CLINICAL INSIGHTS

Summary of the product theater presented at American Head and Neck Society

LIBTAYO® (cemiplimab-rwlc) is the first and only treatment indicated for patients with locally advanced basal cell carcinoma (laBCC) previously treated with a hedgehog pathway inhibitor (HHI) or for whom an HHI is not appropriate, as well as the first FDA-approved therapy in patients with metastatic cutaneous squamous cell carcinoma (mCSCC) or locally advanced cutaneous squamous cell carcinoma (laCSCC) who are not candidates for curative surgery or curative radiation[1]

July 22, 2021

LIBTAYO® (cemiplimab-rwlc) Is FDA-approved in Locally Advanced BCC and Offers Over 4 Years of Clinical Treatment Experience in Advanced CSCC[1-4,]*

*FDA-approved in advanced CSCC in September 2018.[1]

Presented by:

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BCC overview and risk factors for recurrence

BCC is the most common form of nonmelanoma skin cancer (NMSC), accounting for approximately 80% of all NMSC cases.[5,6] There are several risk factors associated with BCC recurrence.[7] In patients with local BCC, these include various features of the tumor, such as its size, location, and pathology, as well as the history of prior radiation therapy and recurrence of the tumor, whether it had poorly defined borders, and other factors such as immunosuppression. While most patients with BCC benefit from surgical interventions, incomplete surgical resection may increase the risk for recurrence.[8] Incomplete surgical resection has been reported to increase the likelihood of disease recurrence up to 27%.[8]

Important Safety Information for LIBTAYO (cemiplimab-rwlc)

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.

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

This supplement is sponsored by Regeneron and Sanofi Genzyme.
Eric Whitman, MD, FACS presented at the product theater, and was compensated for participation.

Progression to locally advanced BCC (laBCC)

Progression to advanced BCC can cause significant invasion of surrounding tissue (locally advanced) or, more rarely, nodal or distant metastasis.[9] In the United States, over 2 million patients are diagnosed with BCC each year; of these, over 20,000 patients will progress to advanced BCC and may no longer be amenable to surgery or radiotherapy.[10,11]

Systemic therapies can play a critical role in the management of laBCC

Systemic therapy is the recommended treatment option for patients with laBCC who are not candidates for surgery or radiotherapy.[9] Some factors that may be used to determine if systemic therapy is appropriate in patients with laBCC include tumor characteristics (eg, large tumors, significant local invasion, potential for deformity/morbidity, aggressive growth), patient characteristics (eg, advanced age, presence of comorbidities, poor performance status, patient preference), and treatment history (eg, multiple recurrences, prior radiotherapy, prior surgery).[9,12] HHIs are a recommended systemic therapy option for patients with laBCC who are no longer candidates for curative surgery or curative radiotherapy.[7] LIBTAYO® (cemiplimab-rwlc) is a treatment option for those patients with laBCC who discontinue HHI therapy (eg, due to disease progression/lack of response or intolerance) or for whom HHI therapy is not appropriate.

A multidisciplinary approach is key to treating advanced BCC

In the management of patients with advanced BCC, the following guidelines unanimously recommend consultation with a multidisciplinary team: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®),[7] American Academy of Dermatology guidelines,[13] and European multidisciplinary guidelines (composed of experts from the European Association of Dermato Oncology, the European Dermatology Forum, and the European Organisation for Research and Treatment of Cancer).[14] While these various guidelines do not specify a list of disciplines that must be involved, the multidisciplinary team may include dermatologists, medical oncologists, pathologists, radiation oncologists, Mohs surgeons, head and neck surgeons, physician assistants, nurses or nurse practitioners, and pharmacists.

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

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.

