



ESMO 2022

Phase-II-Studie mit Cemiplimab bei Patient*innen mit fortgeschrittenem kutanen Plattenepithelkarzinom (CSCC):
Finale Analyse der Gruppe 1, 2 und 3 der EMPOWER-CSCC 1-Studie

Michael R Migden,¹ Chrysalyn D Schmults,² Nikhil I Khushalani,³ Alexander Guminski,⁴ Anne Lynn S Chang,⁵ Karl D Lewis,⁶ George Anstas,⁷ Samantha Bowyer,⁸ Brett G Hughes,⁹ Dirk Schadendorf,¹⁰ Badri Modi,¹¹ Lara A Dunn,¹² Lukas Flatz,¹³ Axel Hauschild,¹⁴ Suk-Young Yoo,¹⁵ Jocelyn Booth,¹⁵ Frank Seebach,¹⁵ Israel Lowy,¹⁵ Matthew G Fury,¹⁵ Danny Rischin¹⁶

¹Departments of Dermatology and Head and Neck Surgery, University of Texas MD Anderson Cancer Center, Houston, TX, USA; ²Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; ³Department of Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL, USA; ⁴Department of Medical Oncology, Royal North Shore Hospital, St Leonards, New South Wales, Australia; ⁵Department of Dermatology, Stanford University School of Medicine, Redwood City, CA, USA; ⁶University of Colorado Denver Cancer Center, Aurora, CO, USA; ⁷Surgical Oncology, Washington University School of Medicine, St Louis, MO, USA; ⁸School of Medicine and Pharmacology, University of Western Australia, Nedlands, Western Australia, Australia; ⁹Royal Brisbane & Women's Hospital and University of Queensland, Brisbane, Queensland, Australia; ¹⁰University Hospital Essen, Essen and German Cancer Consortium, Essen, Germany; ¹¹Department of Surgery, Division of Dermatology, City of Hope, Duarte, CA, USA; ¹²Department of Medicine, Head and Neck Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; ¹³University Hospital Tübingen, Tübingen, Germany; ¹⁴Schleswig-Holstein University Hospital, Kiel, Germany; ¹⁵Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; ¹⁶Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia

Introduction

- CSCC is the second most common malignancy in the USA, with approximately 186,000–420,000 cases diagnosed each year.¹
- While most cases of CSCC are cured by complete surgical excision, a small but substantial number of patients develop advanced disease, including locally advanced (laCSCC) or metastatic (mCSCC) disease.^{2,3}
- Cemiplimab is a high-affinity, fully human, hinge-stabilised, immunoglobulin G4 anti-programmed cell death-1 (PD-1) antibody that blocks the interaction of the PD-1 receptor with its ligands, PD-L1 and PD-L2.⁴
- Cemiplimab is approved in the US and Europe, and by multiple other health authorities, for the treatment of patients with metastatic or locally advanced CSCC who are not candidates for curative surgery or curative radiation.^{5–8} Additionally, cemiplimab is recommended for the treatment of patients with metastatic or locally advanced CSCC not amenable to curative surgery or curative radiation by the European Association of Dermato-Oncology, European Organisation for Research and Treatment of Cancer, and the National Comprehensive Cancer Network.^{9,10}
- In the primary and follow-up analysis from the EMPOWER-CSCC 1 Phase 2 study, cemiplimab demonstrated substantial clinical benefit and an acceptable safety profile in patients with advanced CSCC (NCT02760498).^{11–14}
 - Cemiplimab achieved an objective response rate (ORR) of 46.1% in patients with advanced CSCC, with complete response rates of 20.3%, 12.8% and 16.1% for groups 1, 2 and 3, respectively.¹¹
- Here, we provide the final update from study Groups 1, 2 and 3.

