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POSTER

Pembrolizumab for Locally Advanced or Recurrent/ Metastatic Cutaneous Squamous Cell Carcinoma: Long-Term Results of the Phase 2 Keynote-629 Study

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Background

- Cutaneous squamous cell carcinoma (cSCC) is the second common non-melanoma skin cancer and primarily treated with surgical resection [1]
- Patients with locally advanced (LA) or metastatic cSCC may not be candidates for curative surgery or radiation, and long-term prognosis is poor for metastatic disease [1-3]
- Pembrolizumab monotherapy is approved in certain countries, including the US, for treatment of LA or recurrent/metastatic (R/M) cSCC not amenable to surgery based on results from the open-label phase 2 KEYNOTE-629 trial (NCT03284424) [4]
  - Objective response rate (ORR) was 50.0% (95% CI, 36.1-63.9) with 9 (16.7%) complete responses (CRs) in the LA cohort and 35.2% (95%CI, 26.2-45.2) with 11 (10.5%) CRs in the R/M cohort
  - 69.2% of patients in the total population experienced a treatment-related adverse event (AE) and 11.9% experienced a grade 3-5 treatment-related event

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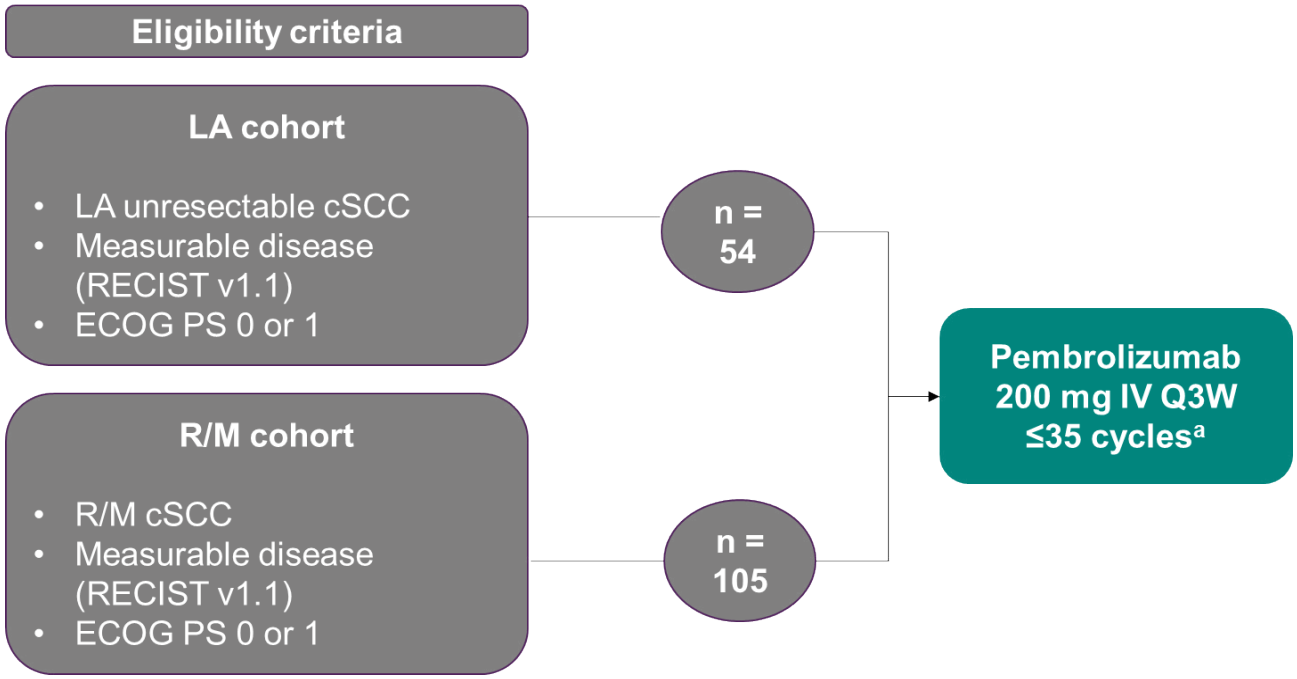

Figure 1: Study design.