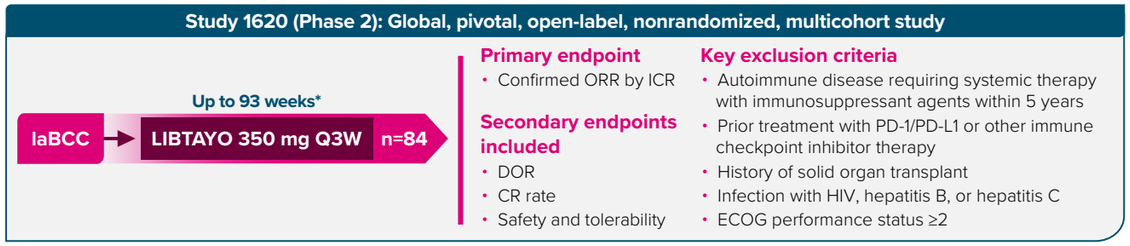
LIBTAYO® (cemiplimab-rwlc) was evaluated in the largest prospective clinical study of a PD-1 inhibitor in patients with laBCC previously treated with an HHI

LIBTAYO is the first and only treatment indicated for patients with laBCC previously treated with an HHI or for whom an HHI is not appropriate.[1] The safety and efficacy of LIBTAYO were evaluated in an open-label, nonrandomized, multicohort study (Study 1620); this study included 84 patients with laBCC who had progressed on HHI therapy, had not had an objective response after 9 months on HHI therapy, or were intolerant of prior HHI therapy, as shown in **Figure 1**.[1] Study 1620 excluded patients with autoimmune disease that required systemic therapy with immunosuppressant agents within 5 years; a history of solid organ transplant; prior treatment with anti–PD-1/PD-L1 therapy or other immune checkpoint inhibitor therapy; infection with human immunodeficiency virus, hepatitis B, or hepatitis C; or an Eastern Cooperative Oncology Group performance status of at least 2.

Tumor response assessments were performed every 9 weeks during cycles 1 to 5 and every 12 weeks during cycles 6 to 9. The major efficacy outcome measures were confirmed objective response rate (ORR), defined as complete response (CR) rate plus partial response (PR) rate as assessed by independent central review (ICR), and ICR-assessed duration of response (DOR). For patients 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, ORR was determined by a composite endpoint that integrated ICR assessments of radiologic data (RECIST 1.1) and digital medical photography (World Health Organization [WHO] Criteria).

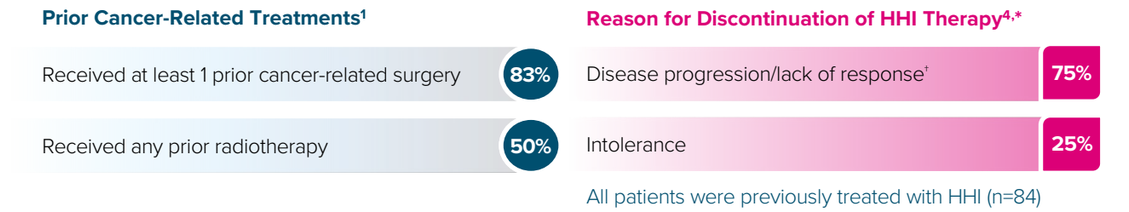
The baseline characteristics of patients with laBCC enrolled in Study 1620 are shown in **Figure 2**.

Figure 1. Clinical Study of LIBTAYO, a PD-1 Inhibitor, in Patients with laBCC Previously Treated with an HHI[1]



*Treatment continued until progression of disease, unacceptable toxicity, or completion of planned treatment. CR, complete response; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HHI, hedgehog pathway inhibitor; HIV, human immunodeficiency virus; ICR, independent central review; laBCC, locally advanced basal cell carcinoma; ORR, objective response rate; Q3W, every 3 weeks.

