OPTIMIZING IRRADIATION THROUGH MOLECULAR ASSESSMENT OF LYMPH NODE: PRELIMINARY RESULTS OF OPTIMAL TRIAL COMPARING INCIDENTAL VERSUS CONVENTIONAL IRRADIATION IN EARLY BREAST CANCER

Manuel Algara, Elvira Rodríguez, Amanda Flauger, Inmaculada Beato, Francisco Martín, José-Reyes Rodríguez, Xavier Sanz, Juan Salinas, Miguel Soler, Andreu Frias, Germán Juan, Aurora Manso, José Luis López-Guerra, Ana Calin, Inmaculada Díaz, Ezequiel González, Antonio José Lozano, Francisco Carrasco, Ignacio Andrés García, Ana Manterola

Hospital del Mar Parc de Salut Mar (Barcelona)

Background

In early breast cancer after conservative surgery there is no consensus about the extension of regional irradiation in case of low burden involvement of lymph nodes after sentinel node biopsy. The objective is to know the doses administrated to lymph node areas in a trial comparing intentional irradiation respect incidental irradiation in breast cancer, with low burden node involvement demonstrated by a molecular test.

Material and methods

The OPTIMAL Trial is designed to show the non-inferiority of incidental irradiation, as compared to intentional irradiation of the auxiliary nodes in terms of 5-year disease-free survival of early breast cancer patients. Inclusion criteria were: patients with node negative early breast cancer, treated with conservatory surgery and lymph node involvement assessed by means OSNA (One Step Nucleic Acid Amplification) and total tumor load between 250-5000 copies (micro-metastasis) or between 5000-15000 copies (macro-metastasis), at final pathological analysis.

Figure 1. Randomization

Patients were randomized (figure 1) to intentional irradiation to breast and lymph node levels I to II and supracavitary fossa (arm 1) or incidental irradiation only treatment directed to breast was allowed (arm 2). In all cases, all lymph node areas and internal mammary chain were contoured, and measures of the dose administered were recorded. Patients were treated at standard fractionation of 2 Gy up to 50 Gy and a boost was administered according to guidelines of each participating department. On figure 2 is presented an example of variability of received dose to lymph nodes with intentional irradiation with tangents.

Figure 2. Dose to lymph node levels variability

The same values in the range of macro-metastases were 6862 and 7503 in the both arms respectively. There was one local relapse in intentional arm and 2 cases of metastatic spread in the incidental arm. There was no regional relapse in both arms. The mean doses at lymph node in arm 1 was 49.7 Gy at level I, 49.1 at level II, 49.4 Gy at level III, and 48.9 at supracavitary fossa. The doses for the same node levels in arm 2 were 31.9 Gy, 18.6 Gy, 7.3 Gy and 1.4 Gy respectively. The median doses at internal mammary chain were similar in both groups (239 Gy in arm 1 and 16.7 in arm 2), see figure 4.

Results

More than 300 patients have been included and the first 247 have been analyzed (125 in arm 1 and 122 in arm 2). Patients presented micro-metastasis in 98 and 104 cases, and macro-metastasis in 23 and 14 patients of incidental or armical arm respectively. Both arms were well balanced according to the characteristics of the patients: age, tumor, stage and molecular profile. The mean copies by OSNA in the range of micro-metastases were of 1263 in intentional arm and 1121 in incidental arm (figure 3).

OSNA

<table>
<thead>
<tr>
<th>Intentional arm</th>
<th>INCIDENTAL arm</th>
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<tbody>
<tr>
<td>n = 122</td>
<td>number of copies</td>
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<tr>
<td>104 (85.6%)</td>
<td>1263 (1115.5)</td>
</tr>
<tr>
<td>14 (11.5%)</td>
<td>6602 (2683.3)</td>
</tr>
<tr>
<td>4 (3.3%)</td>
<td>7903 (2650.8)</td>
</tr>
</tbody>
</table>

Figure 3. OSNA copies distribution in both arms

Conclusion

At the time there are no differences in local control, regional control and metastasis in both arms of the trial. The doses diminish as it increases the level of the lymph nodes in incidental arm.

Figure 4. Comparison of doses to axillary lymph node levels and internal mammary chain