## Genitourinary malignancies – Renal and Other
## Tuesday 22 September 2009, 09:00–11:15

**17LBA** LATE BREAKING ABSTRACT

**TRIST: A randomised, double blind, placebo controlled phase III study of MVA-5T4 in metastatic renal cancer patients**

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**Background:** TRIST (TroVax Renal Immunotherapy Survival Trial; 2006–001246–13) is a randomised, placebo controlled phase III study which investigated whether TroVax® (MVA delivering the tumour antigen 5T4), added to first-line standard of care (SOC), prolonged the survival of patients with locally advanced or metastatic clear cell renal adenocarcinoma.
**Methods:** Patients (n = 700 planned) with histologically proven clear cell renal cancer who had undergone prior nephrectomy, were classified as good or intermediate prognosis (MSKCC 0–2) and who required first line treatment for locally advanced or metastatic disease were randomised 1:1 to receive up to 13 immunisations of MVA-5T4 or placebo in combination with either Sunitinib, low-dose IL-2 or IFN-a. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), overall response rate (ORR) and safety. The study had 80% power to detect a hazard ratio in favour of TroVax of 0.725.
**Results:** A total of 733 patients were recruited (365 MVA-5T4, 368 placebo), and received a median of 8 MVA-5T4 vaccinations (range 0–13). Patient characteristics were generally well balanced between MVA-5T4 and placebo arms for SOC (IL-2: 23.8%/22.6%; IFNa: 51.2%/51.9%; Sunitinib: 24.9%/25.5%) and good prognosis (MSKCC score 0/1; 63.6%/66.6%). The most commonly occurring TEAEs (>20% patients) were pyrexia, fatigue, weight loss and nausea. There was no significant difference in TAEs or SAEs either related or unrelated to study medication. Survival data censored to March 13th 2009 demonstrated no significant improvement in OS (20.1 vs 19.2 mos; HR: 1.07; 95% CI: 0.86, 1.33; p = 0.55). A prospectively planned analysis demonstrated a significant survival advantage in good prognosis patients treated with IL-2 (not reached vs 19.5 mos; HR: 0.54; 95% CI: 0.30, 0.98; p = 0.04). Antibody responses against 5T4 were induced in most MVA-5T4-treated patients and were associated with enhanced survival irrespective of the health status of the patient.
**Conclusions:** MVA-5T4 was well tolerated when administered alongside IL-2, IFNa and Sunitinib. The primary endpoint was not met in this study. However, a significant survival benefit was evident in a prospectively defined sub-set of patients who had a good prognostic profile. Furthermore, exploratory analyses suggest that a number of baseline haematology factors could be used to identify patients who may derive significant benefit from this vaccine.

## Gynaecological cancer
## Thursday 24 September 2009, 09:00–11:15

**18LBA** LATE BREAKING ABSTRACT

**A GCIG randomized phase III study of carboplatin (C) & pegylated liposomal doxorubicin (PLD) (C–D) vs carboplatin (C) & paclitaxel (P) (C–P): CALYPSO results in partially platinum-sensitive ovarian cancer (OC) patients**

