LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

LIBTAYO is a programmed death receptor-1 (PD-1)–blocking antibody indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) who are not candidates for curative surgery or curative radiation.[1]

Updated LIBTAYO® (cemiplimab-rwlc) results in

Patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation

Adapted from data presented at the American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program; May 29-31, 2020

Important Safety Information

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue at any time after starting treatment. While immune-mediated adverse reactions usually occur during treatment, they can also occur after discontinuation. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously. Early identification and management are essential to ensuring safe use of PD-1/PD-L1–blocking antibodies. The definition of immune-mediated adverse reactions included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

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LIBTAYO is indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) who are not candidates for curative surgery or curative radiation.[1]

Study designs for Study 1423 and Study 1540

The efficacy of LIBTAYO in 219 patients with metastatic (nodal or distant) cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) who were not candidates for curative surgery or curative radiation was evaluated in 2 open-label, multicenter, nonrandomized, multicohort studies: Study 1423 and Study 1540. Both studies excluded patients with autoimmune disease who required systemic therapy with immunosuppressant agents within 5 years; history of solid organ transplant; prior treatment with anti–PD-1/PD-L1–blocking antibodies or other immune checkpoint inhibitor therapy; infection with HIV, hepatitis B, or hepatitis C; or ECOG PS ≥2.[1]

Patients received LIBTAYO 3 mg/kg intravenously every 2 weeks for up to 48 weeks in Study 1423 or up to 96 weeks in Study 1540. An additional cohort of patients in Study 1540 received 350 mg every 3 weeks for up to 54 weeks. Among 193 patients enrolled in Study 1540, 115 had mCSCC and 78 had laCSCC. Among 26 CSCC patients enrolled in Study 1423, 16 had mCSCC and 10 had laCSCC. Treatment continued until progression of disease, unacceptable toxicity, or completion of planned treatment. Tumor response assessments were performed every 8 or 9 weeks. The major efficacy outcome measures were confirmed objective response rate (ORR), defined as complete response (CR) plus partial response (PR) as assessed by independent central review (ICR), and ICR-assessed duration of response (DOR). For patients with mCSCC without externally visible target lesions, ORR was determined by Response Evaluation Criteria in Solid Tumors (RECIST 1.1). For patients with externally visible target lesions (laCSCC and mCSCC), ORR was determined by a composite endpoint that integrated ICR assessments of radiologic data (RECIST 1.1) and digital medical photography (WHO Criteria).[1]

The cutoff for Study 1540 data in the USPI is September/October 2018.[2]

ECOG=Eastern Cooperative Oncology Group; PD-1=programmed death receptor-1; PD-L1=programmed death ligand 1; PS=performance status; WHO=World Health Organization.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

No dose reduction for LIBTAYO is recommended. In general, withhold LIBTAYO for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue LIBTAYO for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Withhold or permanently discontinue LIBTAYO depending on severity. In general, if LIBTAYO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Immune-mediated pneumonitis: LIBTAYO can cause immune-mediated pneumonitis. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 4 (0.5%), Grade 3 (0.5%), and Grade 2 (2.1%). Pneumonitis led to permanent discontinuation in 1.4% of patients and withholding of LIBTAYO in 2.1% of patients. Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 58% of the 26 patients. Of the 17 patients in whom LIBTAYO was withheld, 9 reinitiated after symptom improvement; of these, 3/9 (33%) had recurrence of pneumonitis. Withhold LIBTAYO for Grade 2, and permanently discontinue for Grade 3 or 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

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Select information from the LIBTAYO® (cemiplimab-rwlc) Prescribing Information (continued)

For the responding patients presented in the table below, the median time to response was 1.9 months (range: 1.7–9.1 months).[1]

Response rates in patients with mCSCC or laCSCC who were not candidates for curative surgery or curative radiation receiving 3 mg/kg every 2 weeks in Study 1540[1]