Figure 2. Baseline Characteristics of Patients with laBCC Enrolled in Study 1620[1]

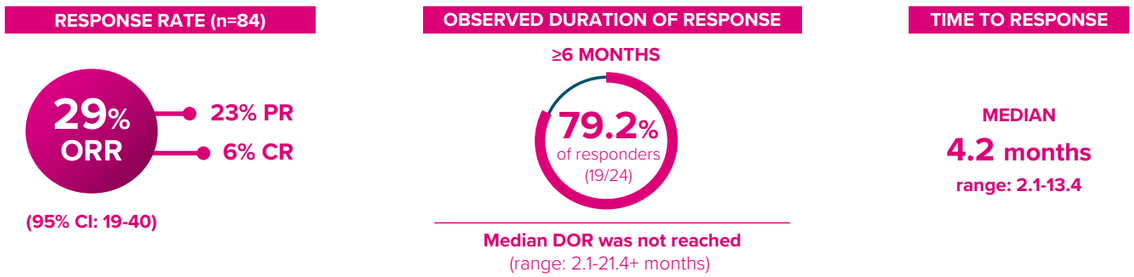


*Investigators were allowed to select more than 1 reason for discontinuation of prior HHI therapy for an individual patient. †Lack of response was defined as not having an objective response after 9 months on HHI therapy. HHI, hedgehog pathway inhibitor; laBCC, locally advanced basal cell carcinoma.

LIBTAYO® (cemiplimab-rwlc) demonstrated clinically meaningful responses in a study of patients with laBCC previously treated with an HHI

Among 84 patients with laBCC, the ORR was 29% (95% CI: 19-40); 23% of patients achieved a PR and 6% achieved a CR (**Figure 3**). The median duration of follow-up was 15.1 months (range: 0.5-25.1). Among the patients with laBCC who achieved an objective response, 79.2% demonstrated a DOR of at least 6 months. The median DOR was not reached (range: 2.1-21.4+). For the responding patients, the median time to response was 4.2 months (range: 2.1-13.4).[1]

Figure 3. Efficacy Results for Patients with laBCC in Study 1620: 350 mg Q3W[1]



Median duration of follow-up was 15.1 months (range: 0.5-25.1) for patients with laBCC. CR, complete response; DOR, duration of response; laBCC, locally advanced basal cell carcinoma; ORR, objective response rate; PR, partial response; Q3W, every 3 weeks.

In an exploratory subgroup analysis of patients with laBCC, the ORR by reason for HHI discontinuation was 29% (18/63) in patients who had disease progression/lack of response while on HHIs, and 29% (6/21) in patients who were intolerant to HHIs. Please note, this analysis may not have had enough power for hypothesis tests.[4]

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

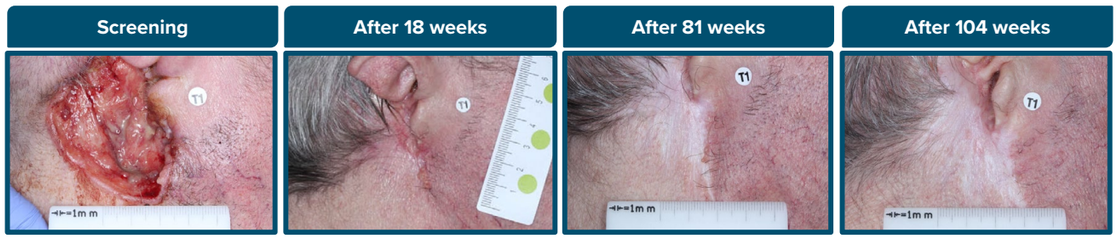
Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

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.

