ANNUAL MEETING ON WOMENS' CANCER®

BUILDING BRIDGES // BREAKING BARRIERS

SGO // PHOENIX, ARIZONA // MARCH 18 – 21, 2022

Phase 2 study of tislelizumab monotherapy in previously-treated, locally advanced unresectable or metastatic microsatellite instability-high/mismatch repair-deficient solid tumors: Gynecological cancer subgroup

Dr Yunong Gao[2*]

On behalf of Dong Wang,[1†] Naiyi Zhang,[2] Aimin Zang,[3] Jing Wang,[4] Yi Huang,[5] Lin Shen,[2] Jian Li,[2] Yanqiao Zhang,[6] Tianshu Liu,[7] Yanhong Deng,[8] Yaling Xu,[9] Zhezhen Li,[9] Yidi Wang[9]

[1]Chongqing University Cancer Hospital, Chongqing, China; [2]Beijing Cancer Hospital, Beijing, China; [3]Affiliated Hospital of Hebei University, Hebei, China; [4]Hunan Cancer Hospital, Hunan, China; [5]Hubei Cancer Hospital, Hubei, China; [6]Harbin Medical University Cancer Hospital, Harbin, China; [7]Zhongshan Hospital of Fudan University, Shanghai, China; [8]The Sixth Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China; [9]BeiGene (Shanghai) Co, Ltd., Shanghai, China. *Corresponding author; †Lead author

ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 18 – 21, 2022

SGO Society of Gynecologic Oncology

Financial Disclosures

- I have the following financial relationships with ACCME defined ineligible companies to report over the past 24 months:
  - I have no financial relationships with ACCME defined ineligible companies to report

Background

- MSI-H/dMMR tumors share common histopathologic characteristics that may render them susceptible to immune checkpoint inhibitors such as anti-PD-(L)1 monoclonal antibodies[1–3]
- Clinical data indicate MSI-H/dMMR as a strong predictive biomarker for immunotherapy.[4] This is of particular interest in tumor types such as endometrial cancer, in which the incidence of MSI-H/dMMR has been reported to be nearly 30%[5]
- Tislelizumab is a humanized, IgG4 monoclonal antibody with high affinity and binding specificity for PD-1 that was engineered to minimize Fcγ receptor binding on macrophages, thereby abrogating antibody-dependent cellular phagocytosis[6,7]
- Primary results from the Phase 2 RATIONALE 209 study showed that tislelizumab was generally well tolerated and demonstrated a clinically meaningful improvement in the ORR in patients with previously treated, locally advanced, unresectable or MSI-H/dMMR solid tumors compared with the historical control rate (45.9% vs 10%, respectively)[8]
- Here, we report results from the updated analysis for patients with gynecological MSI-H/dMMR tumors

dMMR, mismatch repair-deficient; MSI-H, microsatellite instability-high; ORR, objective response rate; PD-(L)1, programmed cell death protein 1/programmed death- ligand 1

1. Dudley JC, et al. Clin Cancer Res 2016;22:813–20; 2. Llosa NJ, et al. Cancer Discov 2015;5:43–51; 3. Giannakis M, et al. Cell Rep 2016;15:857–65; 4. Yan L, et al. Cancer Commun 2018;38:6; 5. Hause RJ, et al. Nat Med 2016;22:1342–50; 6. Cheng A,et al. Ann Oncol 2018;29:v27-8; 7. Huang D, et al. J Clin Oncol 2018; 36:TPS3112; 8. Li J, et al. J Clin Oncol 2021;39;(15_suppl):2569

Study design

RATIONALE 209 (NCT03736889) is an ongoing single-arm, open-label, multicenter study conducted at 26 sites in China

Key eligibility criteria:

- Adults (≥ 18 years) with locally advanced unresectable or metastatic histologically-confirmed MSI-H/dMMR solid tumors
- Received/refused prior cancer therapy regimen(s) for advanced or metastatic disease*
- ≥ 1 measurable lesion per RECIST v1.1
- ECOG PS ≤ 1
- No prior checkpoint inhibitor treatment

