

applications with 20–160 W over 75 min. In group 2, median epicutaneous temp. of 41.2°C (40.0–42.0°C) and max. temp. 41.9–44.0°C were recorded in a median 10 (3–23) applications with 10–45 W over 60 min. In group 1 2/6 pat. presented with blisters/necrosis whereas no blisters were seen in group 2. Moist desquamation occurred in 2/6 pat. and 3/11 pat. in group 1 and 2, respectively.

**Conclusion:** To avoid hyperthermia induced blisters/necrosis epicutaneous temp. mapping is most important. In case of lymphangiosis cutis or infiltrated skin, bolus temp. of 40°C provide homogeneous heating of the chest wall. Large applicators increases the risk of "hot spots" and blisters/necrosis.

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PUBLICATION

### Taxol (T) and mitoxantrone (M) as first line treatment in advanced breast cancer (ABC) patients. A phase II study of the Southern Italy oncology group (GOIM)

F. Giotta<sup>1</sup>, L. Manzione<sup>2</sup>, V. Gebbia<sup>3</sup>, D. Bilancia<sup>2</sup>, N. Gebbia<sup>3</sup>, G. Colucci<sup>1</sup>. <sup>1</sup>Dept of Medicine Oncology Institute, Bari; <sup>2</sup>Oncology Service S. Carlo Hospital, Potenza; <sup>3</sup>Chemotherapy Service, University of Palermo, Italy

**Purpose:** In phase I/II studies the combination of T with anthracyclines yielded response rate ranging from 63% to 94%, sometimes with significant cardiotoxicity. In prospective randomized trials, M has shown a clinical activity only slightly inferior to that of anthracyclines, but with less incidence of alopecia, nausea/vomiting and cardiotoxicity. In view of these considerations, in April 1996 we started a phase II study with the combination of T and M as first line treatment of ABC.

**Methods:** Patients with histologically proven diagnosis of ABC, age between 18 and 65 years, adequate haematologic and normal renal, hepatic and cardiac functions, were eligible for the study. T was administered as a 3-hour intravenous infusion after standard premedication with steroid, anti-histamine and H<sub>2</sub>-blockers at a dosage of 175 mg/m<sup>2</sup>; M was administered intravenously at a dosage of 12 mg/m<sup>2</sup>. Courses were repeated every 3 weeks.

**Results:** To date, 23 patients were enrolled in the study and 16 are fully evaluable for clinical efficacy and toxicity. We obtained 4 CR, 7 PR and 5 SD for a total of 11 OR (69%) with a median duration of response of 6+ months and a median duration of survival of 7+ months. Toxicity was mild and mainly of grade I–II according to WHO criteria.

**Conclusion:** From our preliminary data of this ongoing study, the combination of T and M seems to be an effective and safe chemotherapy regimen for patients with ABC.

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### Factors predicting response to chemo-endocrine treatment in advanced breast cancer

F. Giesecking, V. Müller, H. Maass, Ch. Lindner, F. Jänicke. Department for Obstetrics and Gynecology, University Hospital of Hamburg, Germany

**Purpose:** Chemo-endocrine treatment as used in our institution is well tolerated even by heavily pretreated patients with advanced breast cancer. In a retrospective study the response rate and duration of response to this treatment regime was evaluated to find factors that predict good response to this treatment.

**Methods:** Response (CR, PR, NC) of 129 patients with metastatic breast cancer to chemo-endocrine treatment using Cyclophosphamide (100 mg/d p.o.), Methotrexate (25 mg/week i.v.), 5-Fluorouracil (500 mg/w i.v.), Prednisone (10 mg/d p.o.) and Methenolone (300 mg/w i.m.) was evaluated in correlation to steroid receptor status, prior disease-free interval, site of metastatic disease and previous treatment.

**Results:** Response rates were higher in patients with estrogen-and/or progesterone receptor positive tumors (80% vs. 37% in hormone-receptor negative), with long disease-free interval (78% in patients >2 years vs. 66% in patients <2 years), and with endocrine pretreatment (85% vs. 35% with chemotherapeutic pretreatment). Patients with bone metastasis showed better response (77%) than women with other metastatic sites (61%). Response rates were 73% with two and 68% with three previous treatment regimes.

**Conclusions:** Combined chemo-endocrine treatment is most effective in patients bone metastasis, positive receptor status and after response to prior endocrine therapy and is showing good response rates even in pretreated patients.

