Safety and Efficacy of Dostarlimab in Patients With Recurrent/Advanced Non-Small Cell Lung Cancer (NSCLC)

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Background

- Dostarlimab (TSR-042) is a humanized programmed death (PD)-1 receptor monoclonal antibody that blocks interaction with PD-1 ligands, PD-L1 and PD-L2
- PD-1 and PD-L1 inhibitors have shown efficacy and safety in patients with advanced NSCLC[1]
- Dostarlimab is being evaluated as monotherapy in patients with advanced solid tumors in the ongoing phase 1 GARNET trial (NCT02715284)
- Here, we report efficacy and safety data from patients within the NSCLC cohort of part 2B of the GARNET trial

Conclusions

- Dostarlimab demonstrated antitumor activity regardless of TPS scores in a PD-L1 unselected population of patients with recurrent/advanced NSCLC who have progressed from platinum-based therapy
- Despite the majority of enrolled patients having PD-L1–low or PD-L1–negative tumors, because of the availability of immunotherapy for patients having tumors with TPS ≥50, dostarlimab showed encouraging ORR and DOR
- Disease control rate was similar across all TPS scores
- Dostarlimab demonstrated a low discontinuation rate due to treatment-related adverse events (TRAEs)
- TRAEs were characteristic of anti–PD-1 agents
- Dostarlimab is currently being investigated as monotherapy and combination therapy in multiple tumor types

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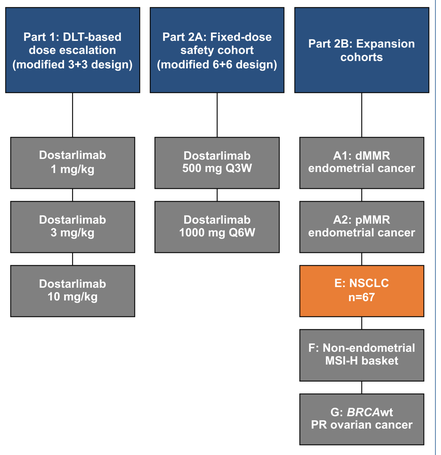
Objective

- To evaluate the antitumor activity of dostarlimab in patients with NSCLC, as measured by investigator-assessed immune-related overall response rate (irORR) per immune-related Response Evaluation Criteria in Solid Tumors (irRECIST)

Methods

- GARNET was conducted in 2 parts: part 1 was a weight-based dose escalation phase to characterize the pharmacokinetic/dynamic profile; part 2A was a fixed-dose safety phase to determine the RP2D to be tested in the expansion cohorts of part 2B (**Figure 1**)
- Patients with disease progression after ≥1 prior platinum-based chemotherapy regimen for recurrent/advanced NSCLC and were PD-(L)1 naive were enrolled
- Patients with a known epidermal growth factor receptor (*EGFR*) mutation (or anaplastic lymphoma kinase [*ALK*] translocation) must have received a prior chemotherapy regimen and EGFR tyrosine kinase inhibitor (or ALK inhibitor)
- Patients received 500 mg of dostarlimab every 3 weeks (Q3W) for cycles 1 to 4, and 1000 mg every 6 weeks (Q6W) until disease progression
- Tumor PD-L1 expression was measured on tumor samples collected prior to enrollment; PD-L1 tumor proportion scores (TPS) were categorized as <1%, 1 to 49%, and ≥50%

Figure 1. GARNET Study Design



DLT, dose-limiting toxicity; dMMR, mismatch repair deficient; MSI-H, microsatellite instability-high; NSCLC, non-small cell lung cancer; pMMR, mismatch repair proficient; PR, platinum resistant; Q3W, every 3 weeks; Q6W, every 6 weeks; RP2D, recommended phase 2 dose; wt, wild-type.

Results

- A total of 67 patients were enrolled; 3% of patients were *EGFR*-positive and 18% had unknown *EGFR* status (Table 1)
- No patient had a known *ALK* translocation
- At the data cutoff date, July 08, 2019, 55 (82.1%) patients had discontinued treatment

Table 1. Baseline Demographics and Patient Characteristics

Characteristic	NSCLC N=67
Age, years	
Mean (median)	64.8 (66.0)
Age group, n (%)	
<65 years	30 (44.8)
≥65 years	37 (55.2)
Sex, n (%)	
Female	27 (40.3)
Male	40 (59.7)
ECOG performance status, n (%)	
0	14 (20.9)
1	52 (77.6)
2	1 (1.5)
Most recent cancer stage, n (%)	
I-II	0 (0)
III	4 (6.0)
IV	63 (94.0)
Histology at diagnosis, n (%)	
Adenocarcinoma	46 (68.7)
Squamous cell carcinoma	17 (25.4)
Other[a]	4 (6)
Number of prior anticancer regimens, n (%)	
1	41 (61.2)
2	16 (23.9)
≥3	10 (14.9)
Previous anticancer treatments received, n (%)	
Any anticancer treatment	67 (100.0)
Radiotherapy	34 (50.7)
Surgery	19 (28.4)
Bevacizumab	9 (13.4)

[a]One patient had undifferentiated carcinoma, 1 had large cell carcinoma, 2 were listed as 'other'.
ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer.

