Sixteen years follow-up results of a randomized phase II trial of neoadjuvant FAC compared with CMF in stage III breast cancer.

Background

Neoadjuvant chemotherapy (NAC) is a standard treatment for locally advanced and inflammatory breast cancer but it has also become an alternative option for early stages of disease. The progressive use of chemotherapy has considerable advantages including the direct assessment of the tumor’s sensitivity to therapy, the early eradication of systemic micrometastatic disease, and the possibility of performing breast conserving therapy in women who might otherwise need a mastectomy.

The management of locally advanced breast cancer remains challenging, with high rates of locoregional and distant recurrences and significant morbidity and mortality. Moreover, a subset of patients fails to respond or even show tumor progression in NAC.

The use of chemotherapy with cyclophosphamide, methotrexate and 5-fluorouracil (CMF) was first described by Bonadonna et al. in the adjuvant setting. Another commonly used chemotherapy regimen consisted of 5-fluorouracil, doxorubicin and cyclophosphamide (FAC). A prospective randomized study described an objective response rate of 71% for CMF in the neoadjuvant setting, whereas another study conducted at our institution showed similar results with the use of FAC.

Based on this data, we developed a randomized phase II study to compare FAC vs CMF at doses intensity of equivalent activity in the neoadjuvant setting for patients with locally advanced breast cancer.

Objective

The aim of this study was to describe long-term results of FAC vs CMF neoadjuvant chemotherapy in stage III breast cancer patients (pts).

Primary endpoints were:

- Response rate.
- Toxicity.

Secondary endpoints were:

- Breast conservation surgery after NAC.
- Loco-regional control.
- Disease-Free Survival (DFS).
- Overall Survival (OS).

Materials and Methods

Study design

Before treatment:
- Complete history and clinical examination.
- Blood biochemistry profile before each cycle of CT.
- Performance status (ECOG-Zubrod).
- Menopausal status.
- Hormonal receptor status.
- Laboratory complete blood count, liver and renal function, electrolytes, lipids, albumin, alkaline phosphatase, lactate dehydrogenase.
- Imaging: (B-) mammography, chest X-ray, bone scan, hepatic, ultrasounds or computed tomography, echocardiogram.

During treatment:

- Evaluation of treatment:
  - Complete physical examination at each cycle of CT.
  - CBC and biochemical profile before each cycle of CT.

- Results:

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<tr>
<th>Arm A</th>
<th>Arm B</th>
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<td>FAC</td>
<td>CMF</td>
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  - **Arm A (FAC)**
  - **Arm B (CMF)**

  - **Efficacy criteria:**
    - Histological diagnosis of breast cancer by local needle biopsy.
    - Stage: disease according to UICC criteria.
    - Measurable disease.
    - Performance-status (ECOG-Zubrod).
    - Adequate bone marrow.

  - **Irrelevancy criteria:**
    - Inflammatory breast cancer.
    - Prior systemic or surgical therapy.
    - Synchronous bilateral breast cancer.
    - Evidence of myocardial dysfunction.

  - **Patient selection**

  - **Results**

  - **Clinical Response (%)**

  - **Pathological Tumor down staging**

  - **Pathological LN down staging**

  - **Haematological toxicity (WHO grade 3-4)**

  - **Non-haematological toxicity (WHO grade 3-4)**

  - **Conclusions**

  - **Bibliography**

Conclusions

To the best of our knowledge, this is the first study to report long-term outcomes of FAC and CMF in the neoadjuvant setting. Within the sensitivity of our study, both regimens showed similar OR, long-term toxicity, DFS and OS rates at 16 years. After 5 years of follow-up, the hazard of death seems to decline (nearly 40% of pts are still alive), a finding that is similar to what has been reported for other regimens.

Bibliography