LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

LIBTAYO demonstrated meaningful tumor reduction in clinical trial patients with advanced CSCC[1,2]

LIBTAYO, a programmed death receptor-1 (PD-1) inhibitor, is the first and only FDA-approved therapy indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation.[1]

47.2% ORR (51 of 108 patients; 95% CI: 37.5%, 57.1%)[1,2*]

- **43.5% PR[†]; 3.7% CR[‡]**

61% of responders (31 of 51 patients) reached a DoR of ≥6 months.[1,2*§]

Median DoR was not reached (range: 1-15.2+ months).[1-3*§]

*At time of data cutoff; based on a combined analysis of Studies 1423 and 1540, which were single-arm, open-label, multicenter, nonrandomized, multicohort studies. Median duration of follow-up was 8.9 months.[1] See additional study design details on the following page.
[†]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 diameters of target lesions, per WHO Criteria. Responses had to be maintained for at least 4 weeks.[2]
[‡]Complete response is defined as disappearance of all target lesions for at least 4 weeks. 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; locally advanced CSCC patients in Study 1540 required biopsy to confirm CR.[1,2]
[§]Group 2 patients (locally advanced CSCC; cemiplimab-rwlc 3 mg/kg every 2 weeks) who started treatment less than 9 months prior to the data cutoff date and all Group 3 patients (metastatic CSCC; cemiplimab-rwlc 350 mg every 3 weeks) from Study 1540 are excluded from the efficacy analysis set.[2]

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 and usually occur during treatment; however, they can also occur after discontinuation. Early identification and management are essential to ensuring safe use of PD-1–blocking antibodies. Monitor for symptoms and signs of immune-mediated adverse reactions. Evaluate clinical chemistries, including liver tests and thyroid function tests, at baseline and periodically during treatment. Institute medical management promptly to include specialty consultation as appropriate.

CR, complete response; DoR, duration of response; ORR, objective response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; WHO, World Health Organization.

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Study design for Study 1423 and Study 1540

The efficacy of LIBTAYO in patients with metastatic (nodal or distant) CSCC or locally advanced CSCC 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 human immunodeficiency virus, hepatitis B, or hepatitis C; or Eastern Cooperative Oncology Group (ECOG) performance score ≥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. Treatment continued until progression of disease, unacceptable toxicity, or completion of planned treatment. Tumor response assessments were performed every 8 weeks. The major efficacy outcome measures were confirmed ORR, as assessed by independent central review (ICR) and ICR-assessed DoR. For patients with metastatic CSCC 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 (locally advanced and metastatic CSCC), 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 efficacy analysis was conducted when all patients had the opportunity for at least 6 months of follow-up.[1]

The cutoff for the data in the USPI is October 2017.

The recommended dose 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

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

In general, withhold LIBTAYO for Grade 3 or 4 and certain Grade 2 immune-mediated adverse reactions. Permanently discontinue LIBTAYO for Grade 4 and certain Grade 3 immune-mediated adverse reactions. For Grade 3 or 4 and certain Grade 2 immune-mediated adverse reactions, administer corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) or other appropriate therapy until improvement to Grade 1 or less followed by a corticosteroid taper over 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reaction is not controlled with corticosteroids. Institute hormone replacement therapy for endocrinopathies as warranted.

CSCC, cutaneous squamous cell carcinoma; DoR, duration of response; ORR, objective response rate; PD-1, programmed death receptor-1; PD-L1, programmed death ligand 1.

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LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Challenging surgery

Case discussion: **65-year-old male with locally advanced CSCC[2]**

Medical and treatment history

- Patient history indicated that the primary site of the CSCC lesion was on the left cheek
- Tumor staging was T4/N0/M0 at initial diagnosis
- Well-differentiated histology
- Relevant comorbidities (not comprehensive) included allergic rhinitis and sarcoidosis
- Patient underwent a surgical intervention
  - Excision of skin lesion

Patient experienced a series of medical complications

- Grade 2 neuropathy to the left side of the face
- Grade 2 pain to the left side of the face
- Grade 1 left facial paralysis

Patient experienced recurrence/relapse.

Important Safety Information

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated pneumonitis: Immune-mediated pneumonitis occurred in 2.4% of 534 patients receiving LIBTAYO, including Grade 5 (0.2%), Grade 3 (0.7%), and Grade 2 (1.3%). Pneumonitis led to permanent discontinuation of LIBTAYO in 1.3% of patients. Systemic corticosteroids were required in all patients with pneumonitis, including 85% who received prednisone ≥40 mg/day or equivalent. Pneumonitis resolved in 62% of patients. 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.

