Integrated Analysis of a Phase 2 Study of Cemiplimab in Advanced Cutaneous Squamous Cell Carcinoma: Extended Follow-up of Outcome and Quality of Life Analysis

[[Please note, where text is underlined, an animation will be timed with the recording to highlight those data]]

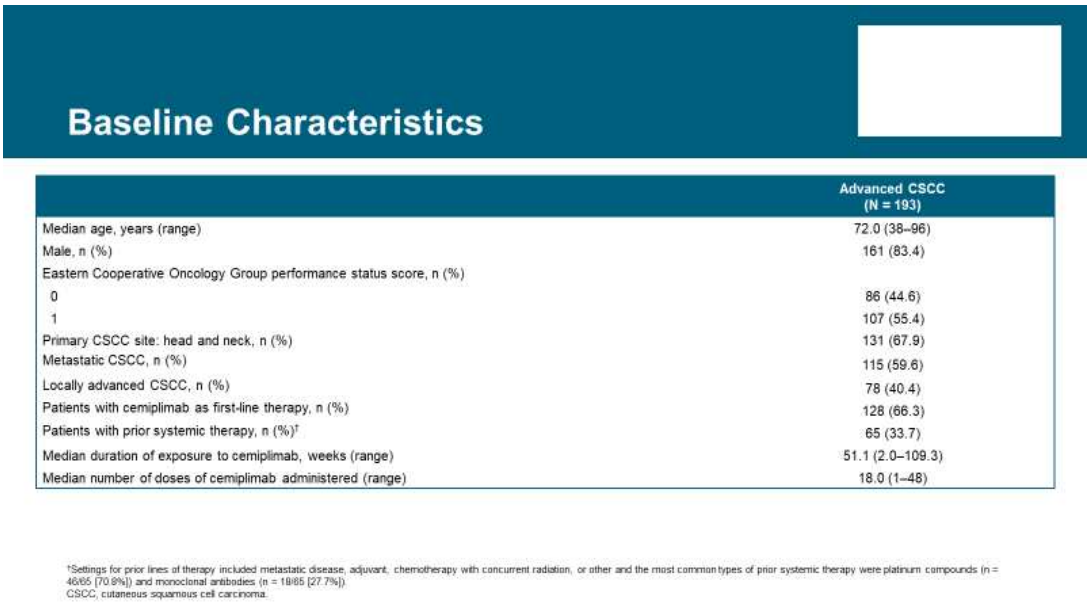
Slide 1

My name is Professor Danny Rischin, MD, from the Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia. On behalf of my coauthors, this video abstract will provide an overview of our manuscript titled 'Integrated Analysis of a Phase 2 Study of Cemiplimab in Advanced Cutaneous Squamous Cell Carcinoma: Extended Follow-up and Quality of Life Analysis'.

Cemiplimab is a high affinity and highly potent human IgG4 monoclonal antibody that binds to the PD-1 receptor. We have previously reported primary data from Groups 1 to 3 of the open-label, international Phase 2 study of patients with advanced CSCC, and the methods for this study have previously been presented. Here, we present up

to 3-year follow-up from the largest and most mature prospective dataset for this disease.

Slide 2



	Advanced CSCC (N = 193)
Median age, years (range)	72.0 (38–96)
Male, n (%)	161 (83.4)
Eastern Cooperative Oncology Group performance status score, n (%)	
0	86 (44.6)
1	107 (55.4)
Primary CSCC site: head and neck, n (%)	131 (67.9)
Metastatic CSCC, n (%)	115 (59.6)
Locally advanced CSCC, n (%)	78 (40.4)
Patients with cemiplimab as first-line therapy, n (%)	128 (66.3)
Patients with prior systemic therapy, n (%)†	65 (33.7)
Median duration of exposure to cemiplimab, weeks (range)	51.1 (2.0–109.3)
Median number of doses of cemiplimab administered (range)	18.0 (1–48)

†Settings for prior lines of therapy included metastatic disease, adjuvant, chemotherapy with concurrent radiation, or other and the most common types of prior systemic therapy were platinum compounds (n = 46/65 [70.8%]) and monoclonal antibodies (n = 18/65 [27.7%]).
CSCC, cutaneous squamous cell carcinoma.

