Background

Iniparib (BR201205) is a novel investigational PARP inhibitor that has demonstrated clinical activity in the treatment of advanced breast cancer.

Methods

●  Using in vitro cell assays in the SUM-149 cell line, we investigated the effects of various concentrations of iniparib on cell proliferation and survival.

●  For the in vivo studies, we used a xenograft model of human breast cancer cells implanted subcutaneously into nude mice. The mice were treated with iniparib at different doses and the effects on tumor growth were monitored over time.

●  The main outcome measure was tumor volume at the end of the treatment period.

●  To evaluate the antitumor activity of iniparib, we performed tumor histology and immunohistochemistry analyses to assess the effects on cell death modes.

●  Statistical analysis was performed using the two-tailed Student's t-test and the Mann-Whitney U-test for continuous variables.

●  The significance level was set at p < 0.05.

●  All data were expressed as mean ± standard deviation (SD).

●  The sample size was determined based on our previous studies and was calculated to detect a 25% difference in tumor volume with 80% power at a 5% significance level.

●  The study was approved by the Institutional Review Board of our institution.

●  All participants provided written informed consent before enrolling in the study.

●  We used commercial PARP inhibitors and drugs such as gemcitabine and carboplatin to confirm the selectivity of iniparib.

●  The ECOG PS (Eastern Cooperative Oncology Group performance status) was assessed in all patients at baseline.

●  The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Results

●  In vitro studies showed that iniparib inhibited cell proliferation and induced apoptosis in a dose-dependent manner.

●  In vivo studies demonstrated that iniparib reduced tumor growth and induced tumor regression when administered orally or intraperitoneally.

●  Tumor histology revealed that iniparib induced apoptosis and cell death by promoting PARP inhibition and DNA repair defects.

●  The average tumor volume reduction was 30% in the iniparib-treated group compared to the control group (p < 0.05).

●  No significant differences were observed in the toxicity profiles between the iniparib-treated and control groups.

Conclusions

Iniparib shows promising antitumor activity in vitro and in vivo, and its development as a PARP inhibitor for the treatment of advanced breast cancer is warranted.

References