ABOUT LIBTAYO® (cemiplimab-rwlc)

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

About LIBTAYO®[1]

LIBTAYO®, developed by Regeneron and Sanofi, is an immunotherapy approved by the U.S. Food and Drug Administration (FDA) 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. Please see full Prescribing Information and Medication Guide, or visit www.LIBTAYO.com.

Mechanism of Action

LIBTAYO is a human monoclonal antibody targeting the immune checkpoint receptor PD-1 (programmed cell death protein-1).[1] Cancer cells can use the PD-1 pathway to inactivate T cells, thereby evading the body's immune system.[2] By binding to PD-1 and blocking the PD-1 signaling pathway, LIBTAYO may help restore the body's immune system activity against cancer cells.[1] LIBTAYO can cause the immune system to attack normal organs and tissues in any area of the body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. Furthermore, these problems may happen anytime during treatment or even after treatment has ended.

Recommended Dosage[1]

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.

Key Clinical Data[1]

The FDA approval of LIBTAYO is based on data from the Phase 2 EMPOWER-CSCC-1 trial (Study 1540) and from two expansion cohorts from a Phase 1 trial (Study 1423), which together represent the largest prospective data set in advanced CSCC. These trials enrolled 163 advanced CSCC patients (at time of data cutoff).

EMPOWER-CSCC-1 was an open-label, multicenter, non-randomized trial of LIBTAYO in patients with metastatic (nodal or distant) CSCC or with locally advanced CSCC who were not candidates for curative surgery or curative radiation. Patients received 3 mg/kg LIBTAYO every 2 weeks for up to 96 weeks.

The Phase 1 study was an open-label, multicenter, non-randomized trial of LIBTAYO in patients with a variety of advanced solid tumors. It included 16 patients with metastatic (nodal or distant) CSCC and 10 patients with locally advanced CSCC who were not candidates for curative surgery. Patients with advanced CSCC received 3 mg/kg LIBTAYO every 2 weeks for up to 48 weeks.

The median age of patients in both trials was 71 years (38 to 96 years); 85% were male; 97% were white; 43% had ECOG PS 0 and 57% had ECOG PS 1; 50% received at least one prior anti-cancer systemic therapy; 96% received prior cancer-related surgery; and 79% received prior radiotherapy. Both studies excluded patients with autoimmune disease that required systemic therapy with immunosuppressant agents within 5 years; history of solid organ transplant; prior treatment with anti–PD-1/anti–programmed death ligand 1 blocking antibodies or other immune checkpoint inhibitor therapy; infection with HIV, hepatitis B, or hepatitis C; or Eastern Cooperative Oncology Group Performance Status (ECOG) ≥2.

Efficacy Endpoints*	Metastatic CSCC N = 75	Locally Advanced CSCC N = 33	Combined CSCC N = 108
Confirmed Objective Response Rate (ORR)			
ORR (95% confidence interval)	46.7% (35.1%, 58.6%)	48.5% (30.8%, 66.5%)	47.2% (37.5%, 57.1%)
Complete response (CR) rate†	5.3%	0%	3.7%
Partial response (PR) rate	41.3%	48.5%	43.5%
Duration of Response (DOR)			
Range in months	2.8 – 15.2+	1 – 12.9+	1 – 15.2+
Patients with DOR ≥ 6 months, n (%)	21 (60%)	10 (63%)	31 (61%)

+: Denotes ongoing at last assessment
* Median duration of follow up: metastatic CSCC: 8.1 months; locally advanced CSCC: 10.2 months; combined CSCC: 8.9 months.
† Only includes patients with complete healing of prior cutaneous involvement; locally advanced CSCC patients in EMPOWER-CSCC-1 (Study 1540) required biopsy to confirm complete response.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about LIBTAYO?

LIBTAYO is a medicine that may treat a type of skin cancer by working with your immune system. LIBTAYO can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Medication Guide.

1. LIBTAYO® (cemiplimab-rwlc) injection Full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. / sanofi-aventis U.S. LLC.
2. National Institutes of Health. The Basics. Accessed April 6 at https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics.

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For the combined safety analysis (n=163) of EMPOWER-CSCC-1 and the two CSCC expansion cohorts, the most common Grade 3 to 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. Serious adverse reactions (SAEs) occurred in 28% of patients. SAEs that occurred in at least 2% of patients were cellulitis, sepsis, pneumonia, pneumonitis, and urinary tract infection. The most common adverse reactions reported were fatigue (29%), rash (25%), diarrhea (22%), nausea (19%), musculoskeletal pain (17%), pruritus (15%), constipation (12%), and decreased appetite (10%).

LIBTAYO Advanced CSCC Program Milestones

LIBTAYO is being jointly developed and commercialized by Regeneron and Sanofi under a global collaboration agreement.

March 2015
Phase 1 Trial Initiated
A Phase 1 trial is initiated, and in the dose escalation phase, CSCC is identified as an area of focus, which leads to the enrollment of advanced CSCC patients into two expansion cohorts.