Efficacy endpoints*	Metastatic CSCC n=59	Locally advanced CSCC n=78	Combined CSCC N=137
Confirmed objective response rate (ORR)			
ORR (95% CI)	49% (36, 63)	44% (32, 55)	46% (37, 55)
Complete response (95% CI)†	17% (8, 29)	13% (6, 22)	15% (9, 22)
Partial response (95% CI)‡	32% (21, 46)	31% (21, 42)	31% (24, 40)
Duration of response (DOR)			
Median DOR, months (range)	NR (2.8–21.6+)	NR (1.9–24.2+)	NR (1.9–24.2+)
Patients with observed DOR ≥6 months, n (%)§	27 (93%)	23 (68%)	50 (79%)
Patients with observed DOR ≥12 months, n (%)§	22 (76%)	12 (35%)	34 (54%)

*Median duration of follow-up: mCSCC: 16.5 months; laCSCC: 9.3 months; combined CSCC: 11.1 months.
†Complete response is defined as disappearance of all target lesions for at least 4 weeks. Nontarget lesions also had to be a complete response, and there could be no new lesions. Any pathological lymph nodes (whether target or nontarget) must have reduction in short axis to <10 mm (<1 cm). Only includes patients with complete healing of prior cutaneous involvement; laCSCC patients in Study 1540 required biopsy to confirm CR.[1,2]
‡Partial response is defined as a decrease of 30% or greater in the sum of the diameters of target lesions, taking as reference the baseline sum of diameters, per RECIST 1.1. Partial response of externally visible disease is defined as a decrease of 50% or greater in the sum of products of perpendicular longest dimensions of target lesions, per WHO Criteria. Responses had to be maintained for at least 4 weeks. Nontarget lesions could not have progressive disease, and there could be no new lesions.[2]
§The numerator includes the number of patients whose observed DOR reached at least the specified times of 6 or 12 months. Patients who did not have the opportunity to reach the specified time point were included in the denominator only.

Plus sign (+) denotes ongoing at last assessment.

In an additional cohort in Study 1540, 56 mCSCC patients received LIBTAYO at a dose of 350 mg intravenously every 3 weeks for up to 54 weeks. With a median duration of follow-up of 8.0 months, the confirmed ORR was 41% (95% CI: 28, 55), and 65% of responders had a DOR ≥6 months.[1]

Among 26 CSCC patients in Study 1423, 16 had mCSCC and 10 had laCSCC. One patient in the mCSCC group was dosed at 1 mg/kg every 2 weeks. The rest received 3 mg/kg every 2 weeks. With a median duration of follow-up of 13.3 months, the confirmed ORR was 50% (95% CI: 30, 70); all responses were PRs. The median time to response was 1.9 months (range: 1.7–7.3 months), and 85% of responders had a DOR ≥6 months.[1]

In these trials, responses lasted between 1 month and more than 2 years (24.2+ months); plus sign (+) denotes ongoing at last assessment.[1,2]

The recommended dosage of LIBTAYO is 350 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity.[1]

CI=confidence interval; CR=complete response; NR=not reached; PR=partial response; RECIST=Response Evaluation Criteria in Solid Tumors; WHO=World Health Organization.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated colitis: LIBTAYO can cause immune-mediated colitis. The primary component of immune-mediated colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1–blocking antibodies. In cases of corticosteroid-refractory immune-mediated colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2.2% (18/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (1.1%). Colitis led to permanent discontinuation in 0.4% of patients and withholding of LIBTAYO in 1.5% of patients. Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 39% of the 18 patients. Of the 12 patients in whom LIBTAYO was withheld, 4 reinitiated LIBTAYO after symptom improvement; of these, 3/4 (75%) had recurrence. Withhold LIBTAYO for Grade 2 or 3, and permanently discontinue for Grade 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

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Adverse reactions in ≥10% of patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation receiving LIBTAYO in Study 1423 and Study 1540[1]

Adverse reactions	LIBTAYO (N=219)	
	All Grades (%)	Grades 3-4 (%)
General and administration site		
Fatigue*	34	3
Skin and subcutaneous tissue		
Rash†	31	1
Pruritus‡	18	0
Gastrointestinal		
Diarrhea§	25	0.5
Nausea	21	0
Constipation	13	0.5
Vomiting	10	0.5
Musculoskeletal and connective tissue		
Musculoskeletal pain‖	24	3
Arthralgia	11	1
Respiratory		
Cough¶	14	0
Hematology		
Anemia	11	4
Endocrine		
Hypothyroidism	10	0
Metabolism and nutrition		
Decreased appetite	10	0

