and GCIG CA125 criteria. 3 core PTB obtained before and after 4 weeks of GSK795, were analysed by immunohistochemistry (IHC) and Reverse Phase Protein Array (RPPA). Sequenom mutation profiling (SMP) of archival tissue and PTB was also done.
Results: The most common drug related AE was G1/2 vomiting (33%); there was only one G3 drug related AE: hepatotoxicity. A PK-PET PD relationship was observed between GSK795 plasma C_{max} and Ki for best responding lesions. Although no RECISTv1.1 responses were noted, CA125 GCIG criteria PR rate was 20% (n = 2/10). A direct correlation was observed between best CA125 response, best CT response and disease stabilization ($p < 0.05$). IHC of available PTB from 2/3 pts dosed at 50 or 75 mg indicated robust increases in pAKT levels and decreases in pPRAS40 levels in 4/5 pts indicating clear PD effect. Ki67 levels also decreased in 4/5 pts after treatment. 2/2 clear cell pts had PIK3CA mutations in their original archival samples; one of these pts had disease stabilization for 50 weeks while the other pt with a concurrent Kras mutation did not respond. Kras and MET mutations were identified in 2 other non-responders (serous). These data are consistent with the genetic signature associated with GSK795 sensitivity (PI3K pathway activation) and resistance (MAPK pathway activation). RPPA of fresh frozen PTB from 11 pts identified 15 putative biomarkers including S6 as a predictive, Bid as a response and CCNE1 as a resistance biomarker of clinical AKT inhibition; currently undergoing validation.
Conclusions: GSK795 was tolerable with evidence of activity. Currently 1 patient (PR by GCIG) remains on the trial >52 weeks. IHC and RPPA showed PD evidence of PI3K/AKT pathway inhibition (pAKT/PRAS40) irrespective of response status. SMP demonstrated mutations associated with response (PIK3CA) and resistance (Kras, MET) to GSK795. RPPA identified putative predictive (S6), resistance (CCNE1) and response (Bid) biomarkers suitable for validation for AKT inhibitor therapy.

Head and Neck Cancer

Saturday 24 September 2011, 11:15−13:50

25LBA LATE BREAKING ABSTRACT

Safety and Efficacy of Panitumumab (pmab) in HPV Positive (+) and HPV Negative (−) Recurrent/metastatic (R/M) Squamous Cell Carcinoma of the Head and Neck (SCCHN): Analysis of the Phase 3 SPECTRUM Trial

J. Vermorken[1], J. Stöhlmacher[2], K. Oliner[3], C. Villanueva[4], P. Foa[5], E. Winquist[6], L. Licitra[7], K. Skladowski[8], Z. Pan[3], B.A. Bach[3].
[1]Antwerp University Hospital, Medical Oncology, Edegem, Belgium; [2]Universitätsklinikum Carl Gustav Carus, Dresden, Germany; [3]Amgen Inc., Thousand Oaks, USA; [4]CHU Jean Minjoz, Besançon, France; [5]San Paolo University Hospital, Milan, Italy; [6]London Health Sciences Centre, London, Canada; [7]Istituto Nazionale Tumori, Milan, Italy; [8]Instytut Onkologii im. M. Sklodowskiej-Curie, Gliwice, Poland

Background: Pmab is a fully human monoclonal antibody against the epidermal growth factor receptor. SPECTRUM (ClinicalTrials.gov Identifier: NCT00460265; Sponsor: Amgen) evaluated the safety and efficacy of pmab + platinum-based chemotherapy (CT) vs CT in patients (pts) with R/M SCCHN. This prespecified analysis presents outcomes by tumor HPV status.
Methods: All tumor samples were centrally reviewed. HPV status was determined using a validated immunohistochemistry assay to $p16^{INK4A}$ by an independent laboratory blinded to treatment assignments. Tumor samples were scored positive, negative, or failed according to prespecified guidelines.

	ITT (n = 657)	HPV^+ (n = 83)	HPV^- (n = 294)
OS			
Events, %	74	76	77
Stratified HR (95% CI)	0.87 (0.73–1.05)	1.02 (0.59–1.77)	0.71 (0.54–0.94)
Stratified LRT p-value	0.14	0.95	0.01
Median OS (pmab + CT vs CT), mos	11.1 vs 9.0	10.9 vs 12.1	11.8 vs 8.7
Quantitative interaction test p-value		0.144	
PFS			
Events, %	86	92	89
Stratified HR (95% CI)	0.78 (0.66–0.92)	1.25 (0.74–2.12)	0.64 (0.50–0.83)
Stratified LRT p-value	0.004	0.41	0.001
Median PFS (pmab + CT vs CT), mos	5.8 vs 4.6	5.5 vs 5.3	6.3 vs 5.1
Quantitative interaction test p-value		0.018	
ORR	**ITT (n = 566)***	**HPV^+ (n = 74)***	**HPV^- (n = 255)***
ORR (pmab + CT vs CT), %	36 vs 25	41 vs 25	37 vs 27
P-value odds ratio	0.007	0.21	0.11

*Pts with baseline measurable disease per modified RECIST.
HR: hazard ratio; LRT: log-rank test; OS: overall survival; PFS: progression-free survival; ORR: objective response rate.

