Preliminary Results With Tislelizumab in Chinese Patients With Non-Small Cell Lung Cancer

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Immune Checkpoint Inhibitors in NSCLC

- Non-small cell lung cancer (NSCLC) accounts for 80–85% of all lung cancers[1]
- The prognosis for patients with NSCLC is particularly poor when it is diagnosed in later stages where 5-year survival rates are approximately 36% for Stage IIIA, 26% for Stage IIIB, and 1% for Stage IV[2]
- Recent studies of immune checkpoint inhibitors have shown efficacy in patients with PD-L1-positive (PD-L1^{+}) advanced NSCLC[3–5] as well as in patients with PD-L1-negative (PD-L1^{-}) NSCLC[5]

[1]PDQ Adult Treatment Editorial Board. Available from: https://www.ncbi.nlm.nih.gov/books/NBK65909/. Accessed April 2018; [2]Non-small cell lung cancer survival rates, by stage. American Cancer Society. 2017. Available from: https://www.cancer.org/content/cancer/en/cancer/nonsmall-cell-lung-cancer/detection-diagnosis-staging/survival-rates.html. Accessed May 2018; [3]Gettinger SN, Horn L, Gandhi L, et al. *J Clin Oncol*. 2015;33(18):2004–2012; [4]Herbst RS, Bass P, Kim DW, et al. *Lancet*. 2016;387(10027):1540–1550; [5]Rizvi NA, Mazières J, Planchard D, et al. *Lancet Oncol*. 2015;16(3):257–265.

Tislelizumab: A Uniquely Engineered Anti–PD-1 Monoclonal Antibody

- Tislelizumab is a humanized IgG4 monoclonal antibody with high affinity/specificity for PD-1
- Tislelizumab as specifically engineered to minimize FcγR binding on macrophages, thereby abrogating antibody-dependent phagocytosis, a potential mechanism of T-cell clearance

