

# Intralesional cemiplimab for patients with early-stage cutaneous squamous cell carcinoma: results from a phase 1 pilot study expansion cohort

Michael Migden,<sup>1</sup> Sherrif Ibrahim,<sup>2</sup> John Strasswimmer,<sup>3</sup> Nathalie Zeitouni,<sup>4</sup> Gary S. Rogers,<sup>5</sup> Jennifer DeSimone,<sup>6</sup> Meenal Kheterpal,<sup>7</sup> Hyunsil Han,<sup>8</sup> Suk-Young Yoo,<sup>8</sup> Mia Bao,<sup>8</sup> Frank Seebach,<sup>8</sup> Israel Lowy,<sup>8</sup> Mihaela Cristea,<sup>8</sup> Matthew Fury<sup>8</sup>

<sup>1</sup>The University of Texas MD Anderson Cancer Center, Houston, TX, USA; <sup>2</sup>Rochester Dermatologic Surgery, P.C., Victor, NY, USA; <sup>3</sup>Dermatology Associates of the Palm Beaches, Delray Beach, FL, USA; <sup>4</sup>Medical Dermatology Specialists, Phoenix, AZ, USA; <sup>5</sup>Beth Israel Lahey Health, Beverly, MA, USA;

<sup>6</sup>Inova Schar Cancer Institute, Fairfax, VA, USA; <sup>7</sup>Duke University Medical Center, Durham, NC, USA; <sup>8</sup>Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA

## SYNOPSIS

- CSCC is a malignant proliferation of epidermal keratinocytes with invasion of the dermis. Risk factors include ultraviolet skin damage due to chronic sun exposure, advanced age, light-colored skin, and immunosuppression.<sup>1,2</sup>
- Cemiplimab (350 mg IV Q3W) is approved for the treatment of adult patients with locally advanced or metastatic CSCC who are not candidates for curative surgery or radiation.<sup>3,4</sup>
- Primary surgery is the standard of care for early-stage CSCC.<sup>5</sup> However, there is an unmet need for patients who prefer a non-surgical option.
- Low-dose IL cemiplimab demonstrated promising clinical activity in a phase 1, single-arm, open-label, sequentially enrolling, dose-escalation pilot study (NCT03889912).<sup>6</sup> The dose escalation results have been previously presented.

## OBJECTIVE

- This study aims to evaluate the safety, tolerability, and efficacy of IL cemiplimab in patients with CSCC or BCC. Here, we report results from the expansion Cohorts A and B of the pilot trial that evaluated low-dose IL cemiplimab in patients with early-stage CSCC.

## METHODS

- Cohort A received 5 mg IL cemiplimab QW × 6, and Cohort B received 5 mg IL cemiplimab Q2W × 3 on weeks 1, 3, 5 (Figure 1). Key eligibility criteria are shown in Table 1.
- Visual response assessments were performed at Weeks 7 and 13, following modified World Health Organization criteria. Planned surgery was performed at Week 13.
- Primary endpoints were safety and tolerability. Secondary endpoints were visual ORR (vCR, vPR, vSD, and vPD) and pCR rate in index lesions.
- Safety analyses were based on treatment received (as treated) and were conducted in all patients who received any study treatment.

Figure 1. Study design.



Table 1. Key inclusion and exclusion criteria.

| Key inclusion criteria  | Key exclusion criteria  |
|---|---|
| <ul style="list-style-type: none"> <li>Age ≥18 years</li> <li>Index lesion ≥1.0–≤2.0 cm (longest diameter)</li> <li>ECOG PS ≤1</li> <li>Adequate hepatic, renal, and bone marrow function, as detailed in the protocol</li> </ul> | <ul style="list-style-type: none"> <li>Immunosuppression and ongoing or recent (within 5 years) autoimmune disease requiring systemic immunosuppressant treatment</li> <li>Prior systemic therapy (PD-1/PD-L1 or any other systemic immune-modulating agent)</li> <li>Any anticancer treatment within 30 days of the initial administration of cemiplimab or planned to occur during the study period</li> <li>An index lesion in the dry red lip or anogenital area</li> </ul> |

## ABBREVIATIONS

BCC, basal cell carcinoma; CCR, clinical complete response; CSCC, cutaneous squamous cell carcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; HN, head and neck; IL, intralesional; ORR, objective response rate; pCR, pathologic complete response; PD-1, programmed cell death-1; PD-L1, programmed cell death-ligand 1; QW, every week; Q2W, every 2 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event; vCR visual complete response; vPD, visual progression of disease; vPR, visual partial response; vSD, visual stable disease.