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.03.
*Fatigue is a composite term that includes fatigue and asthenia.
†Rash is a composite term that includes rash, rash maculopapular, erythema, dermatitis, dermatitis bullous, rash generalized, pemphigoid, rash erythematous, rash macular, rash pruritic, drug eruption, psoriasis, and skin reaction.
‡Pruritus is a composite term that includes pruritus and pruritus allergic.
§Diarrhea is a composite term that includes diarrhea and colitis.
‖Musculoskeletal pain is a composite term that includes back pain, pain in extremity, myalgia, musculoskeletal pain, and neck pain.
¶Cough is a composite term that includes cough and upper airway cough syndrome.

- The most common Grades 3-4 adverse reactions (≥2%) were cellulitis, anemia, hypertension, pneumonia, musculoskeletal pain, fatigue, pneumonitis, sepsis, skin infection, and hypercalcemia[1]
- LIBTAYO was permanently discontinued due to adverse reactions in 8% of patients[1]
- Adverse reactions resulting in permanent discontinuation were pneumonitis, cough, pneumonia, encephalitis, aseptic meningitis, hepatitis, arthralgia, muscular weakness, neck pain, soft tissue necrosis, complex regional pain syndrome, lethargy, psoriasis, rash maculopapular, proctitis, and confusional state[1]
- Serious adverse reactions occurred in 35% of patients[1]
- Serious adverse reactions that occurred in at least 2% of patients were pneumonitis, cellulitis, sepsis, and pneumonia[1]

Grade 3 or 4 laboratory abnormalities worsening from baseline in ≥1% of patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation receiving LIBTAYO in Study 1423 and Study 1540[1]

Laboratory abnormality	Grades 3-4 (%)*
Chemistry	
Increased aspartate aminotransferase	2
Increased INR	2
Hematology	
Lymphopenia	9
Anemia	5

Laboratory abnormality	Grades 3-4 (%)*
Electrolytes	
Hyponatremia	5
Hypophosphatemia	4
Hypercalcemia	2

Toxicity graded per NCI CTCAE v4.03.
*Percentages are based on the number of patients with at least 1 post-baseline value available for that parameter.
CSCC=cutaneous squamous cell carcinoma; INR=international normalized ratio.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

Background

The following are updated data adapted from Study 1540 (EMPOWER-CSCC 1), which were presented at the American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program.

Rischin D, Khushalani NI, Schmults CD, et al. Phase 2 study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma (CSCC): longer follow-up.

These longer follow-up data (predetermined data cutoff was October 11, 2019) for patients with advanced CSCC will be reviewed.

CSCC=cutaneous squamous cell carcinoma.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated hepatitis: LIBTAYO can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 2% (16/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (1.4%), and Grade 2 (0.2%). Hepatitis led to permanent discontinuation of LIBTAYO in 1.2% of patients and withholding of LIBTAYO in 0.5% of patients. Systemic corticosteroids were required in all patients with hepatitis. Additional immunosuppression with mycophenolate was required in 19% (3/16) of these patients. Hepatitis resolved in 50% of the 16 patients. Of the 5 patients in whom LIBTAYO was withheld, 3 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence.

For hepatitis with no tumor involvement of the liver: Withhold LIBTAYO if AST or ALT increases to more than 3 and up to 8 times the upper limit of normal (ULN) or if total bilirubin increases to more than 1.5 and up to 3 times the ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 8 times the ULN or total bilirubin increases to more than 3 times the ULN.

For hepatitis with tumor involvement of the liver: Withhold LIBTAYO if baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN. Also, withhold LIBTAYO if baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 10 times ULN or if total bilirubin increases to more than 3 times ULN. If AST and ALT are less than or equal to ULN at baseline, withhold or permanently discontinue LIBTAYO based on recommendations for hepatitis with no liver involvement.

Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated endocrinopathies: For Grade 3 or 4 endocrinopathies, withhold until clinically stable or permanently discontinue depending on severity.