This table provides baseline characteristics of the 193 patients included in the study. Most patients were male, with a median age of 72 years. Most patients had a primary cancer site of head and neck. The median duration of exposure was 51.1 weeks, and the median number of doses was 18.

Slide 3

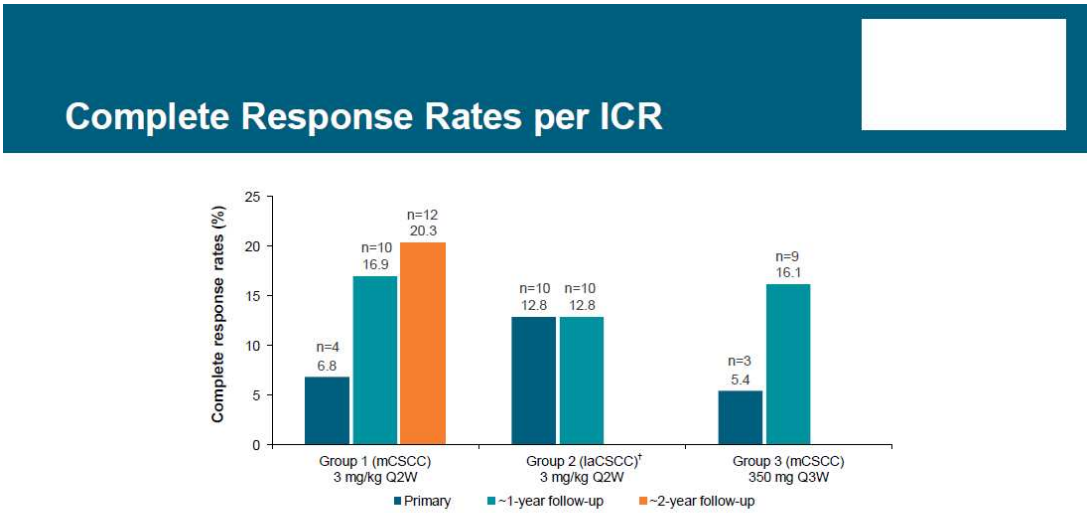
-

	Group 1 (mCSCC) 3 mg/kg Q2W (n=59)	Group 2 (laCSCC) 3mg/kg Q2W (n=78)	Group 3 (mCSCC) 350 mg Q3W (n=56)	Total (N=193)
Median duration of follow-up, months (range)	18.5 (1.1–36.1)	15.5 (0.8–35.6)	17.3 (0.6–26.3)	15.7 (0.6–36.1)
ORR, % (95% CI)	50.8 (37.5–64.1)	44.9 (33.6–56.6)	42.9 (29.7–56.8)	46.1 (38.9–53.4)
Best overall response, n (%)				
Complete response, n (%)	12 (20.3)	10 (12.8)	9 (16.1)	31 (16.1)*
Partial response, n (%)	18 (30.5)	25 (32.1)	15 (26.8)	58 (30.1)
Stable disease, n (%)	9 (15.3)	27 (34.6)	10 (17.9)	46 (23.8)
Non-complete response/non-progressive disease, n (%)	3 (5.1)	0	2 (3.6)	5 (2.6)
Progressive disease, n (%)	10 (16.9)	10 (12.8)	14 (25.0)	34 (17.6)
Not evaluable, n (%)	7 (11.9)	6 (7.7)	6 (10.7)	19 (9.8)
Disease control rate, % (95% CI)	71.2 (57.9–82.2)	79.5 (68.8–87.8)	64.3 (50.4–76.6)	72.5 (65.7–78.7)
Durable disease control rate, % (95% CI)†	61.0 (47.4–73.5)	62.8 (51.1–73.5)	57.1 (43.2–70.3)	60.6 (53.3–67.6)
Median observed time to response, months (IQR)‡	1.9 (1.8–2.0)	2.1 (1.9–3.8)	2.1 (2.1–4.2)	2.1 (1.9–3.7)
Median observed time to complete response, months (IQR)§	11.1 (7.5–18.4)	10.5 (7.4–12.9)	12.4 (8.2–16.6)	11.2 (7.4–14.8)
Median DOR, months (range)‡	NR (20.7, NE)	NR (18.4, NE)	NR (NE, NE)	NR (28.8, NE)
Kaplan-Meier 12-month estimate of patients with ongoing response, % (95% CI)	89.5 (70.9–96.5)	83.2 (64.1–92.7)	91.7 (70.6–97.8)	87.8 (78.5–93.3)
Kaplan-Meier 24-month estimate of patients with ongoing response, % (95% CI)	68.8 (46.9–83.2)	62.5 (38.4–79.4)	NE (NE, NE)	69.4 (55.6–79.6)