Patient case studies

The following cases highlight 2 patients with laBCC who underwent treatment with LIBTAYO in Study 1620. **They are examples of the 23% of patients with laBCC who achieved a PR in Study 1620. Individual responses may vary.**

Patient Case 1: In a 79-Year-Old Male Patient with laBCC Who Discontinued Prior Vismodegib Due to Disease Progression Presenting with a Right Auricular Lesion

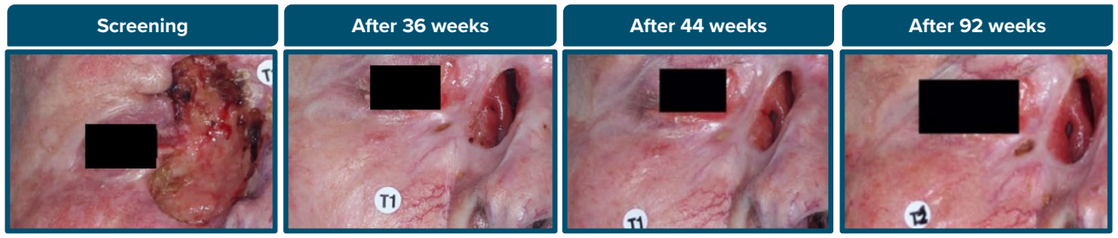


Clinical outcomes:
As of data cutoff
February 17, 2020

- **Best response: PR** by composite evaluation (RECIST 1.1 + WHO Criteria) per ICR
- **Time to response: 4.2 months**
- **DOR: 19.7+ months**

Patient Case 2: In a 77-Year-Old Female Patient with laBCC Who Discontinued Prior Vismodegib Due to Disease Progression Presenting with a Right Nasal Cavity Lesion

The duration of response for this patient was 4.8 months. At the time of data cutoff, this patient was no longer in response due to having disease.



Clinical outcomes:
As of data cutoff
February 17, 2020

- **Best response: PR** by composite evaluation (RECIST 1.1 + WHO Criteria) per ICR
- **Time to response: 8.2 months**
- **DOR: 4.8 months**

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.
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LIBTAYO® (cemiplimab-rwlc) demonstrated a favorable safety profile in Study 1620

In the safety analysis for Study 1620, LIBTAYO was permanently discontinued due to adverse reactions in 13% of patients. Adverse reactions resulting in permanent discontinuation in >1.5% of patients (at least 2 patients) were colitis and general physical health deterioration. Dosage delays of LIBTAYO due to an adverse reaction occurred in 34% of patients. Adverse reactions that required dosage delay in >2% of patients (at least 3 patients) included blood creatinine increased, diarrhea, colitis, fatigue, headache, pneumonitis, and urinary tract infection. The adverse reactions of any grade occurring in at least 10% of patients and respective Grades 3-4 are shown in **Table 1**. The most common adverse reactions reported in at least 15% of patients were fatigue, musculoskeletal pain, diarrhea, rash, pruritus, and upper respiratory tract infection. The most common Grade 3-4 adverse reactions (>2%) were hypertension, colitis, fatigue, urinary tract infection, pneumonia, increased blood pressure, hypokalemia, and visual impairment. Serious adverse reactions occurred in 32% of patients. Serious adverse reactions that occurred in >1.5% of patients (at least 2 patients) were urinary tract infection, colitis, acute kidney injury, adrenal insufficiency, anemia, infected neoplasm, and somnolence. Fatal adverse reactions occurred in 1.5% of patients who received LIBTAYO, including acute kidney injury and cachexia. The Grade 3 or 4 laboratory abnormalities in at least 1% of patients are shown in **Table 2**. The most common (>3%) laboratory abnormality worsening from baseline to Grade 3 or 4 was hyponatremia.

Warnings and Precautions for LIBTAYO include severe and fatal immune-mediated adverse reactions such as immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated nephritis with renal dysfunction, immune-mediated dermatologic adverse reactions, and other immune-mediated adverse reactions; infusion-related reactions; complications of allogeneic hematopoietic stem cell transplantation (HSCT); and embryo-fetal toxicity. Monitor for symptoms and signs of immune-mediated adverse reactions.

For more information on Warnings and Precautions, see additional Important Safety Information throughout and in Section 5 of the full Prescribing Information.

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

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.

