2.1 Mammakarzinom

2.1.1 Adjuvant Chemo-Immuno-Therapy with LMF+BCG in Node-Negative and Node-Positive Breast Cancer*

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Introduction

Breast Cancer is by far the most common neoplastic disease of women in western industrialized countries. Contrary to public hope and prevailing medical opinion, this tumor is apparently hard to cure, since eventually 60—70% of “radically” resected patients are going to succumb to their disseminated disease within 10 years after surgery [1, 2, 3]. Survival expectancy and mortality have essentially remained unchanged over the past 40 years.

The traditional surgical approach and the role of routine post-operative radiotherapy following “radical” mastectomy have therefore been seriously challenged recently [4, 5]. While early attempts involving short term adjuvant systemic treatment have either failed or yielded inconclusive results [6, 7], this logic therapeutic concept has been greatly stimulated by early results of two randomized trials conducted by American and Italian authors [8, 9]. Both investigations showed effective reduction of tumor recurrences within 2—3 years post mastectomy by adding either L-PAM intermittently for 2 years or CMF-combination chemotherapy for 1 year to surgery. Only patients with known histologic proof of homolateral axillary tumor involvement were entered in these two as well as several other current adjuvant trials.

It is however well known from the natural history of breast cancer, that at least 25—30% of patients with node-negative disease at the time of surgery will finally die of disseminated tumor within 5 years and about 35% within 10 years after “radical” mastectomy [1, 4, 5, 6]. This percentage seems to be higher in certain areas as for example in Eastern Switzerland [10]. We therefore felt justified to include both node-negative as well as node-positive breast cancer patients in

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a well stratified, controlled trial to determine the effectiveness of a relatively short 6-months adjuvant oral chemotherapy with Leukeran + Methotrexate + 5-Fluorouracil (LMF) followed by BCG skin scarifications on recurrence rate and survival. Chemo-immuno-therapy at the time of study design (1974) seemed to be a logic combination in postoperative adjuvant treatment due to its potential of eliminating small numbers of residual tumor cells after cytoreductive chemotherapy and to possibly reduce immunodepressive side effects of chemotherapy [11].

**Patient Group and Study Methods**

*Patient Selection*

A total of 242 breast cancer patients were entered in our trial between April 1974 and July 1977. Besides our centrally located oncology center several affiliated neighbourhood hospitals also participated in the current study. All patients had to fulfill the following study criteria:

- “radically” operable breast cancer T_{1-3a}, N_{0-1} (histologically N− or N +), M₀
- less than 70 years of age at surgery
- geographically accessible to at least 3-monthly follow-up

Table 1 shows the main characteristics and risk factors of our study population. A total of 9 cases out of 242 were not evaluable due to clear cut staging errors (4 cases), concomitant second tumor (1 case) and lost to follow up or refusal to continue the adjuvant treatment program (4 cases). Risk factors and mean age are nearly ideally balanced within the 2 treatment regimens and nodal subgroups.

**Adjuvant Treatment Program**

After a standardized technique of “modified radical mastectomy”, all patients underwent the usual diagnostic workup, including chest film, bone scan, bone

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>Regimen A (Surgery only)</th>
<th>Regimen C (Surg. + LMF/BCG)</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>116</td>
<td>117</td>
<td>233</td>
</tr>
<tr>
<td>N_</td>
<td>60</td>
<td>59</td>
<td>119</td>
</tr>
<tr>
<td>N_</td>
<td>56</td>
<td>58</td>
<td>114</td>
</tr>
<tr>
<td>N (1—3)</td>
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<td>40</td>
<td>75</td>
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<td>N (4)</td>
<td>20</td>
<td>18</td>
<td>38</td>
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<tr>
<td>T_{1-2a}</td>
<td>104</td>
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</tr>
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<tr>
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<td>57</td>
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</tr>
<tr>
<td>Postmeno</td>
<td>61</td>
<td>60</td>
<td>121</td>
</tr>
</tbody>
</table>

Total randomized = 242 patients. 9/242 not evaluable due to staging errors or lost to follow up.