N=80

Tislelizumab 200 mg IV Q3W → Treatment until disease progression, unacceptable toxicity, or withdrawal for other reasons → Continued safety and survival follow-up

Primary endpoint: IRC-assessed ORR per RECIST v1.1

Secondary endpoints: IRC-assessed DoR, TTR, DCR and PFS per RECIST v1.1, OS, investigator-assessed ORR, DoR, TTR, DCR and PFS per RECIST v1.1; and safety and tolerability

Exploratory endpoints: Retrospective analysis of PD-L1 expression

*≥ 2 prior regimens for CRC; ≥ 1 prior regimens for other cancer types

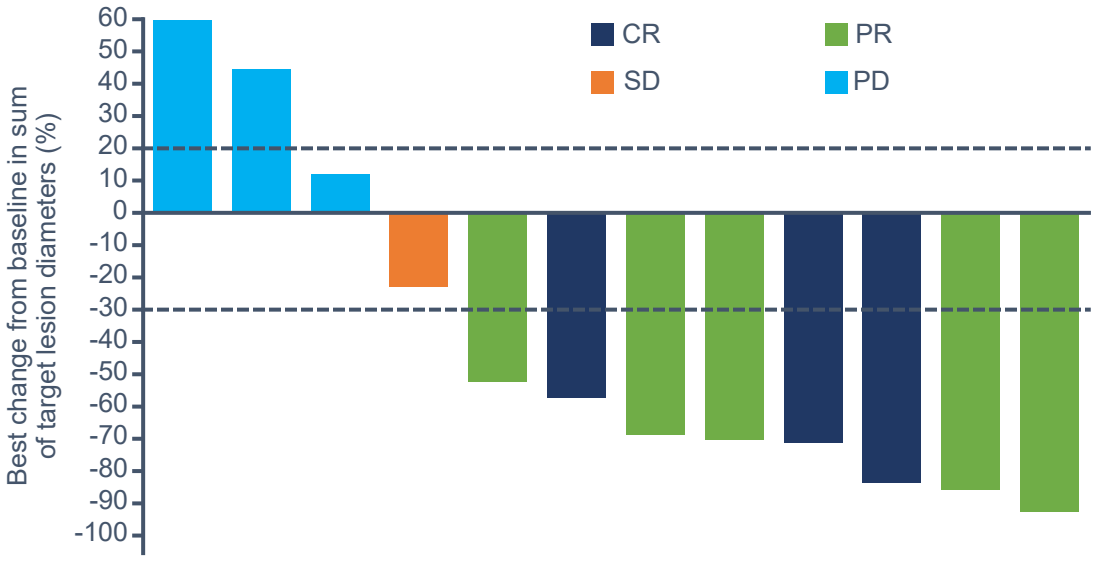
CRC, colorectal cancer; DCR, disease control rate; dMMR, mismatch repair-deficient; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICR, independent review committee; IV, intravenously; MSI-H, microsatellite instability-high; ORR, objective response rate; OS, overall survival; PD-L1, programmed death- ligand 1; PFS, progression-free survival; Q3W, every three weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response

Results: Efficacy

Tumor response by IRC per RECIST v1.1 (EE analysis set)

	All gynecological (N=15)	Cervical cancer (n=1)	Endometrial cancer (n=13)	Ovarian cancer (n=1)
ORR (CR + PR)				
n (%) 95% CI p-value	8 (53.3) 26.6, 78.7 < 0.0001	1 (100) 2.5, 100 -	6 (46.2) 19.2, 74.9 -	1 (100) 2.5, 100 -
Confirmed best overall response, n (%)				
CR PR SD PD NA*	3 (20.0) 5 (33.3) 1 (6.7) 4 (26.7) 2 (13.3)	0 1 (100) 0 0 0	3 (23.1) 3 (23.1) 1 (7.7) 4 (30.8) 2 (15.4)	0 1 (100) 0 0 0
Disease control rate (CR + PR + SD)				
n (%) 95% CI	9 (60.0) 32.3, 83.7	1 (100) 2.5, 100	7 (53.8) 25.1, 80.8	1 (100) 2.5, 100
Time to response				
Median (range), weeks	9.1 (8.4–39.1)	9.1 (9.1–9.1)	9.1 (8.4–39.1)	8.7 (8.7–8.7)