ECOG PS: Eastern cooperative oncology group performance status; IV: Intravenously; Q3W, every 3 weeks.

[a]Patients who discontinued treatment after achieving complete response may be eligible to receive an additional 17 cycles of pembrolizumab if disease progression occurred.

Objective

- Present updated efficacy and safety results for pembrolizumab in LA and R/M cohorts of KEYNOTE-629 with an additional 38 months of follow-up

Methods

Figure 1

Statistical analysis

- Efficacy and safety were assessed in all patients who received ≥ 1 dose of study treatment
- The primary end point was ORR per RECIST v1.1 by blinded independent central review (BICR)
- The secondary end points were disease control rate (DCR; defined as CR + partial response (PR) + stable disease ≥ 12 weeks), duration of response (DOR) and progression-free survival (PFS) per RECIST v1.1 by BICR, overall survival (OS), and safety
- DOR was assessed in all patients with a confirmed CR or PR
- 95% CIs for ORR and DCR were calculated using the exact binomial Clopper-Pearson method
- Event rates over time for DOR, PFS, and OS were estimated using the Kaplan-Meier method

Results

- Median time from first dose to the data cutoff date of September 13, 2023, was 52.4 months (range, 47.6-56.9) for the LA cohort, 64.7 months (range, 62.1-69.5) for the R/M cohort, and 63.1 months (range, 47.6-69.5) in the total population (Figure 2, Figure 3, Figure 4, Figure 5, Table 1, Table 2 and Table 3).

Conclusions

- With an additional 38 months of follow-up (median follow-up 63.1 months in the total population), pembrolizumab monotherapy continued to demonstrate durable antitumor activity in patients with LA or R/M cSCC
- In the current analysis, ORR, median PFS, and median OS are consistent with the initial analysis at a median time from first dose to data cutoff of approximately 15 months [4]
  - One additional patient in the LA cohort achieved a CR since the last data cutoff
- Responses were durable, with a median DOR of 52.5 months and 61.2% of responders in the total population having extended responses that lasted ≥ 36 months
- The safety and tolerability of pembrolizumab remained manageable
- These findings continue to support the use of pembrolizumab monotherapy in patients with LA or R/McSCC

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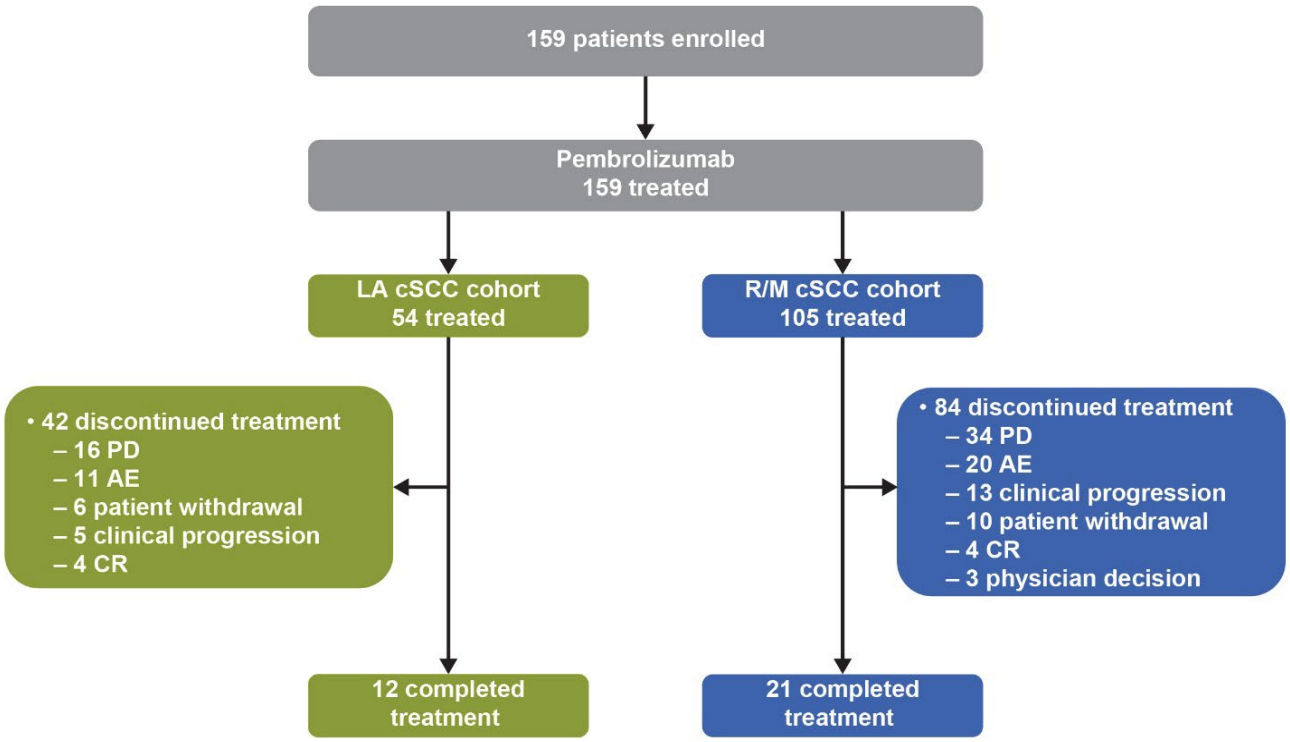

