Poster 24: Understanding Mirvetuximab Sensitivity in Platinum Sensitive versus Platinum Resistant Cell Lines

Presenting Author: Sadhvi Batra, MD, University of Michigan

Topic
Ovarian

Objectives
To determine differential response differences to Mirvetuximab soravtansine among platinum sensitive versus resistant patient-derived high grade serous ovarian cancer cell lines.

Methods
Four patient-derived cisplatin resistant isogenic cell line pairs OV81.2 and OV81.2 CP40 and OV231 and OV231 CP30 were used. Increasing doses of MIRV (concentration ranging from 0.1nM to 1000nM),in DMEM medium were added to 48 well plate containing OV81.2, OV81.2 CP40 (2x104 cells per well), and OV231,OV231 CP30 (2.4x104 cells per well). The plates were incubated at 37C, 5% CO2 for 48 hours and cell viability was determined using CellTiterGlo in accordance with manufacture's protocol. IC50 were generated using a sigmoidal dose-response (variable slope) nonlinear regression curve fit (GraphPad Software Inc.).

Results
The IC50 for each cell line was as follows: OV81.2 13.7nM, OV81.2 CP40 3nM, OV231 3.2nM, and OV231 CP30 2.8nM, suggesting that the resistant cells were more sensitive to MIRV. T-tests comparing the IC50 within the isogenic pairs showed no statistically significant findings with p=0.10 (OV81.2 & OV81.2 CP40) and p=0.14 (OV231 & OV231 CP30). Two-way ANOVA showed that for both sets of lines, there was a significant difference at 7.96nM.

Conclusions
Based on findings, there is biological plausibility that platinum resistant cell lines may be more sensitive to MIRV. This is notable by significant differences between isogenic lines at 7.96nM, which is near the IC50 in all lines. This is presumably due to differences in mRNA expression conferred by platinum resistance and may suggest a trend towards differences in response among those treated with MIRV in the platinum sensitive setting versus those treated in platinum resistant setting. Further studies are needed to understand sensitivity differences and if these are clinically meaningful.

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