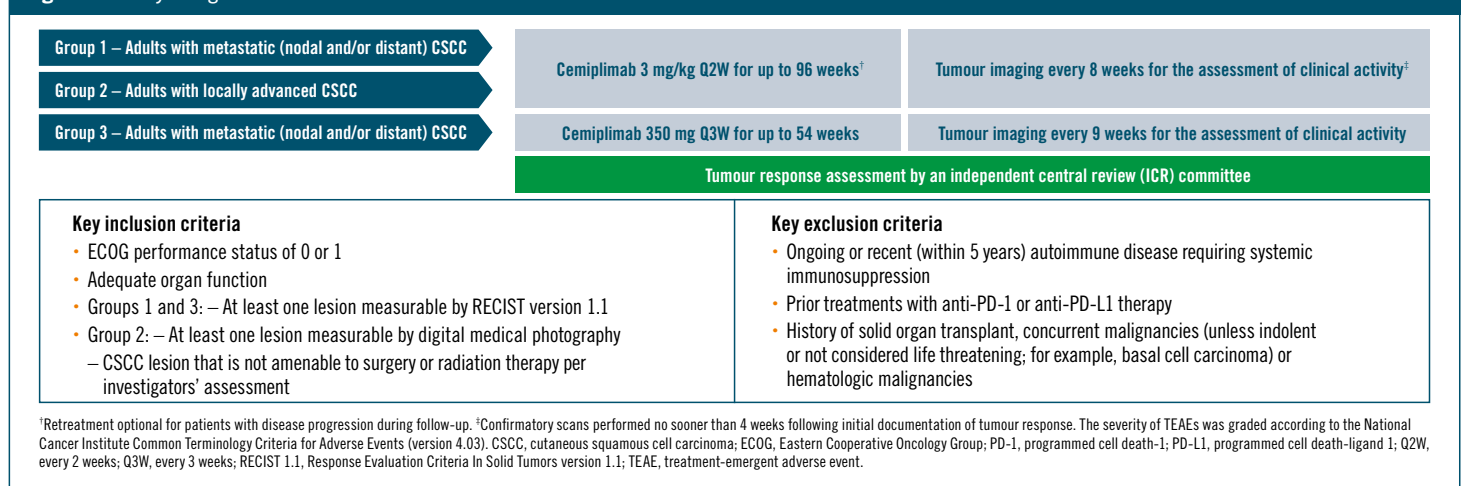
Objectives

- Primary objective: To assess the clinical benefits of cemiplimab as measured by ORR (complete + partial response) per independent central review (ICR).
- Key secondary objectives: Duration of response (DOR), progression-free survival (PFS), overall survival (OS), complete response rate, and safety and tolerability.

Methods

- EMPOWER-CSCC 1 is an open-label, non-randomised, multicentre, international Phase 2 study of patients with advanced CSCC (NCT02760498).
- Patients with histologically confirmed mCSCC or unresectable laCSCC received cemiplimab 3 mg/kg intravenous (IV) every 2 weeks for up to 96 weeks (Group 1, mCSCC; Group 2, laCSCC) or cemiplimab 350 mg IV every 3 weeks for up to 54 weeks (Group 3, mCSCC) (**Figure 1**).
- This is the final analysis and the data cutoff was 1 March 2022.

Figure 1. Study design



Results

Patients

- A total of 193 patients were enrolled (Group 1, n=59; Group 2, n=78; Group 3, n=56) with a median age of 72.0 years (range, 38–96). Most patients had a primary cancer site of the head and neck (n=131, 67.9%) (**Table 1**).
- Median duration of follow up was 15.7 months (range, 0.6–43.4) and median duration of exposure was 51.1 weeks (range, 2.0–109.3).

Response

- Tumour response per ICR, median PFS and OS remained generally consistent with the previous update (data cutoff: 11 October 2020) (**Table 2**).
- Median PFS was 22.1 months (95% confidence interval [CI], 10.4–32.3) and the overall median DOR was 41.3 months (95% CI, 38.8–46.3) (**Figures 2 and 3A**).
- Median OS was not reached. The Kaplan–Meier estimated probability of OS at 48 months was 61.8% (95% CI, 54.0–68.7) (**Figure 3B**).

