Proffered Papers

Breast cancer, advanced disease

643 ORAL

Letrozole (FEMARA®), a new potent, selective aromatase inhibitor (AI): Superior to another AI, aminoglutethimide (AG), in postmenopausal women with advanced breast cancer (ABC), after relapse or progression on previous anti-estrogen therapy

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Over 2 years, 555 pts with ABC previously treated with anti-estrogens were randomly assigned open-label od letrozole 2.5 mg (185), or 0.5 mg (192) or AG 250 mg bid with corticosteroid replacement (178). Pts had to have measurable or evaluable disease, positive or unknown ER/PgR status. Tumor response and progression were evaluated by blinded peer review applying UICC criteria to serial tumor images, obtained 3-monthly for up to 33 mos. Dominant site was visceral in 44% pts, bone in 30%. Treatment comparisons were adjusted for relevant baseline covariates using multivariate regression models.

Letrozole was superior to AG in TTP (2.5 mg, risk ratio 0.68, P = 0.004 and 0.5 mg, risk ratio 0.76, P = 0.03) and TTF (2.5 mg, risk ratio 0.66, P = 0.001 and 0.5 mg, risk ratio 0.75, P = 0.02). Letrozole 2.5 mg was superior in survival to AG (risk ratio 0.68, P = 0.02) and to letrozole 0.5 mg (risk ratio 0.72, P = 0.04). There was no significant difference in survival between letrozole 0.5 mg and AG. Overall ORR (CR+PR) was 17.8% for letrozole 2.5 mg (median duration 23.2 mos), 16.7% for 0.5 mg (median duration 20.6 mos) and 11.2% for AG (median duration 14.0 mos). Duration of clinical benefit (CR+PR+NC > 6 mos) was 23.2 mos for letrozole 2.5 mg, 17.5 mos for letrozole 0.5 mg and 12.3 mos for AG (P = 0.01).

Both doses of letrozole were well tolerated, with discontinuation because of AEs in <3%. Rash ascribed by the investigator to trial treatment occurred in 8.4% pts on AG, 2.2% on letrozole 2.5 mg (P < 0.05). No serious related AEs wee reported for letrozole 2.5 mg.

Letrozole is the first new AI to show superior antitumor efficacy to another established AI, aminoglutethimide. Letrozole 2.5 mg was superior to 0.5 mg and is the recommended dose.

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Significantly improved survival with 'arimidex' (anastrozole (A)) compared with megestrol acetate (MA) in postmenopausal women with advanced breast cancer (ABC): Updated results of two randomised trials

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Purpose: Two randomised studies of similar design comparing 2 doses of A (1 mg and 10 mg daily) with MA (40 mg 4 times daily) in 764 postmenopausal women with ABC which had relapsed or progressed whilst on tamoxifen treatment, have recently undergone updated analyses based on mature survival data.

Methods: Data from the 2 studies were combined for a single analysis. Treatments were compared using a Cox regression model adjusting for predefined factors.

Results: Median follow-up was 31 months. 62% of patients overall had died. Significant improvement in survival was associated with A 1 mg compared with MA (hazard ratio (HR) 0.78, p = 0.02). A 1 mg resulted in a longer median survival (26.7 vs 22.5 months), and a higher 2 year survival (56.1% vs 46.3%) than MA. Analysed individually the 2 studies were consistent: each demonstrated a lower risk of death on A 1 mg than on MA (HRs 0.74, p = 0.048, and 0.85, p = 0.34). A 10 mg also demonstrated improved survival over MA (HR 0.83, p = 0.10). Response and time to progression were not significantly different between treatment arms.

Conclusion: A 1 mg results in improved survival compared with MA in postmenopausal women with ABC. There is no dose-response between the 2 doses of A, thus confirming the choice of 1 mg as the therapeutic clinical dose.

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Taxol (T) versus doxorubicin (D) as first-line chemotherapy (CT) in advanced breast cancer (ABC): An EORTC randomized study with crossover

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Three-hundred-thirty-one anthracycline-naive patients (pts) with ABC have been randomized to receive either T 200 mg/m^2 over 3 h or D 75 mg/m^2 q 3 weeks. Pts who progressed within 7 courses of first-line CT were crossed to the alternative drug, while the crossover was optional for later progression (PD). Data regarding pt characteristics and toxicity have already been given (Sem Oncol 23 suppl 11: 11–15, 1996). Dose-reductions in pts receiving first-line T or D were needed in 10% and 28% of pts, respectively. Regarding second-line T or D, dose was reduced in 14% and 22% of pts, respectively. The overall response rate for first-line CT, according to an intent to treat analysis is 36%; 28% of pts had stable disease. So far, among 76 pts crossed to D and 51 to T, 106 have completed second-line CT. Considering only pts who did mandatory crossover (T and D resistant pts), the tumor response rate is as follow:

No. of evaluable pts	CR + PR%	NC%	PD%
55	36	44	20

Updated data regarding response rates, time to progression and quality of life (assessed by Rotterdam Symptom Checklist and EORTC QLQ-C30) by treatment arm will be presented.

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Mitoxantrone (N) vs. 5-fluorouracil/epirubicin/ cyclophosphamide (FEC) as first line therapy in high-risk metastatic breast cancer

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Purpose: To evaluate the effectivity and tolerability of a mono- (N) versus a polychemotherapy (FEC) patients (P) with high-risk metastatic breast cancer (HRBC).

Patients and Method: From 7/92 to 8/96 248 P with HRBC (≤35 years, visceral involvement, DFI ≤ 18 months) were prospectively randomised for line 1st line therapy. By now 224 P are evaluable for toxicity and 171 for effectivity. 110 P received F = 500 mg/m^2, E = 50 mg/m^2, C = 500 mg/m^2 every 3 weeks and 114 P N = 12 mg/m^2 every 3 weeks until progression.

Results: An interim analysis revealed that thin there was no significant difference in response rates (CR + PR) between the FEC and the N. Time to progression was identical in both groups. N showed a more extensive myelotoxicity, however nausea & vomiting and hairloss were less