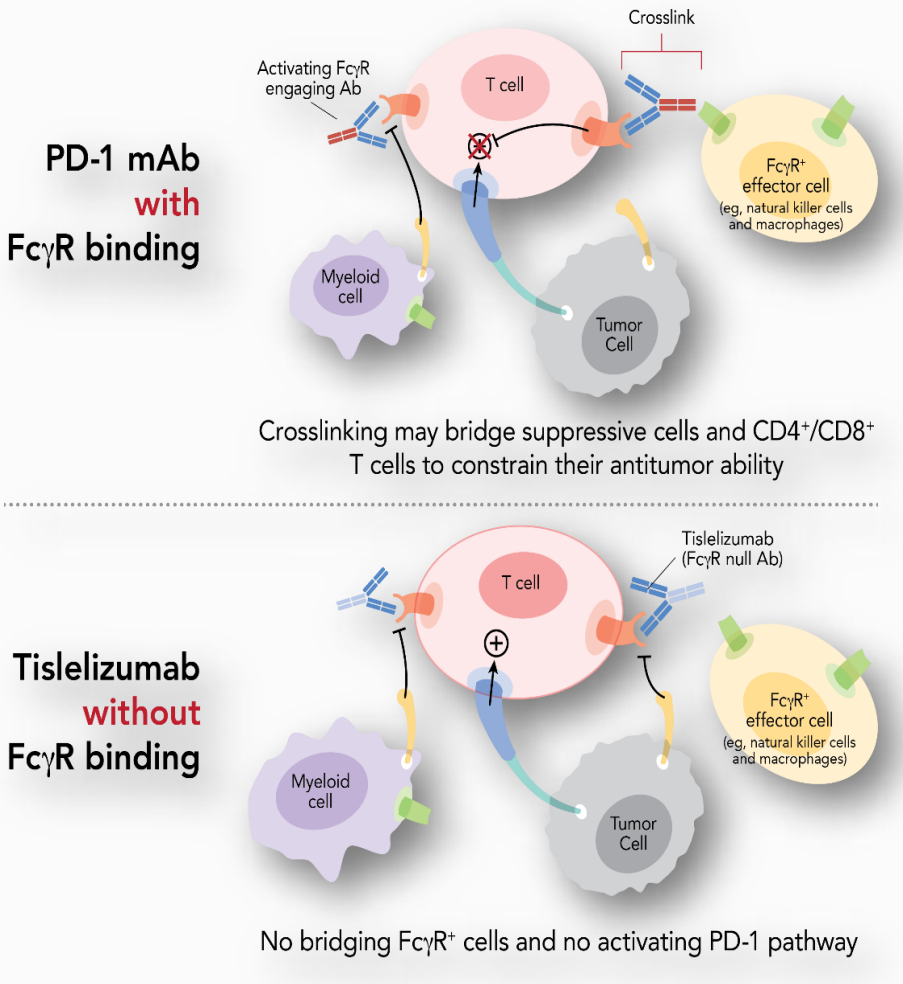


Figure modified from Dahan R, et al. *Cancer Cell*. 2015;28:285–295.
Abbreviations: Ab, antibody; PD-1, programmed cell death-1.

BGB-A317-102 Study: Ongoing, Phase 1/2 Study of Tislelizumab in Chinese Patients

1: Dose verification*

200 mg Q3W

RP2D

2: Indication expansion**

- Arm 1: Melanoma (n=20)
- Arm 2: NSCLC† (PD-L1 ≥10%; n=20)
- Arm 3: NSCLC† (PD-L1<10%; n=20)

PD-L1 expression status was tested prospectively at a central laboratory (using Ventana PD-L1 protocol [SP263 antibody])
PD-L1⁺ (Arm 2) was defined as expression of PD-L1 in ≥10% tumor cells; otherwise tumors were considered PD-L1⁻ (Arm 3)

- Arm 7: Urothelial carcinoma (n=20)
- Arm 8: MSI-H or dMMR CRC (n=20)
- Arm 9: TNBC, HNSCC, SCNEC, or other tumors with MSI-H or dMMR (n=20)
- Arm 10: Nasopharyngeal carcinoma (n=20)
- Arm 11: Child-Pugh A HCC (n=20)

Here, we report the preliminary results from the phase 2 cohorts (indication expansion) of this multicenter clinical study of tislelizumab in Chinese patients with NSCLC

Abbreviations: CRC, colorectal cancer; HCC, hepatocellular carcinoma; HNSCC, head and neck squamous cell carcinoma; dMMR, mismatch repair deficiency; MSI-H, microsatellite instability high; NSCLC, non-small cell lung cancer; PD-L1, programmed cell death ligand-1; Q3W, every 3 weeks; RP2D, recommended phase 2 dose; SCNEC, small cell neuroendocrine carcinoma; TNBC, triple-negative breast carcinoma.

†Patients must be EGFR wild-type and of no known ALK gene rearrangements

Patient Disposition

- As of May 11, 2018, 46 patients with NSCLC (n=21, PD-L1^{+}; n=25, PD-L1^{-}) were enrolled in the study; 15 remained on treatment and 31 discontinued tislelizumab
  - One patient discontinued due to a grade 3 AE (hypotension) considered not related to treatment
- Across the 46 patients, the median treatment duration of tislelizumab was 4.1 months (range: 0.2–11.27 months)

	PD-L1^{+} (n=21)	PD-L1^{-} (n=25)	Overall (N=46)
Active on tislelizumab, n (%)	**7 (33.3)**	**8 (32.0)**	**15 (32.6)**
Reason for tislelizumab discontinuation, n (%)	**14 (66.7)**	**17 (68.0)**	**31 (67.4)**
AE	0	1 (4.0)	1 (2.2)
Death	1 (4.8)	1 (4.0)	2 (4.3)
Withdrawal of consent	2 (9.5)	2 (8.0)	4 (8.7)
Disease progression	10 (47.6)	13 (52.0)	23 (50.0)
Other	1 (4.8)	0	1 (2.2)
Median treatment duration, months (range)	**3.5 (0.2 – 11.2)**	**4.4 (0.69 – 11.3)**	**4.1 (0.2 – 11.3)**
Median follow-up duration, months (range)	**6.3 (0.2 – 11.8)**	**8.6 (2.0 – 10.8)**	**8.4 (0.2 – 11.8)**

Abbreviations: AE, adverse event; PD-L1, programmed cell death ligand-1.

