

RM-1929 photoimmunotherapy in patients with locoregional, recurrent head and neck squamous cell carcinoma: Efficacy and safety results from a subgroup analysis in anti-PD-1–treated and anti-PD-1–naïve patients

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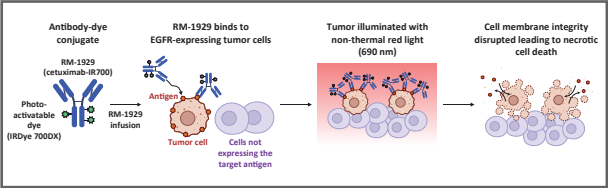
Background

- More than 65% of patients with head and neck squamous cell carcinoma develop recurrent or metastatic disease:¹
 - The mainstay of treatment for these patients is systemic therapy with platinum, taxanes, fluoropyrimidines, and cetuximab,² but responses are limited.
 - The introduction of programmed death 1 (PD-1) immune-checkpoint inhibitors has greatly improved outcomes in a limited number of patients.^{3,4}
 - However, the prognosis for most patients remains poor with limited treatment options.
- ASP-1929* photoimmunotherapy is an investigational anticancer therapy that has recently been approved in Japan. It comprises a targeted antibody that binds specifically to receptors overexpressed on tumor cells conjugated to a photoactivatable dye:
 - Binding of such an antibody-dye conjugate to cancer cells followed by photoactivation induces rapid cell necrosis with minimal damage to surrounding tissues.^{5,6}
 - RM-1929 (cetuximab sarotalocan) is a conjugate of cetuximab, a monoclonal antibody targeting the epidermal growth factor receptor (EGFR) that is highly expressed in HNSCC, and IRDye®700DX, a dye that is activated with non-thermal red light (690 nm).
 - RM-1929 photoimmunotherapy involves two sequential steps: (1) intravenous (IV) infusion of RM-1929; and (2) tumor illumination approximately 24 hours later (**Figure 1**).
 - In a phase 1/2a study of RM-1929 photoimmunotherapy, an objective response rate (confirmed and unconfirmed responses) of 43%, and a median overall survival of 9.3 months was reported in heavily pretreated patients with recurrent HNSCC (rHNSCC) in the Phase 2a part.⁷

Objective

- This *ad hoc* subgroup analysis explores the safety and efficacy of RM-1929 photoimmunotherapy in patients with rHNSCC with or without a history of anti-PD-1 treatment.

Figure 1. RM-1929 (cetuximab sarotalocan) photoimmunotherapy



Methods

Study design

- Ad hoc* pooled analysis of data from two early-phase studies (RM-1929-101 and RM-1929-102) in patients with rHNSCC.
- Only patients treated with RM-1929 640 mg/m² were included in the analysis (N=36).
- Study RM-1929-101
 - Phase 1/2a, open-label, dose-escalation study conducted in the United States (ClinicalTrials.gov identifier: NCT02422979).⁷
 - Treatment: RM-1929 160, 320 or 640 mg/m² IV for 1 cycle (Phase 1, Part 1) or RM-1929 640 mg/m² IV for up to 4 cycles (Phase 2a, Part 2) plus fixed light dose (690 nm laser) 50 J/cm² for superficial illumination or 100 J/cm fiber length for interstitial illumination.

- Study RM-1929-102

- Phase 1, single-center, open-label study conducted in Japan (Japanese Registry of Clinical Trials, identifier: jRCT2031200133).⁸
- Treatment: RM-1929 640 mg/m² IV plus fixed light dose (690 nm laser) 50 J/cm² for superficial illumination or 100 J/cm for interstitial illumination for 1 cycle.

Outcomes

- Treatment-emergent adverse events (TEAE) were graded according to National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03. AEs were coded using the MedDRA Dictionary (version 21.0).
- Tumor response was evaluated according to modified Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 by central review.
- Overall survival was defined as time from first RM-1929 administration to death from any cause.

