

**2009 AACR Annual Meeting**

**April 18-22, 2009**

**Denver, CO**

**Abstract Number:** 684  
**Session Title:** Biomarkers to Predict Treatment Response  
**Presentation Title:** Reovirus infection in combination with chemotherapy improves the efficacy of treatment in primary cultures of patient derived epithelial ovarian cancer  
**Presentation Start/End Time:** Sunday, Apr 19, 2009, 8:00 AM -12:00 PM  
**Location:** Hall B-F, Poster Section 30  
**Poster Section:** 30  
**Poster Board Number:** 3  
**Author Block:** Luci P. MacCormac, Julia V. Cockle, Matt C. Coffey, Philip A. Burns, Geoff D. Hall. University of Leeds, Leeds, United Kingdom, Oncolytics Biotech Inc., Calgary, AB, Canada, St James's Institute of Oncology, Leeds, United Kingdom

Relapse of epithelial ovarian cancer (EOC) with drug-resistant disease is all but inevitable, supporting the need to identify new therapeutic strategies. One potential strategy involves the use of oncolytic viruses that preferentially replicate in tumor cells. The main aim of this study was to assess the cytotoxicity of one such agent, reovirus (Reolysin(tm), Oncolytics), on primary cultures of EOC derived from patient samples, both alone and in combination with standard chemotherapy drugs. A further aim was to identify biomarkers of activity that could be applied to later clinical trials.

Short term primary cultures from ascites were established in autologous ascitic fluid from 37 patients. Reovirus cytotoxicity (assessed at 5 days using a WST-1 assay) was assessed at a multiplicity of infection (MOI) of 0.1, 1 and 10 alone and in combination with pharmacological concentrations of cisplatin, paclitaxel and gemcitabine. Five established EOC cell lines and short term cultures from solid tumor from four of the patients were also used for the purposes of comparison. DNA and RNA were prepared from uninfected samples and were used to assess; *K-ras* mutation status, gene expression profiles using Human Exon 1.0 ST Arrays (Affymetrix), and miRNA expression using Cancer RT<sup>2</sup> miRNA PCR arrays (SABiosciences), in order to identify potential biomarkers of reovirus response.

A range of sensitivity to reovirus was seen in the patient derived samples, with 54% (20/37) displaying <50% viability at an MOI 1. Four primary cultures from solid tumor displayed the same sensitivity as the matched ascites cultures. The 5 established EOC cell lines showed a range of viability from 0% (TR175) to 90% (OVCA433) at an MOI 1. Combination of reovirus with chemotherapy induced an additive effect in most cases. However, a clear synergistic response was seen at certain dose combinations in >30% of samples treated with a combination of reovirus and paclitaxel. Although *K-ras* mutations were not identified in any patient derived sample (consistent with published data for serous ovarian adenocarcinoma), a 36-gene expression profile (92% sensitivity) and overexpression of 3 miRNA markers were found to be predictive for response to reovirus.

The *in vitro* model using primary cultures of patient-derived samples of EOC provides an ideal system in which to assess the efficacy of new agents and in parallel assess potential biomarkers of activity. Our data supports a significant synergistic effect of reovirus and paclitaxel, which could be used to guide the development of future clinical trials. Our eventual aim is to define a reliable *in vitro* marker of response that could be applied to clinical trials.

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