Data cut-off: 11 May 2018

Patient Demographics and Baseline Disease Characteristics

- The majority of patients were male (n=32; 69.6%), former smokers (n=26; 56.5%), and had received ≥1 prior anticancer therapy (n=44; 95.6%)
  - In Arm 2 (PD-L1^{+}, n=21), 81% of patients were male, 71.4% were former smokers, and all had received ≥1 prior anticancer therapy
  - In Arm 3 (PD-L1^{-}, n=25), 60% of patients were male, 44% were former smokers, and 92% had receive ≥1 prior anticancer therapy

	PD-L1^{+} (n=21)	PD-L1^{-} (n=25)	Overall (N=46)
Median age, years (range)	58.0 (26 - 72)	54.0 (37 - 72)	55.5 (26 - 72)
Male, n (%)	17 (81)	15 (60)	32 (69.6)
Smoking status, n (%)			
Former	15 (71.4)	11 (44)	26 (56.5)
Current	0	1 (4)	1 (2.2)
Non-smoker	6 (28.6)	13 (52)	19 (41.3)
Prior anticancer radiotherapy, n (%)	9 (42.9)	7 (28)	16 (34.8)
Number of prior lines of anticancer therapy regimens, n (%)			
0	0	2 (8)	2 (4.3)
1	5 (23.8)	9 (36)	14 (30.4)
2	8 (38.1)	7 (28)	15 (32.6)
≥3	8 (38.1)	7 (28)	15 (32.6)

Abbreviation: PD-L1, programmed cell death ligand-1.

Data cut-off: 11 May 2018

Tislelizumab Response by PD-L1 Expression Status

- A total of 17 of 21 patients (81%) with PD-L1^{+} tumors and all 25 patients (100%) with PD-L1^{-} tumors had ≥1 postbaseline tumor assessment and were evaluable for antitumor activity by the investigator per RECIST v1.1 criteria
- ORR for PD-L1^{+} and PD-L1^{-} NSCLC patients were 11.8% and 20%, respectively

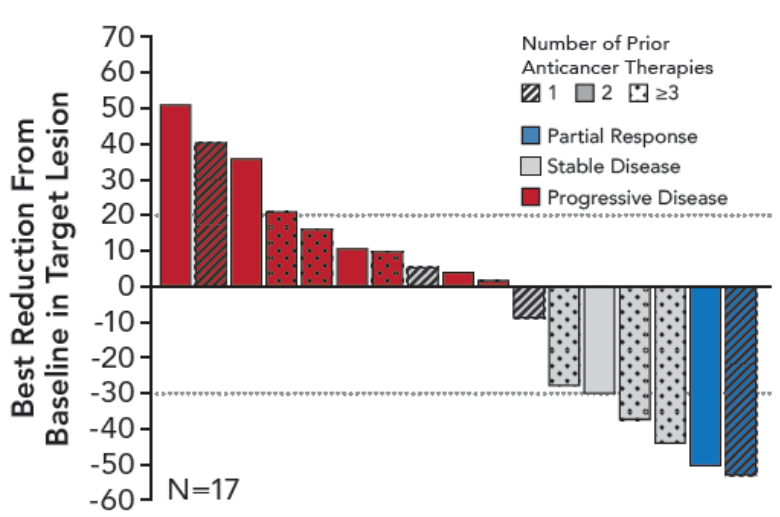
	PD-L1^{+} (n=17)	PD-L1^{-} (n=25)	Overall (N=42)
BOR per RECIST v1.1 (confirmed)			
Complete response (CR)	0	0	0
Partial response (PR)	2 (11.8)	5 (20)	7 (16.7)
Stable disease (SD)	6 (35.3)	11 (44)	17 (40.5)
Progressive disease (PD)	9 (52.9)	9 (36)	18 (42.9)
ORR (CR+PR), % (95% CI)	**11.8 (1.46, 36.44)**	**20.0 (6.83, 40.70)**	**16.7 (6.97, 31.36)**

