**BACKGROUND**

Poly(ADP-ribose) polymerase (PARP) inhibitors have been shown to be particularly beneficial in tumors with DNA repair defects. PARP inhibition and tumor-selective synthetic lethalities. PARP inhibitors have been shown to be particularly beneficial in tumors with DNA repair defects.

**OBJECTIVES**

- Primary objectives
  - To evaluate pharmacokinetics (PK) and pharmacodynamics (PD) of MK-4827 in patients with advanced, refractory solid tumors and ovarian cancer (SOCC). In addition, a preliminary assessment was made of the antitumor activity of PARP inhibition.
- Secondary objectives
  - To evaluate safety and tolerability of MK-4827 in patients with advanced, refractory solid tumors and ovarian cancer.
  - To determine whether inhibition of PARP is associated with clinical benefit.
  - To determine whether inhibition of PARP is associated with clinical benefit.

**METHODS**

- **Patient Eligibility**: Patients with advanced, refractory solid tumors and ovarian cancer, with acceptable organ function and no prior history of thrombocytopenia.
- **Dose Expansion**: MK-4827 was administered orally once daily in cohorts of 3-6 patients.
- **Pharmacodynamics**: Pharmacodynamic end-points included changes in γ-H2AX foci.
- **Statistical Analysis**: Two-tailed t-tests were used to compare the difference in γ-H2AX foci.

**RESULTS**

- **MK-4827 Phase I Study Results**: MK-4827 was well tolerated. The maximum tolerated dose (MTD) was established at 300 mg orally on a continuous schedule.
- **Pharmacodynamic Profile**: MK-4827 inhibited PARP activity in tumor tissues.

**CONCLUSIONS**

- MK-4827 was well tolerated in advanced, refractory solid tumors and ovarian cancers.
- Preliminary antitumor activity was seen in sporadic ovarian cancers.
- MK-4827 may be a promising therapeutic target for DNA repair defects.