Immune-mediated colitis: Immune-mediated colitis occurred in 0.9% of 534 patients receiving LIBTAYO, including Grade 3 (0.4%) and Grade 2 (0.6%). Colitis led to permanent discontinuation of LIBTAYO in 0.2% of patients. Systemic corticosteroids were required in all patients with colitis, including 60% who received prednisone ≥40 mg/day or equivalent. Colitis resolved in 80% of patients. 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.

CSCC, cutaneous squamous cell carcinoma.

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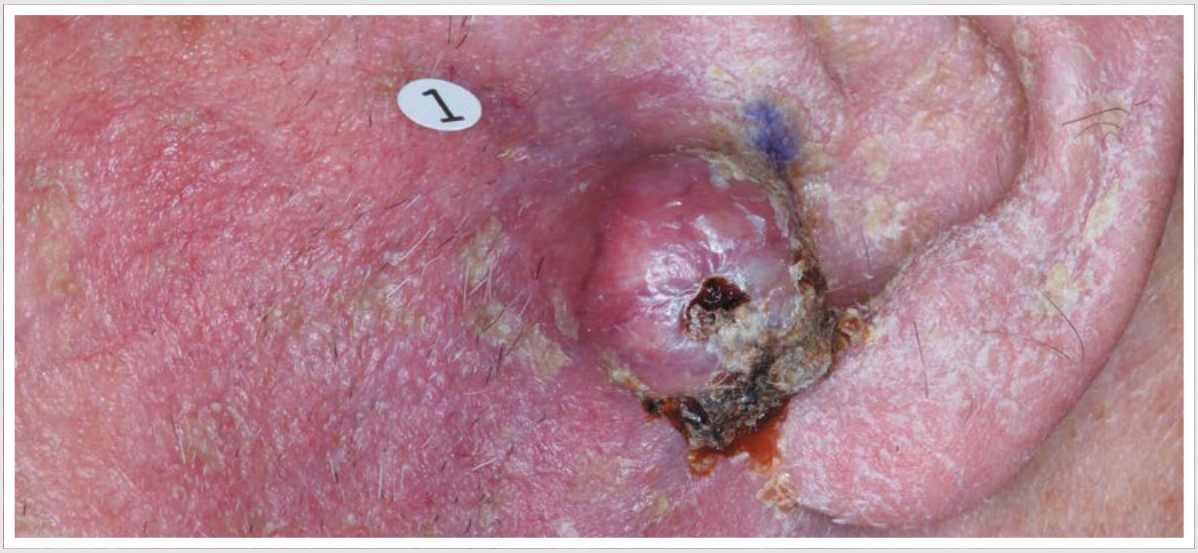
Presentation at screening

Anterior auricular lesion[2]

- Screening -



Actual clinical trial patient.

Important Safety Information

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated hepatitis: Immune-mediated hepatitis occurred in 2.1% of 534 patients receiving LIBTAYO, including Grade 5 (0.2%), Grade 4 (0.2%), and Grade 3 (1.7%). Hepatitis led to permanent discontinuation of LIBTAYO in 0.9% of patients. Systemic corticosteroids were required in all patients with hepatitis, including 91% who received prednisone ≥40 mg/day or equivalent. Hepatitis resolved in 64% of patients. Withhold LIBTAYO if AST or ALT increases to more than 3 and up to 10 times the upper limit of normal (ULN) or if total bilirubin increases up to 3 times the ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 10 times the ULN or total bilirubin increases to more than 3 times the ULN. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper.

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Case discussion: **65-year-old male with locally advanced CSCC who was not a candidate for curative surgery or curative radiation[2]**

Patient was a candidate for LIBTAYO due to the following reasons[2]:

- Locally advanced CSCC
- CSCC in an anatomically challenging location; patient not a candidate for surgery, as it was anticipated to result in severe disfigurement or dysfunction
- Individualized benefit-risk assessment was performed by a multidisciplinary team who deemed that radiotherapy was contraindicated
- Tumor staging was T4/NO/MO at screening
- Well-differentiated histology at screening

Patient received LIBTAYO 3 mg/kg intravenously every 2 weeks in a clinical trial.[1]

The recommended dose 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

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated endocrinopathies: Withhold LIBTAYO if clinically necessary for Grade 2, 3, or 4.

