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Cemiplimab Improves Health-Related Quality of Life (HRQoL) and Reduces Pain in Patients with Advanced Cutaneous Squamous Cell Carcinoma (CSCC): Results from a Post Hoc Exploratory Analysis of a Phase 2 Clinical Trial

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Cemiplimab Improves Health-Related Quality of Life (HRQoL) and Reduces Pain in Patients with Advanced Cutaneous Squamous Cell Carcinoma (CSCC): Results from a Post Hoc Exploratory Analysis of a Phase 2 Clinical Trial

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Synopsis

- Patients with advanced cutaneous squamous cell carcinoma (CSCC) who are not curable by surgery are generally administered palliative systemic therapy.
  - In these patients, pain is an important symptom from the patient and clinician perspectives.[1]
- Cemiplimab is indicated for treatment of patients with metastatic CSCC (mCSCC) or locally advanced CSCC (laCSCC) not eligible for curative surgery/radiation.[2]
- Cemiplimab demonstrated a robust clinical response and a safety profile consistent with other checkpoint inhibitors.[3]
- A Phase 2 clinical trial supported durability of response and reported an overall objective response rate (ORR) of 46.1%[4-6] as measured by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1).[7]
- The Phase 2 trial included the cancer-specific European Organisation for Research and Treatment of Cancer (EORTC) 30-item questionnaire (QLQ-C30)[8] as a measure of patient-reported health-related quality of life (HRQoL).

Objective

- This post hoc analysis explored the effects of cemiplimab on HRQoL and pain using QLQ-C30 data from the Phase 2 clinical trial (NCT02760498) of advanced CSCC, with a focus on the association between time to clinically meaningful changes in pain and clinical tumor response.

Methods

- For inclusion in this non-randomized, global, pivotal trial, adults with advanced CSCC not amenable to curative surgery/radiotherapy according to the investigator were required to have ≥1 lesion, Eastern Cooperative Oncology Group (ECOG) performance status ≤1, and life expectancy >12 weeks.
- Patients (N=193) received intravenous 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 the Q2W groups and 9 weeks for the Q3W group.
- The QLQ-C30[8] was administered at baseline and day 1 of each treatment cycle.
- The QLQ-C30 assesses HRQoL over the past week using a Global Health Status/HRQoL scale and across functional domains (physical, role, cognitive, emotional, and social functioning) and symptoms (fatigue, pain, nausea/vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties).
  - Scores range from 0 to 100; high scores on functional domains and low scores on symptoms reflect better outcomes.
  - A change ≥10 points from baseline is considered clinically meaningful.[9]
- Mixed-effects repeated measures models (MMRM) estimated changes from baseline to each cycle on all QLQ-C30 scales; results are expressed as least squares (LS) mean and standard error (SE).
  - The model included fixed effects of treatment, visit, treatment-by-visit interaction, and baseline value.
- Changes from baseline in pain were also stratified by clinical responders, defined by ORR assessed by independent central review, and clinical non-responders (stable or progressive disease).
- For patients with data from baseline to cycle 6 and cycle 12, proportions with clinically meaningful (≥10 points) improvement or worsening, or stability (<10 points) on each item was determined.
- Kaplan–Meier (KM) survival analysis was used to estimate time to first clinically meaningful change in QLQ-C30 pain score and its relationship to tumor response in patients who had baseline pain scores that allowed for at least a 10-point change.
- Since pain medication use was captured over treatment duration, opioids were analyzed at each cycle.
  - Opioid use was adjusted for duration to calculate cumulative number of days on opioids per patient-year using Poisson regression with treatment group as fixed factors and patients' treatment exposure duration as offset variable.

Results

- Demographic characteristics of enrolled patients (N=193) were generally similar across 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 indicated moderate to high levels of functioning and moderate to low symptom burden (**Table 2**).
- At cycle 3, significant improvements from baseline were observed for emotional and social function and symptoms of pain, insomnia, appetite loss, nausea/vomiting, and constipation (all $P<0.05$) (**Table 2**).
- Improvements increased or were maintained at cycle 12 and were clinically meaningful for pain, insomnia, appetite loss, and constipation (**Table 2**).
- These improvements likely contributed to the improved HRQoL that was significant at cycle 3 ($P<0.001$) and clinically meaningful at cycle 12.

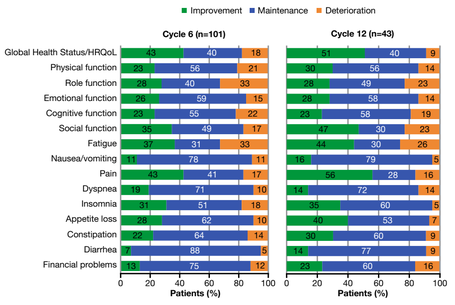
Table 2. Baseline scores and change from baseline (MMRM) in patients in the full analysis set who had baseline and post-baseline assessments on each QLQ-C30 scale or item

QLQ-C30 scale/item	Baseline, mean ± SD (n)	LS mean change ± SE (n)	
		Cycle 3	Cycle 12
Global Health Status/HRQoL	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.