Disease assessment by radiographic imaging was performed every 9 weeks during first 12 months and every 12 weeks thereafter.
Abbreviation: CI, confidence interval; PD-L1, programmed cell death ligand-1.

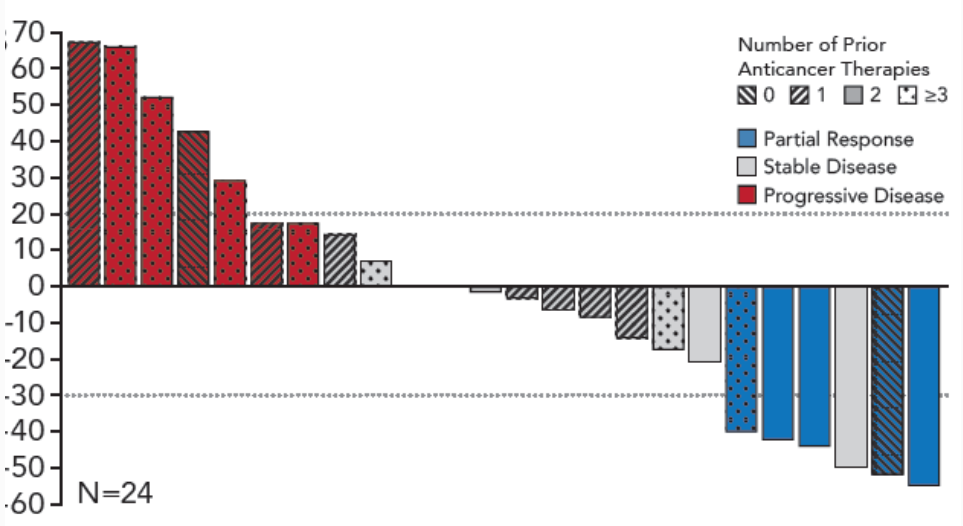
Data cut-off: 11 May 2018

Maximum Tumor Reduction in Evaluable Patients With PD-L1+ NSCLC or PD-L1– NSCLC

Patients With PD-L1^{+} NSCLC



Patients With PD-L1^{-} NSCLC



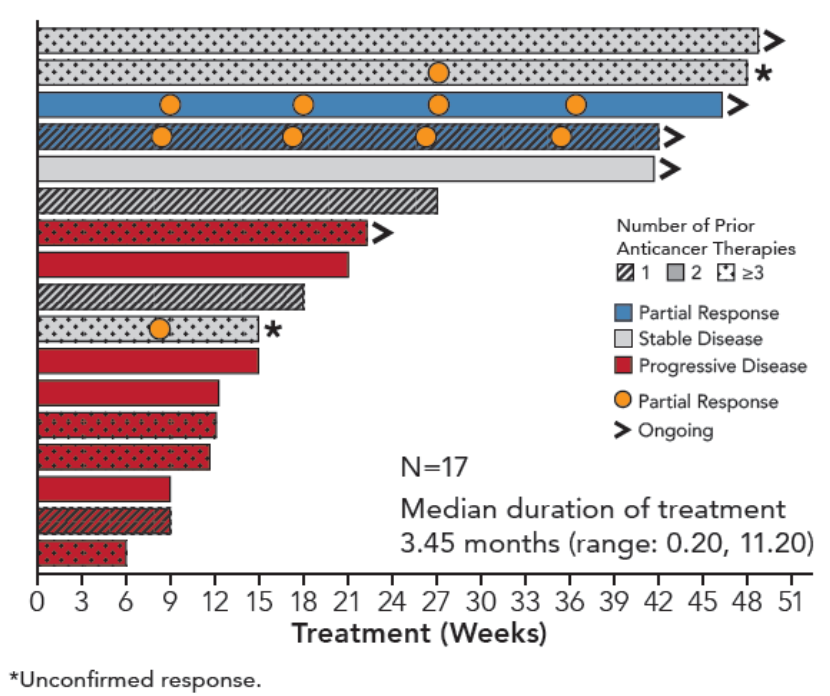
One patient with PD-L1^{-} NSCLC did not have a postbaseline target lesion result and was excluded. The patient experienced progressive disease due to the development of a new lesion.

