Camonsertib (RP-3500), an ataxia telangiectasia- and Rad3-related kinase inhibitor (ATRi) in combination with low dose gemcitabine (gem) in patients with solid tumors with DNA damage response (DDR) aberrations: Preclinical and Phase 1b results (NCT04497116)

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Methods

Camonsertib, a highly selective ATR kinase inhibitor: Rationale for synergy with gemcitabine

ATR: mediator of cellular DDR, activated in response to DNA replication stress

Responses observed across range of gem doses

Proposed RP2D: 80 mg cam (D1-3, 15-17) + 400 mg/m² gem

Response: response evaluation in solid tumors

Camonsertib pharmacokinetics

ATM, ATRIP, BRCA1/2, CDK12, CHTF8, etc.

Preliminary RP2D: 160 mg QD (3/4)

Other

ctDNA TF signal low and goes to undetectable at month 8 after treatment

3 lines of prior therapy: platinum and PARPi resistant

Figure 1. Preclinical data demonstrate combination synergy at low doses of cam and gem

Table 1. Patient demographics

Table 2. Treatment-related adverse events and neutrophil dynamics

Table 3. Patients with responses to cam + gem combination

Results

Figure 2. Comprehensive dose and schedule finding

Figure 3. ATRi molecular response analysis

Figure 5. Prolonged tumor response in patient with PARPi-deficient ovarian cancer

Conclusions

- The synergy of low doses of cam + gem, demonstrated in preclinical studies, was confirmed in this trial.
- ATRI: mediator of cellular DDR, activated in response to DNA replication stress
- Responses observed across range of gem doses
- Proposed RP2D: 80 mg cam (D1-3, 15-17) + 400 mg/m² gem
- Response: response evaluation in solid tumors
- Camonsertib pharmacokinetics
- ATM, ATRIP, BRCA1/2, CDK12, CHTF8, etc.
- Preliminary RP2D: 160 mg QD (3/4)
- Other
- ctDNA TF signal low and goes to undetectable at month 8 after treatment
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