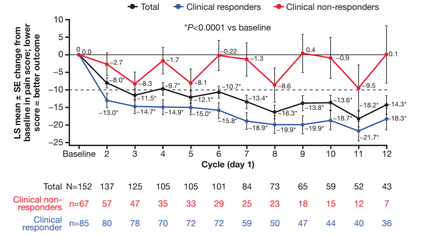
- Clinically meaningful improvement or stability was experienced by 77%–86% of patients across QLQ-C30 scales by cycle 6, and by 74%–95% at cycle 12 (**Figure 1**).

Figure 1. Proportion of patients reporting clinically meaningful change at cycle 6 and cycle 12



- In all patients, reductions from baseline in pain were statistically significant as early as cycle 2, clinically meaningful by cycle 3, and sustained to cycle 12 (**Figure 2**).
- In contrast to clinical non-responders, clinical responders reported a clinically meaningful reduction in pain from baseline at cycle 2 with further reductions that were sustained to cycle 12 (all $P<0.0001$) (**Figure 2**).

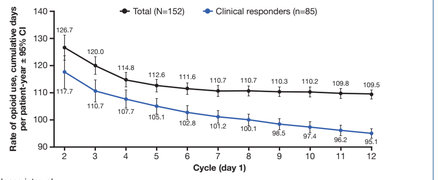
Figure 2. Change from baseline in QLQ-C30 pain score by cycle among patients who had baseline and post-baseline assessment of the QLQ-C30 pain scale



Horizontal broken line indicates threshold for a clinically meaningful change.

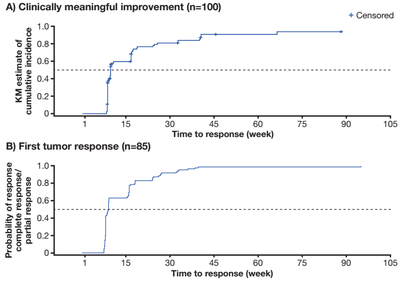
- Opioid use decreased over study duration (**Figure 3**), suggesting that clinically meaningful improvement in pain was independent of opioid use.
- Median time to first clinically meaningful pain improvement in all patients approximated the median time to first tumor response that was estimated for clinical responders, 2.0 months and 2.1 months, respectively (**Figure 4; Table 3**).
  - Among clinical responders, the median time to first clinically meaningful pain improvement was also 2.1 months.
- The change from baseline in pain score at first tumor response was statistically significant and clinically meaningful versus non-responders ($P<0.0001$) (**Table 3**).
- Median time to first clinically meaningful deterioration in pain approximated the median time to progression-free survival (PFS), 14.8 months and 18.4 months, respectively (**Figure 5; Table 3**).
  - Median time to first clinically meaningful pain deterioration among clinical responders was 20.6 months (**Table 3**).

Figure 3. Cumulative number of days on opioids over time among patients who had baseline and post-baseline assessment of the QLQ-C30 pain scale



CI, confidence interval.

Figure 4. KM survival analysis of time to first clinically meaningful improvement in pain score (A) and first tumor response (B)



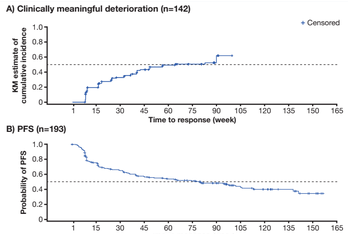
Time point where horizontal broken line (50% survival probability) crosses curve indicates median time to response.

Table 3. Summary of relationship between clinically meaningful changes in pain and clinical response among patients with CSCC treated with cemiplimab*

	Clinical responders (complete + partial)	Clinical non-responders (stable + progressive)	All
Baseline pain score, mean ± SD (n)	26.5 ± 29.1 (85)	33.7 ± 31.1 (83)	30.1 ± 30.3 (168)
Change from baseline in pain score at first tumor response, n	85	67	—
LS mean change ± SE	−15.2 ± 1.5†	−3.9 ± 2.1	—
LS mean (95% CI) difference vs non-responders	−11.3 (−16.3, −6.3)‡	—	—
Median time to clinical response, months (n)	2.0 (85)	—	—
Median PFS, months (n)	—	—	18.4 (193)
Median time to first pain improvement, months (n)	2.1 (53)	—	2.1 (100)
Median time to first pain deterioration, months (n)	20.6 (80)	—	14.8 (142)

*Ns reflect the number of patients who had baseline and post-baseline assessment scores on the QLQ-C30 pain scale. †$P<0.0001$ relative to baseline; ‡$P<0.0001$ compared with non-responders.

Figure 5. KM survival analysis of time to first clinically meaningful deterioration in pain score (A) and PFS (B)



Time point where horizontal broken line (50% survival probability) crosses curve indicates median time to response.

Study Limitations

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

Summary and Conclusion

- These results support cemiplimab as a standard of care option for treatment of advanced CSCC, with clinically meaningful benefits on HRQoL and clinically meaningful reductions in pain that appear to be independent of opioid use and may correlate with tumor response.

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For any questions regarding this poster presentation, please contact Dr Michael R Migden, mrmigden@mdanderson.org

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