The predictive value of BP for chemotherapy response in advanced breast cancer is currently being assessed.
Conclusions: The study demonstrates that BP is highly expressed in LAPC. However, it does not predict for response to neo-adjuvant anthracycline chemotherapy.

O-53 Biomarkers predicting response to a novel oral taxane DJ-927 in metastatic breast cancer (MBC)

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Background: DJ-927 is a novel oral taxane, whose *in vitro* tumour sensitivity is independent of p-glycoprotein (pgp) expression. Our phase 2 study in anthracycline pre-treated MBC patients showed that DJ-927 was well tolerated (response rate: 21.2%) [ESMO 06 #411P]. This single-centre analysis of 18 patients treated in the mentioned study aimed to investigate biomarkers of sensitivity to DJ-927 and assess cross-resistance to docetaxel.
Methodology: 18 patients received oral DJ-927, 27 or 35 mg/m^2, 3 weekly. 10 subsequently received single agent docetaxel. Primary tumour biopsies (n = 17, 1 unavailable) were studied for pgp, thioredoxin (Trx-1), thioredoxin reductase (TrxR1), Ki67, p53, Bcl2, VEGF, Her2, ER and progesterone expression by immunohistochemistry and correlated to response (RECIST).
Results: Best response (investigator assessed) to DJ-927 was: 7 PR (39%); 7 SD (39%) and 4 PD (22%). Response to subsequent docetaxel was: 4 PR (40%); 3 SD (30%) and 3 PD (30%). ER, Her2, vascular invasion, grade or histology did not predict for sensitivity to DJ-927. DJ-927 response was independent of pgp, Trx1, TrxR1, Ki67 and Bcl2. However, all 4 patients with PD on DJ-927 had high nuclear p53, inferring that p53 may predict DJ-927 resistance ($p = 0.015$, Fisher's exact test). Patients who had PR/SD to docetaxel following progression on DJ-927 had high pgp (5/7) and high Trx1 (6/7) levels, known docetaxel resistance markers. This raises the possibility of biomarker modulation by DJ-927.
Conclusion: Clinical sensitivity to DJ-927 appears to be independent of pgp (as *in vitro*) or Trx1/TrxR1. On progression, tumour response to docetaxel was high.

O-54 Switching to an aromatase inhibitor provides mortality benefit in early breast-carcinoma: Pooled analysis of 2 consecutive trials

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Background: The superiority of new generation aromatase inhibitors over tamoxifen in the adjuvant treatment of early breast carcinoma has emerged from several randomized trials. However, until now, only a couple trials (both ones implying early switching to an aromatase inhibitor: the ARNO 95 and the IES trials) have shown a moderate mortality benefit.
Methods: A pooled analysis of 2 prospective multicentric trials, sharing the same study design and nearly identical inclusion criteria, was performed. In both trials, women treated previously with tamoxifen for 2 or 3 years were randomly assigned to either continuing tamoxifen for an additional 2 or 3 years or to having their treatment switched to aminoglutethimide or anastrozole for a comparable time period. Mortality was analyzed according to allocated treatment and other patient and tumor variables. **Results:** In all, 828 postmenopausal women, mostly with estrogen receptor (ER)-positive and node-positive tumors who had been monitored for a median time of 78 months (range, 6–141 months) were analyzed. Of these women, 415 were randomly selected to continue tamoxifen and 413 switched to aminoglutethimide or anastrozole. All-cause mortality and breast cancer-specific mortality were significantly improved by the switch: all-cause-mortality:hazard ratio (HR) = 0.61 (0.42–0.88) $P = 0.007$; breast cancer-specific mortality: HR = 0.61 (0.39–0.94) $P = 0.025$. No increase was recorded in breast cancer-unrelated mortality in women after switching. Multivariate analysis showed that patient age, tumor size, allocated treatment, and nodal status, in that order, were independent mortality predictors.
Conclusions: Switching to an aromatase inhibitor after 2 or 3 years of tamoxifen therapy significantly improves survival compared with continuing 2 or 3 years of additional tamoxifen treatment. These findings fit in with those of a previous metanalysis including the three anastrozole switching trials (Lancet Oncol., 2006, 7: 991–996) and reinforce the indication of early switching to an aromatase inhibitor in women presently receiving adjuvant treatment with tamoxifen.

O-55 Assessment of Her-2 status using a panel of antibodies and FISH

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HER-2 expression in breast cancer has been shown to be of immense clinical importance since the realization that biologically targeted therapies to its transmembrane receptor tyrosine kinases is efficacious in prolonging disease free survival and overall survival not only in the metastatic setting but also for primary operable breast cancer. However, the optimal, most accurate and cost-effective strategy/assay to assess HER-2 status remains elusive.
We have examined HER-2 status using a panel of HER-2 antibodies [Herceptest, A0485, CBE356, and activated HER-2] and fluorescence in-situ hybridisation (FISH) in a large dataset of 800 cases. Staining was mainly membranous with cytoplasmic components ignored for this study. Overall there was good concordance with all antibodies, with HER-2 positive cases seen in 12.4% to 14.4% depending on antibody used. Using the Herceptest antibody as the true population prevalence of HER-2 expression, the best correlation with overexpression was seen with the A0485 antibody (97.8%) and the least with the activated HER-2 antibody. All antibodies showed excellent PPV (>97%) and NPV (>96%).
For borderline cases (2+), this was the least correlation amongst the assays. FISH detected HER-2 gene amplification correlated best with the Herceptest assay with 14.1% of borderline cases being amplified. When negative for FISH, all antibodies correlated excellently. This was also reflected in cases showing overexpression by immunocytochemistry. There were only few cases of unamplified HER-2 which were positive by immunoreactivity.
HER-2 positive disease showed a strong correlation with poor prognostic features. This finding translated to a worsened overall survival and shortened disease free survival. Multivariate analysis showed HER-2 status to be a marker of independent prognostic significance.