1299 PUBLICATION

Safety profile of Herceptin (R) as a single agent and in combination with chemotherapy

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Purpose and Methods: Herceptin (H, trastuzumab) is active in women with HER2-overexpressing metastatic breast cancer. Safety data from all patients in three clinical studies with H as a single agent and in a phase III study of H in combination with chemotherapy (H + chemo) versus chemo alone were pooled and analysed. Chemo was anthracycline-cyclophosphamide (AC) in patients having received no prior adjuvant A, or paclitaxel (T) if the patient had previously received A. Doses used were A (doxorubicin = 60 mg/m^2 or epirubicin = 75 mg/m^2), C = 600 mg/m^2, T = 175 mg/m^2 every 3 hours. All were given every 3 weeks for 6 cycles. In the H alone and H + chemo arm, H was administered as an i.v. 4 mg/kg loading dose followed by i.v. 2 mg/kg per week.

Results: 338 patients from single H studies and 469 patients from the H + chemo study (235 H + chemo); have been analysed. Most of the reported adverse events were mild/moderate; pain, chest pain and dyspnoea occurred most often. Myelosuppression was infrequent and usually occurred in patients with low baseline values. H was associated with infusion-related symptoms, such as fever and/or chills in 25% of cases. These usually occurred with the first infusion only, duration of symptoms was short and prophylaxis was not necessary. Only one patient developed a positive neutralising antibody to H and this was not associated with clinical symptoms. A syndrome of cardiac dysfunction was observed:

	H + AC (n = 143)	AC (n = 135)	H + T (n = 91)	T (n = 95)	H alone (n = 338)
Cardiac dysfunction	27%	7.0%	12.0%	1.0%	4.0%
Grade 3/4 (initial)	16%	3.0%	2.0%	1.0%	3.0%
Grade 3/4 (post treatment)	6%	0.7%	0	0	1.5%
Death from cardiac dysfunction	0.7%	0.7%	0	0	0.9%

Cardiac dysfunction was more common with H + AC although this improved following standard therapy, resulting in only 6% of patients remaining with grade III cardiac dysfunction in the H + AC group. H + T did not increase grade 3/4 cardiac toxicity compared with T or H alone.

Conclusions: H is well tolerated either as a single agent or in combination with chemotherapy. A syndrome of cardiac dysfunction has been observed in some patients treated with H + AC, although this resolves following standard therapy.

1300 PUBLICATION

Role of scintimammography in the assessment of breast lymphoedema

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Introduction: Lymphoedema of the breast may indicate locally advanced, recurrent, or inflammatory cancer. Localising the site of cancer for biopsy is often difficult due to skin thickening, oedema and fibrosis in the conserved breast. Scintimammography using Tc-99 m Sestamibi is a new tool for the diagnosis of cancer, which may help to localise the cancer where mammography is equivocal, or difficult to assess because of the density of the breast.

Patients and Methods: We conducted 43 scans in 29 patients. 25 patients had known primary, or suspected recurrent cancer in the conserved breast. Bilateral breast cancer was present in 7 patients and inflammatory cancer in 13. 4 patients with marked breast oedema were referred for exclusion of cancer.

740 MBq of Tc-99 m Sestamibi was injected into a foot vein using the standard Khalkhali-Diggles regimen and imaging commenced after 5 minutes. Both breasts were imaged anteriorly and laterally, including the axillae.

Results: All patients with bilateral and/or inflammatory breast cancer showed a positive scintimammogram. Of 14 patients with suspected local recurrence in the conserved breast, 10 had sestamibi uptake and proved to have recurrent disease. The remaining 4 were shown to have benign breast change, fat necrosis or fibrosis. 4 patients with marked oedema and negative scintimammograms had negative biopsies or were shown to have normal breasts when the oedema subsided. Of the patients with inflammatory breast cancer, all except one showed less oedema following cytotoxic chemotherapy. In the patient who showed little clinical response to chemotherapy, scintimammography correctly identified residual carcinoma.

Comment: Tc-99 m Sestamibi scintimammography is an important new complementary tool in the diagnosis and assessment of breast cancer and has a special role in imaging the oedematous breast.

1301 PUBLICATION

Bendamustin/mitoxantrone in the treatment of advanced breast cancer

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Purpose: While nausea and emesis are overcome by 5-HT3-antagonists, alopecia remains a major problem in the palliative treatment of patients with advanced breast cancer. Bendamustine and Novantrone are among the cytostatic drugs proven to be effective in the treatment of breast cancer without causing alopecia. Here, we report of our experience with either bendamustine single agent or combination therapy with novantrone.

Methods: From 4/95 to 12/98 we treated 39 patients (41–73 years old, mean age 62), with either Bendamustin (17) or Bendamustin/Novantrone (22). The treatment regimen consisted of Bendamustin 60–100 mg/m^2, d 1–3, with or without Novantrone 8 mg/m^2, d 1–2. The mean number of cycles was 4, 5.

Results: Remission rates for single agent therapy and combination therapy were CR 0/10%, PR 25/38%, NC 44/38%, PD 31/14% respectively. The Overall response rate was 78%.

Overall remission duration was 440 d for patients with CR/PR, 355 d for NC, 312 d for PD. Remission duration for single agent bendamustin was 383 days, for the combination regimen 421 days.

The main toxicity was hematologic, with 8 cases of grade 3/4 leukopenia. Nausea and emesis were observed in 10 cases (g 1–3), There was no alopecia greater than grade 1 in 5 cases.

Conclusion: Bendamustin is a safe and effective drug in the treatment of advanced breast cancer. Toxicity is moderate, especially there is no remarkable alopecia, a fact that is very important for most women. Remission rates of the combination regimen with novantrone are higher, but with more pronounced hematotoxicity and without significant difference in long term survival.

1302 PUBLICATION

Bone marrow scintigraphy in clinical management of advanced breast cancer

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Purpose: To evaluate importance of whole body bone marrow (BM) scintigraphy (BMS) for elaboration of optimal therapeutic decision.

Materials: Whole body bone marrow (BM) scintigraphy (BMS) with radiocolloids was performed in 59 women with advanced breast cancer. Scintigraphic signs of BM involvement were classified in the following way: localized invasion – manifested by isolated focal defect on BM scans, generalized invasion – multifocal defects or diffusely decreased tracer uptake. Metastatic BM invasion was confirmed by biopsy or additional examination (CT, MRI and/or bone scintigraphy).

Results: BM metastases were revealed in 19 patients: 15 of them had focal defects on BMS, another 3 – diffusely diminished tracer uptake and one – multifocal defects. All women with generalized BM involvement had abnormal blood smears (anemia and/or changes in leukocytes count) and very low tolerance to any kind of chemotherapy. All patients of this group died within 12 months of follow-up. On the contrary, all 16 women with isolated focal defects tolerated chemotherapy and/or radiotherapy (2 of them – intensive chemotherapy with BM rescue) and survived, at least, 12 months of follow-up.

Conclusion: BMS permit effective discrimination between localized and extensive metastatic BM invasion. Results of BMS can help to separate women with low tolerance to conventional and experimental chemo- and/or radiotherapy.