- **Adrenal insufficiency:** LIBTAYO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO depending on severity. Adrenal insufficiency occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.4%). Adrenal insufficiency led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. LIBTAYO was not withheld in any patient due to adrenal insufficiency. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these, 67% (2/3) remained on systemic corticosteroids. Adrenal insufficiency had not resolved in any patient at the time of data cutoff
- **Hypophysitis:** LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue depending on severity. Hypophysitis occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient and withholding of LIBTAYO in 1 (0.1%) patient. Systemic corticosteroids were required in 67% (2/3) of patients with hypophysitis. Hypophysitis had not resolved in any patient at the time of data cutoff
- **Thyroid disorders:** LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity
- **Thyroiditis:** Thyroiditis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including Grade 2 (0.2%) adverse reactions. No patient discontinued LIBTAYO due to thyroiditis. Thyroiditis led to withholding of LIBTAYO in 1 patient. Systemic corticosteroids were not required in any patient with thyroiditis. Thyroiditis had not resolved in any patient at the time of data cutoff. Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported

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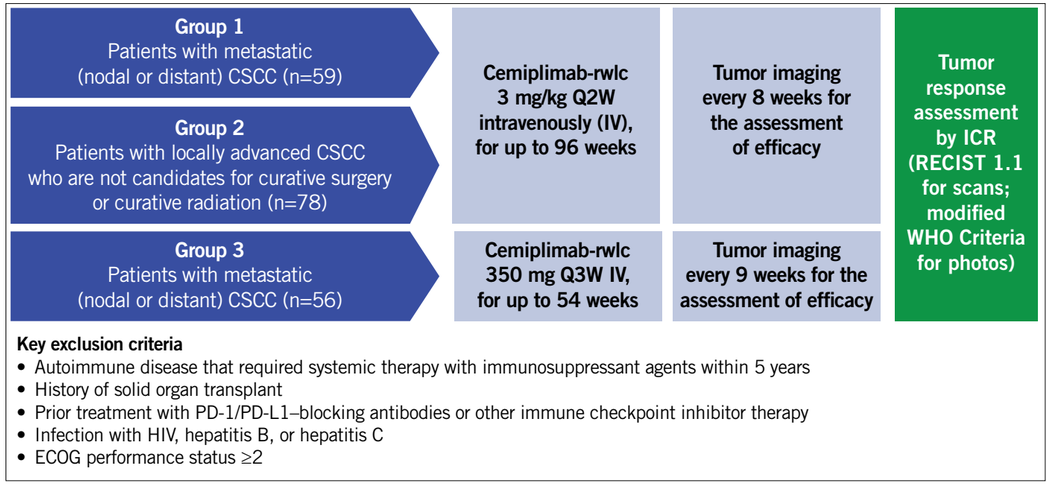
LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Study design for Study 1540[1,3]

Methods

- Global, pivotal, open-label, nonrandomized, phase 2 study that enrolled adult patients with metastatic CSCC or locally advanced CSCC[1,3]



Key exclusion criteria

- Autoimmune disease that required systemic therapy with immunosuppressant agents within 5 years
- History of solid organ transplant
- Prior treatment with PD-1/PD-L1–blocking antibodies or other immune checkpoint inhibitor therapy
- Infection with HIV, hepatitis B, or hepatitis C
- ECOG performance status ≥2

Adapted with permission from Rischin et al, 2020.[3]

The recommended dosage of LIBTAYO is 350 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity.[1]

Endpoints

- **Primary endpoint:** Confirmed ORR as assessed by ICR[3]
- **Secondary endpoints included:** DOR, complete response rate, safety and tolerability[3]

DOR=duration of response; ECOG=Eastern Cooperative Oncology Group; ICR=independent central review; ORR=objective response rate; PD-1=programmed death receptor-1; PD-L1=programmed death ligand 1; Q2W=every 2 weeks; Q3W=every 3 weeks; RECIST=Response Evaluation Criteria in Solid Tumors; WHO=World Health Organization.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated endocrinopathies (continued):