Efficacy

- Confirmed irORR was 27%, with 2 complete responses (Table 2)

Table 2. Tumor Response by irRECIST

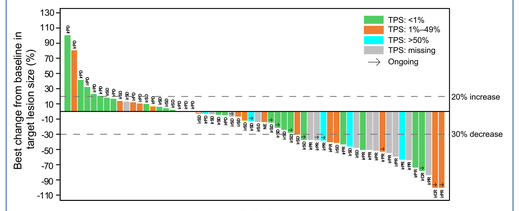
Efficacy outcomes, n (%)	TPS <1% n=24	TPS 1–49% n=20	TPS ≥50% n=5	TPS unknown n=18	Overall N=67
irCR	1 (4.2)	1 (5.0)	0	0	2 (3.0)
irPR	3 (12.5)	3 (15.0)	2 (40.0)	8 (44.4)	16 (23.9)
irSD	11 (45.8)	6 (30.0)	2 (40.0)	5 (27.8)	24 (35.8)
irPD	7 (29.2)	5 (25.0)	1 (20.0)	2 (11.1)	15 (22.4)
Not evaluable	1 (4.2)	2 (10.0)	0	0	3 (4.5)
Not done	1 (4.2)	3 (15.0)	0	3 (16.7)	7 (10.4)
Confirmed irORR	4 (16.7)	4 (20.0)	2 (40.0)	8 (44.4)	18 (26.9)
Response ongoing	2/4 (50.0)	3/4 (75.0)	1/2 (50.0)	3/8 (37.5)	9/18 (50.0)
irDCR	15 (62.5)	10 (50.0)	4 (80.0)	13 (72.2)	42 (62.7)

CR, complete response; DCR, disease control rate; ir, immune-related; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TPS, tumor proportion score.

Efficacy (cont'd)

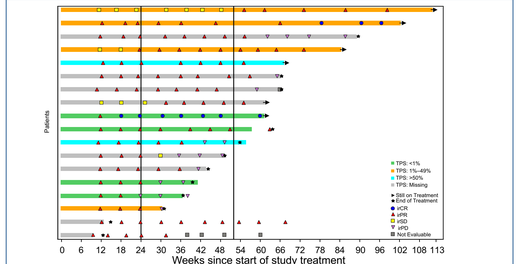
- Median follow-up was 13.8 months; median duration of response (DOR) was 11.6 months (range: 2.8–19.4)
- Figure 2 shows best change from baseline in target lesion size by PD-L1 TPS
- Duration of treatment for all responders is shown in Figure 3
- Progression-free survival is shown in Figure 4
- Overall survival is shown in Figure 5

Figure 2. Best Change in Tumor Size by irRECIST



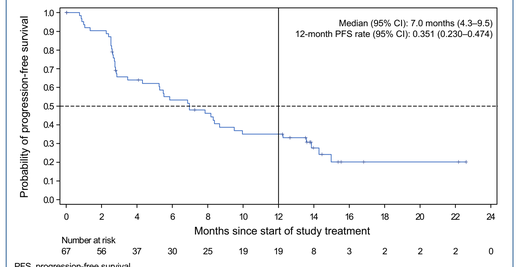
irCR, immune-related complete response; irPD, immune-related progressive disease; irPR, immune-related partial response; irRECIST, immune-related Response Evaluation Criteria in Solid Tumors; irSD, immune-related stable disease; NE, not evaluable; TPS, tumor proportion score.

Figure 3. Duration of Treatment in Responders



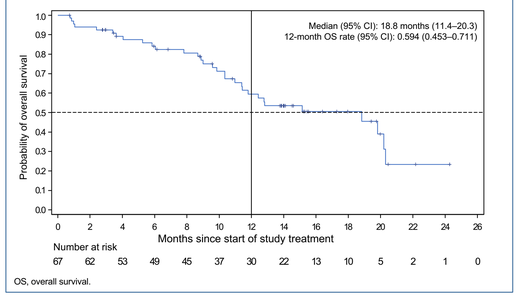
irCR, immune-related complete response; irPD, immune-related progressive disease; irPR, immune-related partial response; irSD, immune-related stable disease; TPS, tumor proportion score.

Figure 4. Progression-Free Survival by irRECIST



PFS, progression-free survival.

Figure 5. Overall Survival



OS, overall survival.

Safety

- Safety data is shown in Table 3 and Table 4
- Five (7.5%) patients had treatment-related any-grade pneumonitis, 1 (1%) had treatment-related grade 3 pneumonitis

Table 3. Adverse Event Summary

Category, n (%)	NSCLC N=67
Any-grade TRAE	45 (67.2)
Grade ≥3 TRAE	8 (11.9)
Any-grade irTRAE	19 (28.4)
Grade ≥3 irTRAE	5 (7.5)
Any TEAE leading to death	3 (4.5)
Any TRAE leading to death	0
Any TRAE leading to discontinuation	4 (6.0)
Any irTRAE leading to discontinuation	3 (4.5)

ir, immune-related; NSCLC, non-small cell lung cancer; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Table 4. Any-Grade and Grade ≥3 irTRAEs

Preferred term, n (%)	NSCLC N=67
Any-grade irTRAE[a]	19 (28.4)
Hypothyroidism	7 (10.4)
Rash	3 (4.5)
Hyperthyroidism	2 (3.0)
Amylase increased	2 (3.0)
Diarrhea	2 (3.0)
Grade ≥3 irTRAE	5 (7.5)
Adrenal insufficiency	1 (1.5)
Lipase increased	1 (1.5)
Rash	1 (1.5)
Pneumonitis	1 (1.5)
Transaminase increased	1 (1.5)

[a]For irTRAEs affecting >1 patient.
NSCLC, non-small cell lung cancer; irTRAE, immune-related, treatment-related adverse event.

References

1. Xia L, et al. *Oncologist.* 2019;24(Suppl 1):S31–S41.

Acknowledgements

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