Advanced cutaneous squamous cell carcinoma (CSCC): Final analysis

Chang S, Lewis K, Anstas G, Bowyer S, Hughes B, Schandendorf D, Modi B, Dunn L, Flatz L, Hauschild A, et al.

1, USA; 2Department of Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL, USA; 3Department of Medical Oncology, Royal North Shore Hospital, St Leonards, New South Wales, Australia; 4Department of Dermatology, Stanford University School of Medicine, Stanford, CA, USA; 5Department of Surgery, Division of Dermatology, City of Hope, Duarte, CA, USA; 6Department of Medicine, Head and Neck Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; 7University Hospital Tübingen, Tübingen, Germany; 8Department of Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL, USA; 9Department of Medical Oncology, Royal North Shore Hospital, St Leonards, New South Wales, Australia; 10Department of Dermatology, Stanford University School of Medicine, Stanford, CA, USA; 11Department of Surgery, Division of Dermatology, City of Hope, Duarte, CA, USA; 12Department of Medicine, Head and Neck Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; 13University Hospital Tübingen, Tübingen, Germany; 14Department of Dermatology, Stanford University School of Medicine, Stanford, CA, USA

Table 1. Patient demographics and baseline characteristics

Advanced CSCC (n=193)	
Age, median (range), years	72.0 (38–96)
Male, n (%)	161 (83.4)
ECOG performance status, n (%)	
0	86 (44.6)
1	107 (55.4)
Primary CSCC site: head and neck, n (%)	131 (67.9)
mCSCC, n (%)	115 (59.6)
laCSCC, n (%)	78 (40.4)
Patients with cemiplimab as first-line therapy, n (%)	128 (66.3)
Patients with prior systemic therapy, n (%) [†]	65 (33.7)
Duration of exposure to cemiplimab, weeks, median (range)	51.1 (2.0–109.3)
Number of cemiplimab doses administered, median (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; ECOG, Eastern Cooperative Oncology Group; laCSCC, locally advanced cutaneous squamous cell carcinoma; mCSCC, metastatic cutaneous squamous cell carcinoma.

Table 2. Tumour response per ICR

	Group 1 (mCSCC) 3 mg/kg Q2W (n=59)	Group 2 (laCSCC) 3 mg/kg Q2W (n=78)	Group 3 (mCSCC) 350 mg Q3W (n=56)	Total (n=193)
Duration of follow-up, months, median (range)	18.5 (1.1–41.0)	15.5 (0.8–43.2)	17.3 (0.6–43.4)	15.7 (0.6–43.4)
ORR, % (95% CI)	50.8 (37.5–64.1)	44.9 (33.6–56.6)	46.4 (33.0–60.3)	47.2 (39.9–54.4)
Complete response, n (%)	12 (20.3)	10 (12.8)	11 (19.6)	33 (17.1)
Partial response, n (%)	18 (30.5)	25 (32.1)	15 (26.8)	58 (30.1)
DOR, months, median (95% CI)	NR (20.7–NE)	41.9 (20.5–54.6)	41.3 (40.8–46.3)	41.3 (38.8–46.3)
PFS, months, median (95% CI)	18.4 (7.3–53.2)	18.5 (11.1–43.8)	21.7 (3.8–43.3)	22.1 (10.4–32.3)
OS, months, median (95% CI)	57.7 (29.3–NE)	NR (58.3–NE)	48.4 (29.5–NE)	NR (56.0–NE)

CI, confidence interval; DOR, duration of response; ICR, independent central review; laCSCC, locally advanced cutaneous squamous cell carcinoma; mCSCC, metastatic cutaneous squamous cell carcinoma; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks.

