with recurrent EOC following niraparib 1LM approval, and that 1LM approval did not markedly change the profile of patients receiving niraparib maintenance therapy in a 2L setting.

2022-RA-722-ESGO PHASE 2 STUDY ASSESSING THE EFFICACY OF ADDING AL3818 (CATEQUENTINIB DIHYDROCHLORIDE, ANLOTINIB HYDROCHLORIDE) TO CHEMOTHERAPIES IN SUBJECTS WITH PLATINUM RESISTANT OVARIAN CARCINOMA

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Introduction/Background AL3818 is a novel, orally administered, small molecule tyrosine kinase inhibitor. The primary objective of this phase 2 study is to evaluate the efficacy of AL3818 in combination with chemotherapies in patients with platinum resistant ovarian carcinoma.

Methodology Patients with a diagnosis of platinum resistant ovarian carcinoma requiring second line or further treatment with chemotherapy were eligible for enrollment. The regimen was a 21-day cycle with oral AL3818 at 8 mg administered on days 8–21, with days 1–7 off. Chemotherapy options included weekly paclitaxel, pegylated liposomal doxorubicin (PLD), and topotecan. Maintenance monotherapy with AL3818 was an option if chemotherapy was discontinued.

Results Most patients were heavily pre-treated with median prior 4 (1–11) lines. At the cut-off date April 8, 2021, n=51 patients with platinum resistant ovarian cancer were enrolled and n=46 were evaluable, 29 of n=46 were treated with weekly paclitaxel. The objective response rate (ORR) and disease control rate (DCR) in intention to treat patient population were 43% (20/46) and 91% (42/46) for n=46 patients, and 55% (16/29) and 90% (26/29) for weekly paclitaxel patients. Median duration of response (DOR) was 5.94 months for n=46 patients and 6.43 months for weekly paclitaxel patients. Median progression free survival (PFS) was 6.27 months for n=46 patients and 6.67 months for weekly paclitaxel patients. Common treatment emergent adverse events (TEAE) included: abdominal pain (14%), alopecia (16%), constipation (10%), cough (12%), diarrhea (50%), dizziness (10%), dry skin (10%), epistaxis (18%), dyspnea (16%) fatigue (64%), fever (10%), headache (20%), hypertension (10%), anorexia (10%), oral mucositis (12%), nausea (52%), neutropenia (12%), vomiting (26%).

Conclusion AL3818 has demonstrated positive combined synergic efficacy with chemotherapies in platinum resistant ovarian cancer patients. These combination regimens are well tolerated in a heavily pre-treated population and a phase 3 registration study is ongoing (NCT02584478).

2022-RA-728-ESGO HIGH EXPRESSION OF VACUOLAR-ATPASE SUBUNIT ATP6V1B1 PREDICTS A POOR PROGNOSIS AND CORRELATES WITH CELL CYCLE PROGRESSION IN EPITHELIAL OVARIAN CANCER

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Introduction/Background Vacuolar-ATPase subunit ATP6V1B1 belongs to the ATP6V1s which participates in the biological process of transporting hydrogen ions and are associated with various cancers in expression and clinicopathological features, while its role its role in epithelial ovarian cancer (EOC) has not been clarified yet. Therefore, in this study we aim to evaluate the function, molecular mechanism and clinicopathological significance of ATP6V1B1 in EOC.

Methodology Expression level of ATP6V1B1 was screened by RNA sequencing of 10 EOCs and normal epithelial ovarian tissues. Expression levels of functional role of ATP6V1B1 were respectively evaluated by immunohistochemistry staining of EOC, borderline, benign and normal epithelial tissues. Associations of clinicopathological features and prognosis with ATP6V1B1 in EOC patients were analyzed both our recruited cohort and GEO datasets. Also, the functional roles of ATP6V1B1 were evaluated in EOC cell lines.

Results ATP6V1B1 protein was elevated in EOCs according to a GEO and TCGA datasets. High mRNA and protein levels of ATP6V1B1 were observed in EOCs compared to borderline, benign and normal nonadjacent ovarian epithelial tissues ($p < 0.001$). Importantly, high expression level of ATP6V1B1 was associated poor overall survival and disease-free survival compared with low expression of ATP6V1B1 in EOCs ($p = 0.006$, $p < 0.001$, respectively), and was associated with platinum-based chemotherapy resistance ($p < 0.001$). In vitro results also demonstrated the knockdown of ATP6V1B1 was associated with decreased cell proliferation and colony forming abilities supporting the oncogenic role in EOC. Also, cell cycle analysis revealed a higher proportion of cells in G1 phase after knockdown of ATP6V1B1 ($p = 0.003$).

Conclusion Our study is the first work to identify an oncogenic role of ATP6V1B1 in EOC tissues and cell lines which may provide insights into the application of ATP6V1B1 as a novel predictor of clinical outcome and a potential therapeutic target in EOC patients.