219 Poster Discussion

Male breast cancer (MBC). Analysis of treatment strategies in 489 cases

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Background: Infiltrating MBC represents less than 1% of all male cancers. Our study analyzes clinico-pathological features, treatments and prognostic factors in a large French cohort.

Materials and Methods: All non metastatic patients treated from 1990 to 2005 in 15 cancer centers were collected: 489 were available. Median age was 66 years (34% over 70 years) and median follow-up 56 months.

Results: Median delay to diagnosis was 3 months and median tumor size was 20 mm. According to TN classification, we found T1: 39%, T2: 41%, T3T4: 9%, Tx: 11% and N1N2: 27%. Lumpectomy (L) and mastectomy (M) were performed in 8.6% and 91.4% of the cases. Axillary dissection (AD), sentinel node biopsy or both were performed in 90%, 2% and 5% of the cases, respectively. 95% of tumors were ductal carcinomas (20% of high grade); 47% were pT1, 20% pT2 and 33% pT3-T4. Axillary nodal involvement (ANI) was present in 52.8% cases (pN 1−3 = 32.3% and pN >3: 20.5%). ER and PgR were positive in 92% and 89% cases. Radiotherapy (RT) was performed in 85% of the patients. After M, chest wall was treated in 83% of the patients, supra-clavicular fossa in 77%, internal mammary chain in 81% and axilla in 13%. Hormonal treatment (HT) was delivered in 72% of the cases (58% and 85% in pN0/pN+; $p < 0.0001$). Tamoxifen and aromatase inhibitors were used in 85% and 12% of the cases. 34% of the patients received chemotherapy (CT): 12% in pN0 and 54% in pN+ ($p < 0.0001$). In 71% cases, an anthracycline-based protocol was used.

Local recurrence (LR), nodal recurrences (NR) and metastases occurred in 2%, 5% and 22% of the cases; 2% and 10% developed contralateral BC and second cancer. The 5 and 10-year overall survival (OS) rates were 81% and 59%; disease-specific survivals (DSS) were 89% and 72%. Death causes were BC 56%, second cancer 8%, complications 3%, intercurrent disease 15% and unknown 18%. In a univariate analysis, metastatic risk factors were T stage (T1: 19%, T2: 26%, T3T4: 40%; $p = 0.013$), pN status (pN0: 12%, pN1−3: 26%, pN >3: 44%; $p < 0.0001$) and presence of locoregional recurrence (62% versus 18% $p < 0.0001$).A multivariate analysis will be further presented.

Conclusions: In comparison with a former cohort (397 pts), earlier diagnosis and wide use of adjuvant treatments (RT/HT/CT) widely decreased LR and increased survival rates in MBC, reaching female ones. Prognostic factors were also very similar to female ones.

220 Poster Discussion

Estimation of the proportion of patients in whom an experimental treatment is effective in a positive randomised trial, using a novel variance-guided equation

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Background: From the results of a positive randomised clinical trial, it cannot be ascertained whether the additional benefit is distributed to all patients or is limited to only a subgroup. We had a new insight: The variance in length of survival in the treated group will be same as the control group if the treatment is effective in every patient; but will be different if the treatment is effective in only a subgroup.

Methods: We devised a new variance-guided equation to estimate the proportion (p) of the patients in whom a treatment is effective:
$p = 1/(1 + [(v(T) - v(C))/(s(T) - s(C))2])$,
where v = variance, s = survival, T and C = logarithms of survival times of treated and control groups; variance = (number of events) × (standard error)2. We tested this equation with the Scottish adjuvant tamoxifen trial (n = 1323) which was initiated in 1978 and allocated patients who had undergone surgery for breast cancer randomly to receive either tamoxifen for 5 years or not. In 1978, it was not appreciated that tamoxifen only benefits patients with tumours that express the estrogen receptor (ER), so the trial included a significant number of patients with ER negative tumours and would not have derived any benefit from tamoxifen. Conveniently, an estimate of this proportion is available from the 742 patients in this trial in whom ER status was ascertained.

Results: Without using any information about the ER status, our equation independently predicted – only from the length of survival of individual patients – that 64% of patients in the Scottish trial benefited from tamoxifen. Thus we accurately predicted the proportion (60−71%) of patients whose tumours were ER positive. This vindication using real clinical data also supports a biologically plausible view that there is a subpopulation amongst those treated that derive absolutely no benefit, while others may derive a variable amount of benefit.

