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CONTROL OF MALIGNANT PLEURAL EFFUSIONS IN BREAST CANCER: A RANDOMIZED TRIAL OF BLEOMYCIN VERSUS INTERFERON ALFA

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The study evaluated the effectiveness of intrapleural infusion of Bleomycin (Bl) vs Interferon alfa (In) to control pleural effusions (PE) secondary to postmenopausal breast cancer. METHODS. 31 pts were randomized to: day 1 simple complete thoracentesis; day 8 thoracentesis plus 60 UI intrapleural Bl (16 pts) vs 18 MU of In (15 pts). Success was defined as absence of PE for 3 weeks. In case of recurrence, the same dose of Bl was repeated and In was increased to 27 MU on day 15. If recurrence again, cross-over of drugs on day 22 and 29. If there was recurrence after success the same effective drug was to be used. RESULTS. Bl was more effective than In as first therapy (63% vs 20%, $p<0.002$) as overall control of PE (32% vs 10%, $p<0.05$). Recurrence rate did not differ significantly (Bl 66%, In 75%). Survival was not affected by response to therapy, but the time of recurrence was significantly longer in Bl-responders ($p<0.05$). Bl effectiveness inversely correlated ($p<0.001$) with PE volume on day 8 (first line therapy) or on day 22 (cross-over therapy). Also in the Bl-responder group there was a significant difference in PE volume between definitive responders and pts who relapsed after success ($p<0.001$) and between pts who needed only one or two Bl infusions ($p<0.05$). In all pts side effects were minor and reversible. Estrogen receptor status (ER) did not affect response to Bl. All In responders were ER+, even if only 28% of the ER+ group was In-responder. CONCLUSIONS. Bl was more effective than In in the palliative control of PE, but achieved only 32% of definitive success. The most predictive factor of Bl response and recurrence-time was PE production rate. In was effective only in a small percentage of ER+ pts.

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LOW-DOSE 6-S LEUCOVORIN (LLV) AND 5-FLUOROURACIL (5-FU) AS SALVAGE TREATMENT IN METASTATIC BREAST CANCER (MBC). Zaniboni A., Arcangeli G., Meriggi F., Arnoldi E.*, Alghisi A. and Marini G.. SEZIONE DI ONCOLOGIA, SPEDALI CIVILI, BRESCIA; *TRESCORE (BG), ITALY.

We have extensively demonstrated that the combination of Leucovorin (both the d,L and the L form) and 5-FU is an active combination for pretreated MBC. However, it is not yet clear which should be the optimal modulatory dose of Leucovorin at least in colorectal cancer. Therefore, we have conducted the present pilot study in 33 pts. with MBC, all previously treated with an anthracycline-based regimen for advanced disease. Pts. received LLV=10 mg/m^2 i.v. day 1 to 5 immediately followed by 5-FU=370 mg/m^2 i.v. bolus day 1 to 5, every 28 days. Ice chips were utilized to prevent oral mucositis. The main characteristics of the 28 evaluable pts. are: median age: 61 yrs. (32-73), ECOG PS=1 (0-2), ER +/- =16/7, dominant metastatic site=visceral:17, soft tissue:9, bone:2.

Nine PR (32%, 95% CI = 15-49), 10 SD and 9 PD were obtained. Median duration of response 4+ mos (3-10), whereas median survival is 7+ mos (1-13+). Side effects were represented by: grade III neutropenia (1 pt.), grade II and III mucositis (7 and 1 pts.), grade II-III diarrhea (2 and 1 pts.). One toxic death occured in 1 pt. with grade IV mucositis and diarrhea after the first cycle (evaluated as PD).

Nausea and vomiting were very mild, alopecia, assessable in 15 pts., was minimal. Minor toxicity was represented by skin rush (2 pts.) and conjunctivitis (4 pts.). Although preliminary, this results suggest that low-dose LLV and 5-FU is an active, well tolerated and relatively inexpensive treatment for pretreated MBC.

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HOW TO OVERCOME THE PROBLEM OF NIPPLE AND AREOLA INVOLVEMENT IN CENTRAL SMALL SIZE BREAST CANCER?