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## RESULTS

### Patient demographics and baseline characteristics

- Twenty-four patients completed the study (12 in each cohort).
- Overall, baseline demographics and disease characteristics were similar between the 2 cohorts (Table 2).
  - In Cohort A, the median age was 76.0 years, and most patients were male (66.7%) with an ECOG PS of 0 (91.7%).
  - Similarly, in Cohort B, the median age was 72.5 years. Most patients were male (66.7%) with an ECOG PS of 0 (83.3%).

Table 2. Patient demographics and baseline characteristics.

|                               | Cohort A (n=12) | Cohort B (n=12) |
|-------------------------------|-----------------|-----------------|
| Age, years, median (min: max) | 76.0 (65:89)    | 72.5 (69:79)    |
| Sex, n (%)                    |                 |                 |
| Male                          | 8 (66.7)        | 8 (66.7)        |
| Female                        | 4 (33.3)        | 4 (33.3)        |
| ECOG PS, n (%)                |                 |                 |
| 0                             | 11 (91.7)       | 10 (83.3)       |
| 1                             | 1 (8.3)         | 2 (16.7)        |
| Primary site of tumor, n (%)  |                 |                 |
| HN                            | 4 (33.3)        | 3 (25.0)        |
| Non-HN                        | 4 (33.3)        | 4 (33.3)        |
| Missing                       | 4 (33.3)        | 5 (41.7)        |
| Histologic grade, n (%)       |                 |                 |
| Well differentiated           | 8 (66.7)        | 7 (58.3)        |
| Moderately differentiated     | 2 (16.7)        | 3 (25.0)        |
| Unknown                       | 1 (8.3)         | 2 (16.7)        |
| Missing                       | 1 (8.3)         | 0               |

### Safety

- Overall, 75% of patients in Cohort A and 83.3% in Cohort B experienced any-grade TEAEs (Table 3).
- The most common TEAE was COVID-19 infection, which occurred during the global COVID pandemic period in 3 (25.0%) patients in Cohort A and 2 (16.7%) patients in Cohort B.
- Other TEAEs included morbilliform rash and post-inflammatory hyperpigmentation in Cohort A (1 event each), and drug eruption, pruritus, injection-site reaction, and elevated thyroid-stimulating hormone in Cohort B (1 event each).
- No TEAEs led to treatment discontinuation or death.

Table 3. Safety summary.

| TEAEs, n (%)                               | Cohort A (n=12) | Cohort B (n=12) |
|--|-----------------|-----------------|
| Any-grade TEAEs                            | 9 (75.0)        | 10 (83.3)       |
| Grade ≥3 TEAEs                             | 0               | 0               |
| Any SAE                                    | 1 (8.3)         | 0               |
| Treatment-related TEAEs                    | 2 (16.7)        | 4 (33.3)        |
| TEAEs leading to dose delay                | 1 (8.3)         | 0               |
| TEAEs leading to treatment discontinuation | 0               | 0               |
| TEAEs resulting in death                   | 0               | 0               |

### Efficacy

- The visual ORR was 66.7% (95% CI, 34.9–90.1%) for Cohort A and 75.0% (95% CI, 42.8–94.5%) for Cohort B at Week 7. At Week 13, the ORR was 66.7% (95% CI, 34.9–90.1%) for Cohort A and 66.7% (95% CI, 34.9–90.1%) for Cohort B (Table 4).
- At Week 7, 5 (41.7%) patients in Cohort A and 2 (16.7%) patients in Cohort B had vCRs.
- At Week 13, vPD was only observed in Cohort B (2 patients).
- The pCR rate was similar in Cohorts A (58.3%) and B (66.7%).