Figure 2. Kaplan-Meier curve of DOR per ICR

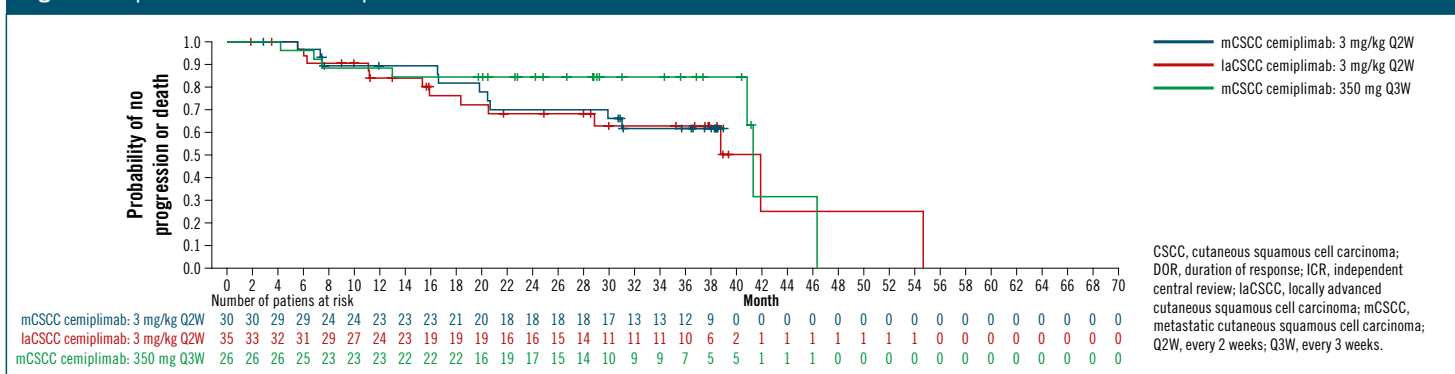
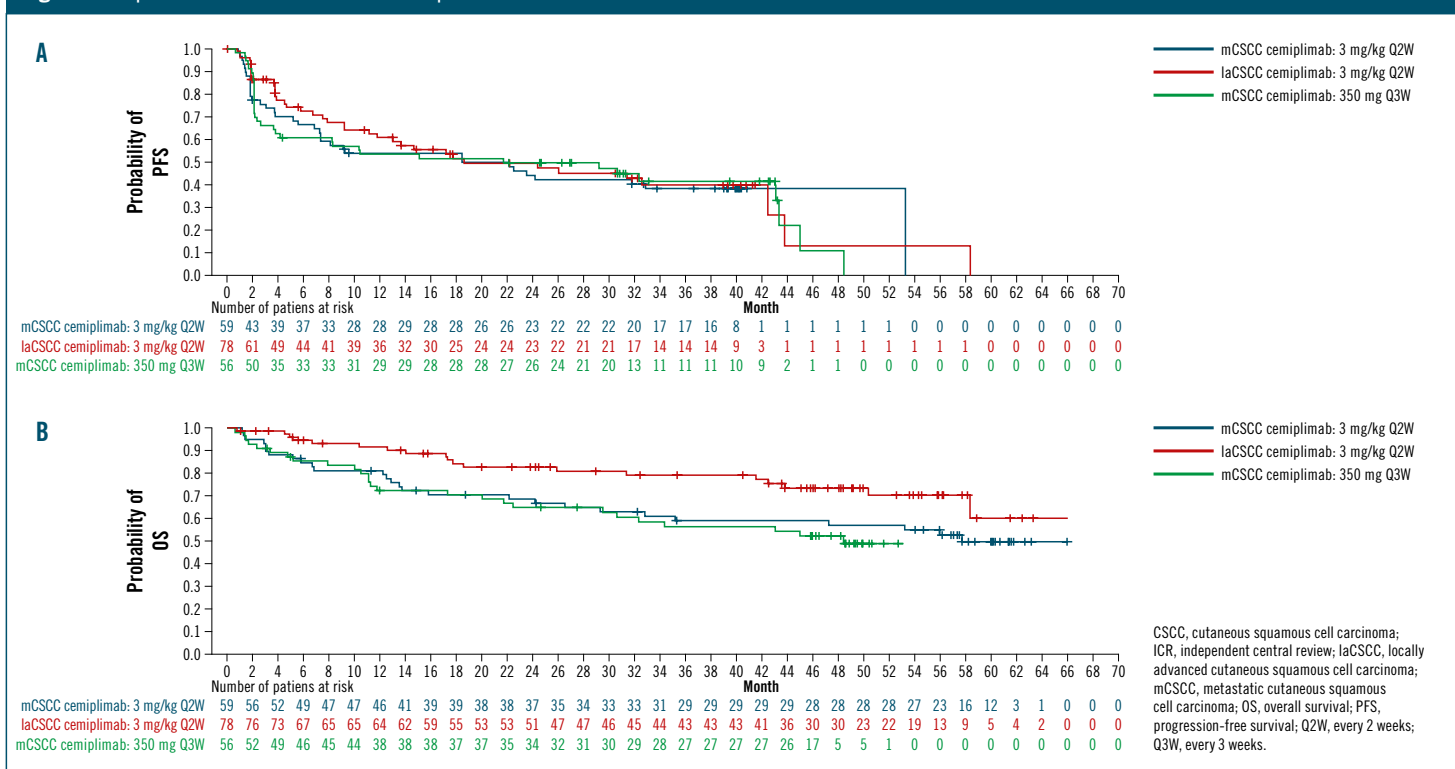