Table 1. Adverse Reactions in ≥10% of Patients in Study 1620[1]

	LIBTAYO (N=132)*	
	All Grades, %	Grades 3-4, %
General and administration site		
Fatigue†	49	3.8
Musculoskeletal and connective tissue		
Musculoskeletal pain‡	33	1.5
Gastrointestinal		
Diarrhea	25	0
Nausea	12	0.8
Constipation	11	0.8
Skin and subcutaneous tissue		
Rash§	22	0.8
Pruritus	20	0
Infections and infestations		
Upper respiratory tract infection¶	15	0
Urinary tract infection	12	2.3
Metabolism and nutrition		
Decreased appetite	14	1.5
Blood and lymphatic system		
Anemia	13	0.8
Nervous system		
Headache	12	1.5
Respiratory, thoracic, and mediastinal		
Dyspnea#	11	0
Vascular disorders		
Hypertension‖	11	4.5

*Of the 132 patients included in the safety analysis of Study 1620, eighty-four patients had locally advanced basal cell carcinoma. †Composite term includes fatigue, asthenia, and malaise. ‡Composite term includes arthralgia, back pain, myalgia, pain in extremity, musculoskeletal pain, neck pain, musculoskeletal stiffness, musculoskeletal chest pain, musculoskeletal discomfort, and spinal pain. §Composite term includes rash maculo-papular, rash, dermatitis, dermatitis acneiform, erythema, rash pruritic, dermatitis bullous, dyshidrotic eczema, pemphigoid, rash erythematous, and urticaria. ¶Composite term includes upper respiratory tract infection, nasopharyngitis, rhinitis, sinusitis, pharyngitis, respiratory tract infection, and viral upper respiratory tract infection. #Composite term includes dyspnea and dyspnea exertional. ‖Composite term includes hypertension and hypertensive crisis.

Table 2. Grade 3 or 4 Laboratory Abnormalities in ≥1% of Patients in Study 1620[1,*]

	LIBTAYO (N=132)[†]
	Grades 3-4, %
Electrolytes	
Hyponatremia	3.1
Hypokalemia	1.5
Coagulation	
Activated partial thromboplastin time prolonged	2.3
Hematology	
Lymphocyte count decreased	2.3

*Percentages are based on the number of patients with at least 1 postbaseline value available for that parameter. †Of the 132 patients included in the safety analysis of Study 1620, eighty-four patients had locally advanced basal cell carcinoma.

LIBTAYO® (cemiplimab-rwlc) was evaluated in the largest prospective clinical study of a PD-1 inhibitor in patients with mCSCC or laCSCC who were not candidates for curative surgery or curative radiation

LIBTAYO is the first FDA-approved therapy for patients with mCSCC or laCSCC who are not candidates for curative surgery or curative radiation.[1]

The efficacy and safety of LIBTAYO were evaluated in two open-label, multicenter, nonrandomized multicohort studies (Study 1423 and Study 1540) in patients with mCSCC (nodal or distant) or laCSCC who were not candidates for curative surgery or curative radiation. Study 1540, shown in **Figure 4**, included 193 patients with mCSCC or laCSCC who were not candidates for curative surgery or curative radiation. Patients received LIBTAYO 3 mg/kg intravenously every 2 weeks for up to 96 weeks (Groups 1 and 2) or LIBTAYO 350 mg every 3 weeks for up to 54 weeks (Group 3).

