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Analysis of radiosensitization effects of different PARP inhibitors on cancer cells

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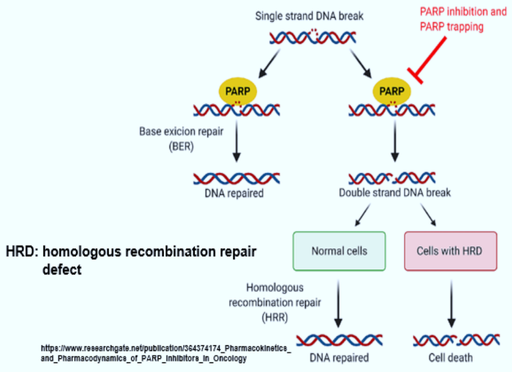
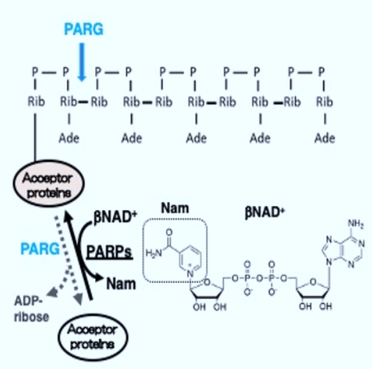
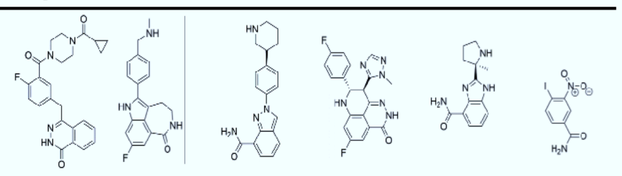
INTRODUCTION

Poly(ADP-ribose) polymerase (PARP)1





Reported clinical PARP inhibitors



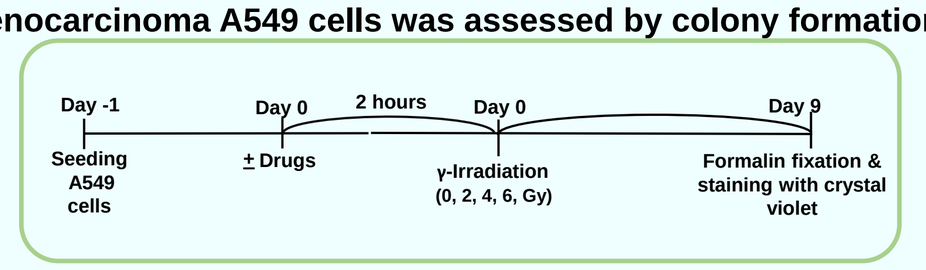
	Olaparib	Rucaparib	Niraparib	Talazoparib	Veliparib	Iniparib
	AZD2281	AG014699	MK-4827	BMN-673	ABT-888	BSI-201
IC50 PARP1	5 nM	NA*(Ki: 1.4 nM)	3.8 nM	0.57 nM	NA*(Ki: 5 nM)	NA*
PARP2	1 nM	NA*	2.1 nM	NA*	NA*(Ki: 5 nM)	NA*
PARP trapping activity	+	+	NA*	++	±	NA*

NA*: data not available

METHOD

1. Colony formation assay

The radiosensitization effect of PARP inhibitors on human lung adenocarcinoma A549 cells was assessed by colony formation assay.

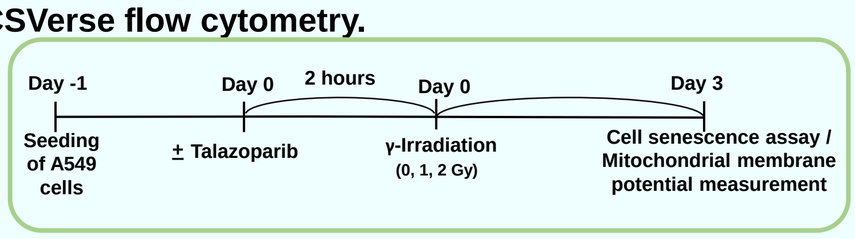


2. Cell senescence assay

A. SA-β-galactosidase activity was measured with X-gal
B. SPiDER-β-gal assay using BD FACSVerse flow cytometry. (BD-Becton, Dickinson & Company)

