Ovarian cancer cells show enhanced response to the novel FGFR inhibitor CPL-304-110

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Background

No selective inhibitor targeting Fibroblast growth factor receptor (FGFR) tyrosine kinases has been clinically approved, so far, although few are tested in preclinical and clinical studies. A novel selective FGFR inhibitor, CPL-304-110, was recently synthesized by Polish company Celon Pharma S.A. Here, we tested this inhibitor against several ovarian cancer cell lines.

Methods

Commercially available ovarian cancer cell lines (A2780, ES2, OAW42, OVCAR3, SKOV3) and our own newly established OVPA8 line, were used. CPL-304-110 was tested in the 0.0001-10 µM concentrations, for 72 hours, and compared to the control inhibitor AZD4547. Cell viability was determined using AlamarBlue assay (data analysis: GraphPad Prism).

Results

Ovarian cancer cell lines were much more sensitive to the novel CPL-304-110 inhibitor (IC50 between 0.98 – 3.51 uM) than to the control inhibitor (IC50: 7.66 – 14.88 uM). SKOV3 cells were the most sensitive (IC50 0.98 uM for CPL304-110, 7.66 uM for control inhibitor; Fig. 1, Tab. 1). Most sensitive cell lines from other cancers had following IC50 values: lung cancer line DMS114: 0.063 uM and 0.043respectively; bladder cancer line UM-UC-14: 0.031 uM and 0.094 uM; gastric line SNU-16: 0.21 nM and 0.09 nM (hypersensitive line).

Figure 1. Antiproliferative effects of CPL-304-110 inhibitor and the control inhibitor (AZD4547) in ovarian cancer cells.

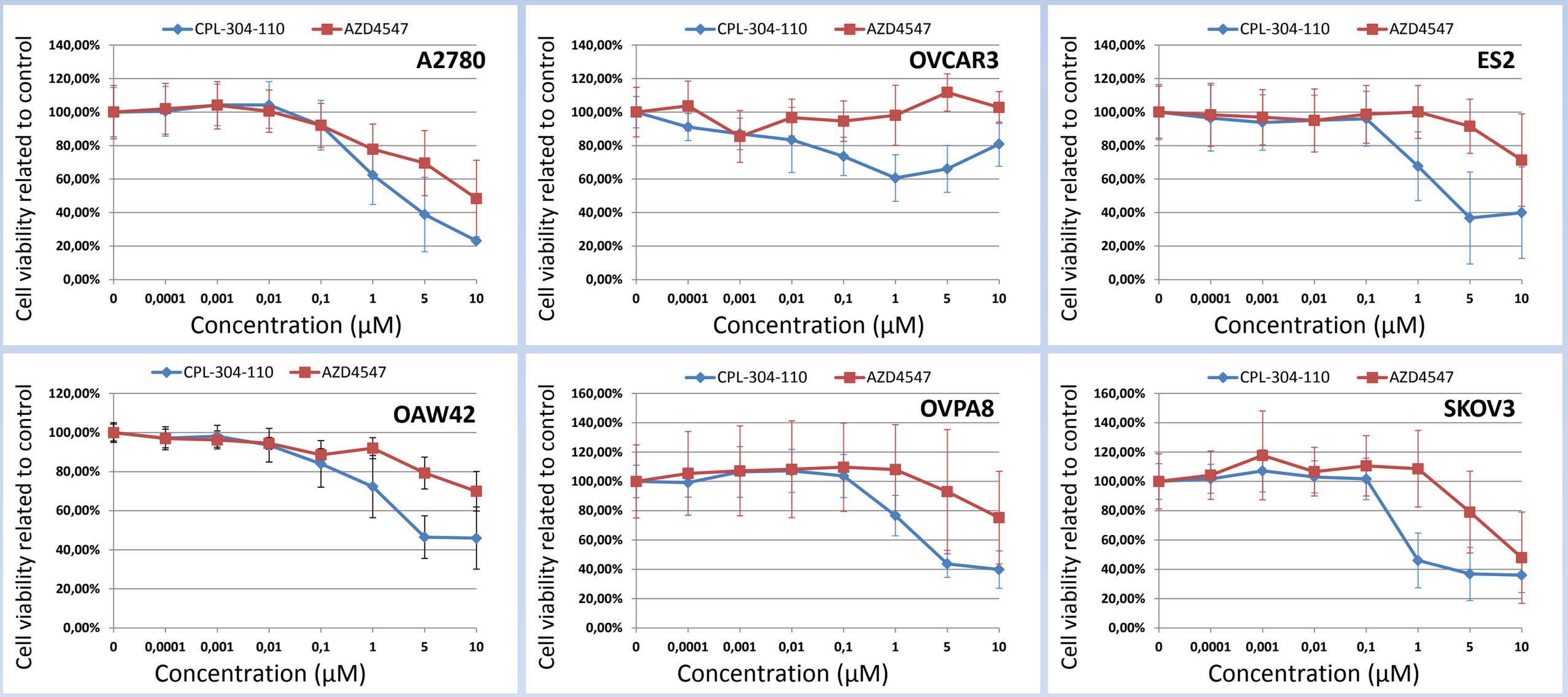

Table 1. IC50 values for ovarian cancer cell lines.

Cell line	Inhibitor FGFR	IC50 (µM)	Cell line	Inhibitor FGFR	IC50 (µM)
A2780	CPL-304-110	1,65	**OVCAR3**	CPL-304-110	> 10
	AZD4547	9,73		AZD4547	> 10
ES2	CPL-304-110	2,316	**OVPA8**	CPL-304-110	3,045
	AZD4547	14,88		AZD4547	12
OAW42	CPL-304-110	3,51	**SKOV3**	CPL-304-110	0,988
	AZD4547	> 10		AZD4547	7,665

Conclusion

Although some cell lines derived from other cancers show greater sensitivity against both inhibitors, in the ovarian cancer lines we observed evident trend toward enhanced efficacy of our novel FGFR inhibitor over the control one. This suggests that FGFR inhibitor effective against ovarian cancer can be synthesized.

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