Data analysis

- Safety and preliminary efficacy data were analyzed by prior and/or concomitant exposure to anti-PD-1 treatment.
- Clopper-Pearson's 95% confidence interval was used for frequency analysis, and the Kaplan-Meier method was used for the analysis of overall survival.

Results

- A total of 36 patients were treated with RM-1929 photoimmunotherapy (640 mg/m²) [RM-1929-101: Part 1, n=3; Part 2, n=30; RM-1929-102: n=3]:
 - Of these, 30 patients received 65 cycles of RM-1929 photoimmunotherapy, at a median of 2 cycles (range 1–4), and 6 patients received a maximum of 1 cycle as specified in the study protocol (RM-1929-101: Part 1, n=3; RM-1929-102, n=3).
- 21 patients (58%) were anti-PD-1–naïve and 15 patients (42%) had received prior anti-PD-1 treatment (pembrolizumab n=6; nivolumab n=9). Of the patients that had received anti-PD-1 treatment, 4 patients received anti-PD-1 (pembrolizumab n=1; nivolumab n=3) concomitantly with RM-1929 photoimmunotherapy.
 - Baseline demographics and clinical characteristics are shown in **Table 1**. All patients were heavily pretreated.

Table 1. Baseline demographics and clinical characteristics

Characteristic	RM-1929 photoimmunotherapy (640 mg/m ²) (N=36)	
	Anti-PD-1–treated (n=15)*	Anti-PD-1–naïve (n=21)
Age, years		
Median (range)	68 (51–86)	68 (39–77)
Sex, n (%)		
Male	10 (66.7)	17 (81.0)
Female	5 (33.3)	4 (19.0)
Race, n (%)		
White	11 (73.3)	16 (76.2)
Asian	3 (20.0)	1 (4.8)
American Indian / Alaska Native	0	1 (4.8)
Other**	1 (6.7)	3 (14.3)
ECOG performance status, n (%)		
0–1	12 (80.0)	18 (85.7)
2	3 (20.0)	3 (14.3)

ECOG, Eastern Cooperative Oncology Group.
*Four patients among anti-PD-1 treated group received anti-PD-1 treatment concomitantly with RM-1929 photoimmunotherapy.
**Includes races not specified on eCRF. Multiple races are counted in each relevant race category; therefore, percentages may exceed 100%.

Safety

- Most adverse events occurred locally at the treatment site (**Table 2**).
- Three patients experienced serious adverse events that led to death occurring more than 19 days after RM-1929 photoimmunotherapy treatment. All were considered unrelated to RM-1929 photoimmunotherapy; 1 in the anti-PD-1–treated subgroup (arterial hemorrhage) and 2 in the anti-PD-1–naïve subgroup (pneumonia and tumor hemorrhage).

Table 2. Safety overview

n (%)	RM-1929 photoimmunotherapy (640 mg/m ²) (N=36)		
	Anti-PD-1–treated (n=15)*	Concomitant anti-PD-1 (n=4)	Anti-PD-1–naïve (n=21)
Any TEAEs	15 (100)	4 (100)	21 (100)
Grade 1	12 (80.0)	4 (100)	20 (95.2)
Grade 2	9 (60.0)	4 (100)	19 (90.5)
Grade 3	5 (33.3)	1 (25.0)	14 (66.7)
Grade 4	2 (13.3)	0	3 (14.3)
Grade 5	1 (6.7)	0	2 (9.5)
Any AEs related to RM-1929 photoimmunotherapy	14 (93.3)	4 (100)	17 (81.0)
RM-1929 photoimmunotherapy treatment-related AEs in >10% of patients in either subgroup			
Application site pain	5 (33.3)	3 (75.0)	3 (14.3)
Face edema	3 (20.0)	1 (25.0)	3 (14.3)
Application site edema	3 (20.0)	1 (25.0)	2 (9.5)
Dysphagia	2 (13.3)	0	3 (14.3)
Erythema	2 (13.3)	0	3 (14.3)
Facial pain	2 (13.3)	0	2 (9.5)
Rash	2 (13.3)	0	2 (9.5)
Oropharyngeal pain	2 (13.3)	0	2 (9.5)
Peripheral edema	2 (13.3)	0	2 (9.5)
Swelling	2 (13.3)	0	1 (4.8)
Stomatitis	2 (13.3)	0	1 (4.8)
Fatigue	1 (6.7)	0	5 (23.8)
Localized edema	1 (6.7)	1 (25.0)	3 (14.3)
Tongue edema	1 (6.7)	0	3 (14.3)
Tumor pain	0	0	4 (19.0)
Oral pain	0	0	3 (14.3)
Anemia	0	0	3 (14.3)
Any serious TEAEs	2 (13.3)	0	10 (47.6)
Any serious TEAEs related to RM-1929 photoimmunotherapy	0	0	3 (14.3)

