unconfirmed partial response was observed in a melanoma patient. The five strata were closed after 12 eligible patients had been entered without responding.
Conclusions: BI-2536 showed limited or no anti-tumour activity based on the Simon optimal design. These data however do not compromise further exploration of this class of agents with optimal documentation of dose, schedule and adequate translational research to optimize the development of polo-kinase 1 inhibitors.

Diagnostic/Biomarkers

Poster presentations (Tue, 22 Sep, 09:00−12:00) **Diagnostic/Biomarkers**

1300 POSTER

Immunohistochemical evaluation of PI3K/p-Akt pathways alterations in combination with conventional biomarkers in early stage breast cancer patients treated with cyclophosphamide/metotrexate/5-fluorouracil based chemotherapy: identification of an Unfavorable Biologic Profile

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Background: Akt activation through PI3K, leads to the phosphorylation of p27 protein thus avoiding nuclear entry and inducing mislocation to the cytoplasm of the protein with consequent inhibition of p27 cell cycle inhibitory function. The prognostic role of PI3K/Akt pathway alterations correlating phenotypic profiles with bio-pathologic variables of known clinical importance have been investigated in a retrospective series of early stage breast cancer patients (BC pts) treated with cyclophosphamide/metotrexate/5-fluorouracil based chemotherapy (CMF).
Materials and Methods: p-Akt, PI3K and p27 expression were evaluated by immunohistochemistry in a series of stage I/II BC pts who underwent conservative surgery and were candidates to receive CMF adjuvant therapy plus radiotherapy. Multiple Correspondence Analysis (MCA) was used to identify sub-groups of pts with different prognosis, while uni- and multivariate Cox regression analyses were applied to determine the impact of parameters identified by MCA on 10-yrs Disease Free Survival (DFS), together with clinico-pathological features. Receiver Operative Curve (ROC) analysis was adopted for optimal cut-off values.
Results: In a series of 133 pts, with a median follow-up of 107 months (range 40 to 141), those pts characterized by high Ki67 index, p53+, p-Akt+, PI3K+ and HER2+ (Adverse Biologic Factors, ABF) were associated with tumor relapse at the MCA analysis. ROC analysis dicotomized between pts with a Favourable Biological Profile (FBP, <3 ABF) and Unfavorable Biologic Profile (UBP $\geqslant$3 ABF). UBP pts showed a significantly shorter 10- yrs DFS than FBP pts at Kaplan-Meier analysis (67.0% vs 91.3%, p = 0.0006). According to the multivariate analysis, the biologic profile was the only significant prognostic indicator for longer DFS (p = 0.002). Significant factors at uni- and multivariate analysis are shown in the table.

Factors	Univariate (HR, 95% CI)	*p-value*	Multivariate (HR, 95% CI)	*p-value*
Grading	3.32 (1.31−8.43)	*0.012*	–	–
PgR	2.37 (1.03−5.48)	*0.043*	–	–
UBP	4.24 (1.73−10.40)	*0.002*	4.24 (1.73−10.40)	*0.002*

Conclusions: These data suggest that the activation of Akt may contribute together with high Ki67 index, p53+, p-Akt+, PI3K+ and HER2+ in predicting recurrence in early stage BC pts homogeneously treated with CMF based therapy.

1301 POSTER

The transcription factor p53 enhances the long-term survival effect of survivin in T4 breast cancer patients – 10-year results from a single institution

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Background: A large proportion of human tumors, including breast cancer, show deregulated expression of a variety of proteins such as survivin or p53, but the prognostic significance of most of them remains controversial. We analysed the expression and the association with survival of survivin (S) in T4 breast cancer pts. In addition we have attempted to correlate whether other molecular markers including p53 may influence the long-term predictive value of S.
Materials and Methods: from 1992 to 2001 53 consecutive T4 breast cancer pts.were included in this study. The median follow up was 125 mth. All 53 pts received primary chemotherapy, surgery, RT, adjuvant chemotherapy and hormone therapy if indicated. The median age was 51 yrs. Pathological characteristics: 28 pts (53%) were ER+ and 25 (47%) ER−; 17 pts (32%) were PR+ and 36 (68%) PR−; 24 pts (45%) were both ER and PR−, 16 (30%) both ER and PR+, 12 (23%) ER+ PR−; 10 pts (19%) HER2+, 43 (81%) HER2−; 18 pts (34%) HER2, ER and PR negative (Triple Negative; TN), and 35 (66%) non-TN. 17 pts (32%) were Ki 67 positive; 13 (24%) were p53 positive and 21 (40%) S positive (SP), 11 pts (21%) were both S and p53 positive.
Results: In the entire group of 53 pts the 5-year and 10-year OS was 60.4% and 43.4% respectively. The 5-year and 10-year OS in the S negative (SN) pts was 75% and 56.3% respectively. The 5-year and 10-year OS in SP pts was 38% and 23.8% respectively (p = 0.009). The overall 5-year and 10 year DFS was 45% and 32.1% respectively. The 5-year and 10-year DFS in 32 SN pts was 59.4 and 37.5% respectively. The 5-year and 10-year DFS in 21 SP pts was 23.8% (p = 0.095). Among pts with p53 positive or negative no statistically significant differences were observed in terms of 5-year and 10-year DFS and OS. A multivariate analysis in SP pts showed an Hazard Ratio (HR) of 2.6 (CI 1.2 to 5.5; p = 0.012). When SP was associated with several prognostic variables (age, ER, PR, G2/3, Ki 67, stage T4 d and HER2) the HR ranged between 2.3 and 2.6, whereas when SP was associated with p53 the HR was 3.27 (CI 1.5 to 7.2).
Conclusions: In our study SP pts had a worse outcome compared to SN in terms of both DFS and OS. Among the prognostic variables evaluated only p53 enhances negatively the effect of S on survival.

1302 POSTER

Assessment of the precursors of heme biosythesis in patients with breast tumour

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Background: Regulation and control of heme/porphyrin biosynthesis is very important for therapy of cancer. Some experimental studies found an increased level of protoporphyrin IX in human breast cancer cells. We tried to assess the precursors of heme biosynthesis in biological media of breast cancer and benign tumour patients.
Materials and Methods: Delta-aminolevulinic acid (delta-ALA) in urine and delta-aminolevulinic acid dehydratase (delta-ALAD) activity in blood of 264 breast cancer patients and 73 benign breast tumour patients were measured by spectrophotometry.
Results: The mean delta-ALA concentration in urine was 16.10 μmol/g creatinine (95% CI = (14.92−17.27) for cancer patients and 14.28 μmol/g creatinine (95% CI = 12.25−16.30) for benign tumour patients (p < 0.05). The figures for delta-ALAD were 38.89 U/L (95% CI = 36.73−41.05), and 41.01 U/L (95% CI =37.72−44.30), respectively (p>0.05).
Conclusion: Our findings show that heme/porphyrin biosynthesis in breast cancer patients is affected more than in benign tumour patients. The mean concentration of delta-aminolevulinic acid in urine of cancer patients is significantly higher than that in benign tumour patients.