Conclusion: This study shows that addition of T to thoracic irradiation either sequentially or concomitantly does not increase the RIPF in rats.

216 Poster Discussion

Interpretation of contrast enhanced MRI for early prediction of breast-cancer response to neoadjuvant chemotherapy: Initial results

C.E. Loo[1], H.J. Teertstra[1], S. Rodenhuis[2], M.J. Van de Vijver[3], J. Hannemann[3], S.H. Muller[1], M.J. Vrancken Peeters[4], K.G.A. Gilhuijs[1]. *[1]Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Radiology, Amsterdam, The Netherlands; [2]Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Medical oncology, Amsterdam, The Netherlands; [3]Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Pathology, Amsterdam, The Netherlands; [4]Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Surgery, Amsterdam, The Netherlands*

Background: The aim of this study was to establish changes in contrast-enhanced MRI of breast cancer during neoadjuvant chemotherapy that are indicative of pathology outcome. Additionally to establish a practical test to identify which tumors will not achieve a complete remission with the given chemotherapy and may benefit from a switch to an alternative regimen.

Material and Methods: Ninety-nine patients with invasive breast cancer >3 cm and/or at least one tumor positive lymph node scheduled to receive neoadjuvant chemotherapy were included. MR imaging was performed prior and during chemotherapy. All selected patients underwent surgery. In case residual vital tumor in the surgical specimen was found at pathology it was defined as non-complete remission. In the first 54 patients (training set), multivariate analysis with cross validation was performed on MRI features describing kinetics and morphology of contrast uptake. ROC analysis was employed to guide switching to a different chemotherapy regimen in patients at risk for non-complete remission, while maintaining first-line therapy in 95% of patients who will achieve complete remission. The practical test was evaluated prospectively on subsequent patients (validation set).

Results: Reduction of <25% in largest diameter of late enhancement in the tumor during chemotherapy was most predictive of non-complete pathological remission ($Az = 0.73$, $p < 0.00001$). The fraction of anticipated non-responders was 41% (22/54) in the training set and 40% (14/35) in the validation set. The fraction of complete remissions in the group of predicted responders was 44% (14/32) in the training set and 43% (9/21) in the validation set. The fraction of non-complete remissions in the group of predicted non-responders was 95% (21/22) in the training set and 79% (11/14) in the validation set after switching therapy.

Conclusion: Reduction of <25% in largest diameter of late enhancement during neoadjuvant chemotherapy shows potential to predict non-complete remission after therapy.

217 Poster Discussion

Impact of early adoption of systemic treatment modalities on mortality trends of breast cancer in Canada – implications for cancer organization processes

J. Ragaz[1], J.J. Spinelli[2], R. Semeniciw[3], W. Hryniuk[4], E. Franco[5]. *[1]McGill University, Medicine & Oncology, Montréal PQ, Canada; [2]British Columbia Cancer Agency, Biostatistics & Epidemiology, Vancouver BC, Canada; [3]Statistics Canada, Biostatistics & Epidemiology, Ottawa Ontario, Canada; [4]Cancer Advocacy of Cancer Canada, Medical Oncology, Toronto Ontario, Canada; [5]McGill University, Epidemiology, Montreal PQ, Canada*

Introduction: Mortality trends require correlation with therapies & interventions delivered.

Methodology: We compared Breast Cancer (BrCa) mortality trends, years 1950–2000, in Canada with data obtained by Statistics Canada. The trends were correlated with therapeutic and screening interventions, comparing data for the entire country (Canada) versus Provinces with different degrees of implementation of Provincial Community Oncology (PCOP) Programs for years 1975–1995, and funding provided.

Implementation was classified as LEVEL I: PCOP most uniform, with most funding (British Columbia); LEVEL II: PCOP medium (Ontario); LEVEL III: least uniform (Maritime Provinces* of New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland).

Results: Mortality was adjusted for each decade between 1950–2000, relative to 1950 (age-standardized BrCa death rate per 100,000 population): 30.1 for Canada, 31.4 for BC; 30.7 Ontario; 26.1 for Maritime Provinces.

We observed an earlier and more substantial BrCa mortality reduction in BC than in the rest of Canada, in parallel with wider and more uniform use of systemic therapies, before the advent of screening mammography.