## DISCLOSURES

MM reports honoraria and travel expenses from Regeneron Pharmaceuticals, Inc., Sanofi, Replimune, Phlogon, Feldan Therapeutics, Stamford Pharmaceuticals Inc., and Sun Pharma; and institutional research funding from Regeneron Pharmaceuticals, Inc., Replimune, and Solgel Technologies. SI reports being a speaker, advisor, and researcher for Regeneron Pharmaceuticals, Inc.; a researcher for Replimune; and a speaker and researcher for Castle Biosciences. JS reports consulting/advisory roles for Regeneron Pharmaceuticals, Inc.; serving on a speaker's bureau for Regeneron Pharmaceuticals, Inc., Sanofi, and Genentech; research funding from Biofrontera and Regeneron Pharmaceuticals, Inc.; and travel, accommodation, or expenses from Regeneron Pharmaceuticals, Inc., and Sanofi. NZ reports being an investigator for Replimune and Dermasensor; an investigator/consultant for Sun Pharma and Biofrontera; and an investigator and speaker for Castle Biosciences and Regeneron Pharmaceuticals, Inc. (all outside the submitted work). GSR has nothing to disclose. JD is an investigator for Merck, Regeneron Pharmaceuticals, Inc., Soligenix, and Kyowa Kirin and is a speaker and consultant for Helsinn. MK reports honoraria and travel expenses from Regeneron Pharmaceuticals, Inc., and Sun Pharma. HH, SY, MB, FS, IL, MC, and MF are employees and shareholders of Regeneron Pharmaceuticals, Inc.

Table 4. Visual and pathological responses.

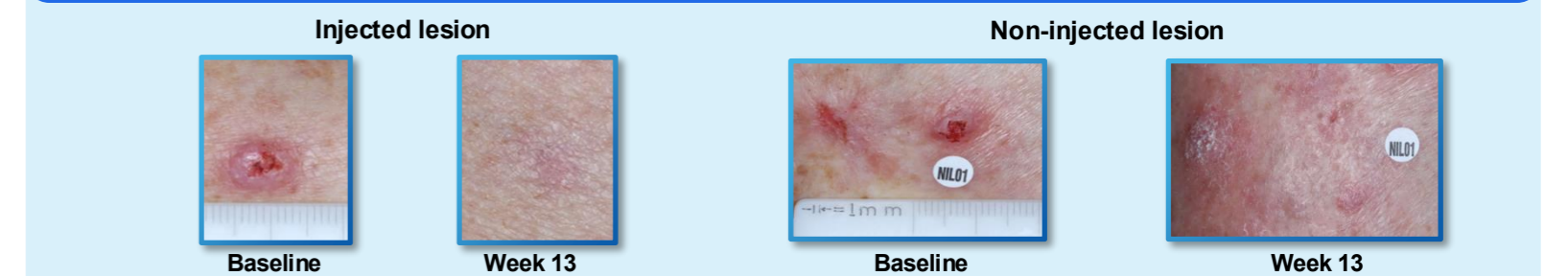
|                                     | Cohort A (n=12)      |                      | Cohort B (n=12)      |                      |
|-------------------------------------|----------------------|----------------------|----------------------|----------------------|
|                                     | Week 7               | Week 13              | Week 7               | Week 13              |
| Index lesion response, n (%)        |                      |                      |                      |                      |
| vCR*                                | 5 (41.7)             | 7 (58.3)             | 2 (16.7)             | 5 (41.7)             |
| vPR                                 | 3 (25.0)             | 1 (8.3)              | 7 (58.3)             | 3 (25.0)             |
| vSD                                 | 2 (16.7)             | 4 (33.3)             | 3 (25.0)             | 2 (16.7)             |
| vPD                                 | 0                    | 0                    | 0                    | 2 (16.7)             |
| Not evaluable                       | 2 (16.7)             | 0                    | 0                    | 0                    |
| ORR (vCR + vPR), n (%) [95% CI]     | 8 (66.7) [34.9–90.1] | 8 (66.7) [34.9–90.1] | 9 (75.0) [42.8–94.5] | 8 (66.7) [34.9–90.1] |
| Pathologic response, n (%) [95% CI] |                      |                      |                      |                      |
| pCR                                 | NA                   | 7 (58.3) [27.7–84.8] | NA                   | 8 (66.7) [34.9–90.1] |

\*Index lesions no longer visible.