Figure 2: Patient disposition.
PD: Progressive Disease

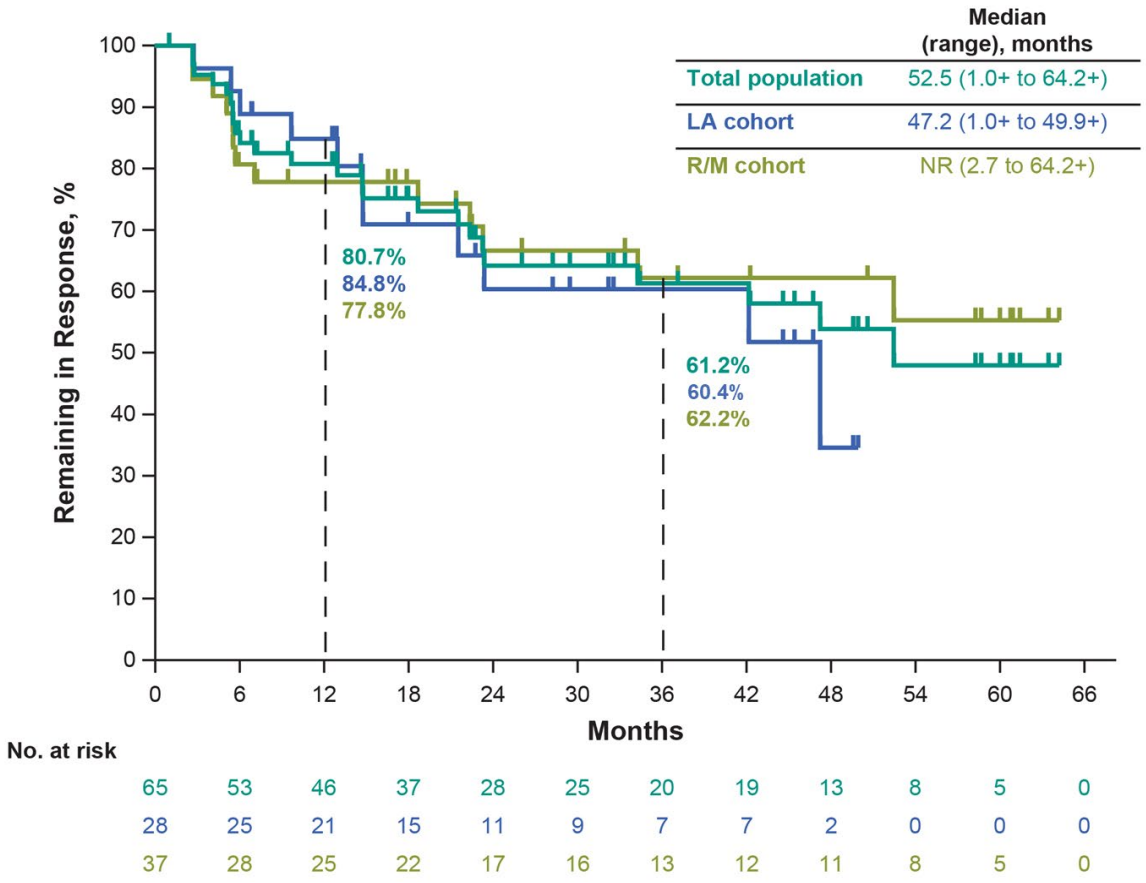

Figure 3: Kaplan-Meier estimates of DOR in patients with a confirmed response per RECIST v1.1 by BICR in the LA cSCC cohort, R/M cSCC cohort, and total population.

