GCIG Translational Committee Agenda
Thursday 31st May 2012
10.30 – 12.30
Doubletree Magnificent Mile Hotel
300 East Ohio Ave.
Chicago, IL, USA

1. Introduction	Iain McNeish (IM) (MRC-NCRI), Mike Birrer (MB) (GOG),
2. Devising HR assays in high grade serous ovarian cancer	Clare Scott (CS) (ANZGOG)
3. Molecular detection of circulating tumour cells in ovarian cancer	Robert Zeillinger (AGO-Austria)
4. MITO16/MaNGO Ov2 trial	Delia Mezzanzanica (MITO)
5. Proposal for evalution of platinum-refractory ovarian cancer	Mike Birrer
6. BriTROC – obtaining biopsies in relapsed ovarian cancer	Iain McNeish
7. AOB	All

1. Introduction

MK and IM welcomed attendees (n=30) and introduced CS as the new co-chair-elect of the Translational Committee. IM thanks MB for his efforts as co-chair in the past 3 years.

2. Clare Scott

CS introduced attendees to Homologous Recombination and its importance in High Grade Serous Ovarian Cancer. Its complexity means that tests of HR competence vs HR deficiency will need to be functional. CS also reminded attendees on the role of Non-homologous end-joining in the activity of PARPi in HRD ovarian cancer.

CS presented data from her own lab on using Rad51AP1 staining in HGSOC explants as a marker of HR repair. Irradiated or cisplatin-treated explants are stained for γH2AX (DNA damage marker) and Rad51AP1 (marker of HR repair). Rad51AP1 antibodies are more reliable that Rad51 for use in IHC on FFPE material. This test offers the possibility of biopsying tumours after cisplatin treatment in patients to assess HR status.

3. Robert Zeillinger

Dr Zeillinger presented data from the EU Framework 6 consortium OVCAD. Using traditional technology to identify CTCs (EpCAM-based isolation), only 3.5% women with ovarian ca had identifiable CTCs. But using novel Ab cocktail (including pan-cytokeratin, EMA, CK5/8), CTCs were identified in 28% samples (range 2 – 187 cells/ml). Using 3q26 amplification as marker, FISH confirms that these are tumour cells.

Gene expression profiling from CTC-enriched blood fraction – 11 gene panel used to identify CTC-positive vs CTC-negative patients. CTC-positivity associated with worse outcome. Most discriminating gene was *PPIC* (cyclophilin C).Correlation between qRT-PCR and Ab cocktail method = 66%.

4. **Delia Mezzanzanica (MITO)**

Dr Mezzananica presented the translational components of the MITO16/MaNGO Ov2 trial, which will investigate role of bevacizumab in relapsed disease in women who have already received it as part of first line treatment. 400 women will receive carboplatin + Taxol and bev first line (phase IV single arm study). On relapse, women will be randomised to receive chemo +/- bev.

Multiple samples to be collected:
FFPE tissue from primary surgery or upon recurrence
Blood and plasma – serial collections
Soluble markers, DNA, CTCs, circ endothelial cells, proteomic analysis
Fresh tumor cells – for xenogafts

Assays to be performed:
TMA construction from FFPE material: IHC for multiple angiogenesis markers
RNA and microRNA extraction – EXIQON analysis
Genomic DNA pharmacogenomics analysis for VEGF SNPs (not GWAS).
Proteomic analyses of serum.
CECs and CEPs (circ endothelial progs) as potential response predictors.

5. **Mike Birrer (GOG)**

MB has already been awarded DOD grant to evaluate expression signatures for predicting recurrence in early stage OC. A consortium of GCIG groups (GEICO, NSGO, MRC, GOG) are already participating – grant due to activate in July 2012. 74 gene signature from Affymetrix 133plus2 arrays.

MB proposed a DOD synergistic leverage grant to expand upon data on original grant, to expand genomic analysis to include Copy Number Variation and methylation to same samples and asked if there any other groups interested in participating.

In addition, DOD has asked for expressions of interest in Outcomes data, specifically biomarkers of long-term survival (>10 years) with associated QoL data. Groups were asked if they wished to participate – would require tumour samples and QoL data from trials where patients had long-term survival data. I.M. suggested that ICON3 and ICON5 should have both.

6. **Iain McNeish**

I.M. introduced the UK ovarian cancer translational consortium (BriTROC), which is going to obtain tumour biopsies from women with relapsed high grade serous ovarian cancer.

First question being addressed by the consortium was role of HR in acquired platinum resistance in ovarian cancer – sequencing of relapsed tumour for HR genes with comparisons with samples taken at diagnosis and germline DNA.

7. **Any other business**

There being none, the meeting adjourned for luncheon.