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Side effects

THE ROLE OF OBSERVATIONAL STUDIES IN MEDICAL ONCOLOGY RESEARCH

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TRIAL SUMMARY: Febrile neutropenia with FEC-T

This study compared rates of febrile neutropenia (FN), overall survival (OS), disease-free survival (DFS), and hormone adherence rates (HA) in women under age 50 and women over 50 years old undergoing FEC-T (5-flurouracil +epirubicin+cyclophosphamide followed by adjuvant chemotherapy) for stage II/III, node-positive, HER2-negative breast cancer. A total of 919 women (274 under age 50 and 645 over age 50) treated with FEC-T in community and tertiary Alberta cancer centres between 2008 and 2012 were included, 88.2% (811) of whom completed recommended treatment.

Results: Rates of FN were similar between patients under age 50 (15.7%; 95% CI: 11.4, 20.0%) and 50 or over (19.4%; 95% CI: 16.3, 22.5%; p=0.202) and occurred with FEC (cycle 1–3; 51%) and taxane (cycle 4–6; 49%) regimens equally. DFS was higher in the under-50 cohort (90.9%) than in patients 50 and over (83.8%), although this was nonsignificant (p=0.251). Differences in breast-cancer-specific OS showed a trend to significance (95% for women under 50 vs 88.1% for women 50 and over; p=0.124). OS was similar in community (87.3%) and tertiary (91.3%) settings (p=0.137). Hormonal adherence rates were significantly higher (p<0.001) for tamoxifen to aromatase inhibitor (AI) switch compared to monotherapy at yearly time-points. Two treatment-related deaths occurred in the under-50 age group (leukemic and treatment related). In this cohort, FN rates occurred with similar frequency in the FEC and taxane groups, regardless of age or place of treatment. Breast cancer-specific OS and DFS were similar for women under 50 and women 50 or older. Hormone adherence rates were significantly higher for those on a hormonal switch strategy compared to monotherapy.
**LANDMARKS**

**TRIAL SUMMARY: Carcinoid heart disease**


Metastatic, functional neuroendocrine tumours (NETs) release bioactive substances into the circulation. Carcinoid syndrome arises due to high levels of circulating serotonin. Carcinoid heart disease (CHD) occurs as a result of longstanding carcinoid syndrome, manifesting as confluent, plaque-like lesions on valvular endocardium, increasing the risk of symptomatic valvular insufficiency and cardiac failure. This study describes the clinical and pathologic characteristics and outcomes of a consecutive series of patients with CHD treated at the Queen Elizabeth II Health Sciences Centre in Halifax, Nova Scotia. A chart review of the 11 patients diagnosed with CHD between January 1, 2000, and July 1, 2015, was performed alongside descriptive analysis of pathologic, clinical, and biochemical variables.

**Results:** Median OS for the entire cohort from time of NET diagnosis was 69 months (range 9 to 217 months). Four patients were diagnosed with CHD within 3 months of initial NET diagnosis, and all underwent valvular surgery within 1 year, with a median postoperative survival of 7.5 months (range 3 to 54 months). The remaining 7 patients had a median time to development of CHD of 57 months (range 18 to 139 months). Of these, 2 were unfit for surgery, 1 died of an unrelated illness and 1 is being observed. Three remaining patients underwent cardiac surgery and had a median postoperative survival time of 30 months (range 12 to 66 months). Median time to hospital discharge was 5 days (range 4 to 8 months) with a 0% 30-day mortality rate.

**TRIAL SUMMARY: Choice of endpoints to assess nausea and vomiting**


Concerned that the choice of study endpoint could potentially change the interpretation of clinical trial results, this study evaluated chemotherapy-induced nausea and vomiting (CINV) rates using different endpoints on a single dataset from a prospective cohort. It also explored the frequency with which published pharmaceutical and non-pharmaceutical company-funded CINV studies involving breast cancer patients included measures of nausea in their primary study endpoint. Data from 177 breast cancer patients receiving anthracycline and cyclophosphamide-based chemotherapy was used to estimate CINV control rates using the 15 most commonly reported CINV endpoints. In a sample of 30 CINV trials involving breast cancer patients that met the final eligibility criteria in a recently published systematic review, the authors examined the number of trials that used a primary endpoint that measured nausea control.

**Results:** CINV control rates ranged from 12.5% (95% CI 7.6%–17.4%) for total control (no vomiting, no nausea and no rescue medication use) to 77.4% (95% CI 71.2%–83.6%) for no vomiting in the overall period. Similar differences were found in the acute and delayed periods. Primary study endpoint(s) measuring nausea control were more commonly found in trials that were not funded by pharmaceutical companies (9/18, 50%) compared to those funded by pharmaceutical companies (1/12, 8.3%). The choice of trial endpoint has important effects on reported CINV control rates and could significantly impact interpretation of results. Primary endpoints of studies, including those mandated by regulatory bodies, should reflect patient experience with nausea. More comprehensive reporting of endpoints would allow for important cross-trial comparisons.

**TRIAL SUMMARY: Acute pain syndrome with taxanes**


Taxane acute pain syndrome (TAPS) is characterized by myalgia and arthralgia starting 24–48 hours after receiving taxane-based chemotherapy and lasting up to 7 days. Despite its negative impact on patient quality of life (QoL), its characteristics and natural history remain poorly defined. This study evaluated the persistence, severity and impact of TAPS on health related QoL. Eligible patients with breast or prostate cancers commencing taxane-based chemotherapy completed the Functional Assessment of Cancer Therapy-Taxane (FACT-T) and Brief Pain Inventory (BPI) questionnaires, and kept a pain medication diary every day for 1 week after each chemotherapy infusion. TAPS was defined as myalgias and arthralgias on these questionnaires.

**Results:** From March to December 2015, 25 of the 52 patients enrolled (21 with breast cancer and 4 with prostate cancer) completed the study. TAPS was reported in 66% of breast cancer patients, starting 24 to 72 hours (range 24 to 96 hours) after treatment infusion, and reaching a peak by day 3 (range 1 to 5 days). TAPS was reported more often in the legs and back. Table 1 shows the characteristics and clinical features. There were no dose reductions, delays or treatment discontinuations required due to TAPS. Medications used to treat TAPS included opioids in 5 patients and nonsteroidal antiinflammatory drugs (NSAIDs) in 9. Mean change in BPI “worst pain” score was +1.61 (p=0.014) and on FACT-T was -6.9 (p=0.017) from baseline to final infusion cycle. TAPS is a common toxicity and is associated with a negative impact on QoL. Further data will help define predisposing risk factors. Prospective patient-reported outcome assessments are crucial to help individualize treatment strategies, as well as improve management of TAPS.
In Brief

Already known
- Randomized controlled trial design is not suited to all questions in oncology.

What these studies showed
- Retrospective, prospective and cross-sectional observational studies provided important information about side effects of chemotherapy, including neutropenia, nausea and vomiting, taxane-induced pain syndrome, as well as the rare condition of carcinoid heart disease.

Next steps
- Results of observational studies should inform future clinical trial design and guide treatment selection for particular subgroups of patients.
References