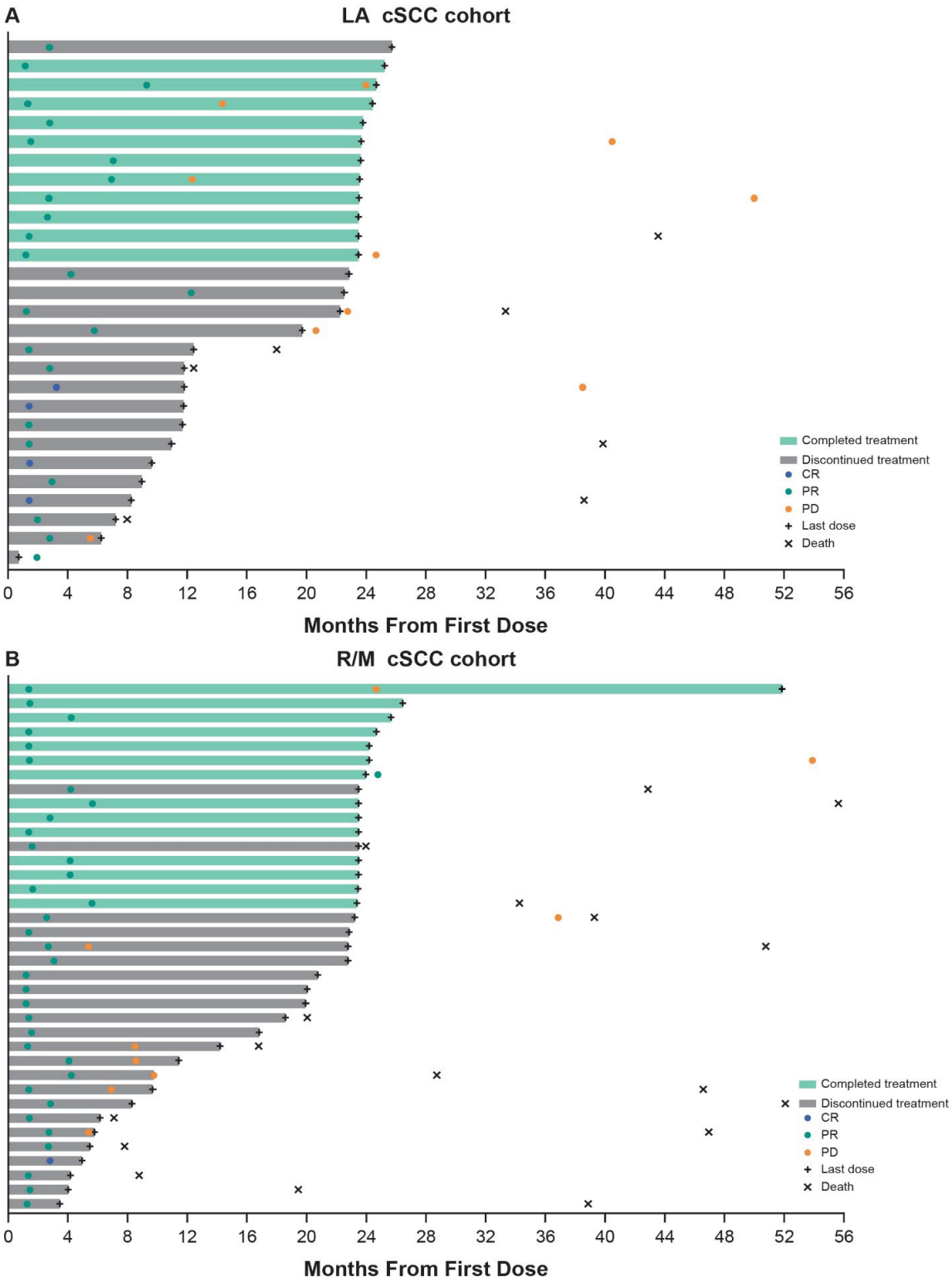

Figure 4: Duration of treatment and time to response in patients with a confirmed response per RECIST v1.1 by BICR in the (A) LAcSCC cohort and the (B) R/M cSCC cohort.