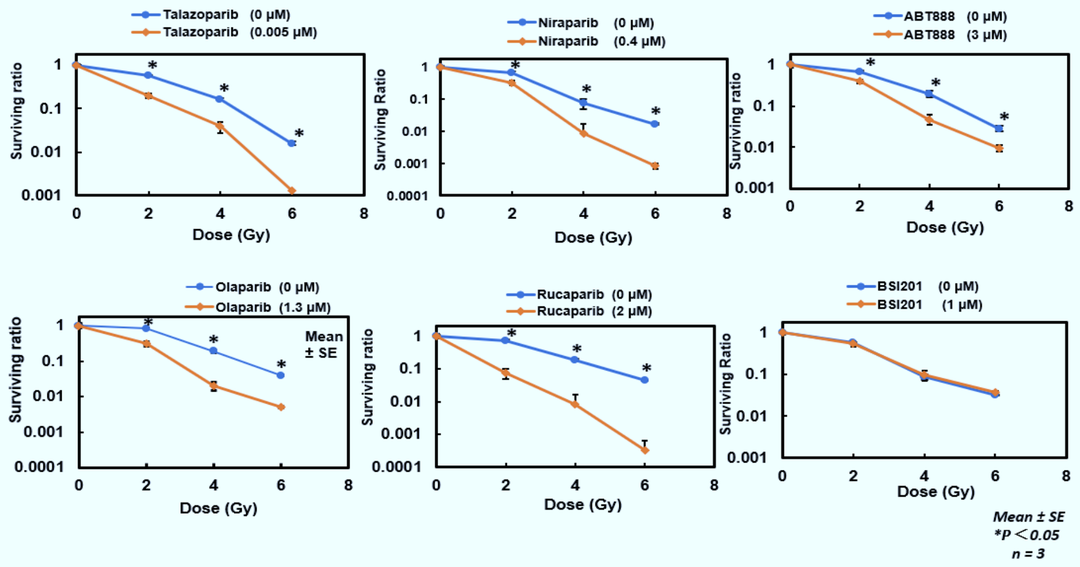
3. Mitochondrial membrane potential measurement

- After incubation with 2 μM JC-1 (fluorescent dye) for 30 min at 37°C on day 3, cells were trypsinized and JC-1 fluorescence was detected using BD FACSVerse flow cytometry.



RESULTS & DISCUSSION

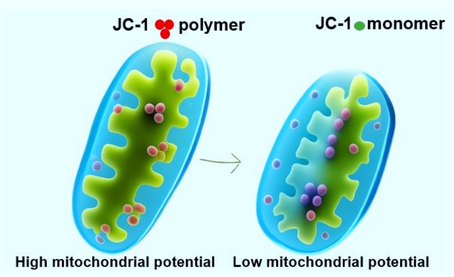
PARP inhibitors except for BSI201 showed a radiosensitization effect on A549 cells



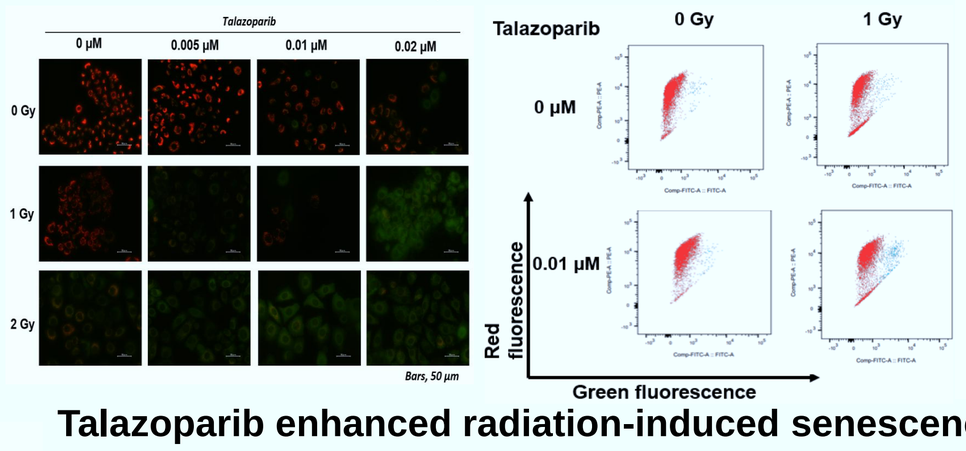
Statistical analysis done by the Tukey-Kramer HSD method

PARP inhibitors	ER10	PE
Talazoparib (0.005 μM)	1.5	0.6
Olaparib (1.3 μM)	1.8	1.1
Rucaparib (2 μM)	2.8	0.5
ABT888 (3 μM)	1.4	0.8
Niraparib (0.4μM)	1.4	0.9

Enhancement ratio (ER) of PARP inhibitors at 10% survival & PE (plating efficiency ratio)