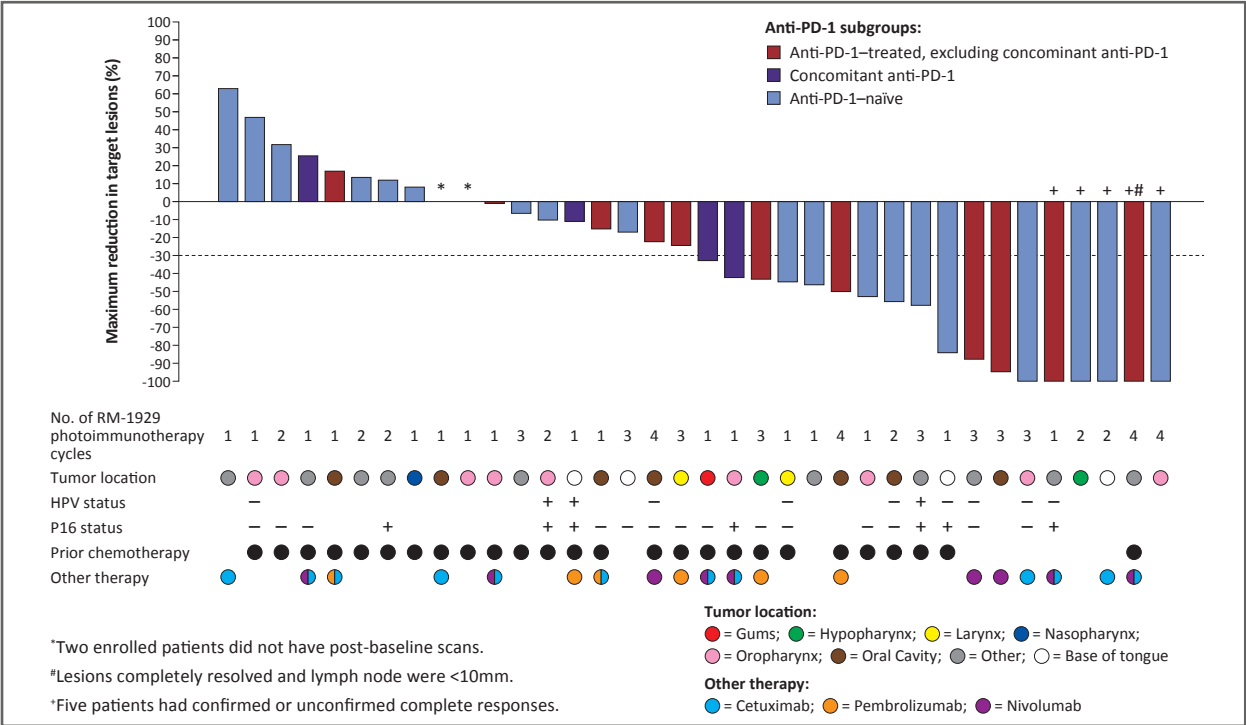
Data expressed as n (%).
PD-1, programmed death 1; TEAE, treatment-emergent adverse event.
*Four patients among anti-PD-1 treated group received anti-PD-1 treatment concomitantly with RM-1929 photoimmunotherapy.

