Methods: Pts with inoperable locally advanced/metastatic gastric/gastro-oesophageal adenocarcinoma and no prior therapy were randomized 1:1 to cis for 6 cycles + cape (5-FU allowed) + bev (7.5 mg/kg) or placebo q3w until progression. The primary endpoint of overall survival (OS) was not met, but the difference in PFS between treatment arms (secondary endpoint) was significant. Clinical outcome differed by region, with increased benefit in European + Pan-American vs. Asian pts. Baseline samples for pVEGFA analysis were available from 712/774 pts, equally distributed across treatment arms. Association with PFS and OS was tested with simple/multiple regression and subgroup analyses using median value as a pre-specified cut-off.
Results: Expression of pVEGFA differed across regions, with higher levels in non-Asian pts. Pts in the control group with high pVEGFA levels had shorter OS than pts with low levels. We also observed a trend towards better effect on PFS/OS for pts with high pVEGFA expression, driven mainly by non-Asian pts (table). This effect was not seen in Asian pts.

BM population	HR PFS VEGFA low vs high *Interaction p-value*	HR OS VEGFA low vs high *Interaction p-value*
Overall (n = 712)	0.89 vs 0.64 *p* = 0.06	1.0 vs 0.73 *p* = 0.08
Non-Asia (n = 345)	0.83 vs 0.54 *p* = 0.08	0.93 vs 0.62 *p* = 0.12
Asia (n = 367)	0.91 vs 0.81 *p* = 0.68	1.02 vs 0.87 *p* = 0.56

Conclusions: pVEGFA shows potential as a prognostic and/or predictive BM candidate for PFS and OS in bev-treated AGC pts, mainly driven by non-Asian pts. The current data are similar to observations for pVEGFA from two other independent analyses in mBC (AVADO) and pancreatic cancer (AVITA, submitted ECCO 2011).

1416 POSTER

Decrease of Regulatory T Cells in Tumour-bearing Sentinel Lymph Nodes Correlates With Non-sentinel Metastases in Node-positive Breast Cancer Patients

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Background: Sentinel lymph nodes (SLNs) form a crucial front-line immune barrier against tumours. Due to the specificity and immunosuppressive activity against tumours, regulatory T cells (Treg) have been noted as a new therapeutic target in breast cancer. However, little is known about the prevalence and clinical significance of Treg in metastases as a primary therapeutic target. The aims of this study were to evaluate the prevalence and prognostic significance of Treg in tumour-bearing SLNs in accordance with the development of metastases in patients with node-positive breast cancer.
Matherial & Methods: We evaluated 30 patients as a training set including 5 patients with ductal carcinoma in situ and 25 patients showing invasive ductal carcinoma (IDC) with various nodal statuses (no metastasis, micrometastasis or macrometastasis), followed by 40 patients with SLN metastases as a validation set: 20 patients without non-SLN metastases (Non-SLN-negative) and 20 patients with non-SLN metastases (Non-SLN-positive). Treg counts were estimated using Foxp3 immunohistochemistry in the training and validation sets and CCL22 in the validation set. We then evaluated the prevalence and correlation to relapse-free survival of Treg in SLN and non-SLN.
Results: In the training set, we confirmed that Foxp3(+) Treg increased specifically in accordance with the development of tumour and lymph node metastases. In the validation set, prevalence of Foxp3(+) Treg in tumour-bearing SLN with Non-SLN-positive was decreased compared to that with Non-SLN-negative. Foxp3(+) Treg accumulation among main tumour, SLN and non-SLN was consistent with the CCL22 intensity gradient. Decreased Foxp3(+) Treg in SLN offered a predictor of patients with node-positive breast cancer.
Conclusions: Our study demonstrated that the dynamic, tumour-specific movement of Foxp3(+) Treg in SLN and non-SLN along the intensity gradient of CCL22 could identify the extent of axillary lymph node metastases, and provided a predictor of patients with node-positive breast cancer. We hope that these findings will provide a basis for a new sentinel concept and clinical applications in the diagnosis and treatment of node-positive breast cancer.

1417 POSTER

A Phase II Trial of Afatinib (BIBW 2992) in Patients With Tumours Prospectively Screened for EGFR And/or HER2 Gene Amplification or EGFR Activating Mutations

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Background: A variety of solid tumours are dependent upon EGFR or HER2 signaling pathways, and inhibition of these proteins using targeted TKIs has been a successful approach in the treatment of tumours such as breast and lung cancer. Afatinib (A), an irreversible ErbB-family receptor TKI has the potential to benefit patients with tumours driven by gene amplification/mutation of these receptors regardless of histology, suggesting the rationality to treat patients based on tumour molecular characteristics rather than primary site of origin.
Methods: A multicenter phase II trial was initiated in the US and Taiwan with an intent to identify patients across 4 different cancer categories (1: esophagogastric, 2: biliary tract or gallbladder, 3: transitional cell carcinoma of the urothelial tract and 4: gynecologic cancers) for EGFR/HER2 gene amplification and/or high polysomy ($\geqslant$4 gene copies in $\geqslant$40% of cells) by FISH, with a goal to treat approximately 48 patients (at least 12 in each category) with A. Patients with known EGFR mutations were also eligible. Other criteria included advanced stage, measurable disease by RECIST, PS 0−2, failure to respond or progression following at least one line of prior chemotherapy and no prior EGFR/HER2 TKI. Eligible patients were treated with A 50 mg, daily oral dosing until progression or undue toxicity. Tumours were tested for EGFR and KRAS mutations. Imaging assessments were performed at 6, 12 weeks, and then every 8 weeks until end of treatment. The primary endpoint was ORR per RECIST with secondary endpoints that included disease control rate, PK and safety.
Results: Trial was closed early due to recruitment challenges. Based on preliminary data pending validation, 385 patients (128, 61, 46 and 150 each in categories 1−4 respectively) were screened to identify 38 patients with FISH+ tumours [23(18%), 5(8.2%), 6(13%) and 4(2.7%) in categories 1−4 respectively] and 20 were treated (10, 1, 5 and 4 in categories 1−4 respectively) with A. Best response included 8 patients with SD, and 1 confirmed CR (HER2+ serous endometrial carcinoma). Eight patients had PD, and 3 were non-evaluable. The median treatment length with A was 83.5 days (range 9–237). Diarrhea, rash and decreased appetite were the most common AEs reported.
Conclusions: Single agent activity of A is limited yet encouraging in select patients with acceptable tolerability. Implementation of a biomarker-driven approach for patient selection in this setting is demanding.

1418 POSTER

Baseline Inflammatory Status Defined by Neutrophil to Lymphocyte Cell Count Ratio (NLR) Predicts Progression Free Survival (PFS) in Metastatic Colorectal Cancer Patients (mCRC) Undergoing Bevacizumab Based Biochemotherapy

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Background: Bevacizumab is a monoclonal antibody (mAb) to the vascular-endothelial-growth-factor (VEGF) which enhances poly-chemotherapy efficacy in mCRC patients. Unfortunately, only part of the patients will receive treatment benefit at the price of additional side-effects and considerable costs. In this context, no biomarker predictive of patients' response to bevacizumab has been identified. Bevacizumab is considered as an anti-angiogenetic agent because it subtracts free VEGF in the tumour tissue, blocking endothelial precursors' recruitment and neo-angiogenesis. VEGF depletion however, also trigger other effects; in fact, it is involved in multiple physiological mechanisms mediated by