Results: A total of 657 pts were enrolled (ITT). As of August 2011, 377 pts (57%) had samples with >10% viable tumor on central review and were evaluable for HPV testing. The assay failure rate was <1%. Eighty-three (22%) tumors were HPV^+ and 294 (78%) were HPV^-. HPV^+ rates varied by tumor site (36% oropharynx, 19% larynx, 16% oral cavity, and 13% hypopharynx) and by geographic region (42% N America, 22% W Europe, 20% Asia Pacific, 19% E Europe, and 17% S America). Demographics were generally balanced except that pts with HPV^+ vs HPV^- tumors were more frequently non-smokers (30% vs 14%), had oropharyngeal primary tumors (45% vs 23%), and had more poorly differentiated tumors (31% vs 15%). Efficacy results are shown in the table. Adverse events (AEs) grade 3+ (pmab + CT vs CT) were 86% vs 87% for HPV^+ and 86% and 77% for HPV^-. Serious AEs (pmab + CT vs CT) were 51% vs 32% for HPV^+ and 53% and 41% for HPV^-.
Conclusions: The addition of pmab to CT improved overall survival and progression-free survival in pts with HPV^- R/M SCCHN. There was no incremental benefit in pts with HPV^+ tumors. These findings should be evaluated in additional studies.

Lung Cancer − Localised/Local Regional

Sunday 25 September 2011, 09:00−10:30

26LBA LATE BREAKING ABSTRACT

Results of a Pilot External Quality Assurance Scheme for Somatic EGFR Mutation Testing in Non-Small Cell Lung Cancer Managed by EMQN, ESMO, ESP, and ETOP

N. Normanno[1], S. Patton[2], S. Murray[3], F. Blackhall[4], K.M. Kerr[5], M. Dietel[6], M. Filipits[7], M. Taron[8], R. Stahel[9], E. Thunnissen[10]. *[1]INT Fondazione Pascale, Cell Biology and Biotherapy Unit, Naples, Italy; [2]St Mary's Hospital, Genetic Medicine, Manchester, United Kingdom; [3]GeneKOR, Athens, Greece; [4]Christie Hospital, Manchester, United Kingdom; [5]Aberdeen Royal Infirmary, Department of Pathology, Aberdeen, United Kingdom; [6]Humboldt-Universität zu Berlin, Berlin, Germany; [7]Medical University of Vienna, Vienna, Austria; [8]Hospital Germans Trias i Pujol, Catalan Institute of Oncology, Badalona, Spain; [9]University Hospital Zürich, Zürich, Switzerland; [10]VU University Medical Center, Amsterdam, The Netherlands*

Background: The clinical significance of somatic epidermal growth factor receptor (EGFR) gene mutations in non-small cell lung cancer (NSCLC) is now well recognised. External Quality Assurance (EQA) has the main objective to establish inter-laboratory consistency. The EQA process can identify systematic errors in methodology that may not be revealed by internal QA processes. The European Molecular Genetics Quality Network (EMQN), the European Society for Pathology (ESP), the European Thoracic Oncology Platform (ETOP) and the European Society of Medical Oncology (ESMO) with other leading European groups collaborated in a pilot EQA scheme for EGFR.
Material and Methods: The EQA process does not specify the methodology to be used for genotyping. Samples generated from cell lines are validated by 4 laboratories and then provided to 30 laboratories participating in the pilot. Each sample is supplied with a mock clinical case. Participating laboratories register with the EMQN, perform DNA extraction and analysis using their usual method, and are requested to submit their results within a 4 week timeframe. The anonymous results are assessed and made available to all participants in order to enable comparisons between laboratories and assess individual laboratory performance.
Results: DNA sequencing (34%) and the DxS Therascreen kit (34%) are the main methodologies used by the participants. There were a significant number of genotyping errors. Five labs made clerical errors which resulted in them reporting the correct genotype for the wrong sample indicating a failure in their checking processes. Two labs made an analytical error, where a mutation was missed leading to a false negative result. No false positive errors were made. Many laboratories did not provide any interpretation of the results in the report and failed to give sufficient details on the techniques used.
Conclusions: The pilot EQA scheme brings together the expertise of pathology (ESP) with genetics (EMQN) and lung cancer clinicians and scientists (ESMO and ETOP). The technical performance of genotyping in EGFR mutation testing for NSCLC is good with a low level of "true" diagnostic errors. The standard of reporting is more variable with many labs reporting the genotyping result in isolation of any interpretation. Robust EQA will harmonize reporting and analytical practices which should ultimately benefit NSCLC patients. A full scheme will be run later in the year including an assessment of pathology review.