

**High-Dose Chemotherapy (HDC) with Autologous Peripheral Blood Progenitor (PBP) Support is not Superior to Cyclophosphamide (CPA), Methotrexate and 5-Fluoruracil (CMF) as Crossover following Doxorubicin (D) Induction in Patients (pts) with Breast Cancer (BC) and 4 or more Involved Axillary Lymph Nodes (4+LN): First Results of the Anglo-Celtic I Study.**

Despite appropriate loco-regional therapy and anthracycline-based adjuvant chemotherapy, the majority of pts with breast cancer which has spread to involve 4+LN will ultimately develop metastases. Bonadonna reported a 48% 10 year disease free survival for 4+LN pts receiving D-CMF crossover chemotherapy. Non-randomised studies in the 1980s and early 1990s suggested that HDC with PBP support might be superior to conventional adjuvant chemotherapy (CDC) in this setting. Anglo-Celtic I, a prospective random assignment adjuvant trial of CDC vs HDC in 4LN+ BC, was opened in 1995 in the UK and Ireland, and subsequently in New Zealand and Belgium. Eligible patients were randomly assigned to receive either HDC or CMF following 4 cycles of D (75 mg/m<sup>2</sup>). Pts randomised to HDC subsequently received a PBP mobilization cycle of CPA 4.0 gm/m<sup>2</sup> supported by filgrastim, followed by a single cycle of PBP-supported HDC (CPA 6.0 gm/m<sup>2</sup>, thioTEPA 800 mg/m<sup>2</sup>) + filgrastim.

Results: 605 patients were randomised between 2/95 and 6/99. There were 5 treatment related deaths (0-CDC, 5 HDC) and xx relapses (xx HDC, XX CDC). for a total of 240 "events". To date 221 patients have experienced relapses and 165 have died. The current estimated event-free survival rates at five years for HDC and CDC are respectively 51% and 54% , and estimated overall survival rates at 5 years are 63% vs 62%. Thus, although the planned first statistical analysis does not take place until another 15 events have occurred, the event rates per arm to date makes it impossible for the study to show superiority for HDC at the first analysis even if the next 15 events all take place on the CDC arm. Unlike the Dutch national study, we have not included a formal early cohort analysis.

Conclusions: While a late emerging benefit for HDC cannot as yet be excluded, the planned first analysis with a median of 4 years of follow-up will not show superiority for HDC.