Abbreviation: NSCLC, non-small cell lung cancer; PD-L1, programmed cell death ligand-1.

Data cut-off: 11 May 2018

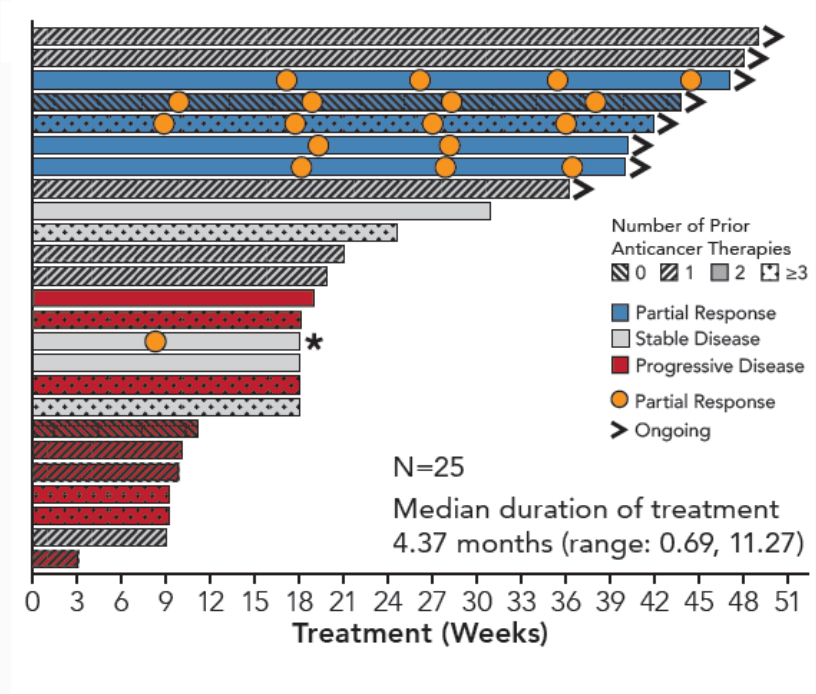
Duration of Tislelizumab Treatment and Response in Evaluable Patients With NSCLC

Patients With PD-L1^{+} NSCLC



*Unconfirmed response.