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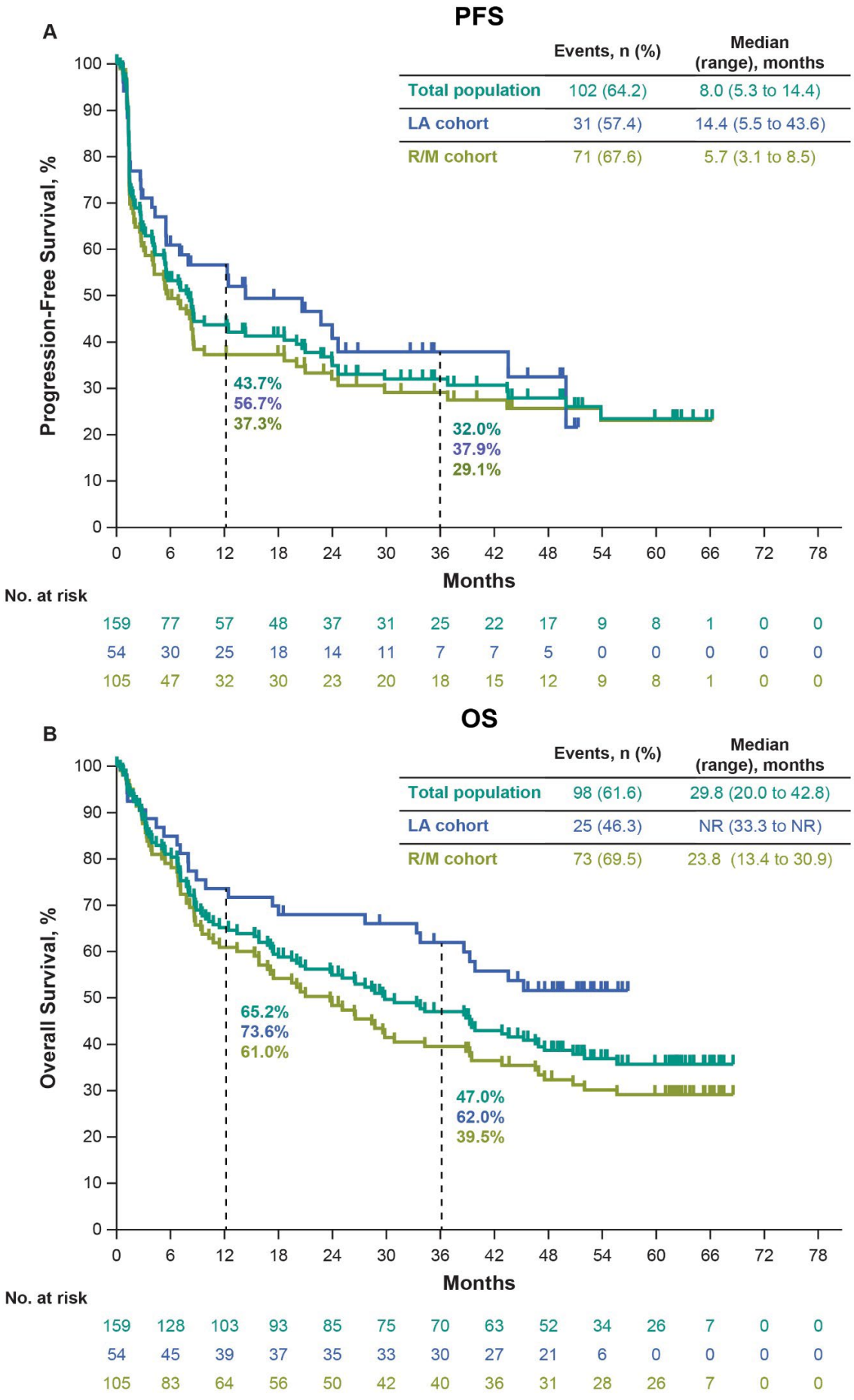

Figure 5: Kaplan-Meier estimates of (A) PFS per RECIST v1.1 by BICR and (B) OS in the LA cSCC cohort, R/M cSCC cohort, and total population.