Figure 3. Kaplan-Meier curves of PFS and OS per ICR



Analysis from EMPOWER-CSCC 1 Groups 1, 2 and 3

Suk-Young Yoo,¹⁵ Jocelyn Booth,¹⁵ Frank Seebach,¹⁵ Israel Lowy,¹⁵ Matthew G Fury,¹⁵ Danny Rischin¹⁶

15University of Colorado Denver Cancer Center, Aurora, CO, USA; ¹⁶Surgical Oncology, Washington University School of Medicine, St Louis, MO, USA; ⁸School of Medicine and Pharmacology, University of Queensland, St. Leonards, Queensland, Australia; ¹University of California, San Francisco, CA, USA; ²University of Colorado Denver Cancer Center, Aurora, CO, USA; ³Surgical Oncology, Washington University School of Medicine, St Louis, MO, USA; ⁴School of Medicine and Pharmacology, University of Queensland, St. Leonards, Queensland, Australia; ⁵Schleswig-Holstein University Hospital, Kiel, Germany; ⁶Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; ⁷Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia

Safety

- All but one patient (n=192, 99.5%) experienced at least one treatment-emergent adverse event (TEAE) of any grade regardless of attribution (**Table 3**).
- The most common TEAE of any grade was fatigue (n=67, 34.7%), followed by diarrhoea (n=53, 27.5%), nausea (n=46, 23.8%) and pruritus (n=41, 21.2%).
- Grade ≥ 3 TEAEs were reported in 95 patients (49.2%). The most common Grade ≥ 3 TEAEs were hypertension (n=9, 4.7%), cellulitis and anaemia (each n=8, 4.1%), pneumonia (n=8, 4.1%), pneumonitis (n=6, 3.1%), sepsis (n=5, 2.6%) and fatigue (n=5, 2.6%).
- In total, 19 patients (9.8%) experienced at least one sponsor-identified Grade ≥ 3 immune-related adverse event (irAE). The most common Grade ≥ 3 irAEs were pneumonitis (n=6, 3.1%), diarrhoea and autoimmune hepatitis (each n=2, 1.0%).
- Twenty patients (10.4%) discontinued treatment due to TEAEs of any grade (**Supplementary Table 1**).
- No new TEAEs resulting in death were reported compared with previous reports.⁶⁻⁸

Table 3. TEAEs[†]