- **Adrenal insufficiency:** Adrenal insufficiency occurred in 0.4% of 534 patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.2%)
- **Hypophysitis:** Hypophysitis, which can result in hypopituitarism, occurred in 0.2% of 534 patients receiving LIBTAYO, which consisted of 1 patient with Grade 3 hypophysitis
- **Hypothyroidism:** Hypothyroidism occurred in 6% of 534 patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (5.6%); no patients discontinued hormone replacement therapy
- **Hyperthyroidism:** Hyperthyroidism occurred in 1.5% of 534 patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.4%); hyperthyroidism resolved in 38% of patients
- **Type 1 diabetes mellitus:** Type 1 diabetes mellitus, which can present with diabetic ketoacidosis, occurred in 0.7% of 534 patients, including Grade 4 (0.4%) and Grade 3 (0.4%); type 1 diabetes mellitus led to permanent discontinuation of LIBTAYO in 0.2% of patients

Immune-mediated nephritis with renal dysfunction: Immune-mediated nephritis occurred in 0.6% of 534 patients receiving LIBTAYO, including Grade 3 (0.4%) and Grade 2 (0.2%). Nephritis led to permanent discontinuation of LIBTAYO in 0.2% of patients. Systemic corticosteroids were required in all patients with nephritis, including 67% who received prednisone ≥40 mg/day or equivalent. Nephritis resolved in all patients. Withhold LIBTAYO for Grade 3, and permanently discontinue for Grade 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper.

CSCC, cutaneous squamous cell carcinoma.

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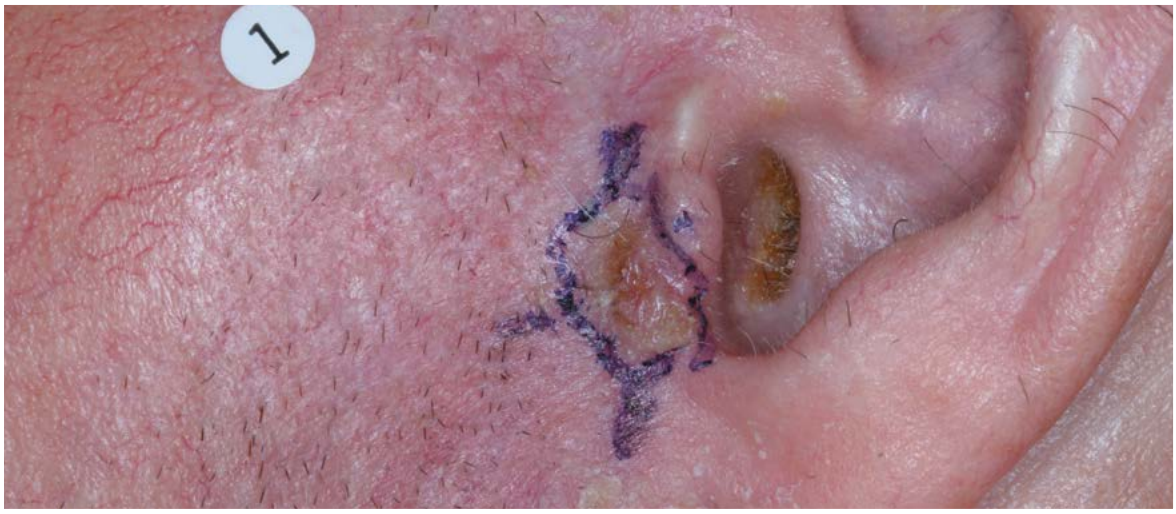
Tumor reduction in a clinical trial patient with locally advanced CSCC who was not a candidate for curative surgery or curative radiation[2]

This is an example from the 43.5% of patients who had a partial response in clinical trials.[1]

By the first assessment, at week 8, a reduction in target lesion of 88.3% from baseline was observed[2]

- After 8 weeks -



Individual patient responses may vary.

Important Safety Information

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated dermatologic adverse reactions: Immune-mediated dermatologic reactions, including erythema multiforme and pemphigoid, occurred in 1.7% of 534 patients receiving LIBTAYO, including Grade 3 (1.1%) and Grade 2 (0.6%). In addition, SJS and TEN have been observed with LIBTAYO and with other products in this class. Systemic corticosteroids were required in all patients with dermatologic reactions, including 89% who received prednisone ≥40 mg/day or equivalent. Dermatologic reactions resolved in 33% of patients. Approximately 22% of patients had recurrence of dermatologic reactions after re-initiation of LIBTAYO. Withhold LIBTAYO for Grade 3, and permanently discontinue for Grade 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper.

CSCC, cutaneous squamous cell carcinoma.

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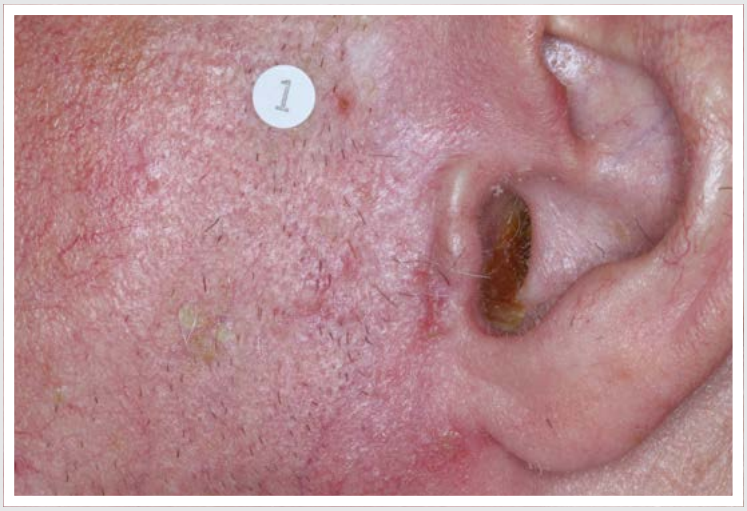
Tumor reduction with LIBTAYO[2]

By week 16, tumor reduction continued with a decrease from baseline of 93.0%[2]

- After 16 weeks -



Individual patient responses may vary.

