the various subgroups. PFS analysis based on central assessment was also significant (HR: 0.36 [95% CI: 0.27–0.47], median 10.6 vs 4.1 months; $p = 3.3 \times 10^{-15}$). Both analyses crossed the pre-specified thresholds for significance. Response rates were 9.5% and 0.4% on EVE+EXE and EXE arms, respectively; $p < 0.0001$. Most common grade 3/4 adverse events were stomatitis (8% vs 1%), anemia (5% vs <1%), dyspnea (4% vs 1%), hyperglycemia (4% vs <1%), fatigue (3% vs 1%), and pneumonitis (3% vs 0%) for the EVE+EXE and EXE groups, respectively.
Conclusion: EVE, when added to an aromatase inhibitor, significantly improves PFS and response rate and has a manageable safety profile. EVE in combination with an aromatase inhibitor is a new therapeutic option for women with previously treated ABC.

Presidential Session III
Monday 26 September 2011, 12:15−14:25
10LBA LATE BREAKING ABSTRACT

The EORTC 10041/BIG 03−04 MINDACT (Microarray in Node Negative and 1 to 3 Positive Lymph Node Disease May Avoid ChemoTherapy) Trial: Patients' Baseline Characteristics and Logistics Aspects After a Successful Accrual

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Background: Personalized medicine and genomic risk profiling have been increasingly demanded for cancer management. The MINDACT trial investigates the added clinical value of the 70-gene profile (Mammaprint™) to standard clinicopathological criteria for the accurate selection of breast cancer (BC) pts for adjuvant chemotherapy (CT).
Material and Methods: All pts had their risk assessed by the 70-gene test [genomic (G) risk: high vs low] and by a modified version of Adjuvant! Online 8.0 [clinical (C) risk: high vs low]. G and C-high risk pts were proposed adjuvant CT. Discordant pts (G-low/C-high or G-high/C-low) were randomised between the two risk assessments to decide on adjuvant CT. Pts assigned to CT were offered a 2nd randomisation between an anthracycline-based regimen and the combination docetaxel–capecitabine. G-low and C-low risk pts were not assigned to CT. HR positive pts were offered an endocrine therapy randomisation (7 years of letrozole vs 2 years of tamoxifen followed by 5 years of letrozole) and ovarian function suppression if premenopausal.

	N (%)		
	G-high	G-low	**Total**
C-high	1827 (28)	1436 (22) CT: 718; no CT: 718	**3263 (50)***
C-low	678 (10) CT: 340; no CT: 338	2586 (40)	**3264 (50)***
Total	**2505 (38)**	**4022 (62)**	**6527**

*The 50−50 split is coincidental

Results: The trial was closed to screening in July 2011. Since March 2007, 11,300 pts were registered, 7,491 had the G test done, and 6,527 (58%) were enrolled in 104 sites in 9 countries. The proportion of registered/enrolled pts increased over time (46% in the 1st year to 63% in the last year). Monthly accrual increased from about 25 in the first year to over 200 pts in the last year. Current pts' baseline characteristics at enrolment are: 33% of pts <50 years of age, 80% were node negative, 71% had LN status verified by sentinel node biopsy, 83% had breast conservation surgery, 72% had tumors $\leqslant 2$ cm, 88% were HR positive (ER or PR+ or both), 11% HER2 positive, and 9% triple negative. Pts' risk allocations at enrolment are described in the table. As per status at enrollment the attribution to chemotherapy would be 11.6% lower using the 70-gene profile.
Conclusions: MINDACT is the largest European randomised prospective trial evaluating the clinical value of a gene expression profile for risk assessment and adjuvant CT prescription for BC. Accrual has been successfully completed and the trial's complex logistics, including real-time collection of frozen tumor tissue, were proven feasible in a multinational, multicentric setting.

Presidential Session IV
Tuesday 27 September 2011, 09:00−11:00
11LBA LATE BREAKING ABSTRACT

Identification of Novel Somatic Mutations in *SF3B1*, a Gene Encoding a Core Component of RNA Splicing Machinery, in Myelodysplasia with Ring Sideroblasts and Other Common Cancers

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Myelodysplastic syndromes (MDS) are a diverse group of chronic hematological malignancies, which, with the ageing population, have become the most prevalent myeloid cancer. Patients with MDS present with peripheral blood cytopenia, bone marrow dysplasia and an increased risk of transformation to acute myeloid leukemia (AML). The more recent WHO classification-based prognostic scoring system (WPSS) classifies MDS patients into five risk groups showing different survivals and probabilities of leukemic evolution. However, MDS patients demonstrate a high degree of morphological heterogeneity and variable clinical course irrespective of WHO subtype.
We reasoned that this heterogeneity may be attributable to distinct molecular lesions that contribute to MDS morphology and clinical outcome. We used massively parallel sequencing technology to identify somatically acquired point mutations across all protein-coding exons in the genome of 9 MDS patients.
We report the identification of novel somatically acquired mutations in patients with MDS. In 6/9 patients, we identified recurrent somatic mutations in a gene that encodes a core component of the RNA splicing machinery, *SF3B1*. To characterize the pevalence of *SF3B1* mutations, we undertook targeted resequencing of the gene in 2,087 samples from MDS patients, primary cancers and core cancer cell lines. Somatic mutations of *SF3B1* were found in 150/533 (28.1%) patients with MDS, 16/83 (19.3%) patients with MDS/MPN, and 2/38 (5.3%) patients with AML. The gene was also mutated in 1−5% of diverse other common tumor types including breast cancer, multiple myeloma and renal cancer. In patients with myeloid neoplasms, there were close relationships between mutant *SF3B1* and presence of ring sideroblasts ($P < 0.001$), and in multivariable analysis, *SF3B1* mutations were independently associated with better overall survival (HR = 0.18, $P = 0.028$) and lower risk of leukemic evolution (HR = 0.32, $P = 0.048$).
The close association between *SF3B1* mutation and ring sideroblasts across MDS is consistent with a causal relationship, and makes this the first gene to be strongly associated with a specific morphological feature in MDS. This molecular lesion has relevant clinical significance, as it is independently associated with a favorable clinical outcome.In conclusion, mutations in *SF3B1* implicate abnormalities of mRNA splicing, a pathway not previously known as a target for mutation, in the pathogenesis of MDS and cancer in general.