Health-Related Quality of Life (HRQL) in Patients with Advanced Cutaneous Squamous Cell Carcinoma (CSCC) Treated with Cemiplimab: Post Hoc Exploratory Analysis of a Phase 2 Clinical Trial

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Background

- Cutaneous squamous cell carcinoma (CSCC) is considered the second most common malignancy in the US, although its exclusion from national cancer registries has presented a barrier to epidemiologic characterization.[1]
  - Estimates suggest an incidence of around 1.5 million cases per year in the US.[2]
  - The incidence of CSCC is increasing yearly in the US.[3]
- Most CSCC patients have a favorable prognosis, but for the patients who are not amenable to curative surgery, palliative systemic therapy has been administered.[1]
- Cemiplimab is a programmed cell death (PD)-1 inhibitor that is indicated for treatment of CSCC in patients with metastatic (mCSCC) or locally advanced (laCSCC) disease not amenable to curative surgery or curative radiation.[4]
  - Cemiplimab demonstrated a robust durable clinical response and a safety profile consistent with other checkpoint inhibitors in a recent Phase 2 study (NCT02760498).[5–8]
  - For the latest data from the Phase 2 study of cemiplimab in patients with advanced CSCC, please see poster 367 reporting longer follow-up data.
  - No new safety signals emerged with longer follow-up. The most common treatment-emergent adverse events of any grade were fatigue (n=67, 34.7%), diarrhea (n=53, 27.5%), and nausea (n=46, 23.8%).
- The Phase 2 trial included the European Organisation for Research and Treatment of Cancer (EORTC) cancer specific 30-item questionnaire (QLQ-C30)[9] as a measure of patient-reported health-related quality of life (HRQL).
- Pain is an important and bothersome symptom in the diagnosis and treatment of CSCC from the patient and clinical perspectives.[10]

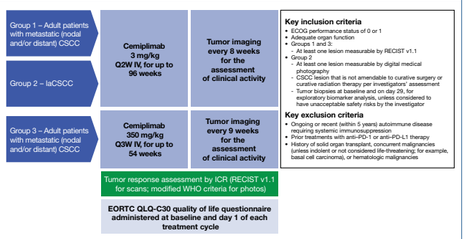
Objective

- This post hoc exploratory analysis examined the QLQ-C30 data from a Phase 2 clinical trial (NCT02760498) to determine the effects of cemiplimab treatment on HRQL and pain.

Methods

- For inclusion in the Phase 2, non-randomized, global, pivotal trial of cemiplimab (**Figure 1**), adults with invasive CSCC not amenable to curative surgery or curative radiotherapy according to the investigator were also required to have ≥1 lesion, Eastern Cooperative Oncology Group (ECOG) performance status ≤1, and life expectancy >12 weeks.
  - Adult patients (N=193) received intravenous (IV) cemiplimab 3 mg/kg every 2 weeks (Q2W; mCSCC n=59; laCSCC n=78) for 12 treatment cycles or 350 mg every 3 weeks (Q3W; mCSCC n=56) for six treatment cycles.
  - Treatment cycle length was 8 weeks for Groups 1 and 2 and 9 weeks for Group 3.
  - The primary efficacy endpoint was objective response rate, defined as the proportion of patients with complete or partial response.

Figure 1. Study design



ICR, independent central review; PD-L1, PD-ligand 1; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; WHO, World Health Organization.

- At baseline and day 1 of each treatment cycle until progression, patients were administered the QLQ-C30.[9]
- The QLQ-C30 assesses HRQL over the past week among cancer patient populations using a global health status/HRQL scale, five functional scales, and nine symptom scales/items.
  - Functional scales include physical, role, cognitive, emotional, and social functioning.
  - Symptom scales/items include fatigue, pain, nausea/vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties.
  - Scores range from 0 to 100; high scores on functional scales and low scores on symptom scales reflect better outcomes.
  - A change ≥10 points from baseline is considered clinically meaningful.[11]
- The full analysis set included patients who had baseline and at least one post-baseline assessment for any QLQ-C30 scale.
- Descriptive statistics were used to summarize HRQL scores over time (only pain and global health status/HRQL scores are shown).
- Mixed effects repeated measures models (MMRM) were used to estimate the mean treatment effect (change from baseline while accounting for missing data) for all QLQ-C30 scales.
  - The model included fixed effects of treatment, visit, treatment-by-visit interaction, and baseline value of the specified individual item.
  - Results are expressed as the least squares (LS) mean and standard error (SE).
- A responder analysis was also conducted at cycle 6 and cycle 12 based on evaluation of average change from baseline among patients who had baseline scores that allowed a ≥10-point change.
  - A responder was defined as a patient who achieved an average 10-point increase in functional scale scores and 10-point decline in symptom scale scores.