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

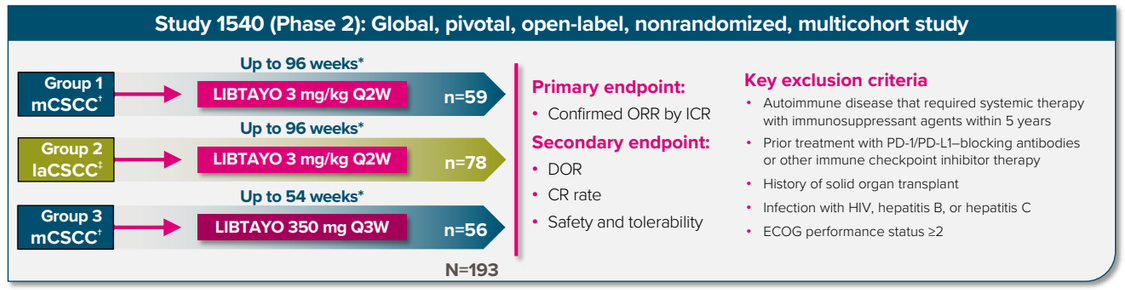
Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

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

Figure 4. Clinical Study of LIBTAYO, a PD-1 Inhibitor, in Patients with mCSCC or laCSCC Who Were Not Candidates for Curative Surgery or Curative Radiation[1]



The recommended dosage of LIBTAYO is 350 mg administered as an intravenous infusion over 30 minutes Q3W until disease progression or unacceptable toxicity

*Treatment continued until progression of disease, unacceptable toxicity, or completion of planned treatment. †Nodal or distant CSCC. ‡Patients with locally advanced CSCC who were not candidates for curative surgery or curative radiation. CR, complete response; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus; ICR, independent central review; laCSCC, locally advanced cutaneous squamous cell carcinoma; mCSCC, metastatic cutaneous squamous cell carcinoma; ORR, objective response rate; Q2W, every 2 weeks; Q3W, every 3 weeks.

LIBTAYO® (cemiplimab-rwlc) demonstrated substantial clinical activity and achieved durable and rapid responses in patients with advanced CSCC

In Study 1540, the ORR was 46% for the combined CSCC population receiving LIBTAYO 3 mg/kg every 2 weeks, with 15% of patients achieving CR and 31% of patients achieving PR. The median time to response for the combined CSCC population was rapid (1.9 months [range: 1.7-9.1 months]), based on an open-label, single-arm study that did not include comparisons with other treatments (first assessment was performed at 8 weeks). Median DOR was not reached (range: 1.9-24.2+ months), and 54% of patients had an observed DOR of at least 12 months* (**Figure 5**).

*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.

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

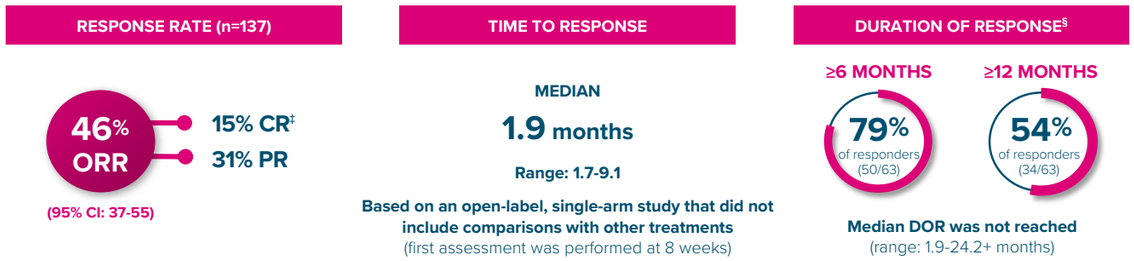
Warnings and Precautions (cont'd)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

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. .

Figure 5. Efficacy Results for Patients with mCSCC or laCSCC Who Received LIBTAYO 3 mg/kg Q2W in Study 1540[1,*,†]



In an additional cohort of patients with mCSCC receiving LIBTAYO 350 mg Q3W (n=56) in Study 1540, the confirmed ORR was 41% (95% CI: 28-55), and 65% of responders reached a DOR ≥6 months.§ Median DOR was not reached (range: 2.1-11.1+ months)

*Data cutoff was September/October 2018. †Median duration of follow-up was 11.1 months and 8.0 months in patients who received LIBTAYO 3 mg/kg Q2W and LIBTAYO 350 mg Q3W in Study 1540, respectively. ‡Only includes patients with complete healing of prior cutaneous involvement; patients with laCSCC in Study 1540 required biopsy to confirm CR. §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. CR, complete response; DOR, duration of response; laCSCC, locally advanced cutaneous squamous cell carcinoma; mCSCC, metastatic cutaneous squamous cell carcinoma; ORR, objective response rate; PR, partial response; Q2W, every 2 weeks; Q3W, every 3 weeks.