TEAEs, n (%)	Advanced CSCC, n=193	
	Any grade	Grade ≥ 3
Any	192 (99.5)	95 (49.2)
Serious	75 (38.9)	60 (31.1)
Leading to discontinuation	20 (10.4)	13 (6.7)
Leading to death	5 (2.6)	5 (2.6)
Occurring in $\geq 10\%$ of patients (any grade)		
Fatigue	67 (34.7)	5 (2.6)
Diarrhoea	53 (27.5)	2 (1.0)
Nausea	46 (23.8)	0
Pruritus	41 (21.2)	0
Constipation	28 (14.5)	1 (0.5)
Vomiting	25 (13.0)	1 (0.5)
Arthralgia	34 (17.6)	1 (0.5)
Cough	32 (16.6)	0
Rash	32 (16.6)	1 (0.5)
Anaemia	22 (11.4)	8 (4.1)
Hypothyroidism	22 (11.4)	0
Actinic keratosis	23 (11.9)	0
Rash, maculo-papular	23 (11.9)	1 (0.5)
Upper respiratory tract infection	21 (10.9)	0
Headache	21 (10.9)	0

[†]TEAEs occurring in $\geq 10\%$ of patients are reported here. Adverse events were coded according to the Preferred Terms of the Medical Dictionary for Regulatory Activities, version 22.1. The severity of adverse events was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03. RTI, respiratory tract infection; TEAE, treatment-emergent adverse event.

Conclusions

- The EMPOWER-CSCC 1 study confirms the efficacy, durability, and safety profile of cemiplimab in patients with advanced CSCC.
- No new safety concerns were identified on longer follow-up.
- Cemiplimab remains a standard-of-care option for metastatic or locally advanced CSCC patients who are not candidates for curative surgery or radiation.

References

- Karia PS et al. *J Am Acad Dermatol.* 2013;68:957–966.
- Stratigos AJ et al. *Eur J Cancer.* 2020;128:60–82.
- Que SKT et al. *J Am Acad Dermatol.* 2018;78:237–247.
- Burova E et al. *Mol Cancer Ther.* 2017;16:861–870.
- Regeneron Pharmaceuticals, Inc and Sanofi-Aventis US LLC. LIBTAYO® (cemiplimab-rwlc) injection full US prescribing information; 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761097s007/b1.pdf. Accessed 31 August 2022.
- European Medicines Agency. LIBTAYO® EPAR; 2022. Available at: https://www.ema.europa.eu/en/documents/product-information/libtayo-epar-product-information_en.pdf. Accessed 31 August 2022.
- Health Canada. LIBTAYO® - Notice of compliance with conditions - qualifying notice; 2019. Available at: <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/notice-compliance/conditions/libtayo-notice-compliance-conditions-218718.html>. Accessed 31 August 2022.
- Ministry of Health Israel. The Israeli Drug Registry - LIBTAYO®; 2021. Available at: https://mohpublic.z6.web.core.windows.net/IsraelDrugs/Rishum01_1_1299478321.pdf. Accessed 31 August 2022.
- Stratigos AJ et al. *Eur J Cancer.* 2020;128:83–102.
- National Comprehensive Cancer Network. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Squamous Cell Skin Cancer (Version 2.2022); 2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed 31 August 2022.
- Rischin D et al. *J Immunother Cancer.* 2021;9:e002757.
- Migden MR et al. *N Engl J Med.* 2018;379:341–351.
- Migden MR et al. *Lancet Oncol.* 2020;21:294–305.
- Rischin D et al. *J Immunother Cancer.* 2020;8:e000775.

Disclosure

Michael R Migden reports 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.

Acknowledgements

The authors thank the patients who participated in this study. Medical writing and editorial support under the direction of the authors was provided by Sameen Yousaf, PhD, of Prime (Knutsford, UK) and funded by Regeneron Pharmaceuticals, Inc. and Sanofi according to Good Publication Practice guidelines. Responsibility for all opinions, conclusions and data interpretation lies with the authors.

