"HER2-positive" and "Triple-negative". The need for specific trials for each of these subtypes is an obvious evolution within the field of adjuvant systemic therapies. While research on HER2-positive disease has progressed rapidly, clinical research on the adjuvant treatment of "Triple-negative" or "Luminal B" breast cancers lack initiatives. Reasons for such limited clinical research include the relatively small size of subpopulations in which niche trials should be performed and the enormous costs involved in conducting and monitoring an adjuvant trial. Nevertheless, results from past trials indicate the need to improve outcomes for several cohorts of breast cancer patients. These include treatment strategies for young women, improved endocrine therapies to reduce the risk of late relapse in endocrine-responsive cohorts, and combined targeted therapy such as novel cytotoxic combinations together with DNA repair inhibitors for patients with triple negative disease.

Presidential Session I
Saturday 24 September 2011, 13:45−15:35
1BA BEST ABSTRACT

A Pivotal Multicenter Trial Evaluating Efficacy and Safety of the Hedgehog Pathway Inhibitor (HPI) Vismodegib in Patients With Advanced Basal Cell Carcinoma (BCC)

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Background: The Hedgehog (Hh) signaling pathway is implicated in pathogenesis of BCC. While most BCCs are mostly surgically managed, rare BCCs can become locally advanced (laBCC) or metastatic (mBCC), leaving no effective therapeutic alternatives. Vismodegib (GDC-0449) is a first-in-class small-molecule inhibitor of Hh signaling. In a phase 1 trial, a 55% response rate was seen in 33 patients (pts) with advanced BCC, and treatment was generally well tolerated (Von Hoff, NEJM 2009), leading to this pivotal trial of vismodegib.
Materials and Methods: This pivotal, multicenter, 2-cohort (laBCC and mBCC) nonrandomized study (NCT00833417; ERIVANCE BCC, SHH4476g; sponsored by Genentech; closed to enrollment). Pts with laBCC had histologically-confirmed BCC that was inoperable or for whom surgery would be significantly disfiguring. Pts with mBCC had histologically-confirmed RECIST-measurable disease. Pts received 150 mg oral vismodegib daily until disease progression. The primary endpoint is overall response rate (ORR) by independent review (IRF), using RECIST for mBCC and a composite endpoint for laBCC including improvements in tumor dimension and ulceration, pathologic clearance of BCC, and RECIST if applicable. Primary hypotheses tested are that ORR is significantly >20% for laBCC and >10% for mBCC. Secondary endpoints include duration of response, response per investigator (INV), and safety.
Results: 104 pts (71 laBCC/33 mBCC) were enrolled at 31 sites in US, Europe and Australia. For laBCC, the IRF ORR was 43% (95% CI 31−56%; $p < 0.0001$) and INV ORR was 60% (95% CI 47−72%). For mBCC, the IRF ORR was 30% (95% CI 16−48%; $p = 0.0011$) and INV ORR was 46% (95% CI 28−62%). Adverse events (AEs) in >30% of pts were muscle spasms, alopecia, taste disturbance, weight loss and fatigue. Serious AEs were reported in 26 pts (25%); 4 patients (4%) experienced serious AEs considered related to vismodegib. Fatal AEs were reported in 7 pts (7%), none considered related to vismodegib. Duration of response, histopathology, and detailed safety will be presented.
Conclusions: This pivotal study confirms the significant clinical benefit of vismodegib in both laBCC and mBCC, as measured by tumor response, and further characterizes the AE profile. These results demonstrate the potential role of vismodegib for the treatment of advanced BCC.

Presidential Session II
Sunday 25 September 2011, 12:20−14:40
2BA BEST ABSTRACT

Synchronous Chemo-radiation Can Reduce Local Recurrence in Early Stage Breast Cancer: Results of the SECRAB Trial (ISRCTN: 84214355) Presented on Behalf of the SECRAB Steering Committee

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Background: The sequencing of chemotherapy (CT) and radiotherapy (RT) after surgery for early breast cancer (EBC) remains controversial. Previous studies using a mitozantrone based regimen have shown that synchronous (Syn) CT-RT does not significantly improve loco-regional recurrence (LLR) and resulted in worse toxicity. SECRAB was designed to determine the optimal sequence of CT and RT in patients having a CMF or anthracycline (A)-CMF regime. The results of a planned analysis looking at local recurrence (LR) are presented.
Materials and Methods: SECRAB was a prospective, randomised multicentre trial comparing sequential (Seq) to Syn RT. RT schedules included 40 Gy/15F over 3 weeks, 45 Gy/20F over 4 weeks and 50 Gy/25F over 5 weeks. Syn RT was administered between cycles 2 and 3 for CMF or 5 and 6 for A-CMF. Seq RT was delivered on CT completion. Key eligibility criteria were completely excised EBC, fit for and requiring adjuvant CT and RT. Between Jul 98 and Mar 04, 2296 women were randomised. LR was defined as a recurrence in the ipsilateral breast or chest wall. Time to LR was calculated as the time from entry until first LR or date of censor.
Results: With a median follow-up of 8.8 years there were 63 and 41 LR in the Seq and Syn arms and 5-year LR rates were 5.1% (95% CI: 3.8%, 6.4%) and 2.8% (95% CI: 1.8%, 3.8%) respectively. There was a significant benefit for Syn RT with a 35% reduction in the risk of LR ($HR_{Syn} = 0.65$, 95% CI: 0.44, 0.96; $p = 0.03$). There was benefit for Syn RT across all treatment (CT regimen, duration of RT, RT boost) and biological subgroups (grade, lymph node status, tumour size, vascular invasion and excision margin). A previous analysis of LRR rates showed no significant difference between Seq and Syn RT ($HR_{Syn} = 0.82$, 95% CI: 0.60, 1.10; $p = 0.19$). Benefit for Syn RT was not seen in patients with regional recurrence, as 80% of these were outside the radiation field. Previously presented results showed an increase in acute skin toxicity in patients treated with Syn treatment however a recent analysis of quality of life data has shown no difference between the two arms.
Conclusions: Syn RT using a CMF or A-CMF regimen has resulted in a significant reduction in LR. The magnitude of benefit is comparable to the effects of chemo-radiation seen in other tumour sites. This is the first study to show this effect in EBC.
Sponsor: University Hospitals Birmingham NHS Foundation Trust

Presidential Session III
Monday 26 September 2011, 12:15−14:25
3BA BEST ABSTRACT

VANTAGE 014: Vorinostat (V) in Patients With Advanced Malignant Pleural Mesothelioma (MPM) who Have Failed Prior Pemetrexed and Either Cisplatin or Carboplatin Therapy: A Phase III, Randomized, Double-Blind, Placebo-Controlled Trial

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Background: V is a histone deacetylase inhibitor that alters gene expression and protein activity. Five of 13 previously treated patients with