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

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
- **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

LIBTAYO® (cemiplimab-rwlc) safety profile in patients with advanced CSCC

Table 3. Adverse Reactions in ≥10% of Patients with Advanced CSCC in Studies 1423 and 1540[1]

	LIBTAYO (N=219)	
	All Grades, %	Grades 3-4, %
General and administrative 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

*Composite term includes fatigue and asthenia. †Composite term includes rash, rash maculopapular, erythema, dermatitis, dermatitis bullous, rash generalized, pemphigoid, rash erythematous, rash macular, rash pruritic, drug eruption, psoriasis, and skin reaction. ‡Composite term includes pruritus and pruritus allergic. §Composite term includes diarrhea and colitis. ¶Composite term includes back pain, pain in extremity, myalgia, musculoskeletal pain, and neck pain. #Composite term includes cough and upper airway cough syndrome. CSCC, cutaneous squamous cell carcinoma.

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

Immune-mediated endocrinopathies (cont'd):

- **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

Table 4. Grade 3 or 4 Laboratory Abnormalities Worsening From Baseline in ≥1% of Patients with Advanced CSCC in Studies 1423 and 1540[1,*]

	LIBTAYO (N=219)
	Grades 3-4, %
Chemistry	
Increased aspartate aminotransferase	2
Increased INR	2
Hematology	
Lymphopenia	9
Anemia	5
Electrolytes	
Hyponatremia	5
Hypophosphatemia	4
Hypercalcemia	2

*Percentages are based on the number of patients with at least 1 postbaseline value available for that parameter. CSCC, cutaneous squamous cell carcinoma; INR, international normalized ratio.

- The most common Grade 3-4 adverse reactions (≥2%) were cellulitis, anemia, hypertension, pneumonia, musculoskeletal pain, fatigue, pneumonitis, sepsis, skin infection, and hypercalcemia
- LIBTAYO was permanently discontinued due to adverse reactions in 8% of patients
- 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
- Serious adverse reactions occurred in 35% of patients
- Serious adverse reactions that occurred in at least 2% of patients were pneumonitis, cellulitis, sepsis, and pneumonia

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

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.

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%).

NCCN Guidelines® recommend cemiplimab-rwlc (LIBTAYO) as follows:[7,15]

Cemiplimab-rwlc (LIBTAYO) is recommended by the NCCN Guidelines for Squamous Cell Skin Cancer as a Category 2A* preferred systemic therapy option for patients across all three of the following categories when curative surgery and curative radiation therapy are not feasible: 1) laCSCC,† 2) regional CSCC, and 3) regionally recurrent/distant metastatic CSCC.[15]

Cemiplimab-rwlc (LIBTAYO) is also recommended by the NCCN Guidelines for Basal Cell Skin Cancer as a Category 2A* recommended systemic therapy option for patients with laBCC previously treated with an HHI or for whom an HHI is not appropriate.[7]

NCCN makes no warranties of any kind whatsoever regarding their content, use, or application, and disclaims any responsibility for their application or use in any way. To view the most recent and complete version of the guidelines, go online to NCCN.org.

*A Category 2A recommendation is based on lower-level evidence and uniform NCCN consensus that the intervention is appropriate. All recommendations are Category 2A unless otherwise specified. †For patients who have complicated cases of locally advanced disease in which curative surgery and curative radiation therapy are not feasible. Assessment of radiation therapy should be made by a radiation oncologist.