### Case study 1: 65-year-old female with CSCC of right lower extremity

- Regressions in lesions in a 65-year-old female with CSCC of the right lower extremity, injected with 5 mg IL cemiplimab QW × 6, are shown in Figure 2; the non-injected lesion was also located on the right lower extremity.

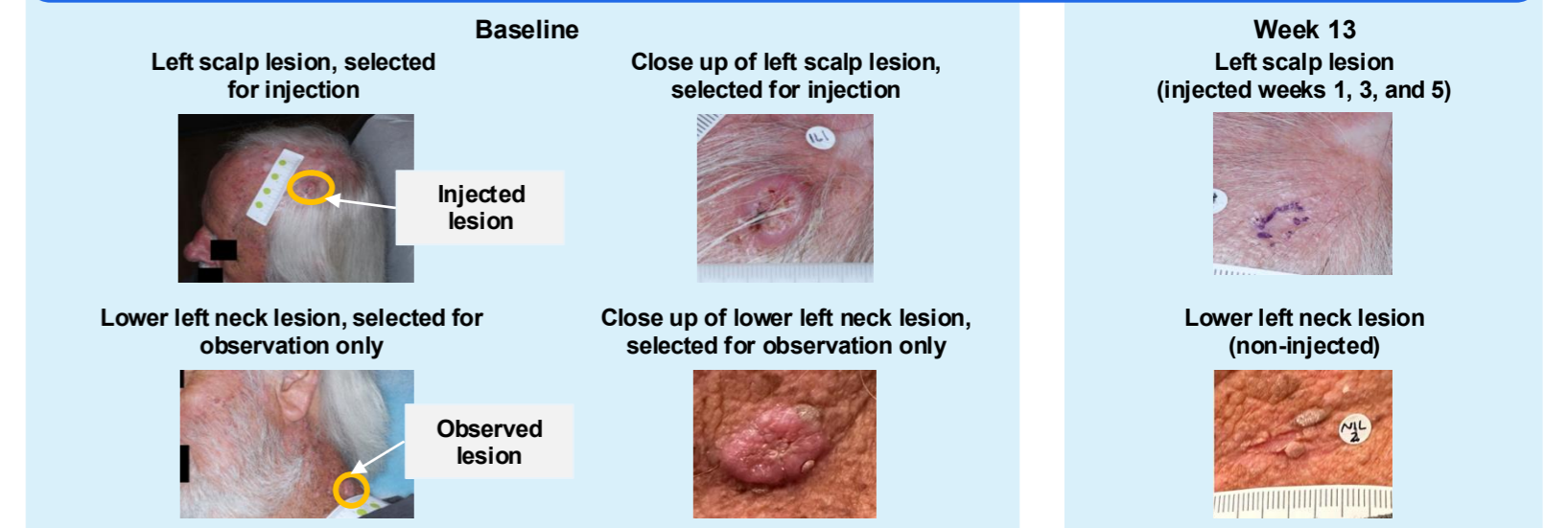
Figure 2. Regressions in injected and non-injected lesions at baseline and Week 13 – results from case study 1.



### Case study 2: 75-year-old male with multiple recurrent CSCC

- Regressions in lesions in a 75-year-old male with multiple recurrent CSCC are shown in Figure 3.
  - The patient had 12 prior procedures (surgery, electrodesiccation) between 2015 and early 2023.
  - On study, the left scalp lesion was injected with 5 mg IL cemiplimab on weeks 1, 3, and 5 only (barely detectable systemic pharmacokinetics).

Figure 3. Regressions in injected and non-injected lesions at baseline and Week 13 – results from case study 2.



## CONCLUSIONS

- Low dose IL cemiplimab (5 mg QW × 6) is highly active against early-stage CSCC.
  - Regressions in both injected and non-injected lesions have been observed.
- The emerging safety profile of low-dose IL cemiplimab differs from the safety profile of the higher IV dose that is approved in the advanced and adjuvant setting.
- Rapid kinetics of response, a lack of disease progression, and a generally acceptable safety profile were observed with the Cohort A regimen (5 mg IL QW × 6).
- This regimen has been selected for a randomized phase 3 study of low-dose IL cemiplimab versus primary surgery in early-stage CSCC (CLEAR CSCC; NCT06585410).<sup>7</sup>