Table 1

Study	Pts (n)	Median follow-up (mo)	Median survival (mo)	Median TTP (mo)	CB (%)
Buzdar et al. 1998:					
Anastrozole	263	31.2	26.7	4.8	42.2
Dombernowsky et al. 1998:					
Letrozole	174	5.5[a]/18–20[b]	25.3	5.6	34.5
Buzdar et al. 2001:					
Letrozole	199	18.0 (max)	29.0	3.2	29.6
Kaufmann et al. 2000:					
Exemestane	366	13.6	NR	4.7	37.4
Rose et al. 2002:					
Anastrozole	357	30.0 (max)	20.3	5.7	23.0
Letrozole	356	30.0 (max)	22.0	5.7	27.0
Robertson et al. 2003:					
Fulvestrant	428	15.1[c]/27.0[d]	27.4[e]	5.5	43.5
Anastrozole	423	15.1[c]/27.0[d]	27.7[e]	4.1	40.9

TTP, time to progression; CB, clinical benefit (complete response + partial response + stable disease ⩾24 weeks); NR, not reached; [a]Follow-up for TTP and CB; [b]Follow-up for TTD; [c]Follow-up for TTP and CB; [d]Follow-up for TTD; [e]Pippen et al. 2003.

Conclusions: Fulvestrant is at least as effective as anastrozole in terms of clinical efficacy and survival with indirect comparisons suggesting that fulvestrant also offers comparable efficacy to other second-line treatments for postmenopausal women with advanced breast cancer.

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Does systemic chemotherapy improve outcome in breast cancer patients with carcinomatous meningitis?

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Introduction: Carcinomatous meningitis is not common, but serious complication of advanced breast cancer, the incidence of which has recently been increasing. The established methods of treatment ie. intrathecal methotrexate and whole brain irradiation (WBI) are not sufficient in term of prolonging survival in these patients (pts).

Purpose: The aim of the study was to assess the role of systemic chemotherapy undertaken after the diagnosis of carcinomatous meningitis in prolonging the survival.

Material and Method: The study is based on the observation of 37 breast cancer pts with carcinomatous meningitis treated in Cancer Center, Warsaw, Poland, between January 2000 and October 2002. The mean age was 51 years (29–78). In 8 (22%) pts leptomeninges were the only site of metastases. The most common clinical signs and symptoms were: headache (73%), confusion (43%), vomiting/nausea (38%), cerebellar syndrome (38%), pain in thoraco-lumbal region (32%) and paresis/plegia (27%). Cancer cells in cerebrospinal fluid were detected in 100% of cases. Two out of 37 pts were not treated because of poor clinical status. Intrathecal methotrexate treatment, 10 mg per dose, was performed in 35 pts. The number of cycles was 1–15, the mean total dose was 70 mg. In 16 (43%) pts the whole brain irradiation was performed. Twenty-one (57%) women apart from intrathecal methotrexate treatment received systemic chemotherapy. Individual schedules of systemic treatment were used, but the most common were vinorelbine with fluorouracil (9 pts), antracyclines (7 pts), cisplatin (5 pts) and taxanes (4 pts).

Results: Clinical and laboratory response was achieved in 28 pts (76%). The mean survival since diagnosis of carcinomatous meningitis was 16 weeks (1–80 weeks), 25 weeks (8–80) for pts treated with systemic chemotherapy and 10 weeks (1–25) for pts without systemic chemotherapy. The comparison of survival depending on systemic chemotherapy was undertaken. Test log rank stratified for Karnofsky status was highly statistically significant (p=0.0003).

Conclusions: Our observations suggest, that systemic chemotherapy added to intrathecal treatment is the important factor prolonging the survival of breast cancer patients with carcinomatous meningitis.

