moderate-to-high emetogenicity of the frequently administered combination of antracycline and cyclophosphamide (AC). Palonosetron (Aloxi®, Onicit®), the 2nd generation $5HT_3$ receptor antagonist (RA) with high binding affinity and long half-life (~40 hours), demonstrated superior and prolonged efficacy versus 1st generation agents in patients with different types of cancer in two phase III, randomized, double-blind, stratified trials comparing single-dose IV palonosetron 0.25 mg (PALO) vs IV ondansetron 32 mg (OND) or dolasetron 100 mg (DOL).

A retrospective subset analysis of BC patients (n = 476) from the two pivotal pooled studies included patients receiving anthracycline- or cyclophosphamide-based chemotherapy (CT) and showed that complete response rates (CR: no emesis, no rescue therapy) in PALO group were significantly higher in acute (Day 1), delayed (Days 2–5), and overall (Days 1–5) intervals than in OND/DOL group: 63% vs 55%, 59%* vs 40%, and 50%* vs 34%, respectively (*p < 0.01).

In these patients, a significantly higher percent of PALO-treated patients had no emesis compared with OND/DOL: 72%* vs 59%, 67%* vs 51%, and 58%* vs 42% (*p < 0.01) for acute, delayed and overall intervals, respectively.

Nausea was also well-controlled, with significantly more patients in the PALO group reporting no nausea on each individual day of the delayed phase than OND/DOL. The impact on daily life due to CINV was diminished with PALO compared with OND/DOL.

A multicenter, open-label study (n = 58) combining PALO 0.25 mg (Day 1) with dexamethasone (12 mg Day 1; 8 mg Days 2–3) and aprepitant (125 mg Day 1; 80 mg Days 2–3) showed high CR rates in the overall population (88%, 78% and 78% for acute, delayed and overall intervals, respectively) and very effective control of emesis and nausea. Of these, 47% were patients with BC, the majority of whom (74%) received AC-based CT. CR rates were 78%, 63% and 63%, while emesis-free rates were 85%, 89% and 85% in the acute, delayed and overall phases, respectively.

In all studies PALO was well tolerated, with a safety profile comparable to that of others in the $5HT_3$ RA class.

Palonosetron, administered alone (single 0.25 IV dose) or combined with currently used antiemetic regimens provides very effective control of CINV in a high-risk population of patients with BC, including patients undergoing AC-based treatment.

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Relative risk for fractures in postmenopausal women, postmenopausal breast cancer survivors and postmenopausal women managed with adjuvant hormonal therapy

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Tamoxifen has a positive effect on bone. In the 'Arimidex', Tamoxifen Alone or in Combination (ATAC) trial the rate of all fracture types for anastrozole was higher than with tamoxifen, although no significant difference was seen in the rate of hip or wrist/Colles' fractures [1].

To better understand the impact of early breast cancer (EBC) treatments on the annual risk of fracture, we conducted a calibrated cross-study comparison of the relative risk of fracture across EBC clinical trial populations of postmenopausal women; healthy women, women who had received treatment for EBC and women enrolled in the ATAC trial. Fracture rates in women with EBC were matched with mean population data for clinical fracture rates among healthy postmenopausal Australian women [2].

Impact of breast cancer and its treatment on fracture rates.

Study	Patient profile	Relative risk of fracture	Annual fracture rate per 1000	Possible impact on annual fracture rate in EBC clinic
Cooley et al. [3]	Healthy	1	17	–
Chen et al. [4]	BC survivor	1.15	20	+1
ATAC [1]	BC survivor on anastrozole	1.36	23	+2
ATAC [1]	BC survivor on tamoxifen	0.91	15	−1

EBC, EBC treatment and anastrozole were associated with an increased risk of fracture; tamoxifen use reduced the risk of fracture (Table). The fracture rate in healthy postmenopausal women in Australia was approximately 17 per 1000 women/year, for women aged 69 years (average age at completion of ATAC). Inputting this value into the model provides the outputs in the table below. In a clinic treating 300 women with EBC per year, this would equate to one extra non-hip fracture in patients not receiving hormonal adjuvant therapy, two extra non-hip fractures in patients receiving anastrozole and one less non-hip fracture in patients receiving tamoxifen, compared with an age-matched postmenopausal population.

Although caution should be exercised when making cross-study comparisons, this conceptual model demonstrates small benefits for tamoxifen in reducing clinical fractures. However, ATAC showed anastrozole to be significantly more effective than tamoxifen at preventing recurrences. Therefore, the use of anastrozole, with a bisphosphonate as required, may provide the best treatment to improve efficacy and extend bone protection.

References

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INC-EU Prospective Observational European Neutropenia Study: preliminary breast cancer results

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Background: Febrile neutropenia (FN) and grade IV chemotherapy-induced neutropenia (CIN) are major side-effects of anti-cancer chemotherapy with a potential for serious sequelae. The aim of this study was to assess the incidence, determinants and impact of FN and CIN in routine practice and to develop disease-specific risk models for these events.

Materials and Methods: A prospective observational study was conducted in 68 centres in 5 European countries (Belgium, France, Germany, Spain, UK). A total of 443 breast cancer patients with disease stages T0–3, N0–2, M0 and at least 4 planned cycles of chemotherapy, were enrolled and observed until the end of their chemotherapy regimen sequence. Treatment was as per usual clinical practice and not influenced by the protocol, except for a blood count at cycle 1 neutrophil nadir.

Results: By November 1, 2005, complete data were available for 305 (69%) of the enrolled patients, who started their chemotherapy treatments between January 2004 and May 2005. They had a mean age at diagnosis ±SD of 53.7±10.5 years and 59% were above 50 years. The diagnostic spread at presentation was stage I 26%, II 52% and III 22%; 66% were oestrogen receptor positive. Chemotherapy regimens used were anthracycline-based in 76%, anthracycline- and taxane-containing in 19%, and CMF-based in 5%. The number of planned chemotherapy cycles ±SD was 6.0±1.4 (range 4–12), and 5.8±1.6 (range 1–12) cycles were administered. Prior or concomitant radiotherapy was reported in 7%. Colony-stimulating factors (CSF) were used in 32% of patients. Cycle 1 primary prophylaxis with CSF occurred in 9%. FN was observed in 5% of patients and CIN in 41%. In the first cycle, 3% had FN and 26% had CIN. Neutropenia-related hospitalisations, dose reductions, and dose delays were seen in 4%, 4% and 11% of patients. Mean average relative dose intensity (ARDI) ±SD was 95±27%. ARDI ⩽ 85% was observed in 27% of patients with FN, 17% of patients with CIN, and 16% of the remainder. These figures correspond to unadjusted odds ratios of 1.9 for those with FN, and of 1.1 for those with CIN, compared to those with no events.

Conclusion: While FN appears to be rare, CIN occurs in a high proportion of patients receiving breast cancer chemotherapy. Further analysis of these data will help to establish and validate clinical risk models suitable for identifying patients at an increased risk of neutropenic events, in order to enable targeted prophylaxis.