347 POSTER

Ciprofloxacin, G-CSF, Pegfilgrastim, Pegfilgrastim+Ciprofloxacin as neutrophil support during neoadjuvant chemotherapy with docetaxel/doxorubicin/cyclophosphamide (TAC) in breast cancer patients

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Background: Febrile neutropenia and associated events are frequently related with the administration of TAC (docetaxel 75 mg/m^2, doxorubicin 50 mg/m^2, cyclophosphamide 500 mg/m^2 day 1, q21). We analysed four prospective consecutive cohorts (total 1201 patients, 7076 TAC cycles) for their protective effect on febrile neutropenia (primary) and associated events.
Patients and Method: Throughout the conduct of the GeparTrio-study, a phase III trial on the use of 6 to 8 cycles of TAC as neoadjuvant treatment in T2-T4 stage primary breast cancer, 4 different primary prophylactic regimens have been recommended: pilot phase: C 500 mg bid d 5–10 (N = 252), Phase III: G 150 μg/m^2 d 5–10 (N = 390), Amendment 1: P 6 mg d 2 (N = 323) Amendment 2: P+C (N = 236)
Results: Incidence rates (%)(C vs. G vs. P vs. P+C): febrile neutropenia per patient: 21.6 vs. 17.5 vs. 7.0 vs. 5.2 ($p < 0.05$); febrile neutropenia per cycle: 5.0 vs. 4.6 vs. 1.4 vs. 1.0 ($p < 0.001$); neutropenia grade III/IV 70.2 vs. 66.9 vs. 44.5 vs. 42.5 ($p < 0.001$); SAEs related to infections 2.4 vs. 4.9 vs. 3.7 vs. 1.3 ($p < 0.001$); toxic deaths due to infection: 0 vs. 2 vs. 1 vs. 0.
Conclusion: Neutropenia, fever, infections and fatal outcome during neoadjuvant chemotherapy with TAC is most effectively be avoided by primary prophylaxis with pegfilgrastim in combination with ciprofloxacin.

348 POSTER

Quality of life and sexual function following high dose or conventional chemotherapy for women with high risk breast cancer: The ACCOG1 trial

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390 patients from 27 centres participated in the QL study of ACCOG1, a high dose versus conventional adjuvant chemotherapy breast cancer trial, for patients with a high risk of relapse. Patients completed the EORTC QLQ-C30, questions on menopausal symptoms and the Sexual Activity Questionnaire (SAQ). Pre-treatment, 6, 12, 24, 36, 48 and 60 month assessments were conducted. At trial entry, 66% of patients were pre-menopausal, 10% peri-menopausal and 23% post-menopausal. Post chemotherapy, approximately 80% received tamoxifen for 5 years.
For the high dose group the median decrease in global QL at six months was significantly greater than in the conventional group. At 12 months however, the median change had returned to 0 for both groups. Social functioning was also significantly lower in the high dose group at six months, again returning to pre baseline levels for both groups after 12 months.
The main conclusion is that despite a greater decrease in global quality of life at six months in the high-dose chemotherapy group, these changes had returned to normal and were equal to the conventional therapy group by twelve months.
Treatment did not have long term affects on sexual habit, which appeared to return to pre-treatment frequency and similar to that of conventional chemotherapy by about twelve months from treatment. However, the most persistent changes were in the effect of treatment in both arms on sexual outcomes, reflected in problems with discomfort and pleasure. Both high dose and conventional chemotherapy showed persisting negative effects on sexual health, which lasted for 5 years following therapy. This has not been previously reported as a long-term complication of high dose chemotherapy.