Best percentage change in target lesion by IRC (EE analysis set)†



Data cut-off: July 8, 2021

*Not assessable captured patients for whom no post-baseline tumor assessments were performed. †One patient was assessed as PD based on new lesion and therefore the target lesion was not evaluated for this patient. CI, confidence interval; CR, complete response; EE, efficacy evaluable; IRC, independent review committee; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease

Results: Safety

Safety summary (safety analysis set)

	All gynecological (N=17)	
Adverse event, n (%)	**TEAE**	**TRAE**
Any/≥ Grade 3	17 (100)/10 (58.8)	17 (100)/9 (52.9)
Serious	6 (35.3)	4 (23.5)
Leading to death	1 (5.9)*	0 (0.0)
Leading to treatment discontinuation	1 (5.9)	1 (5.9)
Leading to treatment modification	4 (23.5)	3 (17.6)

- Immune-mediated TEAEs were reported in 7/17 (41.2%) of patients

TEAEs in ≥ 15% of patients (any grade), by all grades and ≥ Grade 3 safety analysis set

n (%)	All gynecological (N=17)	
	All grade	**≥ Grade 3**
AST increased	9 (52.9)	1 (5.9)
ALT increased	8 (47.1)	1 (5.9)
White blood cell count decreased	7 (41.2)	0 (0.0)
Anemia	7 (41.2)	1 (5.9)
Neutrophil count decreased	5 (29.4)	0 (0.0)
Weight increased	5 (29.4)	0 (0.0)
Pyrexia	5 (29.4)	0 (0.0)
Hypoalbuminemia	5 (29.4)	0 (0.0)
Hypothyroidism	5 (29.4)	0 (0.0)
Vomiting	4 (23.5)	0 (0.0)
Rash	4 (23.5)	0 (0.0)
Blood alkaline phosphatase increased	3 (17.6)	0 (0.0)
Gamma-glutamyltransferase increased	3 (17.6)	1 (5.9)
Platelet count decreased	3 (17.6)	0 (0.0)
Malaise	3 (17.6)	0 (0.0)
Edema peripheral	3 (17.6)	0 (0.0)
Hyperuricemia	3 (17.6)	0 (0.0)
Abdominal pain	3 (17.6)	0 (0.0)
Constipation	3 (17.6)	0 (0.0)
Nausea	3 (17.6)	0 (0.0)
Urinary tract infection	3 (17.6)	3 (17.6)
Cough	3 (17.6)	0 (0.0)

Data cut-off: July 8, 2021

*Due to multiple organ dysfunction syndrome. Treatment modification included dose delay and infusion interruption

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event

Conclusions

- This subgroup analysis demonstrates that tislelizumab was clinically active in patients with gynecological MSI-H/dMMR tumors and was generally well tolerated with no new safety signals
- These data support tislelizumab as a potential new treatment option for patients with gynecological MSI-H/dMMR tumors
- Further investigation with a larger population is warranted to confirm the clinical benefit of tislelizumab in these patients

dMMR, mismatch repair-deficient; MSI-H, microsatellite instability-high

Unlabeled/Investigational Uses

- I will be discussing any unlabeled or investigational uses of any pharmaceutical products or medical devices
  - Tislelizumab in MSI-H/dMMR solid tumors (gynecological subgroup)

dMMR, mismatch repair-deficient; MSI-H, microsatellite instability-high