NR: Not Reached

Table 1: Baseline characteristics.

	LA cSCC n = 54	R/M cSCC n = 105	Total N = 159
Age, median (range)	75 (35-95)	72 (29-95)	74 (29-95)
Sex			
Male	39 (72.2)	80 (76.2)	119 (74.8)
Female	15 (27.8)	25 (23.8)	40 (25.2)
ECOG PS			
0	22 (40.7)	36 (34.3)	58 (36.5)
1	32 (59.3)	69 (65.7)	101 (63.5)
PD-L1 status[a]			
CPS < 1	5 (9.3)	10 (9.5)	15 (9.4)
CPS ≥ 1	46 (85.2)	69 (65.7)	115 (72.3)
Missing	3 (5.6)	26 (24.8)	29 (18.2)
Overall Cancer Stage			
I	1 (1.9)	0 (0)	1 (0.6)
II	7 (13.0)	4 (3.8)	11 (6.9)
III	25 (46.3)	15 (14.3)	40 (25.2)
IV	21 (38.9)	86 (81.9)	107 (67.3)
Disease Status at Baseline			
LA	54 (100)	0 (0)	54 (34.0)
Locally recurrent only	0 (0)	47 (44.8)	47 (29.6)
Metastatic only	0 (0)	25 (23.8)	25 (15.7)
Both locally recurrent and metastatic	0 (0)	33 (31.4)	33 (20.8)

CPS: Combined Positive Score; PD-L1: Programmed Death Ligand 1

Data are n (%) unless otherwise specified.

[a]CPS was calculated as the number of PD-L1-staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

Table 2: ORR per RECIST v1.1 by BICR.

	LA Cohort n = 54	R/M Cohort n = 105	Total Population N = 159
ORR, % (95% CI)	51.9 (37.8-65.7)	35.2 (26.2-45.2)	40.9 (33.2-48.9)
DCR, % (95% CI)	64.8 (50.6-77.3)	52.4 (42.4-62.2)	56.6 (48.5-64.4)
Best overall response, n (%)			
CR	12 (22.2)	13 (12.4)	25 (15.7)
PR	16 (29.6)	24 (22.9)	40 (25.2)
SD	12 (22.2)	30 (28.6)	42 (26.4)
SD ≥ 12 weeks	7 (13.0)	18 (17.1)	25 (15.7)
PD	9 (16.7)	28 (26.7)	37 (23.3)
NE/NA[a]	5 (9.3)	10 (9.5)	15 (9.4)

CR: Complete Response; NA: Not Available; NE; Not Evaluable; PD: Progressive Disease; PR: Partial Response; SD: Stable Disease

[a]Postbaseline assessment not evaluable or no postbaseline assessment available.

Table 3: AE summary.

	Total Population N = 159
Any AE	153 (96.2)
Grade 3-5	93 (58.5)
Resulted in treatment discontinuation	31 (19.5)
Serious	87 (54.7)
Resulted in death	20 (12.6)
Any treatment-related AE	112 (70.4)
Grade 3-5	18 (11.3)
Resulted in treatment discontinuation	14 (8.8)
Serious	16 (10.1)
Resulted in death	2 (1.3)
Immune-mediated AEs[a]	37 (23.3)
Grade 3-5	14 (8.8)
Required systemic corticosteroids	18 (11.3)
High starting dose	11 (6.9)
Low starting dose	7 (4.4)

AE: Adverse Event

[a]Based on a list of preferred terms intended to capture known risks of pembrolizumab and were considered regardless of attribution to study treatment by the investigator

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