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Original Research

Immunohistochemical subtypes predict survival in metastatic breast cancer receiving high-dose chemotherapy with autologous haematopoietic stem cell transplantation☆

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KEYWORDS
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Abstract ***Introduction:*** The objective of this study was to evaluate the outcome of patients affected with different subtypes of metastatic breast cancer (MBC) following treatment with high-dose chemotherapy (HDC) and autologous haematopoietic progenitor cell transplantation (AHSCT).

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Immunohistochemical subtypes;
Autologous haematopoietic stem cell transplantation

Methods: All consecutive female patients treated for MBC with HDC and AHSCT at the Institut Paoli-Calmettes between 2003 and 2012 were included. Patient, tumour and treatment characteristics were collected. Patients were categorised in three subtypes based on hormonal receptor (HR) and human epidermal growth factor receptor 2 (HER2) status of the primary tumour: luminal (L), (HR+/HER2−), HER2 (HER2+, any HR), and triple negative (TN) (HER2− and HR−). The main objective was the analysis of overall survival (OS) according to the immunohistochemical (IHC) subtypes.

Results: A total of 235 patients were included, median age was 46 (range 21–62). Median follow up was 53.28 months (95% confidence interval [CI] 45.12–57.6). The TN subtype appeared to have the worst prognosis with a median OS of 19.68 months (95% CI 11.76–44.4) compared to 44.64 months (95% CI 40.32–67.56) for the luminal subtype and a median OS not reached for the HER2 subtype ($p < 0.01$). In the multivariate analysis, the TN subtype retained an independent poor prognosis value compared to the luminal subtype, with a hazard ratio of 2.03 (95% CI 1.26–3.29, $p = 0.037$).

Conclusion: HDC-AHSCT does not change the prognostic value of IHC subtypes in MBC patients. OS favourably compares with data available in the literature on similar groups of patients. These findings provide additional information and options for patients with MBC and who could potentially benefit of HDC-AHSCT.

1. Introduction

Amongst the many management options evaluated in metastatic breast cancer (MBC), interest for high-dose chemotherapy with autologous stem cell transplantation (HDC-AHSCT) was abandoned [1] after several US and European phase III studies did not show overall survival (OS) benefit [2–6].

However, a meta-analysis of controlled studies has shown benefit in progression-free survival (PFS) for metastatic patients, although no significant statistical benefit in terms of OS, possibly due to a lack of study power [7]. More recently, a retrospective study of the Italian register of MBC patients who had undergone HDC-AHSCT showed that 14% of patients were still alive and disease-free at 10 years [8].

Thus, these findings support the hypothesis that HDC-AHSCT may still have a role in the management of MBC in some selected patients. For example, some retrospective studies have suggested an increased benefit in young, oligometastatic, chemosensitive patients [8–10]. These results, however, have not been confirmed in the prospective studies and identification of the subgroup of MBC that could benefit from HDC-AHSCT remains to be achieved.

Importantly, all of these studies examining the outcome of patients treated in the 1990s and early 2000s. Indeed, systematic testing for human epidermal growth factor receptor 2 (HER2) overexpression allowing the routine use of targeted therapies such as trastuzumab was not carried out at this time [11]. Yet, it is a critical data since it has been extensively shown that prognosis of MBC depends to a large extent on immunohistochemical (IHC) subtypes, defined by overexpression of HER2 and/or hormone receptors (HR) [12], a clinically usable approximation of the molecular subtypes previously described by Perou et al [13]. In addition the prognosis of HER2 MBC has changed dramatically after trastuzumab introduction [14] and little is known about the impact of HDC-AHSCT in the context of anti-HER2 treatments.

Here, we have examined a large single-centre retrospective cohort of MBC receiving HDC-AHSCT. The primary objective of this study was to evaluate OS according to IHC-defined molecular subtypes in a recent patient population treated with this strategy. Secondary objectives included PFS, as well as evaluation of other potential clinico-biological prognostic factors and tolerance of the procedure.

2. Patients and methods

2.1. Patient population

The patient population was identified from our prospectively maintained institutional cell therapy database. Inclusion criteria were as follows: all consecutive female patients treated for MBC with HDC and AHSCT at the Institut Paoli-Calmettes (IPC) between 2003 (the year from which testing for HER2 overexpression was carried out systematically and trastuzumab routinely used) and 2012. A flowchart illustrating consecutive steps in the selection process is provided in Fig. 1.

The study was approved by the IPC Institutional Review Board (IRB, Comité d'Orientation Stratégique). All patients undergoing high-dose chemotherapy supported with autologous transplantation are required to provide