Patients With PD-L1^{-} NSCLC

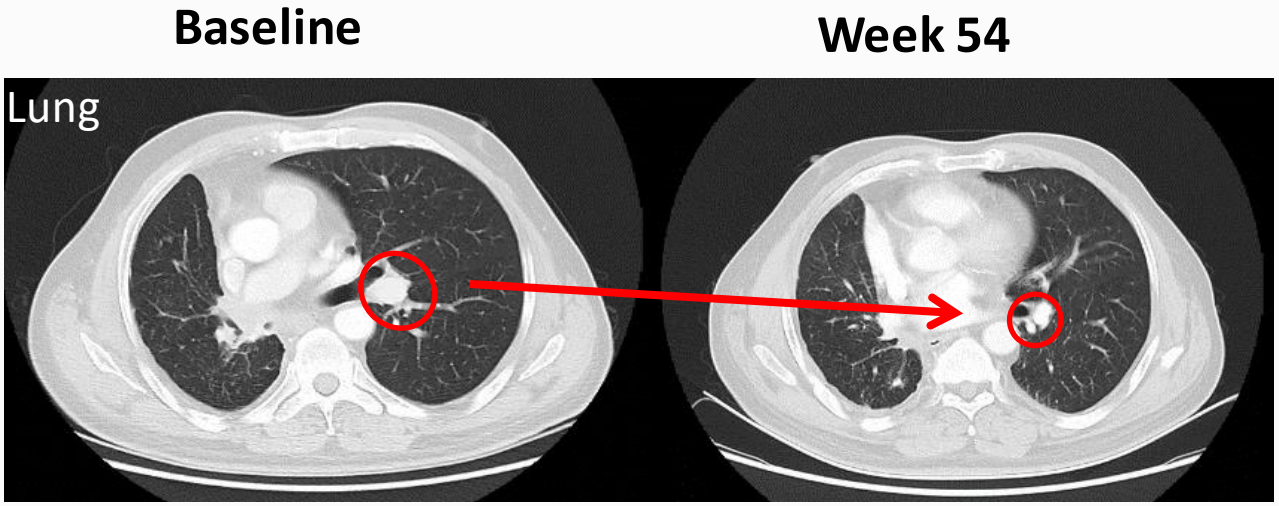


Abbreviations: NSCLC, non-small cell lung cancer; PD-L1, programmed cell death ligand-1.

Data cut-off: 11 May 2018

Case Example: Radiographic Images of a Patient With PD-L1+ NSCLC

- **Gender:** Male
- **Age:** 62 years
- **Former smoker**
- **Histological Type:** Squamous cell carcinoma
- **Metastases:** Lymph node, Lung, pleural effusion
- **Prior line treatments**: 1
- **Best overall response**: PR



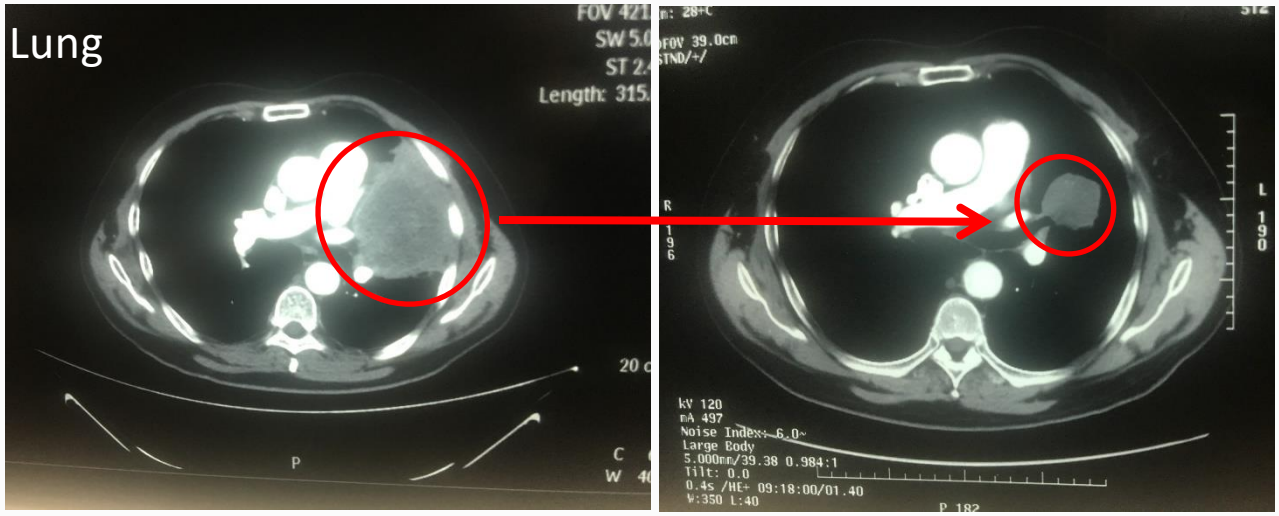
	Baseline	Week 54
Target lesion SLD (mm)	61	29
Non Target Lesion		Non-CR/Non-PD
New Lesion		None

Abbreviations: CR, complete response; NSCLC, non-small cell lung cancer; PD, progressive disease; PD-L1, programmed cell death ligand-1; PR, partial response; SLD, sum of the lesion diameters.