- **Hyperthyroidism:** Hyperthyroidism occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 2 (0.9%). No patient discontinued treatment and LIBTAYO was withheld in 0.5% of patients due to hyperthyroidism. Systemic corticosteroids were required in 3.8% (1/26) of patients. Hyperthyroidism resolved in 50% of 26 patients. Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hyperthyroidism
- **Hypothyroidism:** Hypothyroidism occurred in 7% (60/810) of patients receiving LIBTAYO, including Grade 2 (6%). Hypothyroidism led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. Hypothyroidism led to withholding of LIBTAYO in 1.1% of patients. Systemic corticosteroids were not required in any patient with hypothyroidism. Hypothyroidism resolved in 8.3% of the 60 patients. Majority of the patients with hypothyroidism required long-term thyroid hormone replacement. Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reinitiated LIBTAYO after symptom improvement; 1 required ongoing hormone replacement therapy
- **Type 1 diabetes mellitus, which can present with diabetic ketoacidosis:** Monitor for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity. Type 1 diabetes mellitus occurred in 0.1% (1/810) of patients, including Grade 4 (0.1%). No patient discontinued treatment due to type 1 diabetes mellitus. Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients

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Updated data for patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation

Rischin D, Khushalani NI, Schmults CD, et al. Phase 2 study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma (CSCC): longer follow-up. Data presented at the American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program; May 29-31, 2020.

Patient demographics and baseline characteristics[3]

	Advanced CSCC (N=193)
Median age, years (range)	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)
Metastatic CSCC, n (%)	115 (59.6)
Locally advanced CSCC, n (%)	78 (40.4)
Patients with cemiplimab-rwlc as first-line systemic therapy, n (%)	128 (66.3)
Patients with prior systemic therapy, n (%)*	65 (33.7)

*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%]).[3]

ECOG=Eastern Cooperative Oncology Group.

Adapted with permission from Rischin et al, 2020.[3]

- Median duration of follow-up for the combined advanced CSCC group at the time of data cutoff was 15.7 months[3]

The recommended dosage of LIBTAYO is 350 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity.[1]

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated nephritis with renal dysfunction: LIBTAYO can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 3 (0.1%), and Grade 2 (0.4%). Nephritis led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 0.4% of patients. Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in 80% of the 5 patients. Of the 3 patients in whom LIBTAYO was withheld, 2 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence. Withhold LIBTAYO for Grade 2 or 3 increased blood creatinine, and permanently discontinue for Grade 4 increased blood creatinine. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

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Updated data for patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation

Tumor response assessment by ICR[2,3]

	Group 1 (metastatic CSCC) 3 mg/kg Q2W (n=59)	Group 2 (locally advanced CSCC) 3 mg/kg Q2W (n=78)	Group 3 (metastatic CSCC) 350 mg Q3W (n=56)	Combined advanced CSCC (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)
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)
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 (95% CI)*	Not reached (NR) (20.7, not evaluable [NE])	NR (18.4, NE)	NR (NE, NE)	NR (28.8, NE)
Patients with DOR ≥6 months, n (%)†	28 (93.3%)	30 (85.7%)	23 (95.8%)	81 (91.0%)
Patients with DOR ≥12 months, n (%)†	23 (76.7%)	22 (62.9%)	20 (83.3%)	65 (73.0%)

*Based on number of patients with confirmed complete response or partial response.[3]

†The numerator includes the number of patients whose observed DOR reached at least the specified times of 6 or 12 months. Patients who did not have the opportunity to reach the specified time point were included in the denominator only.[1]

CI=confidence interval; CSCC=cutaneous squamous cell carcinoma; DOR=duration of response; ICR=independent central review; IQR=interquartile range; ORR=objective response rate; Q2W=every 2 weeks; Q3W=every 3 weeks.