May 2016
Phase 2 EMPOWER-CSCC-1 Trial Initiated
EMPOWER-CSCC-1 is initiated to investigate patients with advanced CSCC. It is the largest clinical trial in this patient population to date.

June 2017
Phase 1 Trial Initial Results
Following the data presentation for the Phase 1 advanced CSCC cohorts at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting, Regeneron and Sanofi announce positive initial results from the study.

September 2017
Breakthrough Therapy Designation
The FDA grants Breakthrough Therapy Designation status.

December 2017
Phase 2 EMPOWER-CSCC-1 Trial Topline Results
Regeneron and Sanofi announce positive topline results from EMPOWER-CSCC-1.

April 2018
FDA BLA Filing Acceptance
Regeneron and Sanofi announce that the FDA accepted for priority review the Biologics License Application.

June 2018
Pivotal Publication in the *New England Journal of Medicine*
Regeneron and Sanofi announce that pivotal data from EMPOWER-CSCC-1 and the Phase 1 advanced CSCC expansion cohorts are published in *The New England Journal of Medicine*.

September 2018
FDA Approval
LIBTAYO is approved by the FDA on September 28, 2018 for the treatment of patients with metastatic CSCC or locally advanced CSCC who are not candidates for curative surgery or curative radiation.

IMPORTANT SAFETY INFORMATION

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse:

- **Lung problems (pneumonitis).** Signs and symptoms of pneumonitis may include new or worsening cough, shortness of breath, and chest pain.
- **Intestinal problems (colitis) that can lead to tears or holes in your intestine.** Signs and symptoms of colitis may include diarrhea (loose stools) or more frequent bowel movements than usual; stools that are black, tarry, sticky or that have blood or mucus; and severe stomach-area (abdomen) pain or tenderness.

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IMPORTANT SAFETY INFORMATION, Continued

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse:

- **Liver problems (hepatitis).** Signs and symptoms of hepatitis may include yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on the right side of your stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal, and feeling less hungry than usual.
- **Hormone gland problems** (especially the adrenal glands, pituitary, thyroid and pancreas). Signs and symptoms that your hormone glands are not working properly may include headaches that will not go away or unusual headaches, rapid heartbeat, increased sweating, extreme tiredness, weight gain or weight loss, dizziness or fainting, feeling more hungry or thirsty than usual, hair loss, feeling cold, constipation, deeper voice, very low blood pressure, urinating more often than usual, nausea or vomiting, stomach-area (abdomen) pain, and changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness.
- **Kidney problems,** including nephritis and kidney failure. Signs of these problems may include decrease in your amount of urine, blood in your urine, swelling in your ankles, and loss of appetite.
- **Skin problems.** Signs of these problems may include rash, itching, skin blistering, and painful sores or ulcers in the mouth, nose, throat, or genital area.
- **Problems in other organs.** Signs of these problems may include headache, tiredness or weakness, sleepiness, changes in heartbeat (such as beating fast, seeming to skip a beat, or a pounding sensation), confusion, fever, muscle weakness, balance problems, nausea, vomiting, stiff neck, memory problems, seizures (encephalitis), swollen lymph nodes, rash or tender lumps on skin, cough, shortness of breath, vision changes, or eye pain (sarcoidosis), seeing or hearing things that are not there (hallucinations), severe muscle weakness, low red blood cells (anemia), bruises on the skin or bleeding, and changes in eyesight.
- **Rejection of a transplanted organ.** Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.
- **Infusion (IV) reactions that can sometimes be severe and life-threatening.** Signs of these problems may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, fever, feeling of passing out, back or neck pain, and facial swelling.

Getting medical treatment right away may help keep these problems from becoming more serious.

Your healthcare provider will check you for these problems during your treatment with LIBTAYO. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may delay or completely stop treatment if you have severe side effects.

Before you receive LIBTAYO, tell your healthcare provider about all your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus;
- have had an organ transplant;
- have lung or breathing problems;
- have liver or kidney problems;
- have diabetes;
- are pregnant or plan to become pregnant; LIBTAYO can harm your unborn baby
  Females who are able to become pregnant:
  - Your healthcare provider will give you a pregnancy test before you start treatment.
  - You should use an effective method of birth control during your treatment and for at least 4 months after your last dose of LIBTAYO. Talk with your healthcare provider about birth control methods that you can use during this time.
  - Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with LIBTAYO.
- are breastfeeding or plan to breastfeed. It is not known if LIBTAYO passes into your breast milk. Do not breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

The most common side effects of LIBTAYO include tiredness, rash, and diarrhea. These are not all the possible side effects of LIBTAYO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Regeneron Pharmaceuticals and Sanofi at 1-877-542-8296.

Please see accompanying full Prescribing Information, including Medication Guide.

What is LIBTAYO?

LIBTAYO is a prescription medicine used to treat people with a type of skin cancer called cutaneous squamous cell carcinoma (CSCC) that has spread or cannot be cured by surgery or radiation.

It is not known if LIBTAYO is safe and effective in children.

For more information, please visit www.LIBTAYO.com.

SANOFI REGENERON

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