Health-related quality of life in patients with metastatic basal cell carcinoma treated with cemiplimab: Analysis of a phase 2 open-label clinical trial

Karl D Lewis,[1] Timothy J Inocencio,[2] Ruben GW Quek,[2] Patrick R LaFontaine,[3] Zeynep Eroglu,[4] Anne Lynn S Chang,[5] Cristina Ivanescu,[6] Alexander J Stratigos,[7] Ketty Peris,[8] Aleksandar Sekulic,[9] Matthew G Fury,[2] Chieh-I Chen[2]

[1]University of Colorado Cancer Center, Aurora, CO, USA; [2]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [3]Sanofi, Cambridge, MA, USA; [4]Department of Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL, USA; [5]Department of Dermatology, Stanford University School of Medicine, Redwood City, CA, USA; [6]IQVIA, Durham, NC, USA; [7]Department of Dermatology-Venereology, Andreas Sygros Hospital-National and Kapodistrian University of Athens, Andreas Sygros Hospital, Athens, Greece; [8]Catholic University Fondazione Policlinico Universitario-IRCCS, Rome, Italy; [9]Mayo Clinic Arizona, Scottsdale, AZ, USA

Background

- Patients with metastatic basal cell carcinoma (mBCC) who are not candidates for surgery or radiation therapy are generally treated with hedgehog signaling pathway inhibitors (HHIs).[1]
  - However, intolerance and resistance to HHIs are common.[1]
- Cemiplimab-rwlc is approved in the United States for patients with mBCC and locally advanced BCC (laBCC) following HHI treatment or for whom HHIs are not appropriate.[2]
- In a Phase 2 clinical trial (NCT03132636), cemiplimab demonstrated an objective response rate of 24.1% (95% CI: 13.5–37.6%) in patients with mBCC who progressed on or were intolerant to HHIs.[3]
- Efficacy and health-related quality of life (HRQoL) data for patients with laBCC were previously reported.[4]

Objective

- To evaluate HRQoL in patients with mBCC who were treated with cemiplimab in the phase 2 clinical trial (NCT03132636).

Methods

- In this phase 2, non-randomized, multicenter, pivotal trial of cemiplimab, adults (≥18 years old) with mBCC and Eastern Cooperative Oncology Group performance status ≤1 (N=54) received cemiplimab 350 mg intravenous every 3 weeks for up to 9 treatment cycles.
  - mBCC was based on histologic confirmation of distant BCC metastases to lung, liver, bone, or lymph node, and included patients with both nodal and distant metastatic disease.
- At baseline and Day 1 of each treatment cycle, patients were administered the European Organisation for Research and Treatment of Cancer Quality of Life-Core 30 (EORTC QLQ-C30)[6] and Skindex-16[7] questionnaires (**Table 1**).
  - Follow-up assessment was conducted 28–42 days after the last study treatment administration if a patient discontinued early.
- Analyses were conducted on the full analysis set, which consisted of all enrolled patients who were deemed eligible for the study.
- Mixed-model repeated-measures (MMRM) analyses were used to estimate overall least-squares (LS) mean change from baseline and 95% CI across Cycles 2–9 on all scales for patients with baseline and ≥1 post-baseline value.

Table 1. EORTC QLQ-C30 and Skindex-16 assessments

EORTC QLQ-C30[6]	Skindex-16[7]
The EORTC QLQ-C30 is a standard instrument in oncology for the evaluation of new cancer therapies to provide comprehensive assessment of GHS/QoL, functioning, and symptoms over the past week. • Scores range from 0 to 100; higher scores on functional domains and lower scores on symptoms reflect better outcomes. • A change ≥10 points was considered clinically meaningful.[8]	The Skindex-16 assesses impact of skin disease on patients' HRQoL over the past week with results on 3 subscales (emotional, symptom, and functional). • Scores on the subscales range from 0 to 100; lower scores reflect lower impact of disease. • A change ≥10 points was considered clinically meaningful.[7,9]

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life-Core 30; GHS/QoL, global health status/quality of life; HRQoL, health-related quality of life.

- Responder analyses were conducted in patients with non-missing data to determine the proportions with clinically meaningful improvement or deterioration, or maintenance from baseline on QLQ-C30 and Skindex-16 at Cycles 2, 6, and 9.
  - Maintenance was defined as neither improvement nor deterioration that was clinically meaningful.