Table. BrCa mortality trends relative to year 1950, by decade, between years 1950–2000

Years	1950	1960	1970	1980	1990	2000
Canada:	100%	102.6%	102.7%	99.8%	100.2%	81.7%
BC	100%	98.7%	96.5%	92.2%	85.2%	69.1%
Ontario	100%	103.4%	103.2%	101.4%	100.3%	81.7%
Maritime Provinces*	100%	105.2%	108.2%	114.4%	114.8%	104.1%

Conclusions: These data suggest that timely and widespread adoption of state-of-the art systemic therapies may have a strong impact on the extent of mortality reduction. Delaying the introduction of curative systemic therapies may have prevented early survival gains in some regions.

The emergence of multiple candidate agents with curative potential may overwhelm the clinical development pipeline with consequent delays in their introduction in oncological care. We propose an accelerated clinical development strategy that circumvents issues related to delayed implementation of novel interventions.

The five-point strategy includes: 1. the application of stage IV results into adjuvant trials; 2. fast-tracking novel agents into simultaneously-organized randomized stage IV trials; 3. wider use of neoadjuvant trials; 4. trials with concomitant guideline-treated controls; and 5. international coordination. Significance of these finding and proposals, with impact on broad societal implications, will be discussed in more detail.

218 Poster Discussion

Farnesoid X receptor (FXR) status complements the evaluation of estrogen receptor alpha (ER) in breast cancer (BC) patients and predicts benefit from tamoxifen

F. Journe[1], V. Durbecq[1], B. Haibe-Kains[1], C. Chaboteaux[1], G. Rouas[1], G. Laurent[2], D. Larsimont[1], M. Piccart[1], J.J. Body[3], C. Sotiriou[1]. *[1]University of Brussels (ULB), Institut Bordet Translational Research Unit, Brussels, Belgium; [2]University of Mons-Hainaut (UMH), Laboratory of Histology, Mons, Belgium; [3]University of Brussels (ULB), CHU Brugmann, Brussels, Belgium*

Background: FXR is a nuclear receptor for bile acids. It is normally expressed in liver tissue and the GI tract. We recently detected FXR in BC and reported a significant correlation between FXR and ER expressions. Moreover, we observed that FXR is associated with proliferation markers in ER+ BC. We also showed that chenodeoxycholic acid (CDCA) stimulates the proliferation of MCF-7 (ER+) cells through a physical interaction between FXR and ER, the latter resulting in ER activation. Finally, we demonstrated that CDCA increases the expressions of MMP-2/-9 in BC cells, indicating that bile acids/FXR might be involved in the invasiveness of tumor cells.

Material and Methods: We assessed the prognostic value of FXR expression in BC by retrospectively analyzing microarray data in a population of 2473 patients. We evaluated patient overall survival (OS) and distant metastasis-free survival (DMFS) in the total population and in subgroups characterized by ER, node and menopausal (age >50) status. We compared the prognostic value of FXR status with that of the proliferation marker Ki-67. In addition, we examined the predictive value of FXR with regard to response to tamoxifen.

Results: In the total population, a higher FXR expression was significantly associated with a shorter OS ($p = 0.003$; HR = 1.48; 95% CI [1.14−1.91]). The prognostic value of FXR was particularly good the in ER+/node+ subgroup ($p = 0.02$; HR = 2.16; 95% CI [1.32−3.54]), discriminating high versus low proliferative tumors as efficiently as Ki-67 level ($p = 0.008$; HR = 2.33; 95% CI [1.25−4.33]). In this subgroup of patients treated with tamoxifen, high FXR expression was significantly associated with a shorter DMFS ($p = 0.039$; HR = 2.20; 95% CI [1.04−4.64]). Additionally, the FXR prognostic value, with respect to OS evaluation, was also significant in the ER−/age $\leqslant$50 subpopulation ($p = 0.038$; HR = 1.75; 95% CI [1.03−2.97]), where Ki-67 determination is uninformative. In this subgroup, FXR tended to correlate with occurrence of distant relapses, but was significantly associated with late metastatic relapses (>1000 days) ($p = 0.002$; HR = 3.21; 95% CI [1.55−6.65]), which generally developed in skeleton.

Conclusions: FXR evaluation brings additional prognostic/predictive information mainly in ER− BC. In this subpopulation, FXR seems related to the occurrence of distant relapses, especially in young patients.