Results

Patient population and baseline scores

- A total of 193 adult patients were enrolled in the study, and demographic characteristics were generally similar across the treatment groups (**Table 1**).

Table 1. Demographic and clinical characteristics of the full analysis set

Variable	Total (N=193)	mCSCC 350 mg Q3W (n=56)	mCSCC 3 mg/kg Q2W (n=59)	laCSCC 3 mg/kg Q2W (n=78)
Age, mean ± SD, years	71.1 ± 11.4	69.7 ± 12.8	70.4 ± 10.1	72.5 ± 11.2
≥65 years, n (%)	144 (74.6)	42 (75.0)	43 (72.9)	59 (75.6)
Male, n (%)	161 (83.4)	48 (85.7)	54 (91.5)	59 (75.6)
ECOG performance status, n (%)				
0	86 (44.6)	25 (44.6)	23 (39.0)	38 (48.7)
1	107 (55.4)	31 (55.4)	36 (61.0)	40 (51.3)
Primary site, n (%)				
Head and neck	131 (67.9)	31 (55.4)	38 (64.4)	62 (79.5)
Other	62 (32.1)	25 (44.6)	21 (35.6)	16 (20.5)
Prior cancer-related systemic therapy, n (%)	65 (33.7)	20 (35.7)	33 (55.9)	12 (15.4)
Prior cancer-related radiotherapy, n (%)	131 (67.9)	38 (67.9)	50 (84.7)	43 (55.1)

SD, standard deviation.

- Baseline scores for QLQ-C30 indicated generally moderate to high levels of functioning and moderate to low symptom burden (**Table 2**).
  - Pain is of importance as a symptom in patients with advanced CSCC, and the baseline pain score of patients with advanced CSCC receiving cemiplimab (29.8 ± 30.4) was worse than that reported by patients with advanced head and neck cancer (24.9 ± 26.3; n=1722) and the general population (20.9 ± 27.6; n=7802) in the literature;[12] comparisons with both groups were significant, $P<0.05$ and $P<0.0001$, respectively.

Table 2. Baseline scores and change from baseline (MMRM) in patients in the full analysis set who had baseline and post-baseline assessments on each QLQ-C30 scale or item

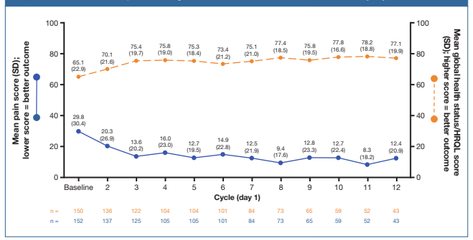
QLQ-C30 scale/item	Baseline, mean ± SD (n)	LS mean change ± SE (n)	
		Cycle 3	Cycle 12
Global health status/HRQL	65.1 ± 22.9 (150)	7.8 ± 1.6 (122)**	11.1 ± 2.6 (43)**
Functional scales†			
Physical function	80.1 ± 22.8 (151)	1.1 ± 1.3 (124)	4.0 ± 2.1 (43)
Role function	75.8 ± 30.0 (151)	0.4 ± 2.1 (123)	5.6 ± 3.4 (43)
Emotional function	80.2 ± 21.2 (151)	4.2 ± 1.3 (123)*	5.3 ± 2.2 (43)*
Cognitive function	83.4 ± 22.2 (151)	1.7 ± 1.4 (123)	2.5 ± 2.3 (43)
Social function	74.4 ± 31.8 (150)	5.3 ± 1.8 (122)*	8.6 ± 3.0 (43)*
Symptoms‡			
Fatigue	30.2 ± 24.6 (152)	−2.8 ± 1.7 (125)	−4.8 ± 2.8 (43)
Nausea/vomiting	4.6 ± 12.2 (152)	−1.6 ± 0.8 (125)*	−2.9 ± 1.3 (43)*
Pain	29.8 ± 30.4 (152)	−11.5 ± 1.9 (125)**	−14.3 ± 3.1 (43)**
Dyspnea	12.9 ± 23.4 (152)	0.7 ± 1.7 (125)	1.5 ± 2.9 (43)
Insomnia	27.4 ± 28.0 (151)	−9.1 ± 2.0 (123)**	−17.4 ± 3.3 (43)**
Appetite loss	19.5 ± 29.3 (152)	−8.4 ± 1.6 (124)**	−13.7 ± 2.7 (43)**
Constipation	13.6 ± 24.1 (152)	−4.5 ± 1.5 (125)*	−11.2 ± 2.5 (43)**
Diarrhea	4.9 ± 13.6 (150)	3.6 ± 1.4 (121)*	0.6 ± 2.3 (43)
Financial difficulty	19.1 ± 30.7 (150)	0.5 ± 2.0 (122)	−3.4 ± 3.3 (43)

