Talazoparib Efficacy Is Enhanced by Noncytotoxic Doses of Temozolomide-Mediated DNA Damage in Prostate Cancer Cell Lines

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BACKGROUND

- Temozolomide (TMZ) is a cytotoxic, orally available, semisynthetic nitrosourea derivative of 3-(2-triazenyl)-1-methyl-2-pyridone that can abrogate DNA damage and cause cell death.
- Talazoparib is a potent, orally bioavailable, small molecule inhibitor of poly(ADP-ribose) polymerase (PARP) enzyme that can irreversibly bind to active PARPs.

METHODOLOGY

- Details of the experimental method are provided in the supplementary methods in the figure legend.

KEY FINDINGS

- In vitro studies of prostate cancer cell lines, single-agent talazoparib had nanomolar efficacy in killing LNCaP and 22RV1 cells (Figure 1A).
- Treatment with talazoparib + TMZ had a synergistic effect, with minimal effect on cell lines treated with talazoparib alone or TMZ alone (Figure 1B).
- The mechanism of this potentiation was explored by examining the formation of DNA damage, which was detected after DNA hydrolysis and quantitated by liquid chromatography–mass spectrometry in multiple combination treatments (Figure 2A).
- The mechanism of this potentiation was further investigated by measuring the activation of caspases (Figure 3A).

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REFERENCES

- Details of the references are provided in the supplementary methods in the figure legend.