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### Phase II study of i.v navelbine (NVB) and doxorubicin (DOX) in previously untreated advanced breast cancer (ABC)

D. Vorobiof<sup>1</sup>, L. Goedhals<sup>1</sup>, P. Barnard<sup>1</sup>, A. Gudgeon<sup>1</sup>, A. Van Der Merwe<sup>1</sup>, L. Smith<sup>1</sup>, E. Murray<sup>1</sup>, D. Pretorius<sup>1</sup>, P. Bassompierre<sup>2</sup>, A. Lategan<sup>2</sup>, F.M. Delgado<sup>2</sup>, I. Lepape<sup>2</sup>, P. Daneel<sup>2</sup>, J.Ph. Burillon<sup>2</sup>, S. Le Couturier<sup>2</sup>. <sup>1</sup>Sandton Oncology Center, Department of Oncology, 2121 Parklands; <sup>2</sup>Pierre Fabre Medicament, South Africa

Promising results have previously been obtained with the combination of NVB and DOX. 74% of the 89 patients (pts) responded with 21% CRs (JCO, 1994 Spielmann). A phase II study was conducted in South Africa in order to confirm these results with i.v NVB 25 mg/m<sup>2</sup> D1 & D8 + DOX 50 mg/m<sup>2</sup> IV on D1, every 21 days, for 8 cycles maximum. Forty chemotherapy-naive pts with ABC were treated. Up to now, 24 pts are evaluable for tolerance and response. Median (m) age was 47.7 y (25–69). All pts had Good PS: 0–1. At the inclusion, 77% pts had metastatic disease and 70% had extensive loco regional disease (m. size of local disease = 80 mm Ø, (range 20–140). 60% pts had ≥3 metastatic sites of which 45% were visceral (38% liver and 7% lung). In total, 223 cycles were administered (m per pts: 5, range 1–8). The overall response rate was 54% (CR 8%, PR 46%/95 CI 34–74%). 2 further pts obtained an objective response but were not available for confirmation. Pt's WHO grade 3 toxicity was as follows: Alopecia 69%, nausea/vomiting 15%, stomatitis 11.5%, phlebitis 4%. WHO grade 3 neutropenia was observed in 27% pts and grade 4 in 15% pts (2 of whom died). Grade 1 peripheral neuropathy was only observed in 4 pts (15%). No cardiac impairment was observed. Given the large tumor bulk of local disease in these patients, very good results and tolerance were documented.

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### The LHRH analogue triptoreline (TRP) with or without the aromatase inhibitor formestane (4-OHA) in premenopausal advanced breast cancer: A study by the I.T.M.O. group

L. Celio<sup>1</sup>, A. Martinetti<sup>2</sup>, L. Ferrari<sup>2</sup>, R. Buzzoni<sup>1</sup>, E. Bombardieri<sup>2</sup>, N. Zilembo<sup>1</sup>, L. Maiorino<sup>3</sup>, E. Bajetta<sup>1</sup>. <sup>1</sup>Medical Oncology B Division; <sup>2</sup>Nuclear Medicine Division, Istituto Nazionale Tumori, Milan; <sup>3</sup>San Gennaro Hospital, Naples, Italy

**Purpose:** This pilot study was undertaken by our group with the aim of acquiring information on the feasibility and toxicity of combined TRP and 4-OHA treatment in premenopausal patients (pts) with previously untreated advanced breast cancer.

**Methods:** 28 consecutive pts were randomised; 15 pts received TRP 3.75 mg i.m. monthly alone, and 13 pts received it in combination with 4-OHA 500 mg i.m. fortnightly. Eligible pts had to have measurable lesions, ECOG PS 0–2, and ER and/or PgR positive tumours. Postmenopausal status was defined as last menstrual period more than 1 year ago. Blood samples for measuring serum oestrogen and gonadotrophin levels were taken before and during treatment.

**Results:** There was no difference in terms of age, DFI, and PS between the two groups; 32% of pts had multiple disease sites. The intent-to-treat analysis showed objective responses in 27% of pts (2 CR + 2 PR) on TRP and in 31% (1 CR + 3 PR) on TRP + 4-OHA. The median duration of response in the two groups was 16+ months (range, 7+–21) and 11+ (range, 7–16), respectively. The sites of response were soft tissue (3 CR) and viscera (5 PR); SD occurred in 5 pts on TRP, and in 4 on TRP + 4-OHA. Local and systemic tolerability was highly satisfactory in both treatment groups. The endocrine evaluations are in progress.

**Conclusion:** In our experience, the concurrent use of TRP and 4-OHA proved to be a feasible and well tolerated approach in the management of premenopausal advanced breast cancer.

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PUBLICATION

### Are new anthracycline dose recommendations needed for patients with liver dysfunction?

N.A. Dobbs, C.J. Twelves<sup>1</sup>. ICRF Clinical Oncology Unit, Oxford; <sup>1</sup>CRC Dept of Medical Oncology, Glasgow, UK

**Purpose:** To investigate whether U.K. oncologist follow current anthracycline dose modifications when treating patients with liver dysfunction.

**Methods:** One hundred and seventy oncologists replied to a questionnaire asking the % of full dose doxorubicin or epirubicin they would prescribe