Important Safety Information

Warnings and Precautions

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 534 patients who received LIBTAYO or were reported with the use of other PD-1–blocking and PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions. Withhold LIBTAYO for Grade 3, and permanently discontinue for Grade 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper.

- **Neurological:** Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome, nerve paresis, and autoimmune neuropathy
- **Cardiovascular:** Myocarditis, pericarditis, and vasculitides
- **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 corticosteroids to reduce the risk of permanent vision loss

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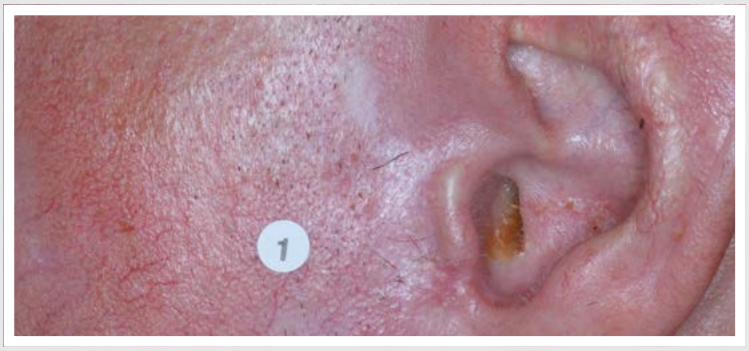
By week 32, reduction in target lesions of 100% from baseline was observed[2]

- After 32 weeks -



Clinical outcomes (as of data cutoff of October 27, 2017)[2]

- Best overall response: PR per composite (RECIST 1.1 + WHO Criteria) evaluation by ICR*
- Best percent change in target lesion(s): 100% by WHO Criteria
- Time to response: 8 weeks (1.9 months)
- DoR: 7.4 months and ongoing

Individual patient responses may vary.

*In order to characterize responses as complete, when possible, composite evaluation of target lesions by both digital medical photography (WHO Criteria) and radiology (RECIST 1.1) was performed, in addition to evaluation of nontarget lesions and appearance of new lesions. This patient did not meet all of the criteria necessary to be classified as an overall CR.

LIBTAYO: A breakthrough for patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation[1]

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Severe and Fatal Immune-Mediated Adverse Reactions

Other immune-mediated adverse reactions (continued):

- **Gastrointestinal:** Pancreatitis to include increases in serum amylase and lipase levels, gastritis, and duodenitis
- **Musculoskeletal and connective tissue:** Myositis, rhabdomyolysis, and associated sequelae, including renal failure, arthritis, and polymyalgia rheumatica

CR, complete response; CSCC, cutaneous squamous cell carcinoma; DoR, duration of response; ICR, independent central review; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; WHO, World Health Organization.

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Severe and Fatal Immune-Mediated Adverse Reactions

Other immune-mediated adverse reactions (continued):

- **Hematological and immunological:** Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, and solid organ transplant rejection

Infusion-related reactions

Severe infusion-related reactions (Grade 3) occurred in 0.2% of patients receiving LIBTAYO. Monitor patients for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or 2, and permanently discontinue for Grade 3 or 4.

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

- Serious adverse reactions occurred in 28% of patients. Serious adverse reactions that occurred in ≥2% of patients were cellulitis, sepsis, pneumonia, pneumonitis, and urinary tract infection. The most common Grade 3-4 adverse reactions (≥2%) were cellulitis, sepsis, hypertension, pneumonia, musculoskeletal pain, skin infection, urinary tract infection, and fatigue
- LIBTAYO was permanently discontinued due to adverse reactions in 5% of patients; adverse reactions resulting in permanent discontinuation were pneumonitis, autoimmune myocarditis, hepatitis, aseptic meningitis, complex regional pain syndrome, cough, and muscular weakness
- The most common adverse reactions (incidence ≥20%) were fatigue, rash, and diarrhea

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 click here for full Prescribing Information.

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

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.** Migden MR, Rischin D, Schmults CD, et al. PD-1 blockade with cemiplimab in advanced cutaneous squamous-cell carcinoma. *N Engl J Med.* 2018;379(4):341-351.

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