PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

High dose chemotherapy in inflammatory breast cancer

ArticleInfo		
ArticleID	:	3639
ArticleDOI	:	10.1186/bcr-1999-66617
ArticleCitationID	:	66617
ArticleSequenceNumber	:	59
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	4
ArticleHistory	:	RegistrationDate : 1999–11–1 OnlineDate : 1999–11–1
ArticleCopyright	:	Current Science Ltd1999
ArticleGrants	:	
ArticleContext	:	1305811

Richard de Boer

Keywords

High-dose chemotherapy, inflammatory breast cancer, rG-CSF, stem cell transplantation

Introduction

Inflammatory breast cancer (IBC) is an uncommon disease, accounting for 2-4% of all breast cancers, but has an aggressive clinical course and a poor prognosis. Single modality therapy (eg radiotherapy or surgery) lead to dismal 5 year survival rates of under 10%. The introduction of primary chemotherapy has improved 5 year survival to around 30-50%, but further improvement is required. Since some studies show that responding patients do much better than non-responding patients, and in particular, that a pathological complete remission (CR) is an important good prognostic factor, it seems reasonable to attempt to improve the efficacy of the primary chemotherapy regimen. One such approach is the use of high dose chemotherapy - a strategy that is also being investigated in both the metastatic and the adjuvant setting.

Aims

To evaluate the feasibility and toxicity of high-dose sequential chemotherapy with stem cell and rG-CSF support in patients with IBC.

Comments

This was a well run multi-institutional study addressing an important question in a difficult disease: In patients with IBC, will an increase in dose intensity in the primary chemotherapy lead to increased response rates (which may translate to improved survival), without an unacceptable increase in toxicity? The results showed that whilst haematological toxicity was common, with high rates of hospital readmission (51% of cycles), the toxicity was manageable. The clinical complete response rate was impressively high (80%). However, despite the fact that the pathological complete response rate (32%) was higher than that reported in comparable studies, it was disappointing that the increased doses of chemotherapy did not translate into a much higher pathological CR rate. While the 3 year survival figures were encouraging, the benefits of this approach and whether they justify the costs (use of rG-

CSF, apheresis, increased hospitalisation etc), are at this stage unclear. Further follow up is required. If the 5 year survival figures appear to be comparable to, or better than, those achieved in other large studies of primary chemotherapy in IBC, then a randomised study pitting this intensive approach against one using a more standard dose schedule would be appropriate.

Methods

The study included 100 consecutive women with true IBC with histological proof. Treatment plan: 4 cycles of chemotherapy given 3 weekly. Cycle 1: cyclophosphamide (CY) 6 g/m^{-2} plus doxorubicin (DOX) 75 mg/m^{-2}. Cycle 2: CY 3 g/m^{-2} plus DOX 75 mg/m2. Cycle 3+4: CY 3 g/m^{-2}, DOX 75 mg/m^{-2} plus 5FU 2500 mg/m^{-2} (5 day continuous infusion). Stem cells were collected after cycle 1 (and 2 if needed), using rG-CSF. Cells were reinfused after cycles 3 and 4. Following chemotherapy, patients went on to receive a mastectomy plus radiation (and tamoxifen if receptor positive).

Results

Of the 100 patients, 95 were valid for analysis. Median age was 46 years and 42% were receptor negative. A total of 87 patients received all four cycles of planned therapy, and cycles 2, 3 and 4 were delayed by more than a week in only 4, 9, and 11, patients respectively. Of 94 evaluable patients, 93 had a clinical response, with 75 (80%) having a complete response. A total of 86 patients underwent a mastectomy at a median of 3.5 months post-chemotherapy. Of these, 28 (32%) had a complete eradication of invasive tumour cells, and in a further 24 patients (28%) there was evidence of major histological changes.

With a 3 year median follow up, the estimated 3 year survival is 70%, the 3 year disease free survival is 44%, and the median survival is not yet reached.

Toxicity: Neutropenia was common (around 80% of patients per cycle) and most hospital readmissions were for febrile neutropenia. Neutropenia tended to last a median of 4-5 days. there was one fatality directly related to therapy (septic shock). Thrombocytopenia was also common and required transfusion support in an average of 29-56% of cycles. Non-haematological grade 3/4 toxicities were mainly vomiting (14% of cycles) and mucositis (10% of cycles).

Discussion

The use of stem cell infusions appeared to allow complete dosing in most patients without the development of increasing toxicities in later cycles. In total, 87 patients received all 4 cycles of

treatment and the schedule delivered about 7.5 times the dose of cyclophosphamide delivered in a standard FAC regimen. Toxicities were manageable and treatment mortality was low (one patient). The clinical response rate was very high and the 3 year survival figures were encouraging.

References

1. Viens P, Palangie T, Janvier M, Fabbro M, Roche H, Delozier T, Labat JP, Linassier C, Audhuy B, Feuilhade F, Costa B, Delva R, Cure H, Rousseau F, Guillot A, Mousseau M, Ferrero JM, Bardou VJ, Jacquemier J, Pouillart P: First-line high-dose sequential chemotherapy with rG-CSF and repeated blood stem cell transplantation in untreated inflammatory breast cancer: toxicity and response (PEGASE 02 trial). Br J Cancer. 1999, 81: 449-456.