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

Immune-mediated dermatologic adverse reactions (cont'd): 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.

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
- **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

Conclusion

LIBTAYO® (cemiplimab-rwlc) is FDA-approved for use in patients with laBCC previously treated with an HHI or for whom an HHI is not appropriate. LIBTAYO was evaluated in the largest prospective clinical study of a PD-1 inhibitor in patients with laBCC previously treated with an HHI. LIBTAYO is also approved for use in patients with mCSCC or laCSCC who are not candidates for curative surgery or curative radiation; it offers over 4 years of clinical treatment experience for patients with advanced CSCC who are not candidates for curative surgery or curative radiotherapy,* and is the most prescribed systemic therapy by oncologists for patients with advanced CSCC.†

*LIBTAYO was approved by the FDA in advanced CSCC in September 2018. †Based on IQVIA medical claims data from October 2018 to June 2020. Claims calibrated with actual vials sold.

Important Safety Information for LIBTAYO (cemiplimab-rwlc) (cont'd)

Warnings and Precautions (cont'd)

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.

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 metastaticcutaneous 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.

This supplement is sponsored by Regeneron and Sanofi Genzyme.
Eric Whitman, MD, FACS presented at the product theater, and was compensated for participation.

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1. LIBTAYO (cemiplimab-rwlc) injection full U.S. prescribing information. Regeneron Pharmaceuticals, Inc., and sanofi-aventis U.S. LLC. **2.** 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. **3.** Study of REGN2810 in patients with advanced cutaneous squamous cell carcinoma. ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/study/NCT02760498. Updated January 26, 2021. Accessed March 24, 2021. **4.** Data on file. Regeneron Pharmaceuticals, Inc. **5.** American Cancer Society. About basal and squamous cell skin cancer. Accessed September 11, 2020. https://www.cancer.org/content/dam/CRC/PDF/Public/8818.00.pdf. **6.** Fahradyan A, Howell AC, Wolfswinkel EM, Tsuha M, Sheth P, Wong AK. Updates on the management of non-melanoma skin cancer (NMSC). *Healthcare (Basel).* 2017;5(4):82. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Basal Cell Skin Cancer V.2.2021 © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed March 5, 2021. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. **8.** Codazzi D, Van Der Velden J, Carminati M, et al. Positive compared with negative margins in a single-centre retrospective study on 3957 consecutive excisions of basal cell carcinomas. Associated risk factors and preferred surgical management. *J Plast Surg Hand Surg*. 2014;48(1):38-43. **9.** Migden MR, Chang AL, Dirix L, Stratigos AJ, Lear JT. Emerging trends in the treatment of advanced basal cell carcinoma. *Cancer Treat Rev*. 2018;64:1-10. **10.** Cameron MC, Lee E, Hibler BP, et al. Basal cell carcinoma: epidemiology; pathophysiology; clinical and histological subtypes; and disease associations. *J Am Acad Dermatol*. 2019;80(2):303-317. **11.** Asgari MM, Moffet HH, Ray GT, Quesenberry CP. Trends in basal cell carcinoma incidence and identification of high-risk subgroups, 1998-2012. *JAMA Dermatol*. 2015;151(9):976-981. **12.** Lear JT, Corner C, Dziewulski P, et al. Challenges and new horizons in the management of advanced basal cell carcinoma: a UK perspective. *Br J Cancer*. 2014;111(8):1476-1481. **13.** Bichakjian C, Armstrong A, Baum C, et al. Guidelines of care for the management of basal cell carcinoma. *J Am Acad Dermatol*. 2018;78(3):540-559. **14.** Peris K, Fargnoli MC, Garbe C, et al. Diagnosis and treatment of basal cell carcinoma: European consensus-based interdisciplinary guidelines. *Eur J Cancer*. 2019;118:10-34. **15.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Squamous Cell Skin Cancer V.1.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed March 5, 2021. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.

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