The differences between 3 and 24m (p= 0.6671), the 6 and 24m (p= 0.5024) and the 12 and 24m (p = 0.1927) samples were not statistically significant. There have been no clinical relapses to date.

Comment: These data show that MRD persists in a proportion of patients despite ongoing adjuvant treatment, suggesting that disseminated tumour cells are relatively resistant to such treatments. Detection of MRD may therefore be used to identify a subgroup of patients who would not benefit from cytotoxic or hormonal therapy. Our results support those of a previous study, which found that tumour cells persisted in the bone marrow after chemotherapy (Braun et al. J. Clin. Oncol. 2000). These findings may be a reflection of the dormant nature of these cells and alternative therapeutic strategies will be required to eliminate them.

550 ORAL

ICI 182,780 (Faslodex™) versus anastrozole (Arimidex™) for the treatment of advanced breast cancer in postmenopausal women - prospective combined analysis of two multicenter trials

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ICI 182,780 (Faslodex, FAS), a novel Estrogen Receptor Downregulator, is the first in a new class of antiestrogen. We report the prospectively planned combined analysis of two phase III trials, comparing FAS 250 mg once monthly and 'Arimidex' (anastrozole, AN) 1 mg once daily in postmenopausal women progressing on prior endocrine treatment for advanced breast cancer.

The trials compared the efficacy and safety of FAS with AN. The primary endpoint was time to progression (TTP). Secondary endpoints included objective response (OR), duration of response (DOR), clinical benefit (CR+PR+SD*24 weeks) and tolerability. Patients were randomised to either FAS 250mg (n=428) by intramuscular injection once monthly or AN 1mg (n=423) taken orally daily. Patients were followed for a median of 15.1 mo. Most (98%) patients had been treated with tamoxifen. At the time of analysis, approximately 83% of patients in each treatment arm had progressed. Median TTP was 5.5 mo and 4.1 mo for FAS and AN, respectively (Hazard Ratio 0.95; CL 0.82*1.10; p = 0.48). The OR (CR+PR) rates were 19.2% and 16.5% (Odds ratio 1.21; CL 0.84*1.74; p= 0.31) and clinical benefit rates were 43.5% and 40.9% for FAS and AN respectively. Both drugs were well tolerated. Withdrawals due to adverse events (drug related) were 2.8% (0.9%) in the FAS group and 1.9% (1.2%) in the AN group. Only 0.5% (2/423) FAS-treated patients withdrew because of an injection site reaction.

At the outset of the trial 7 adverse events were pre-defined for statistical analysis. Incidences of adverse events for FAS vs. anastrozole, which in the majority of cases were mild to moderate were as follows: gastrointestinal disturbances 46.3% vs. 43.7%; hot flushes 21.0% vs. 20.6%; vaginitis 2.6% vs. 1.9%; weight gain 0.9% vs. 1.7%; thromboembolic disease 3.5% vs. 4.0%; urinary tract infection 7.3% vs. 4.3%, and joint disorders (including arthalgia, arthrosis and arthritis) 5.4% vs. 10.6% which is the only adverse event to be significantly different between the two treatments (p=0.0036). Quality of life was maintained to a similar extent with both agents

In conclusion, FAS was found to be at least as effective as the aromatase inhibitor anastrozole in second-line advanced breast cancer in patients previously treated with tamoxifen. All efficacy endpoints are9 in favour of FAS. FAS was well tolerated. Based on these data FAS will provide a valuable new treatment option for advanced breast cancer in postmenopausal women.