*95% CI: 11.2–22.0 †Defined as the proportion of patients with objective response, stable disease, or non-CR/Non-PD without PD for at least 16 weeks, measured at least 105 days to account for scheduling windows in the protocol. ‡Based on number of patients with confirmed complete or partial response. §Based on number of patients with confirmed complete response.
ORR per INV was 54.4% (95% CI: 47.1–61.6) for all patients; 50.8% (95% CI: 37.5–64.1) for Group 1, 56.4% (95% CI: 44.7–67.6) for Group 2, and 55.4% (95% CI: 41.5–68.7) for Group 3. ORR per ICR was 48.4% (95% CI: 39.5–57.4) among treatment-naïve patients and 41.5% (95% CI: 29.4–54.4) among previously treated patients.
CI, confidence interval; DCR, disease control rate; DOR, duration of response; INV, investigator review; IQR, interquartile range; laCSCC, locally advanced cutaneous squamous cell carcinoma; mCSCC, metastatic cutaneous squamous cell carcinoma; NE, not evaluable; NR, not reported; ORR, objective response rate; Q2W, every 2 weeks; Q3W, every 3 weeks.

As you will see in this table, the objective response rate for all three groups combined was 46.1% per independent central review, with a 95% confidence interval of 38.9 to 53.4%. Looking at the data by individual groups, the objective response rate was 50.8% for Group 1, 44.9% for Group 2, and 42.9% for Group 3. Additionally, median duration of response has not been reached. Median duration of follow-up was 15.7 months among all patients.

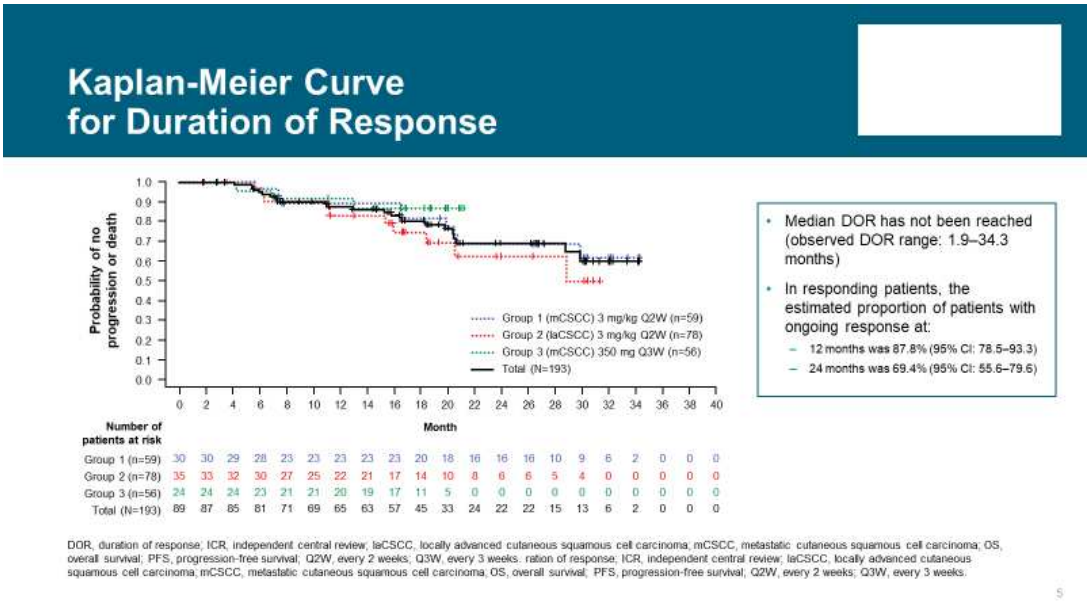
Slide 4



†At the time of the Group 1 primary analysis, a pre-specified Group 2 interim analysis was performed. Among the 23 laCSCC patients included in this pre-specified interim analysis, there were no complete responses.
CSCC, cutaneous squamous cell carcinoma; ICR, independent central review; IQR, interquartile range; laCSCC, locally advanced CSCC; mCSCC, metastatic CSCC; Q2W, every 2 weeks; Q3W, every 3 weeks.

