Abstract #2527: Safety and efficacy of a novel PD-L1/4-1BB bispecific antibody QLF31907 in previously-treated patients with advanced melanoma: results from a phase 2 study

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Background

- QLF31907, a bispecific antibody that simultaneously blocks PD-1/L1 immunosuppressive pathway on cancer cells and conditionally activates 4-1BB co-stimulatory pathway on tumor-specific T cells, was designed to restrict 4-1BB agonism to the tumor microenvironment, which might overcome resistance to PD-(L)1 inhibitor and reduce hepatotoxicity as reported for traditional 4-1BB monoclonal antibodies.
- Although immunotherapy (IO) has revolutionized the treatment of melanoma, a significant proportion of patients, particularly those with mucosal and acral subtypes, either fail to respond initially or experience disease relapse after IO treatment.
- Here, we present results of QLF31907 in previously heavily-treated patients with advanced melanoma, including IO-exposed.

Methods

- This phase 2 trial (NCT05823246) comprised a safety observation stage and an efficacy expansion stage.
- Patients with unresectable locally advanced or metastatic melanoma who failed, were intolerant to, or refused standard treatment were recruited.
- QLF31907 was administered via intravenous infusion from 5 mg/kg to 20 mg/kg every 2 weeks (Q2W) or 3 weeks (Q3W).
- Based on preliminary clinical and pharmacological data, the 5 mg/kg regimen was selected for the efficacy expansion stage. In this regimen, patients received QLF31907 10 mg/kg on C1D1 and 5 mg/kg on C1D15, followed by maintenance dosing of 5 mg/kg Q2W.
- The primary endpoints were dose-limiting toxicity (DLT) and safety in safety observation stage, and was objective response rate (ORR) per RECIST v1.1 assessed by investigator in efficacy expansion stage.

Acknowlegements

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QLF31907 showed potential anti-tumor activity and acceptable safety profile in heavily-treated patients with advanced melanoma, including IO-exposed patients. These results warrant validation in further clinical trials.

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Results

Baseline characteristics

- As of Dec 31, 2025, 59 patients were enrolled.

Table 1. Baseline Characteristics

Baseline characteristics	5 mg/kg Q2W (N = 26)	Total (N = 59)
Median age (range), years	57.5 (37–76)	57.0 (28–76)
Male, n (%)	13 (50.0)	28 (47.5)
ECOG performance status, n (%)		
0	15 (57.7)	34 (57.6)
1	11 (42.3)	25 (42.4)
Subtype, n (%)		
Mucosal	9 (34.6)	24 (40.7)
Acral	10 (38.5)	20 (33.9)
Cutaneous	5 (19.2)	11 (18.6)
Unknown	2 (7.7)	4 (6.8)
Clinical stage, n (%)		
III	1 (3.8)	4 (6.8)
IV	25 (96.2)	55 (93.2)
BRAF mutation status, n (%)		
Positive	2 (7.7)	6 (10.2)
Negative	18 (69.2)	41 (69.5)
Unknown	3 (11.5)	7 (11.9)
No. of prior lines of treatment, n (%)		
1	12 (46.2)	22 (37.3)
2	8 (30.8)	16 (27.1)
≥ 3	6 (23.1)	18 (30.5)
Prior treatment, n (%)		
Chemotherapy	7 (26.9)	21 (35.6)
Targeted therapy	12 (46.2)	37 (62.7)
Immunotherapy	25 (96.2)	55 (93.2)
Prior anti-PD-1/PD-L1 agents, n (%)	24 (92.3)	52 (88.1)

Abbreviations: ECOG, Eastern Cooperative Oncology Group.

Safety

- No DLT occurred.

Table 2. Overall Safety Summary

Safety	5 mg/kg Q2W (N = 26)	Total (N = 59)
TEAE	26 (100.0)	59 (100.0)
TRAE	26 (100.0)	58 (98.3)
Grade ≥ 3 TEAE	12 (46.2)	34 (57.6)
Grade ≥ 3 TRAE	10 (38.5)	28 (47.5)
TEAE leading to drug interruption	13 (50.0)	33 (55.9)
TRAE leading to drug interruption	13 (50.0)	32 (54.2)
TEAE leading to drug discontinuation	5 (19.2)	12 (20.3)
TRAE leading to drug discontinuation	4 (15.4)	10 (16.9)
SAE	15 (57.7)	35 (59.3)
Treatment-related SAE	15 (57.7)	32 (54.2)
irAE	15 (57.7)	37 (62.7)

Data were shown as n (%).
Abbreviations: TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; SAE, serious adverse event. irAE, immune-related adverse event.

Table 3. Common Grade ≥ 3 TRAEs (≥ 10% of Total)

Grade ≥ 3 TRAEs	5 mg/kg Q2W (N = 26)	Total (N = 59)
Liver injury	5 (19.2)*	10 (16.9)
Neutrophil count decreased	4 (15.4)	9 (15.3)
White blood cell decreased	3 (11.5)	6 (10.2)

Data were shown as n (%).
*Most cases occurred in first cycle or second cycle and resolved with glucocorticoids and conventional hepatoprotective agents.
Abbreviations: TRAE, treatment-related adverse event

Efficacy

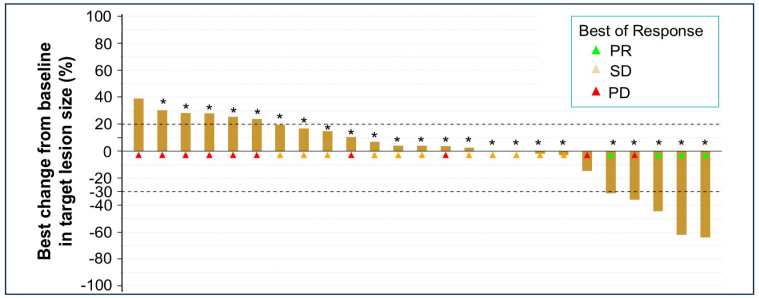
- 57 patients were included in Efficacy Evaluable Analysis Set (EEAS), including 50 patients received prior anti-PD-1/PD-L1 agents.

Table 4. Efficacy Profiles in EEAS

Efficacy	Total population		Prior anti-PD-1/PD-L1-treated	
	5 mg/kg Q2W (N = 25)	Total (N = 57)	5 mg/kg Q2W (N = 23)	Total (N = 50)
ORR, n (%)[§] 95% CI	4 (16.0) (4.5–36.1)	10 (17.5) (8.7–29.9)	4 (17.4) (5.0–38.8)	8 (16.0) (7.2–29.1)
DCR, n (%)[§] 95% CI	15 (60.0) (38.7–78.9)	32 (56.1) (42.4–69.3)	15 (65.2) (42.7–83.6)	29 (58.0) (43.2–71.8)
mDoR, mo (95% CI)[§]	2.5 (1.4, NE)	4.3 (1.4, 13.1)	2.5 (1.4–NE)	4.3 (1.4–NE)
mPFS, mo (95% CI)	3.0 (1.6–4.2)	2.6 (1.6–3.7)	3.0 (1.6–5.6)	2.8 (1.6–3.7)

[§]ORR, DCR and DoR were calculated based on unconfirmed responses.
Abbreviations: ORR, objective response rate; DCR, disease control rate; DOR, duration of response; m, median; PFS, progression-free survival; mo, months; NE, not evaluable.

Figure 1. Best Change from Baseline in Target Lesion Size (5 mg/kg Q2W)



*Patients who received prior anti-PD-1/PD-L1 agents.