Adapted with permission from Rischin et al, 2020.[3]

- In a prespecified analysis by ICR, ORR was 48.4% (95% CI: 39.5–57.4) and 41.5% (95% CI: 29.4–54.4) among those who had not received prior anticancer systemic therapy (n=128) and among those who had received prior anticancer systemic therapy (n=65), respectively[3]
- Overall, the observed time to response was 2 months for 41 patients (46.1%), 2–4 months for 29 patients (32.6%), 4–6 months for 8 patients (9.0%), and >6 months for 11 patients (12.4%)[3]
- In the combined advanced CSCC group, median DOR has not been reached (observed DOR range: 1.9–34.3 months)[3]

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated dermatologic adverse reactions: LIBTAYO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) has occurred with PD-1/PD-L1–blocking antibodies. Immune-mediated dermatologic adverse reactions occurred in 1.6% (13/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.6%). Immune-mediated dermatologic adverse reactions led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 1.4% of patients. Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 69% of the 13 patients. Of the 11 patients in whom LIBTAYO was withheld for dermatologic adverse reactions, 7 reinitiated LIBTAYO after symptom improvement; of these, 43% (3/7) had recurrence of the dermatologic adverse reaction. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold LIBTAYO for suspected SJS, TEN, or DRESS. Permanently discontinue LIBTAYO for confirmed SJS, TEN, or DRESS. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

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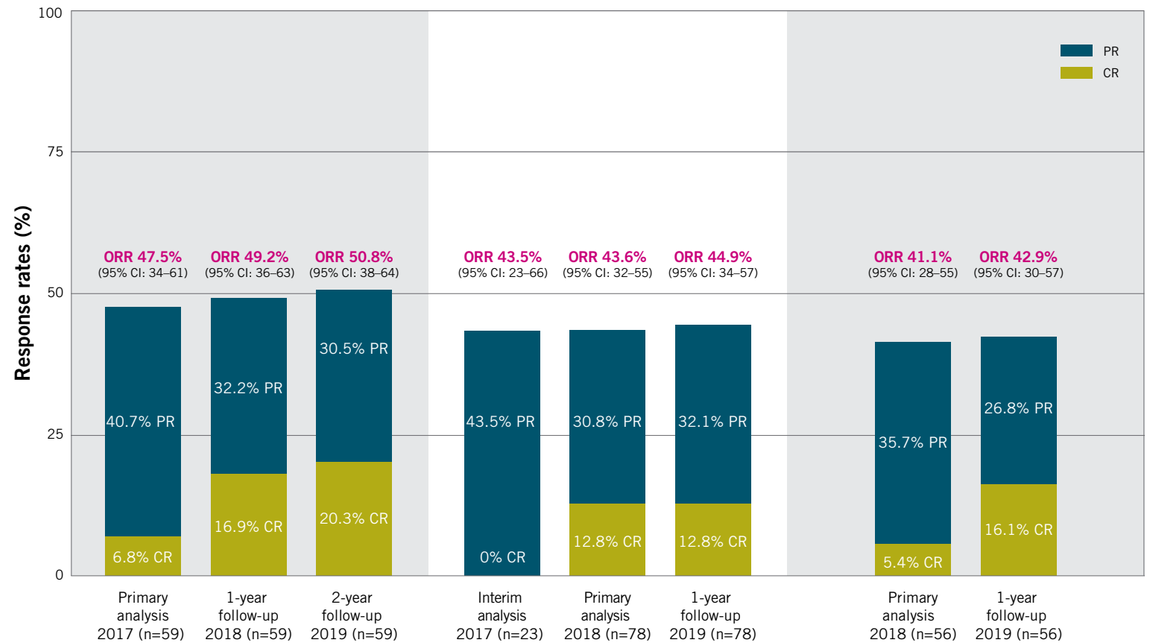
Updated data for patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation

Tumor response assessment in patients by ICR across all data cuts[1-3]



CR=complete response; CSCC=cutaneous squamous cell carcinoma; ICR=independent central review; ORR=objective response rate; PR=partial response; Q2W=every 2 weeks; Q3W=every 3 weeks.