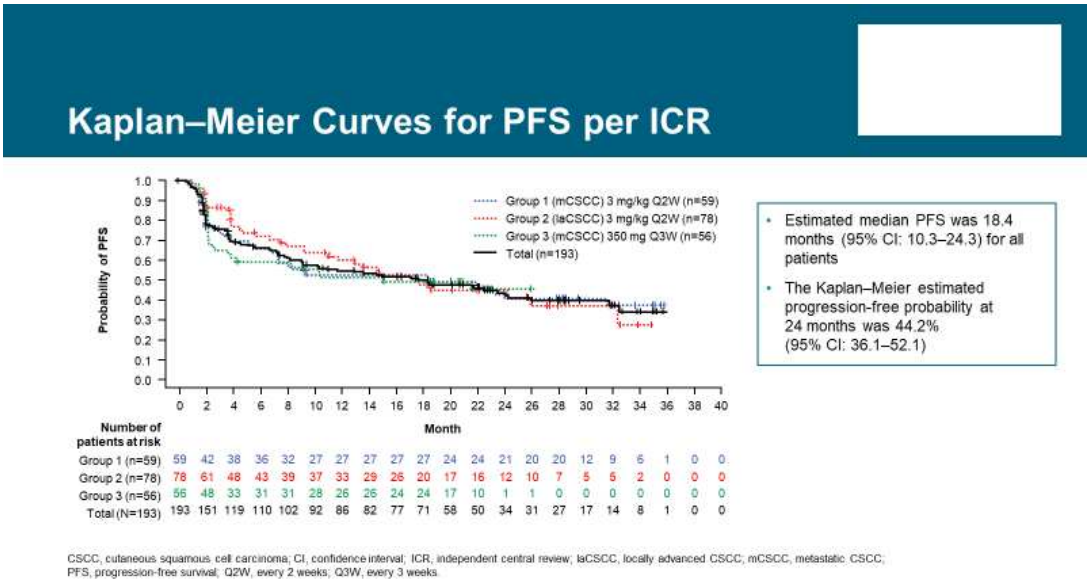
One of the key takeaways from this graph is that cemiplimab had deepening responses over time, evidenced by increasing CR rates compared to primary analyses. Complete responses for Group 1 increased from 6.8% in the primary analysis to 16.9% in the first follow-up analysis and to 20.3% at this subsequent follow-up analysis. For Group 2, there were no complete responses at the interim analysis, but the complete response rate was 12.8% at the primary analysis and is unchanged at this follow-up analysis. For Group 3, the complete response rate increased from 5.4% at the primary analysis to 16.1% at this follow-up analysis.

Slide 5



Another key takeaway from this study is that cemiplimab demonstrates impressive duration of response. Looking at the Kaplan–Meier curve estimating ongoing response over time, among patients who experienced objective responses, 91% of these responses had observed durations of 6 months or greater. The Kaplan–Meier estimated percent of responses ongoing at 12 months is 87.8% and at 24 months is 69.4%.

