favour of Esc. At 10 yr, bPFS was 42% (95% CI = 37−47%) Std and 54% (95% CI = 49−60%) Esc. Long-term HT was reported for 220 with fewer men starting HT and later on Esc: HR = 0.77 (95% CI = 0.59–1.00; p = 0.05). Further data, including prostate-cancer specific survival and metastases-free survival will be presented; a blinded death review is ongoing.

Conclusions: Escalated dose radiotherapy with neo-adjuvant HT showed an advantage in early efficacy outcome measures but this did not translate into an improvement in overall survival. Five extra fractions of RT may have led to less exposure to long-term HT. Survival rates in both arms were much higher than originally expected.

Support: The trial is supported by the UK Medical Research Council

Gynaecological Cancer

Monday 26 September 2011, 09:00−11:55

22LBA LATE BREAKING ABSTRACT

Quality of Life in the ICON7 GCIG Phase III Randomised Clinical Trial

D. Stark[1], M. Nankivell[2], F. Hilpert[3], L. Elit[4], J. Brown[5], A. Lanceley[6], G. Valikova[7], A. Oza[8], A.M. Swart[2], T. Perren[1]. *[1]St James' University Hospital, Institute of Oncology, Leeds, United Kingdom; [2]Medical Research Council, Clinical Trials Unit, London, United Kingdom; [3]University Hospital Schleswig-Holstein, Department of Gynecology and Obstetrics, Kiel, Germany; [4]Henderson Hospital, Juravinski Cancer Centre, Ontario, Canada; [5]Leeds Institute of Molecular Medicine, Clinical Trials Research Unit, Leeds, United Kingdom; [6]UCL, Institute for Women's Health, London, United Kingdom; [7]St James' Institute of Oncology, Cancer Research UK Clinical Centre, Leeds, United Kingdom; [8]Princess Margaret Hospital, University of Toronto, Toronto, Canada*

Background: ICON7 (ISRCTN 91273375) evaluated the addition of bevacizumab (bev) to standard chemotherapy (CT) in the first line treatment of ovarian cancer. Bev was scheduled concurrently with CT (18 weeks) and as maintenance (54 weeks). 1,528 patients were recruited. MRC sponsored the trial, and Roche provided bev for all patients.

The primary endpoint, progression free survival, showed a 15% improvement at 12 months and an overall 1.5 month improvement with bev (restricted mean). This quality of life (QL) sub-study addresses short-term QL of patients during the period on and immediately after trial treatment.

Materials and Methods: QL was collected using the EORTC QLQ-C30 questionnaire at regular intervals until disease progression. The primary QL outcome was Global QL at 54 weeks. Three QL hypotheses were prospectively generated for the addition of bev

1. gastro-intestinal symptoms resolve more rapidly during chemotherapy
2. problems associated with wound healing (pain, body image, social and physical function) are greater at the midpoint of chemotherapy and
3. improvement in fatigue and social functioning is less during continuation of bev.

Other subscales were explored including subgroups from initial survival analyses.

Comparisons were by analysis of variance, controlling for baseline scores. A benefit for bev is indicated by a positive difference in global QL.

Results: Those receiving bev had a clinically small but statistically significant detriment in global quality of life at 54 weeks (table).

None of the hypothesised differences between the treatment arms were supported (all p > 0.05).

Bev was associated with clinically small but statistically significant detriments in exploratory analyses of role and emotional function, appetite, financial worries and chemotherapy side effects (all p < 0.01).

Missing data were present. Sensitivity analyses indicate caution is required in interpreting these observations.

Parameter	N	Comparison	Difference (Bev −CT)	P-value
Global QL	777	Difference in mean QL at 54 weeks	−6.38	<0.0001

Conclusions: Results suggest clinically small deficits in global quality of life and several other patient-reported outcomes associated with the addition of bev to standard CT in ovarian cancer. This should be considered in determining the optimal treatment.

