HIGH-DOSE CEF (CYCLOPHOSPHAMIDE, EPIRUBICIN, FLUOROURACIL) AS PRIMARY CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER: LONG TERM SURVIVAL DATA

F. Conti, P. Perri, I. Sperduti, A. Amodio, S. Carpano, P. Foggi, M. Anzà, M. Della Giulia, M. Lopez. *Regina Elena Institute for Cancer Research, Rome, Italy*

Purpose: To determine wether primary CEF is effective in locally advanced breast cancer, as measured by response, local recurrences, disease free survival (DFS) and overall survival (OS).

Patients and methods: From 1990 to 1998, 62 patients (pts) with stage III disease were enroled into a prospective study at Regina Elena Institute for Cancer Research, Rome. Inflammatory breast cancer (IBC) was included. Pts received three 21 d cycles of chemotherapy that consisted in epirubicin 50 mg/m^2, cyclophosphamide 400 mg/m^2 and fluorouracil 500 mg/m^2 i.v. on days 1 and 8. G-CSF (300 lg) was given subcutaneously every other day from days 5 to 17. After primary chemotherapy, whenever possible, mastectomy or conservative surgery was performed. Subsequently responding pts received the same regimen, whilst non-responders were given a non-cross resistant chemotherapy. In case of conservative surgery or initial T4 tumour radiation therapy was performed at the end of adjuvant chemotherapy. ER positive pts received tamoxifen 20 mg/d for five years.

Results: Median follow for the cohort was 109 months (range, 10–199). The local recurrence rate was 19.3%; two pts developed a new primary cancer in the contralateral breast. Distant metastases occurred in 29 pts (46.7%). The 5 years DFS rate for IIIA pts was 14.3% (median DFS: 27, CI 95% 17–37), for IIIB was 52.5% (median DFS: 87, CI 95% 10–175) for IBC was 20% (median DFS: 27 month, CI 95% 14–40), *p*-value 0.009. The 10-years OS for the IIIA pts was 28.6% (median OS: 43 month, CI 95% 30–56), for IIIB was 47.5% (median OS:116 month, CI 95% 47–185) and for IBC was 26.7% (median OS: 46 month, IC 26–66), *p*-value 0.11.

Conclusion: Ten years of follow up of stage III breast cancer is rarely reported. In IIIB pts we obtained a good local control and interesting long term data of OS.

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EXPERIENCE OF 170 CASES OF DUCTAL CARCINOMA *IN ' (DCIS)*

C. D'Addetta [a], T.P. Latiano [a], A. Piano [a], V.M. Valori [a], M. Morritti [a], G. Cilenti [a], R. Murgo [b], M. Bisceglia [c], S. Parisi [d], M.R. Valvano [e], E. Maiello [a]. [a] *Oncology Unit, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy.* [b] *Surgery Unit, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy.* [c] *Pathology Unit, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy.* [d] *Radiotherapy Unit, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy.* [e] *Statistician, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy*

Background: DCIS currently accounts for up 25% of all newly diagnosed breast cancers, but it can give rise to potentially lethal invasive carcinoma if undetected and left untreated. We are unable to predict which DCIS will progress to invasive cancer and the time interval to the development of recurrent DCIS or invasive carcinoma.

Methods: Retrospectively one hundred seventy patients (pts) with DCIS of the breast were observed between 1996 and 2007 in our Institution. The main characteristics of these pts included: median age 53 years (range 23–78); menopause 112 pts (66%); fertility 139 pts (82%); surgery: mastectomy 39 pts (23%) and local excision 131 pts (77%). After breast-conserving treatment (BCT) 123 pts (94%) received radiotherapy. Overall, 72 pts (42%) received tamoxifen.

Results: With median follow-up of 56 months (range 4–71), recurrence rate was 4.7% (8 pts: 5 ispilateral; 2 controlateral and 1 ipsilateral + controlateral synchronous). Median relapse free survival was 45 months (21–87). Approximately 75% of the of these recurrences have developed invasive cancer and 25% DCIS. All pts had more than 40 years (6/8 between 40 and 50 years) and underwent BCT. The initial histological characteristics of these women were: 7/8 comedo carcinoma and 6/8 presence of disease at the surgical margins. Seven of these pts underwent breast irradiation (87.5%) and only three pts (37.5%) hormonal therapy with tamoxifen. The overall survival of all group was 95.3%.

Conclusions: These retrospective data confirmed that mastectomy treatment is associated with optimal local control. Pts with age between 40 and 50 years and comedocarcinoma histology might be considered at high risk of local recurrence.

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NUOVO RUOLO DEGLI INIBITORI DELL'AROMATASI: IMPIEGO IN TERAPIA ADIUVANTE

A. Molino. *Oncologia Medica Clinicizzata, Università degli Studi di Verona, Italy*

Il trattamento ormonale ha l'obiettivo di impedire che gli estrogeni possano legarsi ai recettori ormonali: requisito fondamentale a tutti i tipi di manipolazione ormonale è dunque l'espressione da parte delle cellule tumorali dei recettori per gli estrogeni e/o per il progesterone.

Le opzioni terapeutiche sono diverse: in premenopausa è necessario abolire l'attività ovarica con i farmaci agonisti LH-RH, che portano alla soppressione della produzione di estrogeni mediante interferenza con l'asse ipotalamo-ipofisi, con conseguente ipogonadismo di origine centrale (castrazione medica); a questi va associato il tamoxifen, che compete con gli estrogeni prodotti in sede extraovarica per il legame con i recettori.

In menopausa il tamoxifen era la terapia standard fino a qualche anno fa, ma negli ultimi anni è stata sviluppata una nuova categoria di farmaci, gli inibitori di terza generazione dell'enzima aromatasi (anastrozolo, letrozolo, exemestane); l'aromatasi è l'enzima responsabile, in menopausa, della conversione degli androgeni surrenalici in estrogeni: questa avviene a livello periferico, cioè osso, fegato, muscolo, tessuto adiposo, tessuto tumorale mammario. Mentre il tamoxifen è un farmaco ampiamente usato da più di 30 anni e quindi ben conosciuto, gli effetti a lungo termine degli inibitori dell'aromatasi sono per certi versi ancora non del tutto noti.