Proffered Papers

Breast cancer advanced disease

1255 ORAL

The added value of the combined evaluation of clinical efficacy, quality of life and cost-effectiveness in a randomized phase III study. Results of an EORTC – NCIC – SAKK neoadjuvant trial in patients with locally advanced breast cancer (LABC)

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Background: Between 05/93 and 04/96, 448 patients (pts) with LABC were randomized into a study comparing: F (500 mg/m^2 i.v. d 1, 8), E (60 mg/m^2 i.v. d1, 8) and C (75 mg/m^2 p.o. d 1–14) q 28 d ' 6 (arm A) Vs E (120 mg/m^2 i.v. d1), C (830 mg/m^2 i.v. d 1) and G-CSF (5 μg/kg/d s.c. d 2–13) q 14 d ' 6 (arm B). The main endpoint was progression free survival (PFS). Other endpoints included overall survival (OS), toxicity, quality of life (QoL) and cost-effectiveness (CE).

Methods: The clinical efficacy based on a potential difference in progression free survival was evaluated on all eligible pts included in the study. The QoL was assessed using the EORTC QLQ-C30 for all pts included in the European component of the study. The CE evaluation was conducted for pts recruited by French, Belgian, Dutch and British centers. The CE evaluation was based on both a specific questionnaire completed by the patients and cost data collected at each institution.

Results: Although the dose intensity delivered in arm B was twice as high as in arm A, there is no significant difference in PFS and OS between the two arms after a median follow-up of 3 years. Compared to arm A, arm B had a significantly poorer Qol score during the first 3 months. However, Qol returned to that of baseline levels earlier for this group of patients and over the first year there was no significant difference in Qol between the two groups. CE analysis disclosed differences in resource use between treatment arms and also between countries and between centers from the same country.

Conclusion: Although arm B provides the same efficacy as arm A with a shorter duration of treatment, its further implementation into day-to-day practice may be hampered by the available Qol and CE data. These exploratory analyses have revealed important aspects of the treatments under investigation that could not have been appreciated solely on the basis of the clinical data.

1256 ORAL

Comparison of outcomes in high risk, locally advanced and inflammatory breast cancer treated with high dose chemotherapy (Quartet) versus standard doxorubicin-based regimens

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From Jan 92 to Dec 95, 87 patients entered a Phase I/II trial of 15 weeks of doxorubicin dose-intense chemotherapy (with cyclo, MTX, Cisplatin, 5 FU, VP 16) followed by 3 days of high dose cyclophosphamide (C), etoposide (V) and cisplatin (P) at week 17 plus GMCSF (Hoescht) or G-CSF (Amgen). CVP total dose (wk 17) between C 4.2–4.8 g/m^2, V 1.5–1.8 g/m^2, P 75 m g/m^2 then RT and TAMxSy. All <56 y, no metastatic disease and either 8 or more +ve nodes (32) or clinically or pathologically locally advanced (T3, 4 or N2) (45) or inflammatory (T4D, any N) (10) breast ca. Failure-free (FFS) and overall survival (OS) were compared with Quartet and 2 matched groups (1) historical group of all similar patients (142) referred to BCCA between Jan 1989 and Dec 1991 who had received a standard dose doxorubicin-based regimen (CAF, AC or ACMF) (2) all similar patients (166) between Jan 92 and Dec 95, concurrent with Quartet study, who were not enrolled and (3) the combination of all pts in groups 1 & 2.

Results: At med-follow-up 4.2 y, overall and failure free for Quartet are 63% and 52%. Comparisons with historical control groups show NO difference for all pts or subsets.

1257 ORAL

Preliminary results of a large comparative multi-centre clinical trial comparing the efficacy and tolerability of Armidex™ (Anastrozole) and Tamoxifen (TAM) in postmenopausal women with advanced breast cancer (ABC)

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Purpose: 'Arimidex' (anastrozole) (AN), a non-steroidal aromatase inhibitor, is available for treatment of ABC in postmenopausal women recurring/progressing on TAM treatment. Here we present the results of a trial comparing the efficacy and tolerability of AN with TAM in postmenopausal women with ABC.

Methods: This randomised, double-blind trial was designed to demonstrate equivalent efficacy of AN 1 mg once-daily relative to TAM 20 mg once-daily in ER+ve and/or PR+ve or unknown patients eligible for hormonal therapy (HT). Patients may have received prior adjuvant HT or chemotherapy; a drug-free period of Ú 12 months was required for those patients who received adjuvant TAM. The primary endpoints of the trial were time to progression (TTP), objective response (OR), and tolerability.

Results: 668 patients were randomised on a 1:1 basis and followed for a median of 19 months. Disease progression was observed in 73% of AN and 75% of TAM patients. Median TTP was 8 months for both groups. OR (CR + PR) was 32% for both AN and TAM. Clinical benefit rates (CR + PR + SDU 24 weeks) were 56% for AN and 55% for TAM.

	Est Value	Lower 95% Conf Limit	Equiv Criterion
Haz Ratio (TTP) TAM/AN	0.99	0.85	0.80
Diff in OR (AN – TAM)	–1%	–7%	–10%

The % incidence of selected pre-defined side effects were as follows for AN and TAM respectively: Hot flushes (21% and 21%), thromboembolic events (5% and 7%), GIT disturbances (23% and 28%) and lethargy (1% and 3%).

Conclusion: 'Arimidex' satisfied the pre-defined criteria for equivalent efficacy to TAM, with a lower observed incidence of thromboembolic events, and may be considered as an alternative first-line treatment to TAM in postmenopausal women with ABC.

1258 ORAL

Side effects of endocrine therapy in patients with breast cancer

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Six hundred women on endocrine therapy were assessed using the C-PET questionnaire [Ray, Brit Med J 1996 313 1484] for symptoms associated with standard hormonal interventions. Tamoxifen caused similar symptoms whether used for advanced disease or in the adjuvant setting and patients were therefore regarded as one group. The groups compared were tamoxifen, T, [505 patients] anastrozole, A, [77 patients] and megestrol, M, [16 patients]. Incidence of side effects was scored as absent or present. The following side effects were reported, hot flushes [H] 54%, sweats [S] 53%, weight gain [W] 39%, fluid retention [F] 21%, nausea [N] 10%, impaired libido [L] 17%, irritability [I] 12%, low energy [E] 26%, dyspnoea [D] 16% and vaginal bleeding [VB] 7% or dryness [VR] 21%.

Multiple 2 × 2 chi-square comparisons, thus $p < 0.01$ significant.