

# 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.<sup>1</sup>
- Cemiplimab is indicated for treatment of patients with metastatic CSCC (mCSCC) or locally advanced CSCC (laCSCC) not eligible for curative surgery/radiation.<sup>2</sup>
- Cemiplimab demonstrated a robust clinical response and a safety profile consistent with other checkpoint inhibitors.<sup>3</sup>
- A Phase 2 clinical trial supported durability of response and reported an overall objective response rate (ORR) of 46.1%<sup>4,5</sup> as measured by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1).<sup>7</sup>
- The Phase 2 trial included the cancer-specific European Organisation for Research and Treatment of Cancer (EORTC) 30-item questionnaire (QLQ-C30)<sup>6</sup> 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  $\geq 1$  lesion, Eastern Cooperative Oncology Group (ECOG) performance status  $\leq 1$ , 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<sup>6</sup> 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  $\geq 10$  points from baseline is considered clinically meaningful.<sup>9</sup>
- 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 ( $\geq 10$  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).

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 $\pm$ SD, years	71.1 $\pm$ 11.4	69.7 $\pm$ 12.8	70.4 $\pm$ 10.1	72.5 $\pm$ 11.2
$\geq 65$ 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)

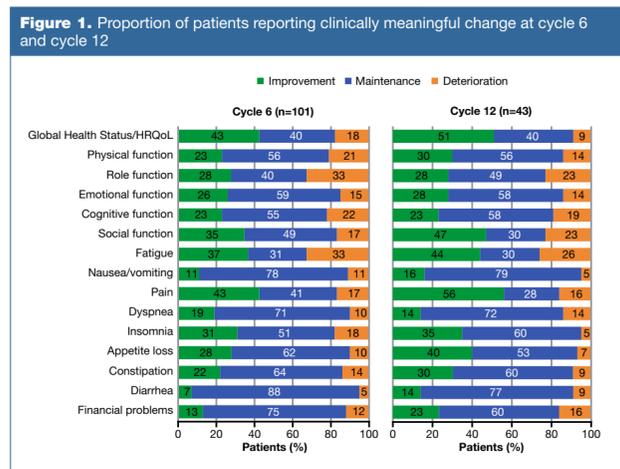
SD, standard deviation.

- 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.

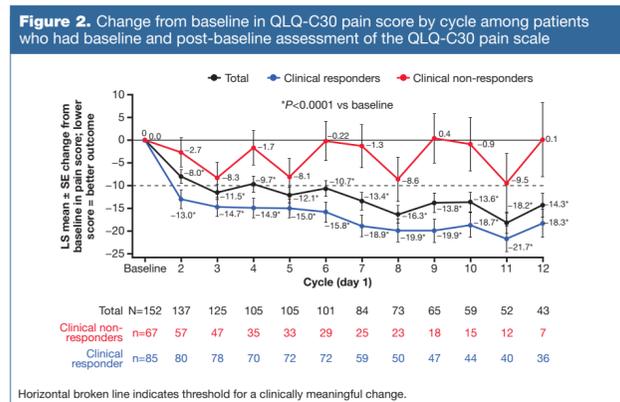
QLQ-C30 scale/item	Baseline, mean $\pm$ SD (n)	LS mean change $\pm$ SE (n)	
		Cycle 3	Cycle 12
Global Health Status/HRQoL	65.1 $\pm$ 22.9 (150)	7.8 $\pm$ 1.6 (122)**	11.1 $\pm$ 2.6 (43)**
Functional scales <sup>1</sup>			
Physical function	80.1 $\pm$ 22.8 (151)	1.1 $\pm$ 1.3 (124)	4.0 $\pm$ 2.1 (43)
Role function	75.8 $\pm$ 30.0 (151)	0.4 $\pm$ 2.1 (123)	5.6 $\pm$ 3.4 (43)
Emotional function	80.2 $\pm$ 21.2 (151)	4.2 $\pm$ 1.3 (123)*	5.3 $\pm$ 2.2 (43)*
Cognitive function	83.4 $\pm$ 22.2 (151)	1.7 $\pm$ 1.4 (123)	2.5 $\pm$ 2.3 (43)
Social function	74.4 $\pm$ 31.8 (150)	5.3 $\pm$ 1.8 (122)*	8.6 $\pm$ 3.0 (43)*
Symptoms <sup>1</sup>			
Fatigue	30.2 $\pm$ 24.6 (152)	-2.8 $\pm$ 1.7 (125)	-4.8 $\pm$ 2.8 (43)
Nausea/vomiting	4.6 $\pm$ 12.2 (152)	-1.6 $\pm$ 0.8 (125)*	-2.9 $\pm$ 1.3 (43)*
Pain	29.8 $\pm$ 30.4 (152)	-11.5 $\pm$ 1.9 (125)**	-14.3 $\pm$ 3.1 (43)**
Dyspnea	12.9 $\pm$ 23.4 (152)	0.7 $\pm$ 1.7 (125)	1.5 $\pm$ 2.9 (43)
Insomnia	27.4 $\pm$ 28.0 (151)	-9.1 $\pm$ 2.0 (123)**	-17.4 $\pm$ 3.3 (43)**
Appetite loss	19.5 $\pm$ 29.3 (152)	-8.4 $\pm$ 1.6 (124)**	-13.7 $\pm$ 2.7 (43)**
Constipation	13.6 $\pm$ 24.1 (152)	-4.5 $\pm$ 1.5 (125)*	-11.2 $\pm$ 2.5 (43)**
Diarrhea	4.9 $\pm$ 13.6 (150)	3.6 $\pm$ 1.4 (121)*	0.6 $\pm$ 2.3 (43)
Financial difficulty	19.1 $\pm$ 30.7 (150)	0.5 $\pm$ 2.0 (122)	-3.4 $\pm$ 3.3 (43)

