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Fulvestrant in heavily pretreated patients with advanced breast cancer: experience from a Named Patient Programme in Switzerland

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Background: Fulvestrant (Faslodex®) is a new oestrogen receptor (ER) antagonist that downregulates the ER and has no agonist effects. Two randomised Phase III trials showed fulvestrant was at least as effective as anastrozole for time to progression, objective response and overall survival in postmenopausal women with advanced breast cancer (ABC) after progression/recurrence on tamoxifen. Here we report the efficacy and tolerability of fulvestrant when used in daily practice in a free of charge Named Patient Programme (supported by AstraZeneca) that was approved by the Swiss National Health Authority (Swissmedic). The majority of patients (98%) had received at least two prior endocrine therapies with or without chemotherapy.
Material and methods: Between December 2000 and May 2004, 179 postmenopausal patients with ABC were included. Therapy duration was measured from first supply of drug to withdrawal or last resupply date (where no withdrawal information was available). 28 patients were excluded from the efficacy analysis because of insufficient baseline/follow-up data; all were included in the safety analysis.
Results: Patients had a median age of 66 years (range: 27–91 years) and 93% had metastatic disease including 93 patients (62%) with bone metastases and 61 patients (40%) with visceral metastases (liver, lung). Most patients (87%) had received ⩾3 prior therapies for ABC (range: 1–10); 137 patients (91%) had received tamoxifen, 138 patients (91%) had received a non-steroidal aromatase inhibitor (AI) and 89 patients (59%) a steroidal AI. 40 patients (26%) were chemotherapy-naïve. 52 patients (34%) received fulvestrant for >6 months, 23 patients (15%) >1 year and six patients (4%) are still receiving treatment (current durations of treatment range up to 51+ months). Duration of therapy by site of metastases is shown in the table.

	Duration of therapy (months)				
Site of metastases (n)	⩽6	6–12	12–18	18–24	>24
No visceral metastases	39	16	3	4	2
Bone only	31	14	2	4	1
With visceral metastases	44	11	3	1	1
Visceral only	8	4	1	1	0

Six patients (3%) had serious adverse events (SAEs); two (1%) were suspected to be related to fulvestrant (facial flush with cough; deep vein thrombosis).
Conclusions: Fulvestrant showed good efficacy and tolerability in this heavily pretreated patient population. Notably several patients experienced prolonged disease stabilisation with fulvestrant, as seen in other studies. Fulvestrant offers a new convenient treatment option for postmenopausal women with ABC.

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A Phase II trial of trastuzumab (H) plus capecitabine (X) as first-line treatment in patients (pts) with HER-2-positive metastatic breast cancer (MBC)

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Background: Breast cancer is one of the most common malignancies among Chinese women. The mortality rate has increased over the past 20 years: in the Zhejiang Province of China (urban area), the mortality increased from 6.56/100,000 in 1990–1992 to 8.01/100,000 in 2000–2002. The addition of H (Herceptin®) to a taxane in pts with HER2-positive MBC provides significant clinical benefit, including prolonged survival. H adds little to the toxicity profile of the taxane alone. As monotherapy, X (Xeloda®) has consistently high activity and a favourable safety profile. The addition of X to docetaxel extends survival in MBC. Preliminary data (Bangemann et al. 2000) indicated that the combination of H and X is an effective and well-tolerated therapy for intensively pretreated HER2-positive MBC (ORR 47%). The current study was initiated to evaluate the activity and safety of the combination of H plus X as first-line therapy in HER2-positive MBC.
Materials and methods: 48 pts were enrolled between March 2003 and October 2004. All pts had measurable (WHO criteria), HER2-positive (IHC 3+ or IHC 2+/FISH positive) MBC, KPS ⩾60, and adequate bone marrow, renal and hepatic functions. Pts had not received prior chemotherapy for MBC. H was administered as a 4 mg/kg loading dose followed by 2 mg/kg i.v. weekly (until disease progression) together with X = 1250 mg/m^2 twice daily on days 1–14 every 3 weeks (maximum 6 cycles).
Results: 43 pts received at least 9 weeks, 38 pts at least 18 weeks, 33 pts at least 26 weeks, 11 pts at least 34 weeks, and 3 pts at least 50 weeks of treatment. Baseline characteristics (n = 43): median age 49 years (range 27–74), median KPS 90 (range 60–100). The principal tumour sites were: lymph nodes (49%); lung (33%); liver (28%); breast (14%); thoracic wall (9%); chest (9%); other (5%). Prior treatment included: surgery (74%); radiotherapy (19%); and adjuvant chemotherapy (65%), including anthracycline (42%), docetaxel (9%), paclitaxel (7%) and other (19%). 43 pts are evaluable for safety. The most common grade 1/2 adverse events were: HFS (23%); leucopenia (9%); SGOT abnormality (9%) and SGPT abnormality (7%). Grade 3 HFS occurred in 4 pts (9%); grade 3 leucopenia occurred in 1 pt (2%). These grade 3 events improved/resolved in all pts. 43 pts are evaluable for efficacy. The ORR is 63% (n = 27), including 8 CR (19%) and 19 PR (44%). 13 pts (30%) have stable disease. Median progression-free and overall survival have not yet been reached.
Conclusions: These results confirm that the combination of H and X is a highly active and well-tolerated regimen for first-line treatment of HER-2-positive MBC.

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Analysis of trastuzumab and chemotherapy in advanced breast cancer after the failure of at least one earlier combination: an observational study

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Introduction: In HER-2 overexpressing advanced breast cancer (ABC) the use of trastuzumab (T) in combination with chemotherapy to increase response rates and survival is well established. It is not known however, if treatment should continue after the failure of an earlier combination. We report our experience in patients with ABC who were treated with at least two lines of T containing regimens.
Patients and methods: We analysed retrospectively for time to tumour progression (TTP) for 1st, 2nd and beyond 2nd line treatment, response rates and overall survival (OS) using the Kaplan-Maier product limit method. Median time of observation was 24 months (m) (range 7–52 m).
Results: Thirty-five patients (pts), median age 50 years (y), range 25–73 y, were included into this study. The most common combination partners were vinorelbine (n = 38), capecitabine (23) and docetaxel (18). Response rates for 1st line treatment were 5.7% complete remission (CR), 40% partial remission (PR), 45.7% stable disease >6 months (SD) and 8.6% of patients experienced disease progression despite treatment (PD). Corresponding numbers for 2nd line were 5.7% CR, 28.6% PR, 37.1% SD and 28.6% PD. Numbers for treatment beyond 2nd line (42 therapies, 3rd to 7th line) were 28.6% PR, 31% SD and 40.5% PD respectively, translating into clinical benefit rate (CR+PR+SD>6 mo) of 91.4% for 1st line treatment, 71.4% for 2nd line and 59.6% for beyond 2nd line. Two pts showed response to a sixth line treatment. TTP was 7 m (range 1–17 m, 95%CI: 6.35–7.65) in the first line setting, 6 m (1–20 m, 95%CI: 4.54–7.46) in the second line and 6 m (1–41 m, 95%CI: 5.05.2–6.95) beyond second line. Log rank test revealed no significant difference. Median OS was not reached yet. Toxicities: A drop of left ventricular ejection fraction below 50% was observed in one patient, necessitating a discontinuation of T treatment. No case of symptomatic congestive heart failure was observed. All other toxicities were well within the range expected from the chemotherapy regimens.
Conclusion: The retrospective character of this study and the relatively low number of pts limit results. We are however able to strengthen existing evidence that pts profit from continuing T beyond 1st line. Further, this is among the first studies reporting a possible beneficial role of T containing