Randomised Phase II Study Evaluating, As First-Line Chemotherapy, Weekly Oral Vinorelbine As a Single-Agent Versus Weekly Paclitaxel As a Single-Agent in Estrogen Receptor Positive, HER2-Negative Patients With Advanced Breast Cancer (NORBreast-231 Trial)


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Background: Chemotherapy (CT) is widely used in the management of estrogen receptor (ER) positive breast cancer patients (pts) pre-treated by hormone therapy (HT). Single-agent CT in this setting has been validated in guidelines of management of the disease. Both paclitaxel and vinorelbine are recommended among the standard available CT agents for advanced breast cancer (ABC). Weekly paclitaxel (P) and oral vinorelbine (OV) as single agents are active with a good tolerance profile for these pts. Oral CT offers significant advantages over intravenous CT because of its greatest convenience, its ease of administration and reduced need for hospitalisation. Since the benefits and safety profile of OV and weekly P have never been compared in a face to face trial, this study will provide key clinical data regarding the optimal management of this patient population: ER positive and HER2-negative disease previously treated by a HT.

Trial design: In this open-label study, pts are randomized to receive: OV 60 mg/m2/week (day 1, 8, 15) for the first cycle, then increased to 80 mg/m2/week from the second cycle in the absence of grade 3 or 4 toxicity or weekly P 80 mg/m2/week (day 1, 8, 15) intravenously. Treatments are continued until disease progression, unacceptable toxicity or pt’s refusal. Main eligibility criteria include: age ≥18 years, documented locally recurrent or metastatic disease previously untreated by CT, ER positive disease previously treated by at least one HT, HER2-negative disease, Karnofsky PS ≥70. Primary objective: disease-control rate (defined as objective response or stable disease for a minimum of 6 weeks). Secondary objectives: other efficacy parameters, evaluation of safety profiles of both arms and quality of life assessment. Statistical methods: the one-sample multiple testing procedure for phase II clinical trials described by Fleming is used. This procedure employs the standard single stage test procedure at the last one of 2 pre-specified testings, while both allowing for early termination (should extreme results be seen) and essentially preserving the size and power of the single stage procedure. 124 pts will be enrolled in this randomized phase II study (62 per treatment arm). Randomisation is stratified according to prior taxane (yes or no) and presence of visceral metastases (yes or no).

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