**$P<0.001$ and *$P<0.05$ versus baseline. †Higher scores reflect better outcomes. ‡Lower scores reflect better outcomes.

Longitudinal analysis

- Among the symptom scales and items, a marked improvement in pain score was observed as early as cycle 2 (**Figure 2**). The initial clinically meaningful improvement (≥10 points) in pain score at cycle 3 (LS mean [SE] change −11.5 [1.9]; $P<0.0001$) was maintained during study treatment to cycle 12 (LS mean [SE] change −14.3 [3.1]; $P<0.0001$) (**Table 2**).
  - At cycle 3, significant improvements from baseline were also observed for symptoms of insomnia, appetite loss, and constipation. At cycle 12, these improvements reached the clinically meaningful threshold (**Table 2**).
  - With the exception of a significant worsening of diarrhea at cycle 3 and a significant improvement of nausea/vomiting at cycle 12, all other domains/symptoms remained stable relative to baseline. By cycle 12, diarrhea remained stable relative to baseline.
- Among the functional scales, significant improvements were observed in emotional and social function at cycle 3 and cycle 12. All other functional scales remained stable relative to baseline (**Table 2**).
- For global health status/HRQL, significant improvement from baseline was observed at cycle 3. At cycle 12, this improvement reached the clinically meaningful threshold (LS mean [SE] change 11.1 [2.6]; $P<0.0001$) (**Table 2**).

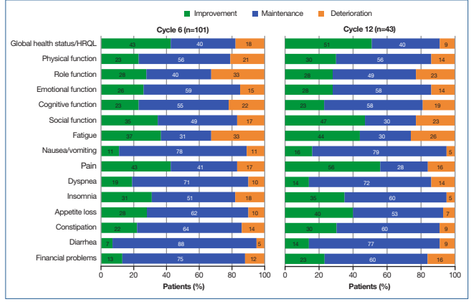
Figure 2. QLQ-C30 pain and global health status/HRQL scores by cycle



Responder analysis

- By cycle 6, the majority of patients experienced clinically meaningful (≥10 points) improvement or stability including pain (83%), nausea/vomiting (89%), diarrhea (95%), constipation (86%), and appetite loss (90%), as well as functional scales (77–86%) (**Figure 3**).
  - These effects likely account for the clinically meaningful improvement or stability also reported on global health status/HRQL among the majority of patients (82%).
- At cycle 12, the majority of patients showed sustained improvement and stabilization across all symptoms and functional scales (74–95%). Ninety-one percent of patients experienced clinically meaningful improvement or stability in global health status/HRQL scores at cycle 12 (**Figure 3**).
- The proportions of patients with clinically meaningful deterioration were generally low at both evaluated time points (**Figure 3**).
  - The highest rate of clinically relevant deterioration among the symptoms was observed for fatigue.

Figure 3. Proportion of patients reporting clinically meaningful change at cycle 6 and cycle 12



Study Limitations

- This was a non-randomized, single-arm, open-label study.
- The 10-point threshold considered indicative of a clinically meaningful change has not been validated for this specific patient population (i.e., advanced CSCC).

Conclusions

- In advanced CSCC patients, treatment with cemiplimab resulted in clinically meaningful reduction in pain as early as cycle 3 with maintenance of effect through cycle 12.
- Improvement in global health status/HRQL was observed as early as cycle 3 with clinically meaningful improvement seen by cycle 12.
- By cycle 6, the majority of patients experienced clinically meaningful improvement or stability in global health status/HRQL and functional status, while maintaining a low symptom burden.
- These results further support cemiplimab as a new standard of care option in the treatment of advanced CSCC.

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