Case Example: Radiographic Images of a Patient With PD-L1⁻ NSCLC

- **Gender:** Male
- **Age:** 56 years
- **Former smoker**
- **Histological Type:** Adenocarcinoma
- **Metastases:** Lymph node, liver, adrenal gland
- **Prior line treatments**: 2
- **Best overall response**: PR

Baseline **Week 54**



	Baseline	Week 54
Target lesion SLD (mm)	100	58
Non Target Lesion		Non-CR/Non-PD
New Lesion		None

Abbreviations: CR, complete response; NSCLC, non-small cell lung cancer; PD, progressive disease; PD-L1, programmed cell death ligand-1; PR, partial response; SLD, sum of the lesion diameters.

Adverse Events Considered Related to Tislelizumab in Chinese Patients With NSCLC

Treatment-related Adverse Events Occurring in ≥2 Patients in overall NSCLC population

	Arm 2 (PD-L1^{+})		Arm 3 (PD-L1^{-})		Overall	
	All grades (n=21)	Grade ≥3 (n=21)	All grades (n=25)	Grade ≥3 (n=25)	All grades (N=46)	Grade ≥3 (N=46)
Subjects who experienced ≥1 TRAE	**15 (71.4)**	**0 (0)**	**15 (60.0)**	**5 (20.0)**	**30 (65.2)**	**5 (10.9)**
Transaminases increased	5 (23.8)	0 (0)	7 (28.0)	3 (12.0)	12 (26.1)	3 (6.5)
Increased AST	*5 (23.8)*	*0 (0)*	*6 (24.0)*	*3 (12.0)*	*11 (23.9)*	*3 (6.5)*
Increased ALT	*4 (19.0)*	*0 (0)*	*6 (24.0)*	*2 (8.0)*	*10 (21.7)*	*2 (4.3)*
Rash	2 (9.5)	0 (0)	3 (12.0)	0 (0)	5 (10.9)	0 (0)
Hypothyroidism	3 (14.3)	0 (0)	2 (8.0)	0 (0)	5 (10.9)	0 (0)
Increased bilirubin	3 (14.3)	0 (0)	1 (4.0)	0 (0)	4 (8.7)	0 (0)
Increased GGT	3 (14.3)	0 (0)	1 (4.0)	1 (4.0)	4 (8.7)	1 (2.2)
Nausea	2 (9.5)	0 (0)	2 (8.0)	0 (0)	4 (8.7)	0 (0)
Pyrexia	2 (9.5)	0 (0)	2 (8.0)	0 (0)	4 (8.7)	0 (0)
Decreased blood TSH	0 (0)	0 (0)	3 (12.0)	0 (0)	3 (6.5)	0 (0)
Increased blood TSH	0 (0)	0 (0)	3 (12.0)	0 (0)	3 (6.5)	0 (0)
Vomiting	1 (4.8)	0 (0)	2 (8.0)	0 (0)	3 (6.5)	0 (0)
Increased free thyroxine	0 (0)	0 (0)	2 (8.0)	0 (0)	2 (4.3)	0 (0)
Decreased weight	0 (0)	0 (0)	2 (8.0)	0 (0)	2 (4.3)	0 (0)
Anemia	2 (9.5)	0 (0)	0 (0)	0 (0)	2 (4.3)	0 (0)

Data presented as n (%). **Abbreviations:** ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; NSCLC, non-small cell lung cancer; PD-L1, programmed cell death ligand-1; TSH, thyroid stimulating hormone.

