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PRELIMINARY SAFETY, EFFICACY, AND PK/PD CHARACTERIZATION FROM GARNET, A PHASE 1 CLINICAL TRIAL OF THE ANTI–PD-1 MONOCLONAL ANTIBODY, TSR-042, IN PATIENTS WITH RECURRENT OR ADVANCED MSI-H ENDOMETRIAL CANCER

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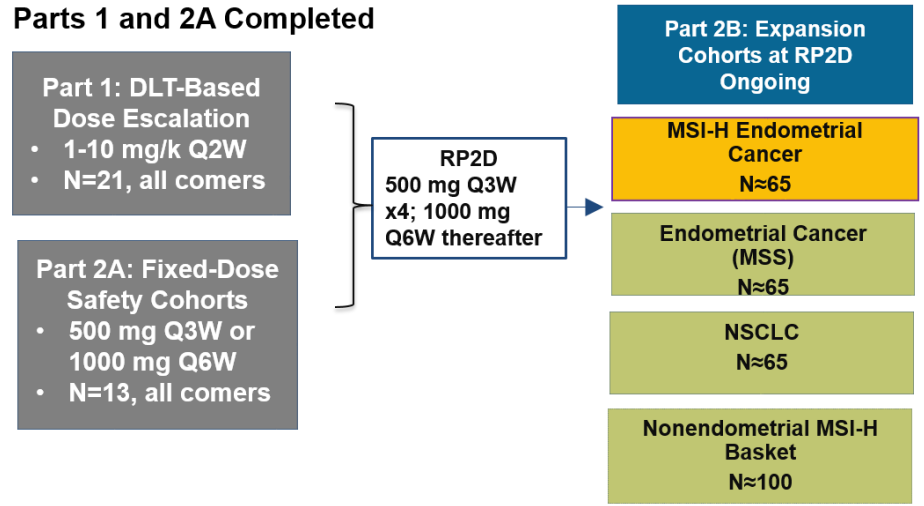
BACKGROUND

- TSR-042 is an investigational, humanized anti-programmed death (PD)-1 monoclonal antibody that binds with high affinity to the PD-1 receptor and effectively blocks its interaction with the PD-1 ligands PD-L1 and PD-L2
- TSR-042 has a safety profile characteristic of approved PD-1 inhibitors[1] and is the only anti-PD-1 therapy administered as a monotherapy every 3 weeks (Q3W) for 4 doses then Q6W until disease progression[2,3]
- The ongoing GARNET trial is evaluating TSR-042 as monotherapy in patients with advanced solid tumors, including endometrial cancer (MSI-H and MSS) and non-small cell lung cancer

GARNET Trial

Part 2B Key Objectives

- Evaluate safety and tolerability at the RP2D in advanced solid tumors
- Objective response rate (ORR), duration of response (DOR), and DOR per irRECIST assessed by investigators
- To further characterize the pharmacokinetic profile and receptor occupancy (RO) of TSR-042
- **Primary Efficacy Endpoints**
- ORR and DOR per irRECIST assessed by investigators



NCT02715284

DLT=dose-limiting toxicity; MSI-H=microsatellite instability-high; EC=endothelial cancer; MSS=microsatellite stable; NSCLC=non-small cell lung cancer; PK=pharmacokinetic; Q2W=every 2 weeks; Q6W=every 6 weeks; RP2D=recommended phase 2 dose.

1.Sachdev JC, et al. *Ann Oncol*. 2017;28(suppl 5):420; 2. OPDIVO (nivolumab) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; 2014; 3. KEYTRUDA (pembrolizumab) [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; 2017.

