positive ABC.

[Guerrero A. et al, Ann Oncol 2013; Bellet M. et al, JCO 2016; Cardoso F. et al, The Breast 2024; Lu Y-S. et al, Clin Cancer Res 2022]

Hypothesis and Sample Size

- On the basis that patients with luminal-ABC treated with Triptorelin in combination with AI and a CDK4/6 inhibitor may have different levels of OF, objectives/endpoint will be:
- **Primary Objective:** describe the incidence of inadequate OFS in pre/perimenopausal ABC patients. The OF will be assessed through serial evaluations of serum estradiol during treatment period.
- **Primary Endpoint:** status of OFS (adequate/inadequate estradiol levels at specific time-points)
- **Secondary/Exploratory Objectives:** determine the effectiveness of Triptorelin as an OFS agent; explore the potential prognostic role of inadequate OFS in terms of progression-free survival (PFS) and overall response rate (ORR); assess differences in clinical characteristics (i.e. age, BMI..) between patients with adequate and inadequate OFS.
- **Sample size:** we aim to recruit 180 patients; this sample size will allow to estimate the rates of patients with adequate levels (about 90% according to *MONALEESA-7* trial) with a 95% confidence interval ranging from 85% to 94%. A description of the estradiol trajectory will be also reported.

Study Plan

Inclusion Criteria

Patients are eligible to be included in the study only if all the following criteria apply:

1. Premenopausal and Perimenopausal (as per local definition) female patients aged ≥ 18 years;
2. Patients have histologically proven, HR-positive and HER2-negative locally recurrent inoperable or metastatic breast cancer according to local definition;
3. Patients have been prescribed first-line treatment with a combination of AI plus CDK4/6i plus triptorelin
4. Written informed consent.

Recruitment/Treatment Plan

- The study will be conducted in 12 centers. Length of Study: 36 months.
- All patients will receive standard treatment consisting of Triptorelin (administered monthly as per clinical practice), AI (letrozole or anastrozole, at the physician's discretion) and a CDK4/6 inhibitor (ribociclib, palbociclib, or abemaciclib according to guidelines and availability).
- The estradiol and FSH samples will be collected (local and central laboratory): baseline, cycle 3, 6 and 12.
- Inadequate OFS will be defined according to plasma estradiol in the premenopausal range defined by central laboratory definition.