Data cut-off: 11 May 2018

Immune-Related Adverse Events

- A total of 26 patients experienced immune-related AEs (irAEs)*
- The most common irAEs (defined as occurring in ≥10% of patients) were increased AST (n=11), increased ALT (n=10), hypothyroidism (n=5), and rash (n=5)
- Most irAEs were grade ≤2 in severity; five patients experienced at least one grade ≥3 irAE
  - Increased AST (n=3), increased ALT (n=2), increased GGT (n=1), maculo-papular rash (n=1), and hyperglycemia (n=1)

*Treatment-related adverse events reported in this study were categorized as immune related according to a predefined list of terms from the study sponsor

Immune-related AEs Occurring in ≥2 Patients overall NSCLC population

	Arm 2 (PD-L1+)		Arm 3 (PD-L1−)		Overall	
	All grades (n=21)	Grade ≥3 (n=21)	All grades (n=25)	Grade ≥3 (n=25)	All grades (N=46)	Grade ≥3 (N=46)
Subjects with at least one immune-related AE	**12 (57.1)**	**0 (0)**	**14 (56.0)**	**5 (20.0)**	**26 (56.5)**	**5 (10.9)**
Transaminases increased	5 (23.8)	0 (0)	7 (28.0)	3 (12.0)	12 (26.1)	3 (6.5)
Increased AST	*5 (23.8)*	*0 (0)*	*6 (24.0)*	*3 (12.0)*	*11 (23.9)*	*3 (6.5)*
Increased ALT	*4 (19.0)*	*0 (0)*	*6 (24.0)*	*2 (8.0)*	*10 (21.7)*	*2 (4.3)*
Hypothyroidism	3 (14.3)	0 (0)	2 (8.0)	0 (0)	5 (10.9)	0 (0)
Rash	2 (9.5)	0 (0)	3 (12.0)	0 (0)	5 (10.9)	0 (0)
Increased bilirubin	3 (14.3)	0 (0)	1 (4.0)	0 (0)	4 (8.7)	0 (0)
Increased GGT	3 (14.3)	0 (0)	1 (4.0)	1 (4.0)	4 (8.7)	1 (2.2)
Decreased blood TSH	0 (0)	0 (0)	3 (12.0)	0 (0)	3 (6.5)	0 (0)

Data presented as n (%).
Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase; PD-L1, programmed cell death ligand-1; TSH, thyroid stimulating hormone.

Data cut-off: 11 May 2018

Safety and Tolerability of Tislelizumab

- Across the two arms, a total of 14 patients had serious AEs
  - Three patients experienced serious TRAEs (nausea and vomiting, increased AST, and hyperglycemia, n=1 each)
- Across these two study arms, three patients had a TEAE with a fatal outcome (multiple organ dysfunction syndrome, central nervous system metastases, hypotension, n=1 each); none were determined to be related to treatment

Abbreviations: AE, adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse events.

Data cut-off: 11 May 2018

Conclusions

- Preliminary data suggest tislelizumab is generally well tolerated and has antitumor activity in patients with advanced NSCLC
  - With a median follow-up of 8.4 months, 15 patients (32.6%) remain on study
  - The rate of treatment discontinuation due to an AE was low (n=1/46)
- Partial responses were observed in both PD-L1^{+} (n=2/17) and PD-L1^{-} (n=5/25) patients with NSCLC
- There was no clear relationship between PD-L1 status and clinical efficacy measures based on the small sample size
- Adverse events reported in the two cohorts of PD-L1^{+} and PD-L1^{-} were consistent with the overall safety profile of tislelizumab observed in previous studies with other tumor types and were generally of low severity
- The preliminary safety profile and antitumor activity support continued development of tislelizumab in patients with advanced NSCLC; phase 3 studies of tislelizumab as treatment for NSCLC have been initiated (NCT03358875 and NCT03594747)

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