Scan for supplementary appendix and a copy of the poster.



Original Abstract

Phase II study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma (CSCC): Final analysis from EMPOWER-CSCC 1 groups 1, 2 and 3

Michael R Migden,¹ Chrysalyn D Schmults,² Nikhil I Khushalani,³ Alexander Guminski,⁴ Anne Lynn S Chang,⁵ Karl D Lewis,⁶ George Anstas,⁷ Samantha Bowyer,⁸ Brett G Hughes,⁹ Dirk Schadendorf,¹⁰ Badri Modi,¹¹ Lara A Dunn,¹² Lukas Flatz,¹³ Axel Hauschild,¹⁴ Suk-Young Yoo,¹⁵ Jocelyn Booth,¹⁵ Frank Seebach,¹⁵ Israel Lowy,¹⁵ Matthew G Fury,¹⁵ Danny Rischin¹⁶

Background

Previous analyses from EMPOWER-CSCC 1 phase 2 study (NCT02760498) demonstrated substantial clinical benefit and an acceptable safety profile with cemiplimab in patients with locally advanced and metastatic CSCC. Here, we provide the final analysis from the study Groups 1, 2 and 3.

Methods

Patients received cemiplimab 3 mg/kg IV every 2 weeks for up to 96 weeks (Group 1, metastatic CSCC; Group 2, locally advanced CSCC) or cemiplimab 350 mg IV every 3 weeks for up to 54 weeks (Group 3, metastatic CSCC). The primary endpoint was objective response rate (ORR; complete + partial response) per independent central review (ICR). This is the final analysis and the final database lock occurred on 01 Mar 2022.

Results

A total of 193 patients were enrolled (Group 1, n=59; Group 2, n=78; Group 3, n=56). Tumour response per ICR, median progression-free survival (PFS) and overall survival (OS) (Table) remain generally consistent with the previous update (data cut-off: 11 Oct 2020). OS at 48 months is 61.8% (95% CI: 54.0-68.7). Overall median duration of response (DOR) was 41.3 months (Table). Fatigue (34.7%) was the most common treatment-emergent adverse event (TEAE) of any grade; hypertension (4.7%) was the most common Grade ≥ 3 TEAE.

	Group 1 (mCSCC) 3mg/kg Q2W (n=59)	Group 2 (laCSCC) 3mg/kg Q2W (n=78)	Group 3 (mCSCC) 350mg Q3W (n=56)	Total (n=193)
Median duration of follow-up, months, (range)	18.5 (1.1–41.0)	15.5 (0.8–43.2)	17.3 (0.6–43.4)	15.7 (0.6–43.4)
ORR, %, (95% CI)	50.8 (37.5–64.1)	44.9 (33.6–56.6)	46.4 (33.0–60.3)	47.2 (39.9–54.4)
Complete response, n (%)	12 (20.3)	10 (12.8)	11 (19.6)	33 (17.1)
Partial response, n (%)	18 (30.5)	25 (32.1)	15 (26.8)	58 (30.1)
Median DOR, months (95% CI)	NR (20.7–NE)	41.9 (20.5–54.6)	41.3 (40.8–46.3)	41.3 (38.8–46.3)
Median PFS, months (95% CI)	18.4 (7.3–53.2)	18.5 (11.1–43.8)	21.7 (3.8–43.3)	22.1 (10.4–32.3)
Median OS, months (95% CI)	57.7 (29.3–NE)	NR (58.3–NE)	48.4 (29.5–NE)	NR (56.0–NE)

CI, confidence interval; DOR, duration of response; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

Conclusion

The final update confirms the durable response, safety and efficacy of cemiplimab in patients with advanced CSCC. There were no new safety signals identified on longer follow-up. Cemiplimab remains a standard of care option for advanced CSCC.

