proliferation was restricted after PART1 knockdown. Western blot experiments showed that PART1 played a role by inactivating the DNA damage response pathway. Subcutaneous tumor formation experiments verified that PART1 can enhance the sensitivity of cells to olaparib and promote proliferation in vivo. The RNA-seq results showed that DNA damage response pathway was significantly activated by PART1 knockdown.

Conclusion/Implications LncRNA PART1 augments PARP1 sensitivity in ovarian cancer by inactivating DNA damage response pathway.

EP322/#101  COL4A6 PROMOTES TUMOR PROGRESSION AND PREDICTS POOR CLINICAL OUTCOME IN OVARIAN CANCER

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Introduction Biomarkers that predict disease progression might assist the development of better therapeutic strategies for aggressive cancers, such as ovarian cancer. Here, we investigated the role of collagen type IV alpha 6 (COL4A6) in cell invasiveness and tumor formation and the prognostic impact of COL4A6 expression in ovarian cancer.

Methods A2780CP70 and OVCAR8 cells transfected with a small interference RNA of COL4A6 (siCOL4A6) and A2780 and OVCAR4 cells transfected with a COL4A6 expression plasmid. Site-directed mutagenesis assay, luciferase assay, chromatin immunoprecipitation assay, invasion assay and xenograft animal study were performed in this study. COL4A6 mRNA expression levels of 160 ovarian tumors were determined by real-time RT-PCR.

Results Small interference RNA-mediated specific reduction in COL4A6 protein levels suppressed the invasive ability and oncogenic potential of ovarian cancer cells and decreased tumor formation. A combination of experimental approaches, including real-time RT-PCR, casein zymography and chromatin immunoprecipitation assays, showed that COL4A6 knockdown attenuated discoidin domain receptors/p-DDR1 expression and suppressed binding of E2F to its putative DDR1 promoter binding site, suggesting that the E2F-DRR1 axis is upregulated by COL4A6. Pharmacological inhibition of DDR1 abrogated the COL4A6-dependent cell invasiveness. Analysis of 160 ovarian cancer patients indicated that high COL4A6 mRNA levels are associated with advanced disease stage. The 5-year recurrence-free and overall survival rates were significantly lower (p=0.001 and p=0.001, respectively) among patients with high expression levels of tissue COL4A6 mRNA compared to those with low expression.

Conclusion/Implications COL4A6 may promote tumor aggressiveness via the E2F/DDR1 axis and that COL4A6 expression can predict clinical outcome in ovarian cancer patients.

EP323/#463  EFFICACY AND SAFETY OF MIRVETUXIMAB SORAVTANSINE IN CHINESE PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER WITH HIGH FOLATE RECEPTOR ALPHA EXPRESSION: RESULTS FROM IMGN853–301 (SORAYA) CHINA STUDY

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Introduction Current therapies for platinum-resistant ovarian cancer (PROC) are primarily non-platinum chemotherapies with limited response and an important unmet clinical need. Mirvetuximab soravtansine (MIRV) is a folate receptor α (FRα)-directed antibody-drug conjugate which has been approved by FDA in Nov-2022 for FRα positive PROC. IMGN853–301 is a single-arm registration study to evaluate the efficacy and safety of MIRV in Chinese PROC patients.

Methods 35 PROC patients were enrolled with 51% of patients with three lines of prior therapy. All patients received prior bevacizumab; 77% of patients received a prior PARP inhibitor. Eligible patients had FRα-high tumor according to PS2+ methodology from Ventana FOLR1 assay. All patients received single-agent MIRV at 6 mg/kg using adjusted ideal body weight on Day 1 Q3W until progressive disease or intolerable toxicity.

Results As of the data cutoff of 25-April-2023, median follow-up was 4.5 months. In all of 35 evaluable patients by investigator per RECIST 1.1, confirmed and unconfirmed ORR was 31.4% (95% CI: 16.85%, 49.29%), and 3-month PFS rate was estimated at 73.5% (95% CI: 55.30%, 85.25%). The most common (≥20%) treatment-related adverse events (all grade and grade 3-4) were Keratopathy (57.1% and 14.3%), Aspartate aminotransferase increased (45.7% and 0%), White blood cell count decreased (37.1% and 2.9%), Alanine aminotransferase increased (37.1% and 0%), Vision blurred (37.1% and 17.1%), Platelet count decreased (37.1% and 5.7%), Neutrophil count decreased (37.1% and 5.7%), and Xerophthalmia (20.0% and 14.3%).

Conclusion/Implications MIRV demonstrated consistent clinically meaningful antitumor activity and favorable tolerability and safety in Chinese patients with FRα-high PROC.