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Oral Vinorelbine in combination with capecitabine: phase I study in patients with metastatic breast cancer

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Intravenous vinorelbine (VRL) associated with capecitabine (CAPE) has shown promising activity in patiënts with metastatic breast cancer (MBC). The present study investigated the combination of oral VRL and CAPE which offers the convenience of an all-oral combination regimen in patients who had received a maximum of one prior line of chemotherapy (CT) for MBC disease. The study was designed to determine the maximal tolerated dose (MTD) and the recommended dose (RD) of oral VRL at 60 or 80 mg/m^2 on days (d) 1 and 8 and CAPE at doses ranging from 1650 to 2500 mg/m^2/d from d1 to d14 every 3 weeks. At the RD, a weekly administration of oral VRL was tested. The protocol was subsequently amended to test an every 4 week-schedule. A total of 35 patients were included in 7 dose levels. Age ranged from 31 to 69 years; 71% had received prior adjuvant CT and 26% were given prior CT for MBC. When using the every 3 week-schedule, MTD was reached at DL3 (VRL 60 on d1, 8 and CAPE 2500) and DL4 (VRL 80 on d1, 8 and CAPE 1650). Dose-limiting toxicities (DLTs) consisted in persisting neutropenia which resulted in delay in starting cycle 2 for 5 patients and febrile neutropenia in 1 patient. The weekly administration of oral VRL was tested at DL2 (VRL 60 and CAPE 2250) but met the criteria of MTD: 2 out of 6 patients experienced DLTs (one persisting neutropenia and one grade 3 thrombocytopenia). The dose level below (VRL 60 and CAPE 2000) was well tolerated and was therefore the recommended dose when using a weekly administration of oral VRL. Five objective responses among 16 evaluable patients were seen. The 4-week schedule is still being investigated: VRL 80 mg/m^2 on d1, 8 and CAPE 1650 mg/m^2/d from d1 to d14 every 4 weeks was well-tolerated. Higher doses of CAPE (1850 and then 2000) are going to be explored.

In conclusion, the combination of oral VRL and CAPE can be safely administered in MBC patients. The currently recommended regimen is oral VRL 60 mg/m^2/week and CAPE 2000 mg/m^2/day from d1 to d14 every 3 weeks.

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Gemcitabine and vinorelbine as first line therapy in elderly advanced breast cancer (ABC)

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Introduction: Based on a previous studies demonstrating the safety and activity of Vinorelbine (V) and Gemcitabine (G) in a first or second-line treatment for ABC, we decided to test the same regimen in elderly patients (>65a).

Materials and methods: From March 2001 to March 2003, we treated 26 consecutive patients (pts) affected by ABC, with the combination of V and G. The dose were for V 25 mg/m^2 intravenous (bolus) and for G 1000 mg/m^2 intravenous (30′ infusion), on day 1 and 8 every 3 weeks. The therapy was continued until progression or for a maximum of 8 cycles. Median age was 74 (range 65–84), PS was 1 in 16 and 2 in 10 cases. 13 patients received prior antracyclin based adjuvant chemotherapy, 8 CMF adjuvant chemotherapy, 5 any therapy. 12 patients had visceral and bone disease, 5 only liver disease, 4 cutaneous disease, 5 bone only.

Results: A median of 4 cycles were performed in all pts (range 3–8). The delivered dose intensity was 89%. The median follow up was 14 months. Objective response (OR) was reached in 14 patients (53.8%). CR was reached by 4 pts (15.3%) (3 skin and 1 liver) and PR by 10 pts (38.5%). Moreover 7 pts (26.9%) had a stable disease (SD) with a mean duration of 6 months (range 3–9). 5 pts out of 26 (19.2%) progressed during therapy. The mean duration of CR and PR were respectively of 10 (range 7–19) and 7 (range 4–14) months. Haematological toxicity was commonly observed, but WHO grade 3–4 neutropenia occurred only in 5 (19.2%) cases without febrile neutropenia and was rapidly resolved by use G-CSF. Grade 3 anemia was noted only in 2 (7.7%) pts after a mean of 5 courses of therapy. Non-haematological toxicity was rare and consisted mainly in grade 2–3 nausea/vomiting (6 pts, 23%) and constipation (3 pts, 11.5%).

Conclusions: These results confirm that the combination of V and G is an effective and well tolerated regimen for the treatment of ABC in elderly patients. The routinely use of haemopoietic growth factors could improve these results permitting to give a Dose Intensity higher than 89% of this study.