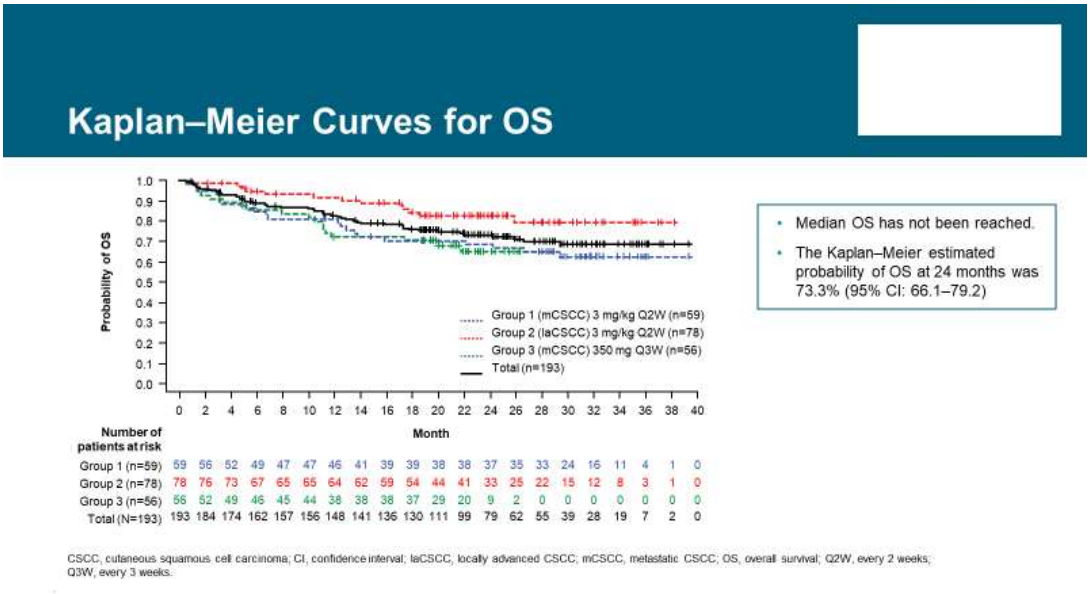
Slide 6



CSCC, cutaneous squamous cell carcinoma; CI, confidence interval; ICR, independent central review; laCSCC, locally advanced CSCC; mCSCC, metastatic CSCC; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks.

In addition to duration of response, as you can see in this graph, the median progression-free survival is 18.4 months. The Kaplan–Meier estimated progression-free probability at 24 months was 44.2%.

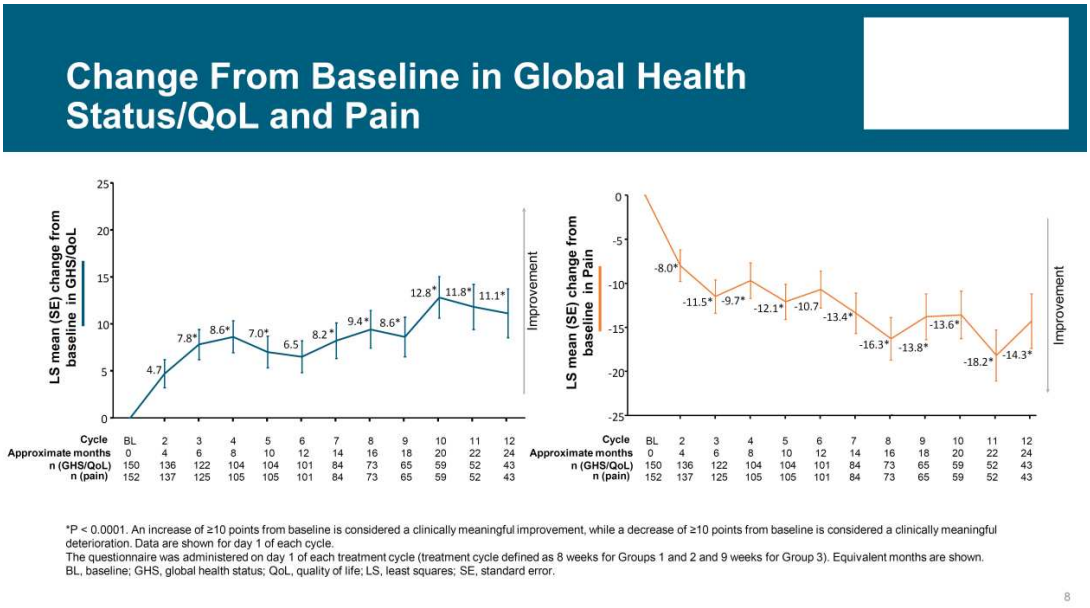
Slide 7



CSCC, cutaneous squamous cell carcinoma; CI, confidence interval; laCSCC, locally advanced CSCC; mCSCC, metastatic CSCC; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks.