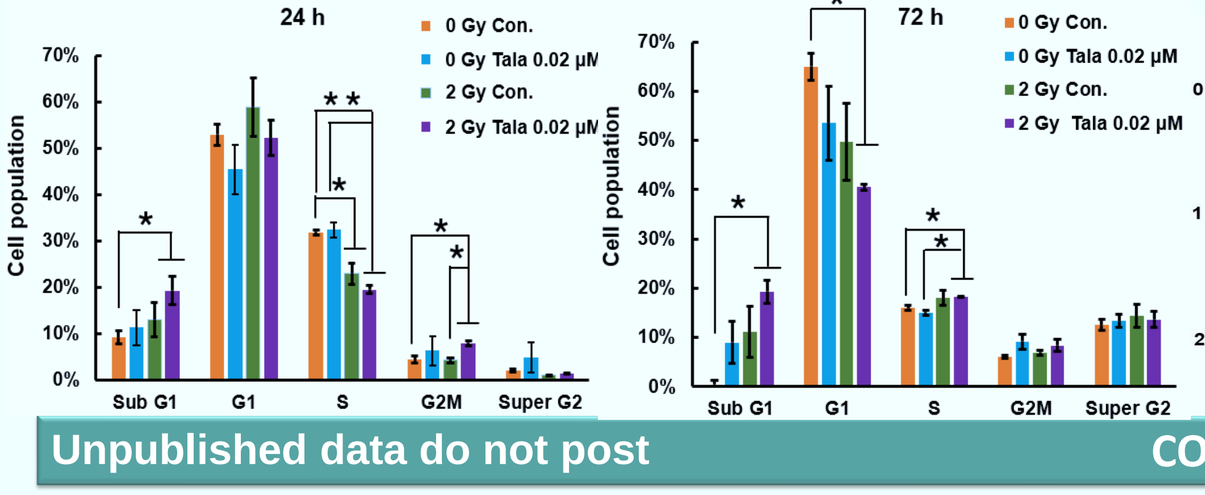


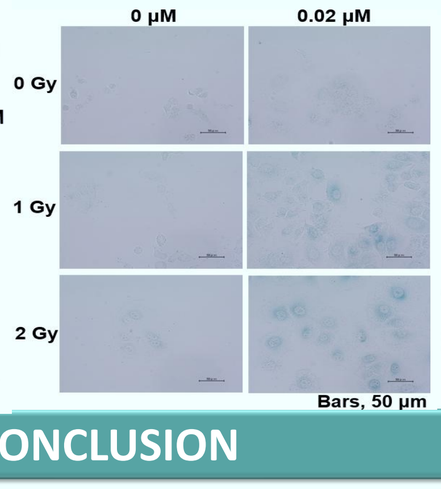
Reduced mitochondrial membrane potential after combined treatment with γ-irradiation & talazoparib on day 3

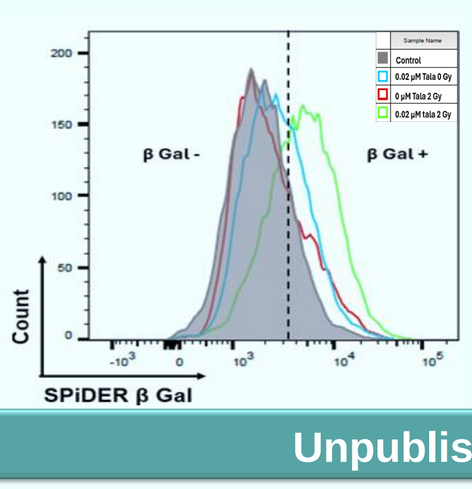


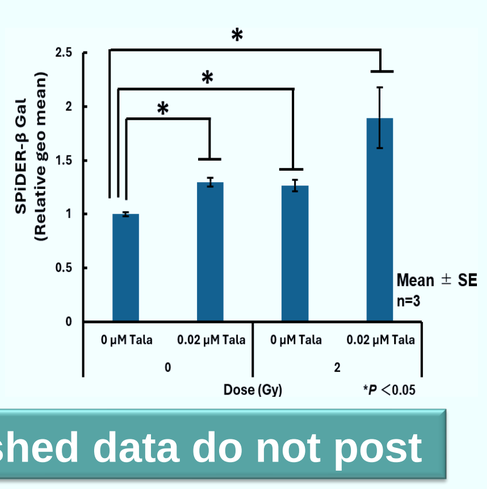
Talazoparib enhanced radiation-induced senescence in A549 cells on day 3

Cell cycle analysis 24 h & 72 h after combined treatment with γ-irradiation & talazoparib in A549 cells









Unpublished data do not post

CONCLUSION

Unpublished data do not post

- Various PARP inhibitors, except for BSI201 showed radiosensitization effects on lung adenocarcinoma A549 cells. Rucaparib showed the highest ER ratio.
- Talazoparib showed a radiosensitization effect at the lowest concentration among the used PARP inhibitors.
- The combination of γ-irradiation and talazoparib increased cellular senescence frequency accompanying the decrease of mitochondrial membrane potential.

FUTURE WORK / REFERENCES

Talazoparib and other PARP inhibitors may be useful for sensitization of radiation therapy. Action mechanisms should be further investigated.

COI Lead presenter: Barkha Saraswat Principal Researcher: Mitsuko Masutani We have no financial relationships to disclose

https://sciforum.net/event/CELLS2025