Conclusions: Thus, using raw survival data from a randomised trial, our method can estimate the proportion of patients that benefit from the new treatment. We can thus foretel the existence and frequency of a predictive factor (such as ER). Widely applicable to positive randomised clinical trials that have found an overall benefit from chemotherapy, hormone therapy, biologic therapy, or radiotherapy, our equation could suggest new biological and therapeutic insights. Clinically, it would enable more precise patient consultation.

221 Poster Discussion

Sentinel node biopsy after neoadjuvant chemoterapy in breast cancer

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Background: To evacuate the accuracy and feasibility of sentinel node biopsy technique in patients with operable clinically node negative breast cancer after chemotherapy irrespective of the initial stage.

Material and Methods: the subject of this study was 101 consecutive patients affected by T2N1M0 core biopsed breast cancer, treated at Istituto Nazionale Tumori, Milano. Age ranger from 24 to 65 years. They underwent neoadjuvant taxanes-antracycline containing chemotherapy. Axillary mapping was performed in all patients using both lynphoscintigraphy with radioactive colloid and blue dye injection. After this a three-levels axillary dissection was performed after sentinel node biopsy at the time of definitive surgery. Breast conserving treatment was allowed in 68 patients; thew remaining received total mastectomy.

Results: The detection rate of sentinel node was 3/101 (97.1%) with a full concordance between the two methods (blue dye and hot). Nodal involvement was found in 40 (39%) patients in agreement with sentinel node status. The sentinel node was the only positive in 14 (35%) of these patients. In this series 52 patients was node negative and false negative rate was 6/58 (10%)

Conclusions: Neoadjuvant chemotherapy downstages axillary lymphnodes and sentinel node biopsy seems to be as accurate and feasible to stage axilla as in case of sentinel node biopsy performed during primary surgery.

222 Poster

Comparison of lipid and cardiovascular (CV) safety data of aromatase inhibitors (AIs)

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Background: The impact of AIs on CV health is of interest, but comparing CV data is difficult due to differences in methodologies and reporting of adverse events (AEs) and is complicated by the cardioprotective effects of tamoxifen (TAM).

Methods: LEAP, MAP.1, ATAC, TEAM, BIG 1-98, and MA.17 were studied to compare the effects of letrozole (LET), anastrozole (ANA), and exemestane (EXE) vs TAM or placebo (PLA) on lipid profile and CV events (CVE). Not all CV safety data were reported in each trial. Some trials had nonspecific requests to report AEs (ATAC), while others had more rigorous AE analysis (BIG 1-98).

Results: In healthy postmenopausal women (PMW) (LEAP), no significant differences between AIs were seen in total cholesterol (TC) levels. In the preventive MAP.1 trial, LET was associated with a transient decrease in TC without affecting other lipid parameters. In trials comparing AIs vs TAM, an increased incidence of hypercholesterolemia (HYP) and CVE were seen. In ATAC, more HYP (9 vs 3%), ischemic CVE (4.1 vs 3.4%), and angina pectoris (2.3 vs 1.6%) was seen with ANA vs TAM at 68 months (mo) follow-up (FU), but similar rates of myocardial infarction were seen on and off treatment at 100 mo FU. In the BIG 1-98 primary core analysis at 25.8 months median FU, more patients on LET had HYP (mostly grade 1) at least once. Median TC did not differ significantly from baseline with LET but decreased with TAM (−13.5%). A similar incidence of cardiac events (4.1% LET vs 3.8% TAM) was also seen. The BIG 1-98 monotherapy arm analysis (51 mo FU) confirmed those results. TEAM and IES found higher serum cholesterol levels with EXE vs TAM, with a numerically higher rate of CVE with EXE (20.8 vs 18.9%, P = 0.09) in IES. A meta-analysis found AIs to have similar overall effects on CVE. Comparisons of AI vs TAM are difficult to interpret, so comparisons with PLA may better indicate the impact of AIs on CV health. No differences were seen in HYP (16 vs 16%, P = 0.79) or CVE (6 vs 6%, P = 0.76) with LET vs PLA in MA.17.

Conclusions: As more PMW remain disease-free with AI therapy, the increased CV risk in this aging population competes with recurrence as a cause of mortality. AIs have similar effects on serum lipids and comparable CV safety profiles. Compared with PLA, AIs (LET, EXE) are not associated with increases in HYP or CVE.