Zusammenfassung

Phase-II-Studie mit Cemiplimab bei Patient*innen mit fortgeschrittenem kutanen Plattenepithelkarzinom (CSCC): Finale Analyse der Gruppe 1, 2 und 3 der EMPOWER-CSCC 1-Studie

Michael R Migden,¹ Chrysalyn D Schmults,² Nikhil I Khushalani,³ Alexander Guminski,⁴ Anne Lynn S Chang,⁵ Karl D Lewis,⁶ George Anstas,⁷ Samantha Bowyer,⁸ Brett G Hughes,⁹ Dirk Schadendorf,¹⁰ Badri Modi,¹¹ Lara A Dunn,¹² Lukas Flatz,¹³ Axel Hauschild,¹⁴ Suk-Young Yoo,¹⁵ Jocelyn Booth,¹⁵ Frank Seebach,¹⁵ Israel Lowy,¹⁵ Matthew G Fury,¹⁵ Danny Rischin¹⁶

Hintergrund

Frühere Analysen der Phase-II Studie EMPOWER-CSCC 1 (NCT02760498) zeigten einen erheblichen klinischen Nutzen und ein akzeptables Sicherheitsprofil von Cemiplimab bei Patient*innen mit lokal fortgeschrittenem und metastasiertem CSCC. Hier stellen wir die finale Analyse der Studiengruppen 1, 2 und 3 vor.

Methoden

193 Patient*innen wurden mit Cemiplimab 3 mg/kg i.v. alle 2 Wochen (Q2W) für bis zu 96 Wochen (Gruppe 1, metastasiertes CSCC; Gruppe 2, lokal fortgeschrittenes CSCC) oder Cemiplimab 350 mg i.v. alle 3 Wochen (Q3W) für bis zu 54 Wochen (Gruppe 3, metastasiertes CSCC) behandelt.

Primäre Endpunkte:

- Objektive Ansprechrate (ORR; komplettes Ansprechen + partielles Ansprechen) bewertet durch ein unabhängiges zentrales Review (ICR)

Wichtigste sekundäre Endpunkte:

- Dauer des Ansprechens (DOR)
- Progressionsfreies Überleben (PFS)
- Gesamtüberleben (OS)
- Komplette Ansprechrate
- Sicherheit und Verträglichkeit

Wirksamkeit

- Die ORR bewertet durch ICR betrug in der gesamten Studienpopulation (über alle 3 Gruppen hinweg) 47,2 % (95 % Konfidenzintervall [KI]: 39,9–54,4) mit 33 Patient*innen mit vollständigem Ansprechen (17,1 %) und 58 Patient*innen mit partiellem Ansprechen (30,1 %).
- Die mediane DOR lag in der gesamten Studienpopulation bei 41,3 Monaten (95 % KI: 38,8–46,3).
- Das mediane PFS der gesamten Studienpopulation betrug 22,1 Monate (95 % KI: 10,4–32,3).
- Das mediane OS der gesamten Studienpopulation wurde nicht erreicht (95 % KI: 56,0 Monate – nicht auswertbar).

Sicherheit und Verträglichkeit

- Die häufigsten Behandlungs-assoziierten unerwünschten Ereignisse (UE) jeglichen Grades waren Fatigue (34,7 %), Diarrhö (27,5 %), Nausea (23,8 %) sowie Pruritus (21,2 %).
- Insgesamt trat bei 19 Patient*innen (9,8 %) mindestens ein UE Grad ≥ 3 auf. Die häufigsten immunvermittelten UE waren Pneumonitis (3,1 %), Diarrhö (1,0 %) und autoimmune Hepatitis (1,0 %).

Fazit

Das finale Update bestätigte das dauerhafte Ansprechen, die Sicherheit und die Wirksamkeit von Cemiplimab bei Patient*innen mit fortgeschrittenem CSCC. Es wurden keine neuen Sicherheitsbedenken im längeren Nachbeobachtungszeitraum festgestellt. Cemiplimab bleibt eine Standardtherapieoption für Patient*innen mit fortgeschrittenem CSCC.