A Phase 1A/1B trial of Tislelizumab, an Anti-PD-1 Antibody (Ab), in Patients (Pts) With Advanced Solid Tumors

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Background Tislelizumab, a humanized IgG4 monoclonal Ab with high affinity and specificity for PD-1, was engineered to minimize binding to FcγR on macrophages, thus abrogating antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Previous reports from this first-in-human study (NCT02407990), and other early phase studies, suggested tislelizumab was generally well tolerated and had antitumor activity in pts with advanced solid tumors. Here we report the effects of tislelizumab in a subset of pts enrolled in phase 1A/1B.

Methods Eligible patients with advanced esophageal [EC], gastric [GC], hepatocellular [HCC], and non-small cell lung [NSCLC] cancers were treated with tislelizumab 2 or 5 mg/kg every 2 wks or 3 wks (Q3W); 97% received 5mg/kg Q3W. Adverse events (AEs) were assessed per NCI-CTCAE 4.03 criteria and tumor assessments performed every 9 wks using RECIST v1.1.

Results Of the 207 pts (EC=54; GC=54; HCC=50; NSCLC=49), 114 were male, 111 were Asian, 78 were Caucasian and all but one received ≥1 prior anticancer therapy. Treatment-related AEs (TRAEs) occurring in ≥5% of pts were fatigue (8.7%), decreased appetite (6.8%), rash (6.8%), hypothyroidism (6.3%), and nausea (6.3%). Grade ≥3 TRAEs occurring in ≥2 pts were pneumonitis (n=3), elevated AST (n=3), and elevated ALT (n=2). Grade 5 TRAEs occurred in two pts: pneumonitis in a pt with NSCLC with compromised pulmonary function and acute hepatitis in a pt with HCC with rapidly progressing disease. As of 27 Apr 2018, a total of 23 pts remained on study treatment; median duration of study follow-up ranged from 4.9–9.9 mo. Responses in each tumor type are presented in the table.

Conclusion Tislelizumab was generally well tolerated and antitumor activity was observed in each tumor type. Tislelizumab, as monotherapy and in combination, is being evaluated in multiple phase 2 and phase 3 studies.

Best Overall Response, Confirmed	EC N=53	GC N=52	HCC N=49	NSCLC N=44
CR, n	1	0	0	0
PR, n	5	7	6	6
SD, n	14	9	19	23
PD, n	25	31	23	12
Not evaluable/missing, n	8	5	1	3
ORR, % (95% CI)	**11.3 (4.3, 23.0)**	**13.5 (5.6, 25.8)**	**12.2 (4.6, 24.8)**	**13.6 (5.2, 27.4)**
DCR, % (95% CI)	**37.7 (24.8, 52.1)**	**30.8 (18.7, 45.1)**	**51.0 (36.3, 65.6)**	**65.9 (50.1, 79.5)**

ORR=CR+PR; DCR=CR+PR+SD.

Abbreviations: CI, confidence interval; CR, complete response; DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.