Docetaxel 100 versus 80 mg/m² as adjuvant treatments of early breast cancer: an exploratory analysis of a randomised trial

Docetaxel-containing regimens are widely used as adjuvant treatment of early breast cancer, and the dose 100 mg/m² is often selected as the starting dose. Yet the optimal starting dose is unknown, since different docetaxel doses have never been compared in a randomised trial in the adjuvant setting. In metastatic breast cancer, three doses of docetaxel (60, 75 or 100 mg/m²) have been compared in one randomised phase III study. More tumour responses but no significant improvement in the time to disease progression or overall survival were achieved with the highest dose in the intention-to-treat population [1].

We compared docetaxel monotherapy with vinorelbine monotherapy as adjuvant treatments of breast cancer in the FinHer trial [2]. A total of 1010 women with axillary node-positive or high-risk node-negative cancer were randomly assigned to receive three cycles of docetaxel or vinorelbine, each followed by three cycles of 5-fluorouracil, epirubicin and cyclophosphamide. Women with amplified Her-2/neu gene were further assigned to receive or not to receive nine weekly trastuzumab infusions. The use of prophylactic antibiotics or granulocyte colony-stimulating factors was not recommended unless febrile neutropenia or severe infection occurred. Adjuvant docetaxel improved recurrence-free survival as compared with vinorelbine [hazard ratio (HR) for recurrence or death 0.58, 95% confidence interval (CI) 0.40–0.85, \( P = 0.005 \)].

While the trial accrual was ongoing, an independent study-monitoring committee recommended the docetaxel dose to be reduced from 100 to 80 mg/m² due to frequently diagnosed neutropenic fever in the docetaxel arm (in 36.9% of the participants). Therefore, 204 (40.6%) of the 502 patients treated with docetaxel received 100 mg/m² and 298 (59.4%) received 80 mg/m² as the starting dose. After docetaxel dose reduction, fewer (14.9%) patients had neutropenic fever. The potential impact of docetaxel dose reduction on treatment efficacy has not been reported.

No significant differences in the baseline characteristics of the patients or the tumours were observed between the

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Distant recurrence No. (%)</th>
<th>Any recurrence No. (%)</th>
<th>Died No./ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel 80 mg/m²–FEC</td>
<td>14 (4.7)</td>
<td>20 (6.7)</td>
<td>6 (2.0)</td>
</tr>
<tr>
<td>(N = 298)</td>
<td></td>
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</tr>
<tr>
<td>Docetaxel 100 mg/m²–FEC</td>
<td>19 (9.3)</td>
<td>22 (10.8)</td>
<td>14 (6.9)</td>
</tr>
<tr>
<td>(N = 204)</td>
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</tr>
</tbody>
</table>

FEC, 5-fluorouracil, epirubicin and cyclophosphamide.

**Figure 1.** Effect of docetaxel 80 mg/m² and 5-fluorouracil, epirubicin and cyclophosphamide (FEC) and docetaxel 100 mg/m² and FEC on the Kaplan–Meier estimates of the time to any recurrence (upper panel) and time to death (lower panel). The 3-year survival figures are shown.
100- and 80-mg/m² groups. Twenty (6.7%) women in the 80-mg/m² group and 22 (10.8%) in the 100-mg/m² group were diagnosed with cancer recurrence during a median follow-up of 36 months (HR 0.76, 95% CI 0.41–1.41, \( P = 0.38 \); Table 1, Figure 1). Similarly, there were no significant differences in the numbers of distant recurrences or deaths between the groups (HR 0.63, 95% CI 0.31–1.27, \( P = 0.19 \); and HR 0.59, 95% CI 0.21–1.66, \( P = 0.32 \), respectively).

Although the present analysis is explorative in nature and based on limited patient numbers, the results indicate that women treated with 80 mg/m² did not receive inferior chemotherapy despite the lower starting dose. The 80-mg/m² dose was less frequently associated with adverse effects and allowed good adherence to the 3-weekly dosing scheme, but frequent administration of prophylactic antibiotics or granulocyte colony-stimulating factors might have improved tolerability of the 100-mg/m² dose. A randomised trial comparing the two starting doses might be warranted, but the present results indicate that the size of such a trial would need to be large to demonstrate a difference, if it exists.

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references


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