551 ORAL

Survival update of so14999 a large phase III trial of capecitabine/docetaxel combination therapy vs docetaxel monotherapy in patients with locally advanced (LABC) or metastatic breast cancer (MBC)

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Capecitabine (Xeloda), an oral fluoropyrimidine, has substantial antitumor activity in colorectal cancer and heavily pre-treated MBC. Capecitabine plus docetaxel (Taxotere) has demonstrated synergy in preclinical studies. Patients with LABC and MBC in whom anthracycline treatment had failed were randomised to oral capecitabine 1250mg/m2 twice daily, days 1-14 plus i.v. docetaxel 75mg/m2 day 1 q3w (n=255), or i.v. docetaxel 100mg/m2 (n=256), day 1 q3w. The baseline patient characteristics in the treatment arms were balanced. Approximately 1/3 of the patients received study treatment as 1st and 1/2 as 2nd line therapy. With a minimum follow up of 15months, overall survival was superior in the combination arm (log rank p=0.0126; HR=0.775), median of 14.5 months (95% CI 12.3-16.3) vs. 11.5 months (95% CI 9.8-12.7) for single agent docetaxel with 72% and 79% of events reached, respectively. The survival curves separate early. One year survival was 56.8% (95% CI 51-63) in the combination arm and 46.9% (95% CI 41-53) in the monotherapy arm. Survival differences were evident in the 1st, 2nd and 3rd line treatment subgroups. Approximately 2/3 of the patients received post study chemotherapy in both treatment arms. The overall tumor response rate (RR) was superior for capecitabine/docetaxel 41.6% vs. for docetaxel 29.7% (p=0.006). Time to progression (TTP) was superior with the combination (log rank p=0.0001; HR=0.652), median of 6.1 months (95% CI 5.4-6.5) vs. 4.2 months (95% CI 3.4-4.5) with docetaxel. Multivariate Cox analysis revealed performance status, ER/PR status, number of metastatic sites and liver metastases as important baseline prognostic factors. Patients receiving monotherapy experienced a higher incidence (all grades) of neutropenia, complications of neutropenia, myalgia, and arthralgia. Diarrhoea, stomatitis, nausea/vomiting and hand-foot syndrome were more common with the combination therapy. The same pattern was generally noted for grade 3/4 adverse events.

Conclusion: The addition of capecitabine to 75mg/m2 docetaxel compared to docetaxel 100mg/m2 monotherapy led to significantly superior RR, TTP and survival, with a manageable safety profile.

552 ORAL

Weekly cisplatin - epirubicin - paclitaxel (PET) with G-CSF support vs. triweekly epirubicin-paclitaxel (ET) in advanced breast cancer (ABC). A SICOG phase III trial

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Background: In a previous study the PET weekly regimen gave an ORR of about 80% in breast cancer patients with metastatic disease, while the ORR exceeded 90% in locally advanced disease. (Frasci G. et al. Breast Cancer Res and Treat 62: 87-97; 2000). The present study aimed at evaluating whether this new regimen could produce a significant prolongation of TTP in ABC patients in comparison with standard ET.

Patients and Methods: ABC pts with locally advanced (T4 or N2) or metastatic disease, who had not received prior chemotherapy (except adjuvant) were considered eligible. Women were randomized to receive PET (P 30 mg/m2/week + E 50 mg/m2/week + T 120 mg/m2/week + G-CSF) or ET (E 90 mg/m2 + T 175 mg/m2 q3wk). A minimum of 6 cycles of PET or 3 cycles of ET were delivered, and the treatment was continued up to 12 and 6 cycles, respectively in absence of disease progression. Study design: Time to treatment failure was the chosen end point. A 3-month TTF prolongation was hypothesized with PET. Thus, at least 120 patients were required in each arm. An interim analysis was planned after the accrual of half of the total planned sample size.

Results: As of April 2001, overall 125 pts have been recruited (PET=61; ET=64), and 121 are evaluable for response (PET=60; ET=61). 65 patients showed locally advanced and 60 had metastatic disease at beginning of treatment. Overall, 17 CRs and 63 PRs have been recorded for a 66% ORR. 11 CRs and 35 PRs occurred in the 63 patients with locally advanced disease (ORR=73%) as compared to 6 CRs and 28 PRs in the 58 patients with metastatic disease (ORR=59%). 12 CRs and 31 PRs (ORR=72%)