Journal Reviews

Journal of Clinical Oncology

MOSAIC Trial Subset Analysis: High-Risk Stage II Elderly Patients

This is a report on the updated survival data from the MOSAIC study first published in 2004. It was a randomised controlled trial of adjuvant chemotherapy in completely resected stage II & III colorectal cancer. The randomisation was between 5-fluorouracil chemotherapy given by the De Gramont regimen with or without oxaliplatin. The first paper reported a significant improvement in overall and disease-free survival, which was confirmed with improved data. This finding was most pronounced for stage III disease, with information that allows re-analysis of stage II disease and in elderly patients aged 70-75 years. There was no statistically significant benefit (OS or DFS) from the combination of oxaliplatin with 5-FU in either stage II or elderly patients. In high risk stage II patients, as defined by the usual criteria – poorly differentiated, obstructed or perforated, T4 stage, vascular invasion and inadequate lymph node harvest - there was a trend towards improvement in DFS & OS, but neither reached significance.

Reviewer's Opinion: On the face of it, this is an open and shut case. Oxaliplatin has no place in the adjuvant treatment of colorectal cancer for stage II (Dukes' B) or in elderly patients. However, there are some caveats. These analyses were exploratory and not specified in the original protocol, although the number of patients and events are large and the follow-up rigorous. The lack of efficacy of oxaliplatin in stage II disease is mirrored in other similar adjuvant trials (C-07) and may be related to differing biology in stage III disease or different molecular findings (such as microsatellite instability). The findings with age are more contentious. The 'elderly' age group was just 70-75 (most of my patients are over 70!) and patients over 75 were ineligible for the study. The numbers involved are small. The safest conclusion is that the data for patients between 70 and 75 is weak and inconclusive at best; and data supporting oxaliplatin-based adjuvant therapy for patients over 76 simply doesn't exist. Oxaliplatin is not without a side-effect profile. Neuropathy and myelosuppression that it can cause may be significant and long lasting. Perhaps we need to think very carefully about using it in cohorts of patients where the data is not compelling, but it is a thought-provoking paper. – SG

Tournigand C, Andre T, Bonnetain F, Chibaudel B, Lledo G, Hickish T, Tabernero J, Boni C, Bachet JB, Teixeira L & de Gramont A.
Adjuvant Therapy with Fluorouracil and Oxaliplatin in Stage II and Elderly Patients (between the ages 70 and 75 years) with Colon Cancer: Subgroup Analyses of the Multicenter International Study of Oxaliplatin, Fluorouracil, and Leucovorin in the Adjuvant Treatment of Colon Cancer Trial.
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Clinical Oncology

Weekly single agent Paclitaxel as neoadjuvant chemotherapy in locally advanced breast cancer

Neo-adjuvant chemotherapy (NACT) has become a standard treatment for locally advanced breast cancers. It was introduced in the last 10 years to treat locally advanced breast cancers ostensibly to facilitate conservative surgery and improve 5-year survival. Compared to adjuvant treatment, however, it has no added survival benefit. Multiple chemotherapeutic regimens were studied in combination for the neo-adjuvant setting; however, the desired clinical benefits from a particular specific 'tailored' regimen could not be established. A commonly practiced regimen includes anthracyclines with cyclophosphomide and 5-fluorouracil. Taxanes (Docetaxel and paclitaxel) were added to anthracycline-based regimens to improve their clinical effectiveness and achieve pathological complete response (pCR). In this small feasibility study, response rates and toxicity profile of a single agent, Paclitaxel, in a short course (8 weeks) regimen was studied in a neoadjuvant setting. Twenty-six patients with locally advance breast cancers were selected and administered 100mg/m2 of Paclitaxel for 8 weeks followed by surgery. The patients also received adjuvant anthracyline-based chemotherapy and radiation treatment post-surgery. There was complete clinical response in 10 patients (38.5%) and complete pathological response, defined by absence of invasive disease from breast and axillary nodes, in 3 patients (11.5%). The levels of grade 3-4 neutropenia, thrombocytopenia and neuropathy were 4, 12 and 4%, respectively. The authors concluded that clinical and pathological responses, and the toxicity profile, seen with Paclitaxel were acceptable and comparable to other regimens.

Reviewer's Opinion: This paper highlights the feasibility and effectiveness of a single agent treatment in neoadjuvant setting for locally advanced breast cancers. Novelty factor of the study was the novel use of only a single agent (Paclitaxel) instead of combination regimen in neoadjuvant setting. Furthermore, Paclitaxel was used as a short course (8 weeks) compared to other studies that have employed it over a 12 weeks in combination with anthracyline-based chemotherapeutics. However, the major limitation of the study was the small number of patients, which precludes definitive interpretation of efficacy. Nevertheless, the study highlights an interesting finding of use and clinical effectiveness of employing a single agent in neoadjuvant treatment. This may lead to larger studies using the same or other chemotherapeutic drugs as a single agent neoadjuvant treatment in breast cancer. – TH

Gupta S, Bharath R, Shet T, Desai SB, Patil VM, Bakshi A, Parmar V, Badwe RA.
Single agent weekly Paclitaxel as neoadjuvant chemotherapy in locally advanced breast cancer: A feasibility study.
CLINICAL ONCOLOGY
2012;24(9):604-9.