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We report on 37 patients with small centrally located breast carcinoma or Paget disease, in whom we performed a new surgical technique at the National Cancer Institute, Milan. The surgery consisted of removal of the "central quadrant" plus the nipple/areola complex and subsequent remodelling, to achieve both oncological radicality and a good cosmetic result. The mean age of the patients was 54 years (range 36-73), 13 were premenopausal and 24 were postmenopausal; 19 had the lesion in the right breast and 18 in the left. Tumor size was from 1-10 mm in 13 cases, 11-20 mm in 10, 21-30 mm in 2 and grater than 30 mm in 1. In 5 patients the lesions were not palpable while in the remaining 6 patients there was nipple involvement only. The new surgical technique involves removal of nipple/areola complex and a cone of glandular tissue down to the fascia, with mobilization of a glandular flap which is rotated into the empty central area and skin graft to replace removed areola. Thirty two patients received homolateral axillary dissection by separate cutaneous incision. The definitive histological result was: invasive ductal carcinoma (19 cases), invasive lobular carcinoma (12 cases) and Paget's disease (6 cases); in 18 (48.7%) cases there was microscopic infiltration of the nipple and in 2 (5.4%) there was infiltration of the retroareolar large ducts. Mean follow up is 32 months (range 6-60). There have been no local recurrences nor distant metastases. This new technique provides a good cosmetic results (the grafted skin can be tatoo later to similate areola) yet assures oncological radicality particularly since the retroareolar ducts are removed.

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MAY HISTOPATHOLOGICAL SUBGROUPS OFFER PROGNOSTIC INDICATION IN INFILTRATING LOBULAR CARCINOMA OF THE BREAST?

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Histopathological variants of breast infiltrating lobular carcinoma (ILC) other than classical, are supposed to have better prognosis, at least in the short term (Fisher et al., 1997; Dixon et al., 1982). In this study, 77 ILC of the breast were, according to Page and Anderson (1987), subgrouped into classical, solid, alveolar and mixed variants . Tumor size, axillary lymphonode status, histopathological variants and patient's 5 year follow-up were recorded, together with Estrogen - (ER-ICA, Abbott) and Progesteron - (PR-ICA, Abbott) receptor status and cytoproliferative activity (Ki-67, Dako) tested on fresh tissue . Clinical-pathological and biological data were statistically analyzed by means of ANOVA and chi-square tests. Our results, confirming that stated in literature, give support to the close relationship among pathological and biological parameters and prognosis. On the contrary, histopathological variants of ILC are not related to prognosis, ER-ica and PR-ICA status, Ki-67 score, tumor size and presence of metastatic nodes.

In conclusion, in our opinion, the subsetting of ILC into different histopathological variants does not seem to offer any additional prognostic indication more than the well estabilished classical parameters.

Fisher et al., Human Pathol 8, 679-683, 1977.
Dixon et al., Histopathology 6, 149-161, 1982.
Page and Anderson, Diagnostic Histopathology of the Breast, Churchill Livingstone, 1987.

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VARIABLES IN THE AXILLA: NEW PROGNOSTIC FACTORS IN N+ BREAST CANCER. ANALYSIS OF 1003 CASES.

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Tumor size and axillary lymphonodal status are established parameters for evaluating prognosis in breast carcinoma. From January 1983 to December 1988, 1003 consecutive cases with positive axillary nodes were surgically treated. In all total axillary dissection was performed and the 3 classic axillary levels identified. Mean age was 52 years (range 23-86). In 440 cases quadrantectomy, and in 563 cases Patey or Halsted mastectomy, were performed. The average number of lymphnodes removed and examined per patient (21) was similar in both treatments. The first level was the site of metastases in 556 cases (55.4%), the 1st and 2nd levels were involved in 214 cases (21.3%) and in 187 cases (18.7%) all 3 levels were affected. Skip metastases (dissemination from 1st level directly to the 3rd) were observed in 26 cases (2.6%), with discontinuous spread (II only, II - III, III only) in 20 cases (2%). Mean follow up was 87 months (range 12-127). Of the 38 patients (3.8%) lost to follow up, 23 without evidence of disease were lost after a median of 72 months (range 1-112) and 15 with disease were lost after median 54 months (range 6-106). 381 patients died from disease after a mean of 47 months. Patients with less than 60 months' follow up were excluded from analysis. Multivariate analysis compared overall and relapse free survival by age, tumor size, number of involved nodes, invasion of lymphnodes by level and perilymphnodal invasion.

All of these factors have strong and independent prognostic significance. Evaluation of all four together is important for accurate prognostic analysis in N+ breast cancer and it is urged that they be universaly adopted in routine prognostic work up.