Gynaecological Cancer

Monday 26 September 2011, 09:00−11:55

23LBA LATE BREAKING ABSTRACT

Quality of Life Outcomes of a Randomized, Placebo-Controlled Trial of Bevacizumab in the Front-Line Treatment of Ovarian Cancer: a Gynecologic Oncology Group Study

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Background: Results of a randomized, double-blind, placebo-controlled phase 3 trial indicate that the addition of bevacizumab to concurrent carboplatin and paclitaxel chemotherapy followed by maintenance bevacizumab (R3) prolongs progression-free survival in the front-line treatment of advanced epithelial ovarian cancer compared to chemotherapy alone (R1) or chemotherapy concurrent with bevacizumab in cycles 2−6 only (R2). Quality of Life (QOL) was compared among groups.

Methods: The Trial Outcome Index of the Functional Assessment of Cancer Therapy-Ovary (FACT-O TOI) was used to assess QOL before cycles 1, 4, 7, 13, and 21; and 6 months after completing study therapy. Differences in QOL scores between groups were assessed using a linear mixed model, adjusting for baseline score and age. Treatment effect size was calculated as the ratio of the treatment difference to the baseline standard deviation in the control group (R1). The significance level is set at 0.0167 to account for multiple comparisons.

Results: A total of 1,693 patients (566 in R1, 554 in R2, and 573 in R3) comprised the sample for the QOL comparisons. At cycle 4, the patients in R2 (p < 0.001) and R3 (p < 0.001) reported QOL scores that were 2.7 points (98.3% CI: 0.88–4.57; p < 0.001; effect size = 0.18) and 3.0 points (98.3% CI: 1.13–4.78; p < 0.001; effect size = 2.0) lower respectively, than those in R1. While the observed differences in QOL were statistically significant, they were not considered clinically significant. The difference in QOL scores between R1 and R3 remained statistically significant up to cycle 7, 2.3 points lower (98.3% CI: 0.33–4.14; p = 0.005; effect size = 0.15) in group R3. These scores were not statistically different between patients in R2 and R3. A similar trend was evident in subscale analyses, in which the patients in R2 and R3 reported statistically (not clinically) lower functioning than those in R1. The percentage of patients who reported abdominal discomfort (AD score >0) dropped over time, without significant differences between study arms.

Conclusion: The addition of bevacizumab compromised QOL to a mild extent during chemotherapy, but had no prolonged effect on QOL after chemotherapy completion. Quality of life improved from baseline to cycle 13 for each treatment group, as did abdominal discomfort.

Gynaecological Cancer

Monday 26 September 2011, 09:00−11:55

24LBA LATE BREAKING ABSTRACT

Mutation and Protein Expression Biomarkers Correlate with Response to AKT Inhibition in a Phase I Trial of the Oral Pan AKT Inhibitor GSK2141795 (GSK795) in Patients (pts) with Platinum Resistant Ovarian Cancer

H. Gungor[1], E. Stronach[1], E. Curry[1], A. Saleem[2], R. Agarwal[1], S. Blagden[1], S. Babar[3], G. Mills[4], S.R. Morris[5], H. Gabra[1]. *[1]Imperial College London, Ovarian Cancer Action, London, United Kingdom; [2]GlaxoSmithKline, Clinical Imaging Centre, London, United Kingdom; [3]Imperial Healthcare NHS Trust, Radiology, London, United Kingdom; [4]MD Anderson Cancer Centre, Systems Biology, Houston, USA; [5]GlaxoSmithKline, Cancer Research, Research Triangle Park, USA*

Background: AKT pathway activation is central to clinical platinum resistance. Molecular analysis of paired tumour biopsies (PTB) was undertaken in a GSK sponsored phase I trial of GSK795, PCS113124, with investigator led translational component in platinum resistant ovarian cancer pts.

Methods: 11 pts received GSK795 in 3 cohorts of 25–50–75 mg for 2 or 4 weeks, escalating to 75 mg following pharmacodynamics (PD) assessment. SUV, Ki and MRglu PET PD parameters were derived by 3 sequential FDG-PET scans. Response assessment was by RECISTv1.1

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

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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

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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.