84% of the patients. The patients were screened for HER2 overexpression by the HercepTest™ and were analysed for *TOP2A* abnormalities with the *TOP2A* FISH pharmDx™ (DakoCytomation, Glostrup). Cases were scored as *TOP2A* amplified when the ratio of *TOP2A* gene signals and centromere 17 control signals was * 2. A deletion was scored when the ratio was < 0.8. Recurrence-free survival (RFS) was used as end-point and was defined as the period from enrolment to relapse (local or distant)

Results: So far *TOP2A* gene copy changes have been evaluated in all 307 tumours known to be HER2 2+ or 3+ positive and in 105 tumours known to be HER2 0 or 1+ positive. *TOP2A* amplification or deletion was found in 37% of the patients analysed so far. When adjusted for classical prognosticators, we found that patients with *TOP2A* alterations had a reduced relative risk of recurrence if treated with CEF (HR = 0.42; CI: 0.27-0.66). This in contrast to patients with a normal *TOP2A* genotype for whom similar outcome was observed in the CMF and CEF treated groups, (RFS: HR = 1.01; CI: 0.68-1.49).

Conclusion: *TOP2A* gene copy number changes seem to predict a favourable effect of adjuvant epirubicin therapy in primary breast cancer. *TOP2A* changes were not restricted to HER2 altered tumours and the *TOP2A* analysis will be completed on all tumours.

675 ORAL

Anastrozole is an effective neoadjuvant therapy for patients with hormone-dependent, locally-advanced breast cancer irrespective of cerbB2 status

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Background: the efficacy and safety of anastrozole 1 mg once daily as neoadjuvant therapy in postmenopausal women with locally-advanced breast cancer (LABC) was investigated in an open-label trial.

Methods: 112 patients were included in the trial; patients had histopathologically-confirmed unilateral, oestrogen receptor-positive LABC (stage IIIA/B). After 3 months of neoadjuvant treatment with anastrozole, clinical responses were evaluated. All patients with a complete or partial clinical response (cCR or cPR) underwent surgery (radical modified mastectomy), then continued on 1 mg anastrozole as adjuvant therapy for 2 years or until progression. Primary end point was objective response (cCR+cPR) rate, secondary endpoints included pathological complete or partial response (pCR or pPR) rate. CerbB2 and Ki67 analysis was carried out on all tumours using the histopathological blocks taken at the time of first diagnosis.

Results: tumour response rates for all patients and according to cerbB2 and Ki67 status are presented in the table.

Tumour response	All patients (%)	cerbB2 status (%)		Ki67 status (%)	
		Negative	Positive	<10%	*10%
	n=112	n=79	n=33	n=61	n=51
Clinical response					
cCR	54.5	60.8	39.4	63.9	43.1
cPR	28.6	34.2	15.2	32.8	23.5
No clinical response	17.0	5.1	45.5	3.3	33.3
Objective response					
(cCR+cPR)	83.0	94.9	54.5	96.7	66.7
Pathological response					
pCR	16.1	21.5	3.0	23.0	7.8
pPR	67.0	73.4	51.5	73.8	58.8
No pathological response	17.0	5.1	45.5	3.3	33.3

Conclusions: the response rates following neoadjuvant anastrozole indicate that it is highly effective in postmenopausal women with hormone-dependent LABC, regardless of cerbB2 or Ki67 status. Further follow-up is required to determine the impact of anastrozole on disease-free, and overall, survival following surgery in these patients.

676 ORAL

An assessment of fracture rates over time (between 6 and 48 months) in the ATAC ('Arimidex', Tamoxifen, Alone or in Combination) trial

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Background: Anastrozole (1 mg once daily [od]) has shown efficacy benefits compared with tamoxifen (20 mg od) for treatment of postmenopausal women with early breast cancer (EBC). An overall assessment of safety data showed a benefit for anastrozole, although incidence of fractures was significantly greater with anastrozole compared with tamoxifen.

Methods: Fracture incidence from the ATAC study was assessed every 6 months up to 48 months of treatment; differences in patterns of time-to-fracture for anastrozole versus tamoxifen were assessed.

Results: At the first analysis (median duration of therapy 31 months), fracture incidence was 5.9 vs 3.7% for anastrozole and tamoxifen, respectively (relative risk [RR] anastrozole/tamoxifen 1.59). Data from a safety update (median duration of therapy 37 months) indicated that risk of fractures did not worsen over time (fracture incidence was 7.1 vs 4.4% for anastrozole vs tamoxifen, respectively; RR 1.60, 95% confidence interval 1.301.97, p<0.0001).

Time (months)	6-monthly fracture rates/100 patients		Anastrozole/tamoxifen 6-month hazard ratio
	Anastrozole (n=3092)	Tamoxifen (n=3093)	
6	1.11	0.99	1.14
12	0.93	0.58	1.61
18	1.36	0.69	1.98
24	1.57	0.61	2.57
30	1.39	0.96	1.45
36	1.09	0.66	1.66
42	1.50	1.37	1.09
48	1.07	0.80	1.34

Fracture rates (see table), remained fairly constant for both anastrozole (range 0.93 to 1.57) and tamoxifen (0.58–1.37), with the 6-monthly fracture rates for anastrozole plateauing after 24 months. The maximum differences between anastrozole and tamoxifen were seen at 18 and 24 months. Similar patterns were seen for osteoporotic fractures' (hip + spine + wrist).

Conclusions: anastrozole leads to an increased fracture incidence compared with tamoxifen, a drug known to have a positive effect on bone mineral density. Importantly, the fracture rate in the anastrozole-treated group appears to stabilise after peaking at 2 years. Although differences in fracture rates exist, the overall benefit to risk in EBC remains unchanged, favouring anastrozole.

Head and neck cancer

677 ORAL

Results of a phase II study of cetuximab in combination with carboplatin in patients (pts) with recurrent or metastatic nasopharyngeal carcinoma (R&M NPC) who failed to a platinum-based chemotherapy

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Background: Recurrent or metastatic NPC pts usually respond well to palliative platinum-based chemotherapy, indeed for a short period. Relapsing or non-responding patients have few valid therapeutic options, if any. Since studies have revealed a high expression rate of epidermal growth factor receptor (EGFR)- up to 94% in NPC pts with its prognostic significance, cetuximab (Erbitux®), a chimeric anti-EGFR monoclonal antibody, has been evaluated in R&M NPC pts.

Design: a multi-center, single arm phase II study in R&M NPC pts with measurable disease and disease progression on or within 12 months after end of a platinum-based chemotherapy. Experimental therapy: cetuximab (Erbitux™) 400 mg/m^2 loading dose followed by 250 mg/m^2 weekly plus carboplatin AUC 5 administered every 3 weeks.