349 POSTER

Global index to summarise health risks versus benefit in the ATAC ('Arimidex', Tamoxifen, Alone or in Combination) trial

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Background: As guidelines now recommend that optimal adjuvant therapy for postmenopausal women with early breast cancer should include the use of an aromatase inhibitor (AI), it is important to ascertain the balance of risks and benefits associated with their use. The Completed Treatment Analysis of the ATAC trial, at a median follow-up of 68 months, demonstrated significant efficacy and tolerability benefits for anastrozole over tamoxifen. Anastrozole is currently the only AI with long-term efficacy and tolerability data in the adjuvant setting, and this now allows the evaluation of the overall risk: benefit of anastrozole relative to tamoxifen.
Methods: Two global risk: benefit indices were constructed using the methodology previously described by the Writing Group of the Women's Health Initiative (WHI) Investigators (Writing Group of the WHI Investigators 2002). The first global index (GI WHI) used the WHI definition of events, and was defined as the time from randomisation to the earliest occurrence of breast cancer recurrence, death or life-threatening adverse event. The second global index of disease-free survival and serious adverse events (GI DFS-SAE), used event definitions more appropriate for the ATAC endpoints: breast cancer recurrence, death or serious adverse event. We mapped the ATAC adverse events to the adverse event terms used by the WHI.
Results: Anastrozole demonstrated a significant reduction in events compared with tamoxifen for both the GI WHI (744 vs. 851; HR = 0.85; 95%CI: 0.77, 0.94; p = 0.0014) and the GI DFS-SAE (1453 vs. 1594; HR = 0.88; 95%CI: 0.82, 0.94; p = 0.0004). Kaplan-Meier curves of cumulative event rates over time started to separate within 1 year and continued to diverge throughout the 6-year follow-up period, beyond the completion of treatment.
Conclusions: This analysis clearly demonstrated the health benefits of anastrozole compared with tamoxifen. In addition to the reduced rates of breast cancer recurrence seen with anastrozole, there was a reduced rate of adverse events resulting in a superior risk: benefit profile for anastrozole compared with that seen for tamoxifen. The benefit was seen early and was maintained throughout follow-up.

350 POSTER

Visualization of fiducial markers for setup verification of partial breast irradiation with kilovoltage imaging

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Introduction: High-precision treatment of early stage breast cancer with postoperative external beam partial breast irradiation requires that fiducial markers be visible on both digital reconstructed radiographs (DRRs) and setup verification images (VIs). This study aimed to determine which types of fiducial markers were best visualised when simulating the geometry of, isocentric gantry-mounted and BrainLAB's Exactrac® floor-mounted, kilovoltage imaging systems.
Methods: Different fiducial markers: small stainless steel surgical clips (3.5 × 1 × 0.5 mm), small & medium titanium surgical clips (3.5 × 1 × 0.5 mm and 6 × 1 × 0.8 mm) and gold seeds (2.5 mm length, 0.8 mm diametre) were inserted into the breast attachments of a supine tissue-equivalent torso phantom (Rando&Harpell Associates Inc.). The fiducial markers were placed in 0, 30, 60, and 90 degree orientations in the x-y-z planes. CT images were acquired using slice thicknesses of 1.5, 2, 3 and 5 mm. Breast tangent, transverse, anterior-posterior (AP) and Exactrac® geometry (148° gantry and 45° couch angle & 212° gantry and 315° couch angle) DRRs were reconstructed. Corresponding simulated kilovoltage verification images were also acquired. Three independent observers located clips on both DRRs and VIs.
Results: To visualise small clips and gold seeds on DRRs, CT slices of 2 mm or less were optimal. All fiducial markers were correctly located on tangential, transverse and AP imaging (DRRs and VIs). Only 38% of Titanium clips (small and medium) were identified on DRRs and 50% on VIs using Exactrac® geometry as they were obscured by bone. However, 82% of stainless steel clips and 100% of gold seeds were located on DRRs and VIs using Exactrac® geometry.
Conclusions: All fiducial markers were easily visualised on DRRs and VIs at beam angles used by isocentric gantry-mounted kilovoltage imaging. Both small and medium titanium surgical clips were poorly visualised on DRRs and VIs if there was bony interference. To provide redundancy when bony interference is anticipated, at least three gold, or six stainless steel fiducial markers should be used to mark the breast surgical cavity.