The author has declared no conflicts of interest.

Saudi Government.

Legal entity responsible for the study:

may offer a new potential approach(s) and implications for future therapeutics.

tive feedback loop during FLYWCH1 repressed genes, regardless of Wnt signaling status. b) Activation of Wnt signaling forms a nega-

FLYWCH1 and the canonical Wnt/b-catenin/TCF4 target gene in carcino-

b-catenin protein while

Results: BMN 673 considerably inhibited HCC1937 and MDA-MB-231 cell viability in dose and time-dependent manner. The cell viability of HCC1937 and MDA-MB-231 cells reduced by 34.9% and 47.5% in concentration of 10 nM BMN 673, respectively (p < 0.01). After 12 days exposure to BMN 673, a significant increase of total apoptotic cells was determined compared to the untreated control. The total percentage of apoptotic cells was 77.8% and 58.3% in HCC1937 and MDA-MB-231 cells treated with 10 nM of BMN 673, respectively (p < 0.01). After the HCC1937 and MDA-MB-231 cells were incubated with 10 nM of BMN 673, the percentage of cells in the G2/M phase significantly increased to 49.5% and 43.5%, respectively (p < 0.01). Additionally, a loss of membrane integrity and the condensation of nucleus were observed in these cells by AO/EtBr staining.

Conclusions: This study has suggested that BMN 673 demonstrates anti-cancer effects by inducing apoptosis in TNBC. However, BRCA mutated TNBC cells are far more sensitive to BMN 673 than to TNBC cells. Nevertheless, BMN 673 is greater potency than other PARP inhibitors at low nanomolar concentrations in TNBC cells.

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Association BRCA mutation status between BMN 673 (talazoparib), an oral PARP inhibitor, in triple-negative breast cancer

G. Gunes Eski0,1, G. Cecenener2, U. Egebi2, B. Tunca2

1Medical Biology, Sakarya University Faculty of Medicine, Sakarya, Turkey, 2Medical Biology, Uludag University Faculty of Medicine, Bursa, Turkey

Background: The poly (ADP-ribose) polymerase (PARP) inhibitors appear to be a promising treatments strategy in BRCA-associated and/or sporadic triple-negative breast cancer (TNBC) due to the molecular heterogeneity of TNBC and the lack of defined molecular targets. However, there is no studies on the association between BMN 673 (talazoparib) efficacy, which is a novel and the most potent PARP1/2 inhibi-

tor, and BRCA mutation status in TNBC. In the current study, we aimed to determine the cytotoxic and apoptotic effects of BMN 673 on TNBC cell lines according to BRCA mutational status.

Methods: HCC1937 [BRCA1 mutant (5382insC)] and MDA-MB-231 (BRCA1 wild-type, TNBC cell lines were treated with 0.01 -10 nM concentration of BMN 673 for 6 and 12 days and the cytotoxic effect was determined by WST-1 assay. Apoptosis induction by BMN 673 treatment was evaluated by Annexin V and cell cycle analysis, as well as the morphologic changes of the apoptotic cells were observed by AO/EtBr dual staining.

Results: BMN 673 considerably inhibited HCC1937 and MDA-MB-231 cell viability in concentration of 10 nM BMN 673, respectively (p < 0.01). After 12 days exposure to BMN 673, a significant increase of total apoptotic cells was determined compared to the untreated control. The total percentage of apoptotic cells was 77.8% and 58.3% in HCC1937 and MDA-MB-231 cells treated with 10 nM of BMN 673, respectively (p < 0.01). After the HCC1937 and MDA-MB-231 cells were incubated with 10 nM of BMN 673, the percentage of cells in the G2/M phase significantly increased to 49.5% and 43.5%, respectively (p < 0.01). Additionally, a loss of membrane integrity and the condensation of nucleus were observed in these cells by AO/EtBr staining.

Conclusions: This study has suggested that BMN 673 demonstrates anti-cancer effects by inducing apoptosis in TNBC. However, BRCA mutated TNBC cells are far more sensitive to BMN 673 than to TNBC cells. Nevertheless, BMN 673 is greater potency than other PARP inhibitors at low nanomolar concentrations in TNBC cells.

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