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Phase II study of Goserelin for ovarian protection in premenopausal patients receiving cyclophosphamide containing chemotherapy: menstruation outcome.

By :

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Introduction

The use of adjuvant chemotherapy in younger women with early breast cancer (EBC) has substantially improved the long-term outcome [1]. However, this benefit is associated with long-term toxic effects which are becoming more important as prognosis improves. These include premature menopause and infertility in young pre-menopausal women. The incidence of premature menopause depends on the type and intensity of chemotherapy and the patient's age. In women <35 years old, the long-term (3 years after diagnosis) incidence of amenorrhea is similar to women who have not received chemotherapy, at ~ 10%, but this increases to 50% in women between 35 and 40 years old, and can be up to 85% in women >40 years [2]. Premature ovarian failure has major consequences including sexual dysfunction and infertility, and the latter may be of great concern to younger patients with breast cancer and has a bearing in influencing treatment decisions in almost 30% of cases [3].

Currently, there is no standard treatment for preventing chemotherapy-induced ovarian failure. Previous studies have suggested that temporary ovarian suppression with a gonadotropin-releasing hormone (GnRH) analogue may preserve ovarian function both in humans and animal models [4–9]. Clinical data are conflicting. For example, a recent Italian multi-center phase III study

Prevention of Menopause-Induced by Chemotherapy: A Study in Early Breast Cancer Patients-Gruppo Italiano Mamella 6 (PROMISE-GIM6) reported that the use of GnRH analogue, triptorelin during chemotherapy in pre-menopausal patients with EBC, reduced the occurrence of chemotherapy-induced early menopause with four pregnancies after a 26-month follow-up [one in the chemotherapy alone arm and three in the triptorelin with chemotherapy arm] [10]. In contrast, another trial suggested that the use of goserelin concurrently with neoadjuvant chemotherapy did not significantly reduce incidence of amenorrhea 6 months after the end of chemotherapy compared with those receiving chemotherapy alone and only two pregnancies were recorded [one in each arm] with a follow-up of 2 years [11].

Study objectives

Determination of the role of Goserelin for ovarian protection in premenopausal patients receiving cyclophosphamide containing chemotherapy**:** menstruation outcome.

Patients and methods

Eligibility criteria:

-Premenopausal cancer patients who will recieve Cyclophosphamide-containing chemotherapy.

-ECOG performance status (PS) ≤ 2.

-Informed consent will be taken from eligible patients before enrollment.

Exclusion Criteria:

Postmenopausal cancer patients

Cancer patients who will receive non Cyclophosphamide containing chemotherapy

Study design:

This study is a randomized prospective phase II study

Study type: interventional

Study design:

Allocation: randomized

Endpoint classification: efficacy study

Primary endpoint: compare rate of ovarian failure at 1 year between the two treatment groups with ovarian failure defined as the absence of menses in the preceding 6 months and levels of FSH in the postmenopausal range.

Secondary endpoint: median time to recovery of menses from the final dose of goserelin.

Official title: **Phase II study of Goserelin for ovarian protection in premenopausal patients receiving cyclophosphamide containing chemotherapy: menstruation outcome.**

Pretreatment assessment:

Eligible patients will be subjected to the following:

-History and physical examination especially menstrual history

-baseline hormonal profile (FSH, LH**,** E2)

Treatment protocol:

In this phase II trial, patients will be randomly assigned, in a 1:1 ratio, to standard adjuvant or neoadjuvant chemotherapy with the GnRH agonist goserelin (goserelin group) or to chemotherapy without goserelin (chemotherapy alone group).

For Patients randomly assigned to the goserelin group, goserelin at a dose of 3.6 mg will be administered subcutaneously every 4 weeks beginning 1 week before the initial chemotherapy dose and will be continued to within 2 weeks before or after the final chemotherapy dose.

Follow up: All patients will be followed for at least 1 year clinically monthly and by laboratory assessment by hormonal profile (FSH, LH**,** E2) every 6 months.

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