The recommended dosage of LIBTAYO is 350 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity.[1]

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Other immune-mediated adverse reactions: The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in 810 patients who received LIBTAYO or were reported with the use of other PD-1/PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

- **Cardiac/vascular:** Myocarditis, pericarditis, and vasculitis. Permanently discontinue for Grades 2, 3, or 4 myocarditis
- **Nervous system:** Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, and autoimmune neuropathy. Withhold for Grade 2 neurological toxicities and permanently discontinue for Grades 3 or 4 neurological toxicities. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Updated data for patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation

Adverse reactions in ≥10% of patients with advanced CSCC[3]

	Advanced CSCC (N=193)	
n (%)	**All Grades**	**Grades ≥3**
Any	192 (99.5)	94 (48.7)
Led to discontinuation	19 (9.8)	14 (7.3)
Most common*		
Fatigue	67 (34.7)	5 (2.6)
Diarrhea	53 (27.5)	2 (1.0)
Nausea	46 (23.8)	0
Pruritus	41 (21.2)	0
Rash	32 (16.6)	1 (0.5)
Cough	32 (16.6)	0
Arthralgia	28 (14.5)	1 (0.5)
Constipation	26 (13.5)	1 (0.5)
Vomiting	24 (12.4)	1 (0.5)
Actinic keratosis	23 (11.9)	0
Maculopapular rash	23 (11.9)	1 (0.5)
Anemia	22 (11.4)	8 (4.1)
Hypothyroidism	22 (11.4)	0
Headache	21 (10.9)	0
Upper respiratory tract infection	20 (10.4)	0

*Adverse reactions reported in ≥10% of patients, ordered by frequency of any grade.
Adapted with permission from Rischin et al, 2020.[3]

- Grade ≥3 adverse reactions occurred in 94 patients (48.7%). The most common Grade ≥3 adverse reactions were hypertension (n=9; 4.7%) and anemia and cellulitis (each n=8; 4.1%)

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Other immune-mediated adverse reactions (continued):

- **Ocular:** Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss
- **Gastrointestinal:** Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis
- **Musculoskeletal and connective tissue:** Myositis/polymyositis, rhabdomyolysis, and associated sequelae including renal failure, arthritis, polymyalgia rheumatica
- **Endocrine:** Hypoparathyroidism
- **Other (hematologic/immune):** Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

LIBTAYO is the #1 most-prescribed systemic therapy by oncologists for patients with advanced CSCC[1]*

*Based on IQVIA medical claims data, October 2018 through November 2020. Claims calibrated with actual vials sold.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Infusion-related reactions

Severe infusion-related reactions (Grade 3) occurred in 0.1% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. The most common symptoms of infusion-related reaction were nausea, pyrexia, rash, and dyspnea. Interrupt or slow the rate of infusion for Grade 1 or 2, and permanently discontinue for Grade 3 or 4.

Complications of allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

Embryo-fetal toxicity

LIBTAYO can cause fetal harm when administered to a pregnant woman due to an increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose.

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LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

To learn more about LIBTAYO, speak with your sales representative or visit LIBTAYOhcp.com

Important Safety Information (continued)

Adverse Reactions

- In the pooled safety analysis of 810 patients, the most common adverse reactions (≥15%) with LIBTAYO were musculoskeletal pain, fatigue, rash, and diarrhea
- In the pooled safety analysis of 810 patients, the most common Grade 3-4 laboratory abnormalities (≥2%) with LIBTAYO were lymphopenia, hyponatremia, hypophosphatemia, increased aspartate aminotransferase, anemia, and hyperkalemia

Use in Specific Populations

- **Lactation:** Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO
- **Females and males of reproductive potential:** Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO

Please see accompanying full Prescribing Information.

Indications and Usage

LIBTAYO is indicated for the first-line treatment of patients with non–small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression (tumor proportion score [TPS] ≥50%) as determined by an FDA-approved test, with no EGFR, ALK, or ROS1 aberrations, and is locally advanced where patients are not candidates for surgical resection or definitive chemoradiation OR metastatic.

LIBTAYO is indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) who are not candidates for curative surgery or curative radiation.

LIBTAYO is indicated for the treatment of patients with locally advanced basal cell carcinoma (laBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.

References: 1. LIBTAYO (cemiplimab-rwlc) injection full U.S. prescribing information. Regeneron Pharmaceuticals, Inc., and sanofi-aventis U.S. LLC. **2.** Data on file. Regeneron Pharmaceuticals, Inc. **3.** Rischin D, Khushalani NI, Schmults CD, et al. Phase 2 study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma (CSCC): longer follow-up. Poster presented at: American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program; May 29-31, 2020.

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