\*\* $P < 0.001$  and \* $P < 0.05$  versus baseline. <sup>1</sup>Higher scores reflect better outcomes. <sup>2</sup>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).

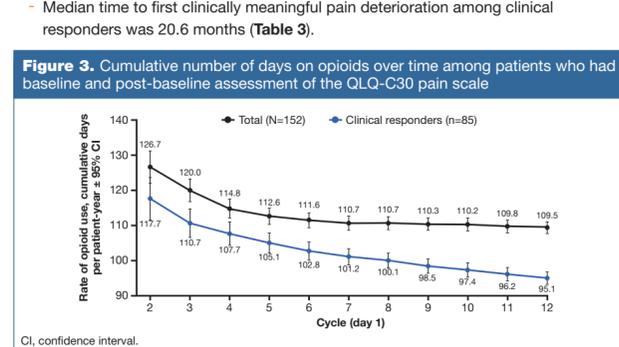


- In all patients, reductions from baseline in pain were statistically significant as early as cycle 2, clinically meaningful by cycle 3, and sustained to cycle 12 (Figure 2).
- In contrast to clinical non-responders, clinical responders reported a clinically meaningful reduction in pain from baseline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



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

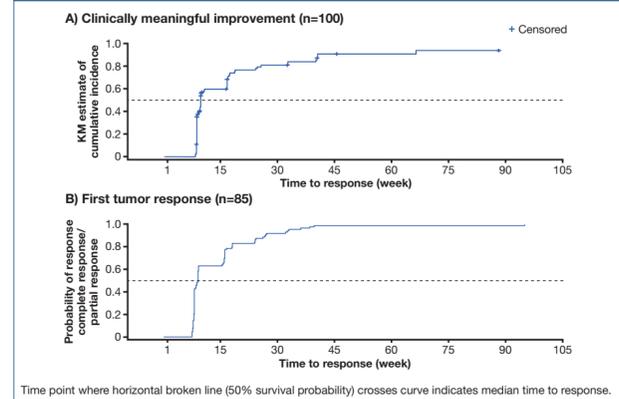
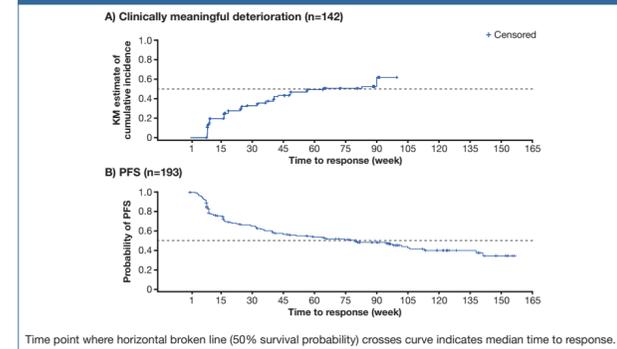


Table 3. Summary of relationship between clinically meaningful changes in pain and clinical response among patients with CSCC treated with cemiplimab\*

	Clinical responders (complete + partial)	Clinical non-responders (stable + progressive)	All
Baseline pain score, mean $\pm$ SD (n)	26.5 $\pm$ 29.1 (85)	33.7 $\pm$ 31.1 (83)	30.1 $\pm$ 30.3 (168)
Change from baseline in pain score at first tumor response, n	85	67	—
LS mean change $\pm$ SE	-15.2 $\pm$ 1.5 <sup>†</sup>	-3.9 $\pm$ 2.1	—
LS mean (95% CI) difference vs non-responders	-11.3	—	—
	(-16.3, -6.3) <sup>†</sup>	—	—
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)

\*No reflect the number of patients who had baseline and post-baseline assessment scores on the QLQ-C30 pain scale. <sup>†</sup> $P < 0.0001$  relative to baseline; <sup>‡</sup> $P < 0.0001$  compared with non-responders.