Results

- The patient population was 70.4% male, with a mean (SD) age of 63.8 (11.1) years (**Table 2**).
  - Two-thirds of the patients (66.7%) had ECOG performance status of 0, and disease progression was the primary reason for discontinuation of prior HHI therapy.

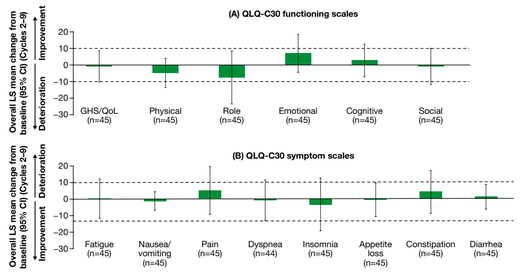
Table 2. Patient characteristics at baseline (N=54)

Variable	Value
Age, mean ± SD, years	63.8 ± 11.1
≥65, n (%)	27 (50.0)
Male sex, n (%)	38 (70.4)
BMI, mean ± SD, kg/m^2	26.2 ± 5.6
ECOG performance status, n (%)	
0	36 (66.7)
1	18 (33.3)
Time from initial diagnosis to first study treatment dose, mean ± SD, months	117.5 ± 110.5
Stage at first known diagnosis, n (%)	
I	2 (3.7)
II	3 (5.6)
III	4 (7.4)
IV	11 (20.4)
Unknown	30 (55.6)
Reason for discontinuation of prior HHI, n (%)†	
Disease progression	41 (75.9)
Intolerance	18 (33.3)

†Sum is >54 because some patients had >1 reason for discontinuation.
BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; HHI, hedgehog inhibitor.

- Baseline scores are presented in **Figure S1 in the supplementary appendix**.
  - These scores were similar to EORTC reference values for overall cancer patients,10 and generally reflect moderate to high levels of functioning and low symptom burden.
- In MMRM analysis, overall changes from baseline across the study period indicated maintenance (change <10 points) on QLQ-C30 global health status (GHS)/quality of life (QoL) and all functioning and symptom scales (**Figure 1**).
  - Changes from baseline were neither clinically meaningful nor statistically significant relative to baseline.

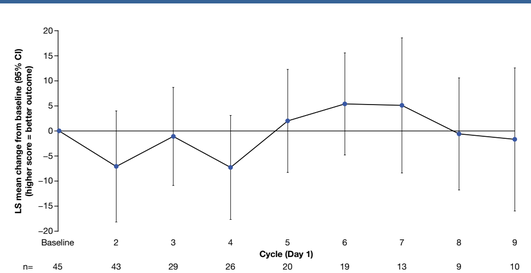
Figure 1. Overall change from baseline (MMRM) on the QLQ-C30 in patients in the full analysis set who had baseline and ≥1 post-baseline value



Broken horizontal lines indicate threshold for a clinically meaningful change.
GHS/QoL, global health status/quality of life; LS, least squares; MMRM, mixed model repeated measures; QLQ-C30, Quality of Life-Core 30.

- Change from baseline in QLQ-C30 GHS/QoL scores at each time point also suggested that overall HRQoL was generally maintained across the study duration (**Figure 2**).

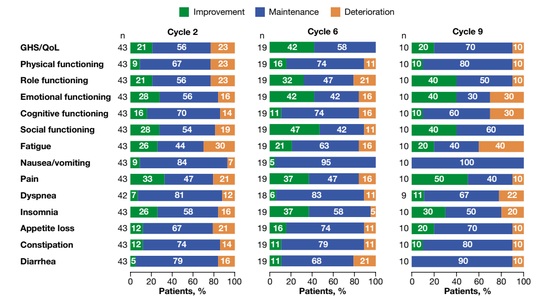
Figure 2. MMRM analysis of change from baseline in GHS/QoL by treatment cycle in patients in the full analysis set who had baseline and ≥1 post-baseline value



GHS/QoL, global health status/quality of life; LS, least squares; MMRM, mixed model repeated measures.

- In the responder analysis, clinically meaningful improvement or maintenance on all QLQ-C30 scales was reported by most patients at Cycle 2 (**Figure 3**).
  - 77% of patients reported clinically meaningful improvement or maintenance on GHS/QoL, with ranges of 77–86% and 70–93% of patients for functioning and symptoms scales, respectively.
- Similar proportions were reported at Cycle 6 (~1 year of treatment), with consistent results at Cycle 9 except for fatigue (**Figure 3**).