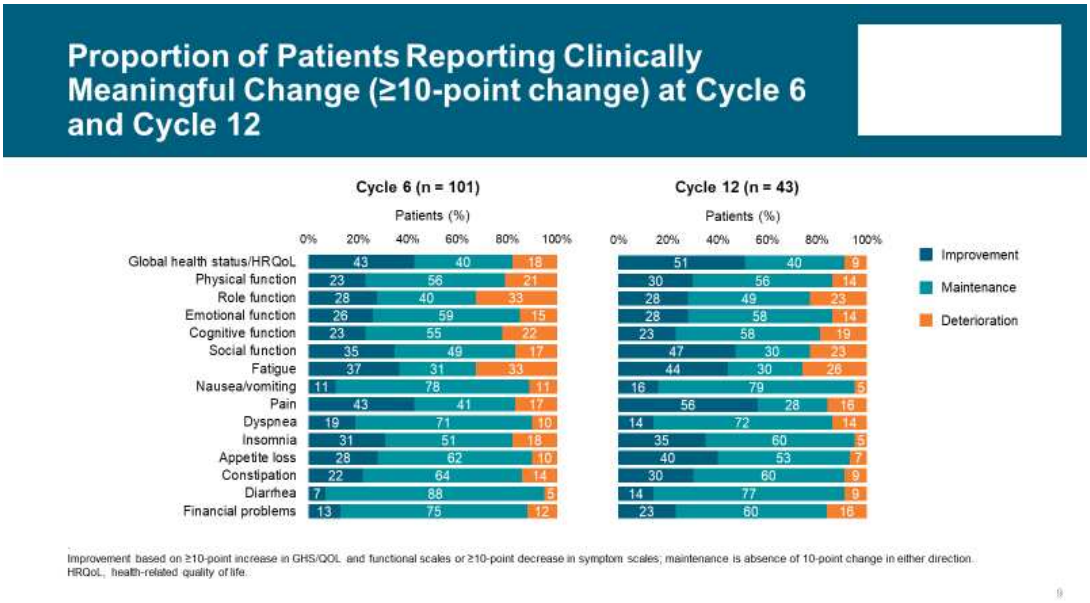
These data show that overall survival was impressive with cemiplimab. Median overall survival has not been reached for the total patient population. The Kaplan–Meier estimated probability of overall survival at 24 months was 73.3%.

Slide 8



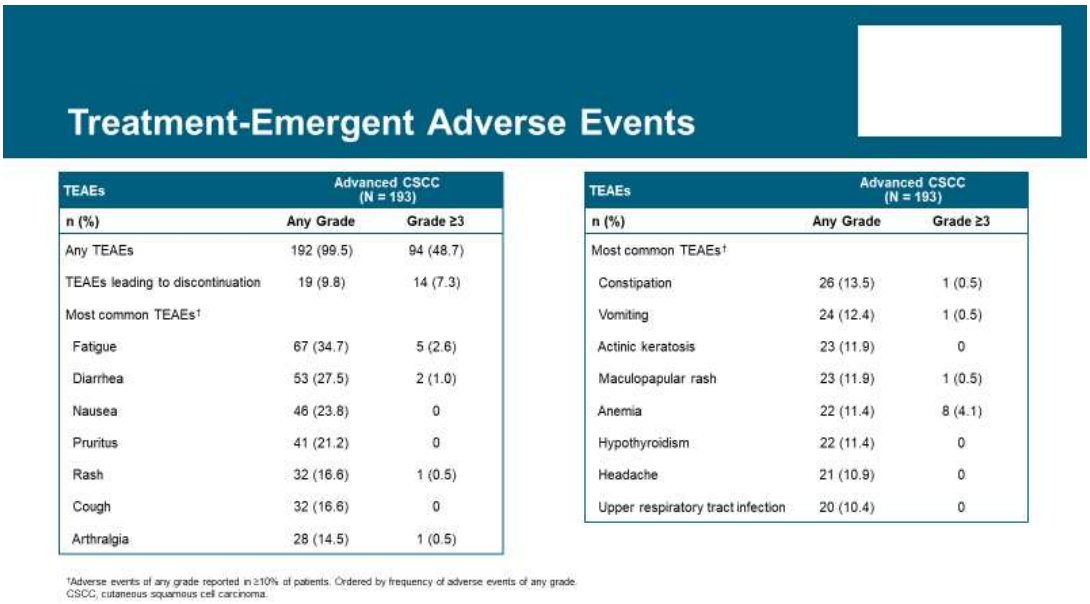
In addition to robust clinical activity, treatment with cemiplimab was associated with improvement in global health status/quality of life as measured by the EORTC QLQ-C30 instrument. Here, we show the least squares mean change from baseline scores in the global health status/quality of life and pain scales over time. As can be seen from this figure, improvements in both scales were observed from cycle 2, with statistically and clinically meaningful improvement from baseline in pain observed as early as cycle 3 and sustained over the course of treatment to cycle 12. Significant improvement in global health status/quality of life was observed during initial cycles and reached the clinically meaningful threshold of 10 points or more by cycle 12.