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



## 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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## Funding sources

Funding was provided by Regeneron Pharmaceuticals, Inc. and Sanofi.

## Acknowledgments

The authors would like to thank the patients, their families, all other investigators, and all investigational site members involved in this study. The study was funded by Regeneron Pharmaceuticals, Inc. and Sanofi. Medical writing support was provided by E. Jay Bieman, PhD, and typesetting was provided by Jenna Lee, of Prime, Knutsford, UK, funded by Regeneron Pharmaceuticals, Inc. and Sanofi.

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

## Disclosures

Michael R. Migden: honoraria and travel expenses from Regeneron Pharmaceuticals, Inc., Sanofi, Novartis, Genentech, Eli Lilly and Sun Pharma; and institutional research funding from Regeneron Pharmaceuticals, Inc., Novartis, Genentech and Eli Lilly. Danny Rischin: institutional research grant and funding from Regeneron Pharmaceuticals, Inc., Roche, Merck Sharp & Dohme, Bristol-Myers Squibb and GlaxoSmithKline; uncompensated scientific committee and advisory board from Merck Sharp & Dohme, Regeneron Pharmaceuticals, Inc., Sanofi, GlaxoSmithKline and Bristol-Myers Squibb; travel and accommodation from Merck Sharp & Dohme and GlaxoSmithKline. Stacie Hudgens: consulting fees from Regeneron Pharmaceuticals, Inc., Chrysalyn D. Schmults: steering committee member for Castle Biosciences; a steering committee member and consultant for Regeneron Pharmaceuticals, Inc.; a consultant for Sanofi; has received research funding from Castle Biosciences, Regeneron Pharmaceuticals, Inc., Novartis, Genentech and Merck, and is a chair for the National Comprehensive Cancer Network. Anna C. Pawlick: honoraria and consulting or advisory roles at Bristol-Myers Squibb, Merck, Regeneron Pharmaceuticals, Inc., Array, Novartis, Seattle Genetics and Amgen; research funding from Bristol-Myers Squibb, Merck, Regeneron Pharmaceuticals, Inc., Celldex and Forance and travel, accommodation, expenses from Regeneron Pharmaceuticals, Inc., Array and Seattle Genetics. Alexander Guminski: personal fees and non-financial support (advisory board and travel support) from Bristol-Myers Squibb and Sun Pharma; personal fees (advisory board) from Merck KGaA, Eisai and Pfizer; non-financial (travel) support from Atollas; and clinical trial unit support from PPD Australia. Axel Hauschild: institutional grants, speaker's honoraria and consultancy fees from Amgen, Bristol-Myers Squibb, Merck Sharp & Dohme, Merck, Regeneron Pharmaceuticals, Inc., Celldex and Forance and consultancy fees from Merck Serono, Phlogon and Regeneron Pharmaceuticals, Inc.; and consultancy fees from OncoSec. Chieh-I Chen, Zhen Chen, Vera Mastey, Matthew G. Fury, Israel Lowy, Siyu Li: employees and shareholders of Regeneron Pharmaceuticals, Inc. Anne Lynn S. Chang: consulting and advisory roles at Regeneron Pharmaceuticals, Inc. and Merck; research funding from Regeneron Pharmaceuticals, Inc., Novartis, Galderna and Merck. Guilherme Rabinowits: consulting and advisory roles for EMD Serono Pfizer, Sanofi, Regeneron Pharmaceuticals, Inc. and Merck and Castle and stock/other ownership interests from Syros Pharmaceuticals and Regeneron Pharmaceuticals, Inc. Sherrif Ibrahim: research funding from Regeneron Pharmaceuticals, Inc. and Castle, speakers' bureau from Genentech and travel and accommodation expenses from Regeneron Pharmaceuticals, Inc. and Genentech. Denise Bury, Medha Sasane: employees and shareholders of Sanofi.