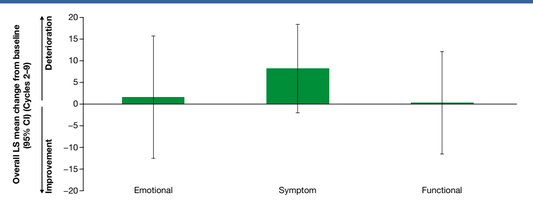
Figure 3. Proportion of patients reporting clinically meaningful improvement, maintenance, or clinically meaningful deterioration on the QLQ-C30 at Cycles 2, 6, and 9



GHS/QoL, global health status/quality of life; QLQ-C30, Quality of Life-Core 30.

- On the Skindex-16, MMRM analysis of overall change from baseline showed maintenance on the emotional, symptom, and functional subscales (**Figure 4**).
  - None of the changes were clinically meaningful or statistically significant relative to baseline.
  - Baseline scores are shown in Figure S2 in the supplementary appendix.

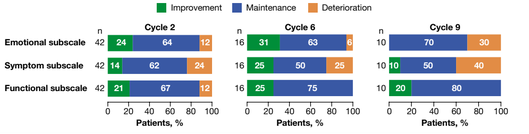
Figure 4. Overall change from baseline (MMRM) on the Skindex-16 in patients in the full analysis set who had baseline and ≥1 post-baseline value (n=43)



LS, least squares; MMRM, mixed model repeated measures.

- Responder analysis showed clinically meaningful improvement or maintenance across all 3 subscales in 76–88% of patients at Cycle 2 (**Figure 5**).
  - Similar results were generally observed at Cycles 6 and 9.

Figure 5. Proportion of patients reporting clinically meaningful improvement, maintenance, or clinically meaningful deterioration on the Skindex-16 at Cycles 2, 6, and 9



Limitations

- This was a single-arm, non-randomized, open-label study.
- The small sample sizes (≤10 patients) in the later cycles (Cycle 8 and 9) limit data interpretability.
- Clinically meaningful changes were based on prior literature,[7–9] and anchor-based approaches to derive clinically meaningful changes within the trial population were not performed.
- In contrast to the QLQ-C30, to the best of our knowledge reference values have not been determined for the Skindex-16.

Conclusions

- Results of this pivotal clinical trial of cemiplimab showed that, in addition to providing clinically meaningful antitumour activity and durable responses in patients with mBCC,[3] patient-reported HRQoL was maintained during the study.
  - From baseline to Cycle 9, most patients treated with cemiplimab reported:
    - Maintenance or improvement in QLQ-C30 GHS/QoL and functioning while maintaining a low symptom burden.
    - Maintenance across all 3 subscales on the Skindex-16.

References

1. Migden MR et al. *Cancer Treat Rev*. 2018;64:1–10.
2. Regeneron Pharmaceuticals, Inc., and sanofi-aventis U.S. LLC. Libtayo® [cemiplimab-rwlc injection for intravenous use] prescribing information. Revised November 2022. Available at: https://www.regeneron.com/downloads/libtayo_fpi.pdf. Accessed January 30, 2023.
3. Lewis K et al. *Cancer Res*. 2022;82(12 suppl):CT165.
4. Stratigos AJ et al. *J Clin Oncol*. 2021;39(15 suppl):9566.
5. Stratigos AJ et al. *Lancet Oncol*. 2021;22:848–857.
6. Aaronson NK et al. *J Natl Cancer Inst*. 1993;85:365–376.
7. Chren MM et al. *J Cutan Med Surg*. 2001;5:105–110.
8. Osoba D et al. *J Clin Oncol*. 1998;16:139–144.
9. Hansson J et al. *Eur J Dermatol*. 2018;28:775–783.
10. Scott NW et al. EORTC QLQ-C30 Reference Values. Available at: https://www.eortc.org/app/uploads/sites/2/2018/02/reference_values_manual2008.pdf. Accessed January 30, 2023.

Acknowledgements

This study was funded by Regeneron Pharmaceuticals, Inc., and Sanofi. Medical writing support was provided by Prime (Knutsford, UK), funded by Regeneron Pharmaceuticals, Inc., and Sanofi.

Disclosures

Karl D Lewis reports research funding from Genentech and Regeneron Pharmaceuticals, Inc.

Scan the QR code for author disclosures and supplementary appendix.

Fall Clinical Dermatology Congress, October 19–22, 2023 (encore previously presented at the National Comprehensive Cancer Network [NCCN] Annual Conference, March 31–April 2, 2023).