Long-term pooled safety analysis of tislelizumab as monotherapy or in combination with chemotherapy in patients with advanced cancers

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Background: The PD-1 inhibitor tislelizumab (TIS) has demonstrated efficacy and tolerability in patients (pts) with advanced cancers. To evaluate long-term safety of TIS as monotherapy (mono) or in combination (combo) with chemotherapy in pts with advanced gastrointestinal (GI) and lung cancers, data were pooled from 8 pivotal phase III studies conducted between 2017 and 2023.

Methods: 2636 adult pts with GI (n=1415) or lung (n=1221) cancers and an ECOG PS of 0-1, who received ≥1 dose of study drug, were included. Endpoints included immune-mediated adverse events (imAEs) by tumor type, treatment (Tx) duration, and race. Early and delayed imAEs, defined as occurring within 1 year (yr) and >1 yr after starting TIS, respectively, were also evaluated.

Results: Median (range) Tx duration in the GI and lung cancer studies was 4.9 (0.1-50.4) and 6.2 (0.2-44.9) months, respectively, with 20.9% and 29.6% of pts, respectively, having ≥1 yr exposure. Most pts were Asian (GI mono: 76.4%; GI combo: 74.9%; lung mono: 79.2%; lung combo: 100%). ImAEs occurred in 32.5% of pts in the GI mono and combo studies (**Table**); most were low grade, with grade ≥3 imAEs reported in 6.2% (mono) and 8.2% (combo) of pts. Incidence of imAEs in the mono and combo lung studies, respectively, was 34.3% and 43.7% (grade ≥3: 6.4% and 9.6%). ImAE incidence was comparable between Asian and White race subgroups, respectively, in the GI mono (33.6% vs 29.5%), GI combo (34.9% vs 23.9%), and lung mono (35.5% vs 32.3%) studies. Most imAEs occurred within 1 yr of starting TIS in the GI (mono: 32.0%; combo: 32.4%) and lung (mono: 34.1%; combo: 42.2%) studies. Delayed imAEs occurred less often than early imAEs; of pts still on Tx or in study follow-up 1 yr after initial Tx, 54/757 (7.1%) in GI studies and 86/804 (10.7%) in lung studies experienced a delayed imAE. Frequently reported imAEs were consistent, regardless of time of onset (early vs delayed).

Conclusions: This long-term, retrospective, pooled analysis supports TIS as a tolerable Tx for pts with advanced GI and lung cancers. Delayed imAEs were relatively infrequent and were consistent with the established safety

ImAEs in GI and Lung Cancer Studies

	GI Mono (n=593)	**GI Mono (n=593)**	**GI Combo (n=822)**	**GI Combo (n=822)**	**Lung Mono (n=534)**	**Lung Mono (n=534)**	**Lung Combo (n=687)**	**Lung Combo (n=687)**
	Within 1 yr	Overall	Within 1 yr	Overall	Within 1 yr	Overall	Within 1 yr	Overall
Pts with any imAE, n (%)	190 (32.0)	193 (32.5)	266 (32.4)	267 (32.5)	182 (34.1)	183 (34.3)	290 (42.2)	300 (43.7)
Most frequent* imAEs, n (%)								
Skin adverse reaction	81 (13.7)	83 (14.0)	93 (11.3)	93 (11.3)	52 (9.7)	53 (9.9)	135 (19.7)	137 (19.9)
Hypothyroidism	61 (10.3)	62 (10.5)	98 (11.9)	101 (12.3)	69 (12.9)	70 (13.1)	105 (15.3)	108 (15.7)
Pneumonitis	28 (4.7)	28 (4.7)	44 (5.4)	45 (5.5)	47 (8.8)	47 (8.8)	61 (8.9)	70 (10.2)
Hyperthyroidism	25 (4.2)	26 (4.4)	25 (3.0)	25 (3.0)	28 (5.2)	28 (5.2)	40 (5.8)	45 (6.6)

*>5% of pts.