Preclinical Evaluation of Mirvetuximab Soravtansine (IMGN853) Combination Therapy in Ovarian Cancer Xenograft Models

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Abstract

Heterogeneous combination therapy for epithelial ovarian cancer (EOC) includes platinum-based doublet regimens until resistance followed by combination chemotherapy plus bevacizumab and then salvage lines of gynecologic monotherapy. However, there are still over 14,000 deaths due to ovarian cancer per year in the US highlighting the significant need for new therapies. Mirvetuximab soravtansine (IMGN853) is an antibody-drug conjugate consisting of the cytotoxic maytansinoid DM4 covalently linked to the humanized monoclonal antibody M9346A, which is highly expressed in ovarian cancer xenografts. The efficacy observed in these models suggests that IMGN853 in combination with pegylated liposomal doxorubicin (PLD), or bevacizumab and/or carboplatin may be promising regimens to evaluate in clinical trials of EOC.

INTRODUCTION

Combination with Bevacizumab (OV90) and Platinum-Resistant EOC PDX

OV90 HS/OCIC Platinum Resistant Model

Combination with Bevacizumab (PDX Model)

Combination with Carboplatin and Bevacizumab

Combination with Pegylated Liposomal Doxorubicin

Methods

Female immunocompromised mice bearing subcutaneous ovarian xenograft tumors (average tumor volume 350-450 mm³ ± 10 animals per group) were treated as described in the Table. Tumors were measured twice weekly with volume calculated as either (length x width x height)/2 for OV90 studies or (length x width²)/2 in PDX studies. A mouse was considered to have a partial regression (PR) when tumor volume was reduced by 50% or greater and to have a complete regression (CR) when no palpable tumor could be detected. Tumor growth inhibition (T/C %) was calculated as the ratio of median tumor volumes at the time when control tumors reached a predetermined size in mm³.

CONCLUSIONS

• Combinations of IMGN853 with bevacizumab or PLD were substantially more effective than monotherapy in models of platinum resistant EOC.

• IMGN853 + bevacizumab therapy was found to be highly active even at doses where single agent IMGN853 was minimally active.

• Carboplatin + IMGN853 was more efficacious than the triple combination of carboplatin + paclitaxel + bevacizumab in the OV90 EOC xenograft model.

• The efficacy observed in these models suggests that IMGN853 in combination with PLD, or bevacizumab and/or carboplatin may be promising regimens to evaluate in clinical trials of EOC.

A phase II clinical study (FORWARD II) assessing doublet combinations of IMGN853 with PLD, bevacizumab and carboplatin in relapsed EOC is planned for 2015.