Presidential session II
Tuesday 22 September 2009, 12.15–14.30

G1 INVITED

Hamilton Fairley Award

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Gordon Hamilton Fairley became the first Professor of Medical Oncology and Director of the Imperial Cancer Research Fund (ICRF) Medical Oncology Unit in 1971. Between then and 1975, when he was tragically murdered, he established an ethos of patient orientated research. Against the background of a large clinical practice, and a team of senior lecturers and clinical research fellows, he established a laboratory in which to investigate the diseases being treated. Critical to this was the creation of both a database and tissue bank, allowing for the correlations of patterns of disease and pathogenesis with the potential of improving therapy. Over the past 35 years, his vision has lead to in-house observations and collaborations which have contributed to our understanding of the pathogenesis of haematological malignancy, and may be illustrated by the increase in our understanding of follicular lymphoma.

Long term observation of the outcome of treatment of patients at Bart's in the last quarter of the last century, delineated the remitting recurring pattern of survival. Initial trials of first line therapy showed no survival advantage to 'intensified treatment' despite improved freedom from progression. In contract, studies of myeloablative chemo-radiotherapy later in the disease appeared to change the prognosis, subsequently confirmed in randomised trials. The pattern of risk of transformation to Diffuse Large B-Cell Lymphoma has been demonstrated on the basis of a rigorous policy of repeat biopsy; with a suggestion that there may two types of follicular lymphoma, one destined to transform, the other not. Studies of the molecular pathogenesis of follicular lymphoma, both in-house and as part of the Leukaemia and Lymphoma Molecular Profiling Project (LLMPP), have identified multiple molecular abnormalities relating to the malignant cell and also highlighted the significance of the 'tumour micro-environment'. Date will be presented to reflect the potential that may be realised from patient orientated research, and the long term contributions of Gordon Fairley.

1BA BEST ABSTRACT

Increased cardiovascular morbidity and mortality following endocrine treatment for prostate cancer: an analysis in 30,642 men in PCBaSe Sweden

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Background: Endocrine treatment (ET), i.e. orchiectomy, gonadotropin releasing hormone (GnRH) agonists or anti-androgen monotherapy (AA), is used in locally advanced and metastatic prostate cancer (PCa). Increased risk of heart disease (HD) is an emerging side-effect as ET is thought to reduce cardio-protective effects of testosterone. Detailed research on types of ET in relation to HD could help to tease out mechanisms involved in the aetiology of HD among these PCa patients. This study is the first large study that addresses cardiovascular side-effects of ET in subgroups of ET and HD.

Material and Methods: PCBaSe Sweden is based on the National Prostate Cancer Register (NPCR) of Sweden and covers 98% of incidence PCa. Analyses focussed on: ischaemic HD (ICD-9: 410–414; ICD-10: I20-I25), myocardial infarction (ICD-9: 410; ICD-10: I21), heart failure (ICD-9: 428; ICD-10: I50), and arrhythmia (ICD-9: 427; ICD-10: I44-I49). Standardized incidence and mortality ratios (SIR and SMR) were calculated to compare observed and expected numbers of HD cases, taking into account age, calendar-time, number of previous HD, and time since last HD. Expected numbers were estimated from the total Swedish population.

Results: Between 1997 and 2006, 30,642 PCa patients received ET as primary treatment in NPCR: 3,391 received anti-androgens (11%), 5,340 orchiectomy (17%), 9,066 GnRH agonists (30%), and 11,646 GnRH agonists and short-time AA (38%). SIR and SMR were >1 for all HD subgroups (see table). Detailed results showed that AA increase (mortality) risk for HD the least (*eg*. SIR for ischemic HD: 1.15 (95% CI: 1.03–1.29) in AA group vs. 1.33 (1.24–1.42) in GnRH group). HD risk following ET was less pronounced for those with HD at baseline (*eg*. SIR for ischemic HD with or without ischemic HD at baseline: 1.17 (1.11–1.24) and 1.41 (1.35–1.47)).

Endocrine treatment	SIR	95% CI	Obs/Exp	SMR	95% CI	Obs/Exp
Myocardial infarction	1.24	(1.19–1.29)	2080/1678.4	1.28	(1.20–1.36)	1062/832.1
Arrhythmia	1.19	(1.13–1.24)	1692/1427.7	1.05	(0.89–1.22)	158/150.8
Ischaemic HD	1.31	(1.26–1.35)	3284/2516.3	1.21	(1.15–1.26)	1828/1514.6
Heart failure	1.26	(1.21–1.31)	2140/1700	1.26	(1.12–1.41)	318/252.5

Conclusions: Use of ET in men with PCa increases risk of HD. The observed lowest risk for AA supports the suggested cardio-protective effect of testosterone. A less pronounced increase in risk for men with history of HD could be due to ongoing treatment for this HD.

2BA BEST ABSTRACT

Results of the TEAM (tamoxifen exemestane adjuvant multinational) prospective randomized phase III trial in hormone sensitive postmenopausal early breast cancer

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Background: The TEAM study is the largest of the 3 trials to compare efficacy of an aromatase inhibitor versus tamoxifen as initial endocrine therapy. Exemestane (E) is a steroidal aromatase inactivator, which has been demonstrated to be more effective than tamoxifen (T) in metastatic breast cancer (BC). The role of E in adjuvant therapy has been established after 2 or 3 years of T compared to 5 years of T in the Intergroup Exemestane Study (Lancet 2007;369:599−70). One objective of the TEAM study was to evaluate E compared to T as initial adjuvant endocrine therapy.

Methods: Using common criteria, eligible postmenopausal patients in 9 countries with invasive ER+ and/or PR+ early BC, were prospectively randomized to either open-label E 25 mg/day or T 20 mg/day. All patients had completed primary therapy of surgery and chemotherapy if indicated. All data were collected and analyzed by the Central Data Center in Leiden, The Netherlands. The trial was initiated in 2001 with a primary endpoint of DFS between T and E. In 2004, based on results of the IES, TEAM was modified such that all patients on T were switched to E at 2.5−3 years. The modified design includes 2 primary endpoints: DFS of T versus E followed up to 2.75 years, and DFS of E for 5 years versus T switched to E treated for a total of 5 years. The present analysis focused on the first primary endpoint: DFS for T compared to E at 2.75 years with censoring of events after 2.75 years. Log rank test with a 2-sided significance level of 2.98% stratified by country and factors nested in protocols was utilized.

Results: At 2.75 years of follow-up (N = 9779), 740 DFS events were reported. Compared with tamoxifen, exemestane was associated with improved DFS (hazard ratio [HR], 0.89; 95% CI, 0.77–1.03; $P = 0.12$) and RFS (HR, 0.85%; 95% CI, 0.72–1.00; $P = 0.056$), and significantly better DFS on study drug (HR, 0.83; 95% CI, 0.71–0.97; $P = 0.022$) and time to first distant metastasis (HR, 0.81; 95% CI, 0.67–0.98; $P = 0.028$). Discontinuation rates were 29.5% (n = 1434) for tamoxifen patients and 18.9% (n = 926) for exemestane patients, and 754 tamoxifen patients switched early to exemestane. No between-group differences were observed for time to contralateral breast cancer or OS, and no unexpected safety issues were reported. Patients $\geqslant$70 years old and those with N1 tumors had significant better DFS on exemestane compared to those on tamoxifen.

Conclusions: Initial adjuvant therapy with exemestane in postmenopausal patients with hormone receptor-positive breast cancer is more effective than tamoxifen and has a favourable safety profile.