Slide 9



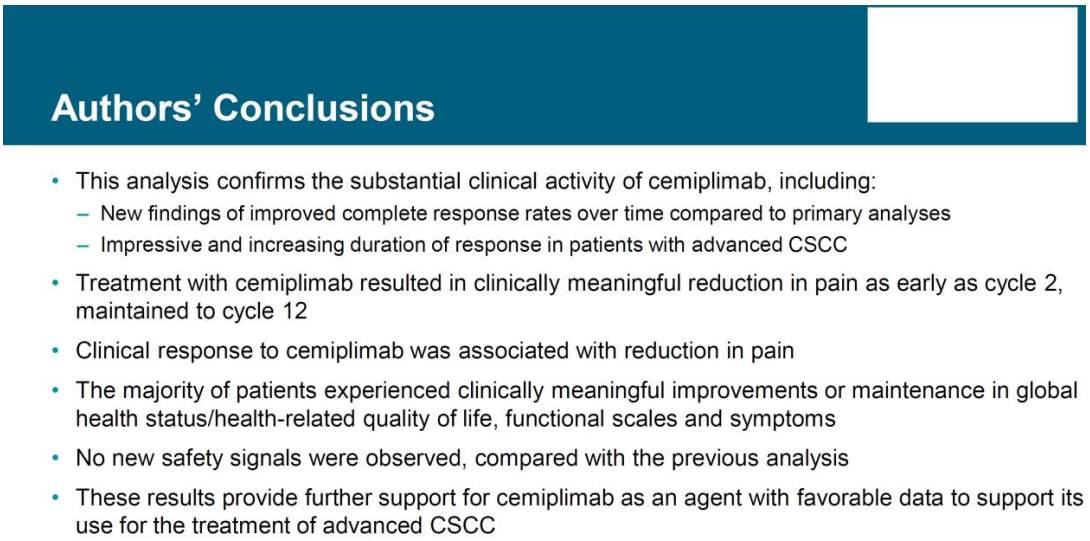
This figure shows the proportion of patients with a clinically meaningful improvement or deterioration (10 point or greater change) or maintenance (absence of a 10 point or greater change) in global health status/quality of life, functioning and symptoms scales at cycle 6 and cycle 12. By cycle 6, most of these patients had experienced clinically meaningful improvements or maintenance in global health status/quality of life, functioning, and symptoms. Overall, 91% of patients experienced clinically meaningful improvement or stability in global health status/quality of life scores at cycle 12, and most patients experienced sustained improvement or maintenance of their functioning and symptoms by cycle 12.

Slide 10



In total, 99.5% of patients experienced at least one treatment-emergent adverse event, TEAE, of any grade regardless of attribution. TEAEs of any grade led to discontinuation in 9.8% of patients, and Grade ≥3 TEAEs led to discontinuation in 7.3% of patients. The most common TEAEs of any grade were fatigue, diarrhea, and nausea. In total, 48.7% of patients experienced at least one Grade ≥3 TEAE regardless of attribution. In addition, 29.5% patients experienced at least one sponsor-identified immune-related adverse event (irAE) of any grade, and 9.3% patients experienced at least one Grade ≥3 irAE. No new TEAEs resulting in death were reported for any group in this longer-term follow up, compared with previous reports.

Slide 11



In summary, this analysis confirms the substantial clinical activity of cemiplimab, including new findings of improved complete response rates over time compared to primary analyses, and impressive and increasing duration of response in patients with advanced CSCC. In addition, treatment with cemiplimab resulted in a clinically meaningful reduction in pain as early as cycle 2, maintained to cycle 12. Further, clinical response to cemiplimab was associated with reduction in pain. The majority of patients experienced clinically meaningful improvements or maintenance in global health status/health-related quality of life, functional scales and symptoms. In addition, no new safety signals were observed compared with the previous analysis. These results provide further support for cemiplimab as an agent with favorable data to support its use for the treatment of advanced CSCC.