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**Background:** This phase III study was designed to compare efficacy & safety of carboplatin-pegylated liposomal doxorubicin (C–D) and carboplatin-paclitaxel (C–P) in patients (pts) with recurrent OC >6 months. Previous analyses of the intent-to-treat population have shown that C–D combination was significantly superior in terms of PFS and tolerance (ASCO 2009 abstract # 32763). We report here progression-free survival (PFS) and toxicity results for the pts with partially platinum sensitive OC (i.e relapsed between 6 and 12 months).
**Methods:** 976 pts after 1st- or 2nd-line platinum-based therapy who had been pretreated with a taxane were randomized to either C–D [C AUC 5 IV + PLD 30 mg/m$^2$ IV] d1 q4 wk, or C–P [C AUC 5 IV + P 175 mg/m$^2$ IV] d1 q3 wk $\times \geqslant$6 cycles. The primary endpoint was PFS. Randomization was stratified according to therapy-free interval of (1) 6–12 months, (2) >12 months.
**Results:** Relapse within 6–12 months was observed in 35% of the 976 pts (n = 344;161 in C–D arm, 183 in C–P arm). 81% of the pts in this subset population received 6+ cycles in C–D arm and 77% in C–P arm. Toxicity profile was similar to the overall study population, with lower rates of long-lasting toxicities (grade $\geqslant$2 neuropathy; 4% C–D vs 29% C–P), alopecia (9% C–D vs 86% C–P) and lower rates of severe hypersensitivity (6% C–D vs 22% C–P). With a median follow-up of 23 months and 326 events, the PFS was significantly superior for pts treated in C–D arm with a HR = 0.73 [95% CI: 0.58–0.9], p = 0.004. Overall survival data are still immature (deaths = 153).
**Conclusion:** In the stratum of partially platinum-sensitive OC (relapse between 6–12 months) PLD-carboplatin combination showed to be superior to paclitaxel–carboplatin in terms of PFS and tolerance, and paralleled the results of the intent-to-treat population.

## Head and neck cancer
## Tuesday 22 September 2009, 14:45–16:45

**19LBA** LATE BREAKING ABSTRACT

**HPV-associated p16-expression and response to radiobiological modifications of radiotherapy in head and neck cancer: results from the randomised DAHANCA trials**

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**Background:** High-risk human papillomavirus (HPV) is etiologically linked to a subgroup of head and neck cancers (HNSCC). The impact of tumour HPV/p16-status on prognosis after radiotherapy (RT) in patients with HNSCC is of such magnitude, that therapeutic implications seem intriguing. Based on our present knowledge of tumour HPV/p16-status, we found it relevant to reanalyse the results from the randomised DAHANCA trials, in order to asses the influence of HPV/p16-expression on the qualitative responses to accelerated fractionation (6fx/wk vs 5fx/wk) and hypoxic modification (nimorazole vs placebo) in RT of HNSCC.
**Material and Methods:** Pre-treatment tumour tissues from 599 patients enrolled in the DAHANCA trials were evaluated for p16-expression by immunohistochemistry and classified dichotomously as either p16-positive or negative. The primary endpoint was loco-regional tumour control 5 years after radiotherapy.
**Results:** The influence of p16-status on accelerated fractionation was analysed in 333 oropharyngeal cancer patients from the DAHANCA 5, 7 and 10 trials. A significant benefit from reducing overall treatment time was observed both in patients with p16-negative tumours (odds ratio [OR] = 0.55[95% CI 0–30–0.99]) as well as in patients with p16-positive tumours (OR = 0.39[0.18–0.83]), the endpoint being loco-regional tumour control.
Similarily, the impact of p16-status on hypoxic modification was evaluated in 331 patients with HNSCC from the DAHANCA 5 trial. In patients with p16-negative tumours there was a significant benefit from nimorazole (OR = 0.55[0.32–0.92]), whereas patients with p16-positive tumours had similar control rates regardless of hypoxic modification during RT (OR = 0.98[0.40–2.41]).
Overall, positive p16-status significantly improved loco-regional control in both study-populations with OR of 0.28 [0.17–0.44] and 0.34 [0.20–0.57], respectively.
**Conclusions:** Expression of HPV/p16 significantly improves prognosis for patients with HNSCC treated with RT. The effect of accelerated fractionation was not influenced by tumour HPV/p16-status, which indicates that the argument for reducing overall treatment time seems to apply also to patients with HPV/p16-positive tumours of the oropharynx. However, hypoxic modification was of no benefit in HPV/p16-positive HNSCC, suggesting that hypoxic radioresistance may not be clinically relevant in these tumours. Knowledge of tumour HPV/p16-status seems essential for optimal treatment planning in HNSCC.