Table 3. Efficacy overview

Endpoint	RM-1929 photoimmunotherapy (640 mg/m ²) (N=36)	
	Anti-PD-1–treated (n=15)*	Anti-PD-1–naïve (n=21)
Objective response rate,^a n (%) [95% CI]	7 (46.7) [21.3–73.4]	9 (42.9) [21.8–66.0]
Complete response	2 (13.3) [1.7–40.5]	3 (14.3) [3.1–36.3]
Partial response	5 (33.3) [11.8–61.6]	6 (28.6) [11.3–52.2]
Disease control,^b n (%) [95% CI]	13 (86.7) [59.5–98.3]	15 (71.4) [47.8–88.7]
Overall survival, median months (95% CI)	10.5 (2.6–NR)	9.3 (3.6–16.9)

CI, confidence interval; NR, not reached; PD-1, programmed death 1.
*Among the anti-PD-1–treated patients, 4 patients received anti-PD-1 treatment concomitantly with RM-1929 photoimmunotherapy.
^aConfirmed and unconfirmed responses across all time points according to modified Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 by central radiology review.
^bComplete response, partial response or stable disease of any duration between Cycle 1 Day 1 and disease progression or death or date of last evaluable tumor assessment.

Figure 2. Waterfall plot of best change in sum of diameters of target lesions from baseline by central review



*Two enrolled patients did not have post-baseline scans.

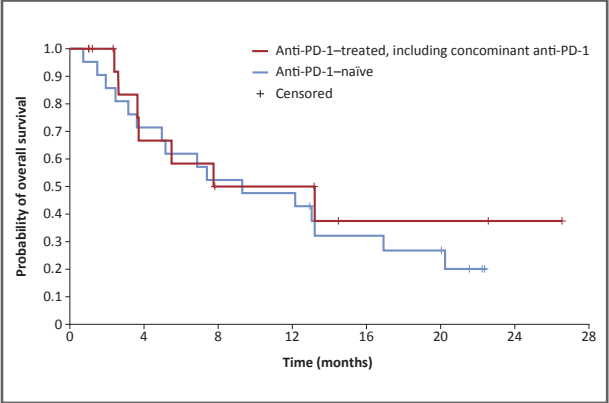
*Lesions completely resolved and lymph node were <10mm.

*Five patients had confirmed or unconfirmed complete responses.

Efficacy

- Efficacy outcomes with RM-1929 photoimmunotherapy according to prior anti-PD-1 exposure are shown in **Figure 2** and **Table 3**.
- Objective response rates (ORR) were 46.7% and 42.9% with or without prior anti-PD-1 treatment, respectively (**Table 3**):
 - Of the 4 patients who received concurrent anti-PD-1 therapy, best responses (confirmed and unconfirmed) were 2 partial responses, 1 stable disease, and 1 progressive disease.
- Median overall survival was 10.5 and 9.3 months with or without prior anti-PD-1 treatment, respectively (**Figure 3** and **Table 3**).

Figure 3. Kaplan-Meier plot of overall survival



Conclusions

- Data from this exploratory subgroup analysis reveals a similar safety profile between anti-PD-1–treated and anti-PD-1–naïve patients.
- To gain further insight on the combination of ASP-1929* photoimmunotherapy with anti-PD-1 treatment, an open-label study in patients with recurrent or metastatic HNSCC or locally advanced or metastatic cutaneous squamous cell carcinoma is currently recruiting.

References

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DISCLAIMER: Outside of Japan, photoimmunotherapy with RM-1929/ASP-1929 is investigational and has not yet been approved as safe or effective by any other regulatory authority.
*RM-1929 and ASP-1929 are analogous. Extensive physiochemical studies showed that they have comparable physical and chemical properties.