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RESULTS

SAFETY[a]

- Thirty-five patients with MSI-H EC received at least one treatment with TSR-042
- The safety profile of the MSI-H EC cohort was consistent with the safety profile seen in the overall GARNET study
- Treatment-related TEAEs were reported in 65.7% of patients, grade ≥3 treatment-related AEs were reported in 11.4%
- irAEs related to anti-PD-1 therapies[1] were infrequent

Grade ≥3 Treatment-Related TEAEs, Preferred Term	MSI-H EC (n=35)
Subjects with at least 1 treatment-related grade ≥3 TEAE, n (%)	4 (11.4)
Alanine aminotransferase increased	1 (2.9)
Anemia	1 (2.9)
Aspartate aminotransferase increased	1 (2.9)
Leukopenia	1 (2.9)
Neutropenia	1 (2.9)

EFFICACY

- Twenty-five patients with MSI-H EC were evaluable
- The overall response rate (including both confirmed and unconfirmed responses) was 52% (95% CI: 31.3, 72.2)
- Ten of the 13 responses (77%) are ongoing. One partial response has continued for >60 weeks
- 11 responders (85%) are still receiving treatment
- Two patients had DOR >6 months
- At RP2D, TSR-042 maintained at least a 7.8-fold margin for full RO through the course of treatment

Best Overall Response by irRECIST	MSI-H EC (n=25)
Complete response[a], n (%)	1 (4)
Partial response[a], n (%)	12 (48)
Stable disease, n (%)	2 (8)
Progressive disease, n (%)	7 (28)
Not evaluated, n (%)	3 (12)
Overall response rate[a], % (95% CI)	52 (31.3, 72.2)
Disease control rate[a,b], % (95% CI)	60 (38.7, 78.9)

[a]Responses include both confirmed and unconfirmed responses.
[b]irCR+irPR+uirPR+irSD.

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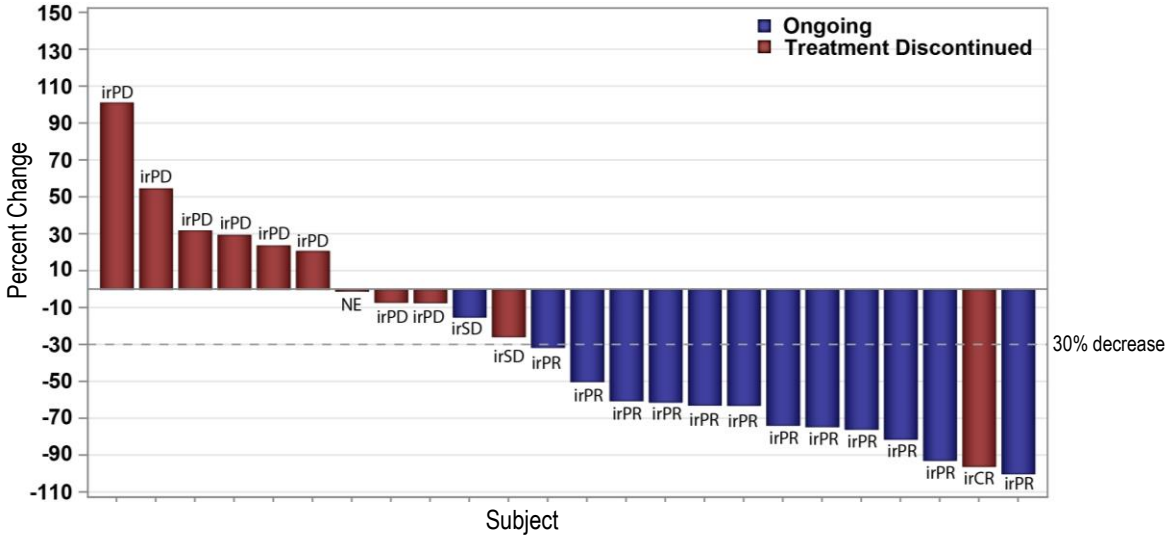
[a]Serious treatment-related TEAEs were reported in 2 patients (5.7%).
CR=complete response; PR=partial response; SD=stable disease.
1. Wang PF, et al. *Front Pharmacol.* 2017;8:730.

TUMOR RESPONSE

Depth of Response



CONCLUSIONS

- Preliminary efficacy data indicates robust activity of TSR-042 in MSI-H EC patients with advanced disease who were previously treated with platinum-based therapy
- Preliminary safety findings indicate that TSR-042 is safe and well tolerated, with a profile characteristic of approved PD-1 inhibitors
- Safety and efficacy data for TSR-042 at the RP2D support the unique and convenient dosing schedule of 500 mg Q3W for the first 4 cycles and 1000 mg Q6W thereafter
- Maximal RO was achieved at the RP2D and maintained through the course of treatment

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