TECENTRIQ® (atezolizumab)

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TECENTRIQ is a cancer immunotherapy, which is a medicine designed to work with the body's own immune system. It is a monoclonal antibody designed to bind with programmed death-ligand 1 (PD-L1). PD-L1 is a protein that plays a role in preventing the body's immune system from fighting cancer. By binding to PD-L1, TECENTRIQ may remove the "stop sign" and activate the immune response.[1]

TECENTRIQ®
atezolizumab INJECTION FOR INTRAVENOUS USE 1200 mg

- TECENTRIQ is the **first and only** approved anti-PDL1 medicine for people with locally advanced or metastatic bladder cancer previously treated with platinum-based chemotherapy **and** for people with metastatic non-small cell lung cancer (NSCLC) previously treated with platinum-based chemotherapy.[2,3,4]
- It was the **first** FDA-approved treatment for people with a specific type of advanced bladder cancer in more than 30 years.[2,3,4]
- Genentech now has **four** medicines available to treat various types of lung cancer.
- Genentech has **11** ongoing or planned Phase III studies with TECENTRIQ across several cancers.

Approved Indications

TECENTRIQ is approved for the treatment of patients with:

Locally advanced or metastatic urothelial carcinoma (UC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Metastatic non-small cell lung cancer (NSCLC) who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving TECENTRIQ.

Important Safety Information

TECENTRIQ can cause the immune system to attack normal organs and tissues in many areas of the body and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death.

(continued on next page)

Please see the following pages and TECENTRIQ full Prescribing Information including Most Serious Side Effects for Important Safety Information.

About Urothelial Carcinoma

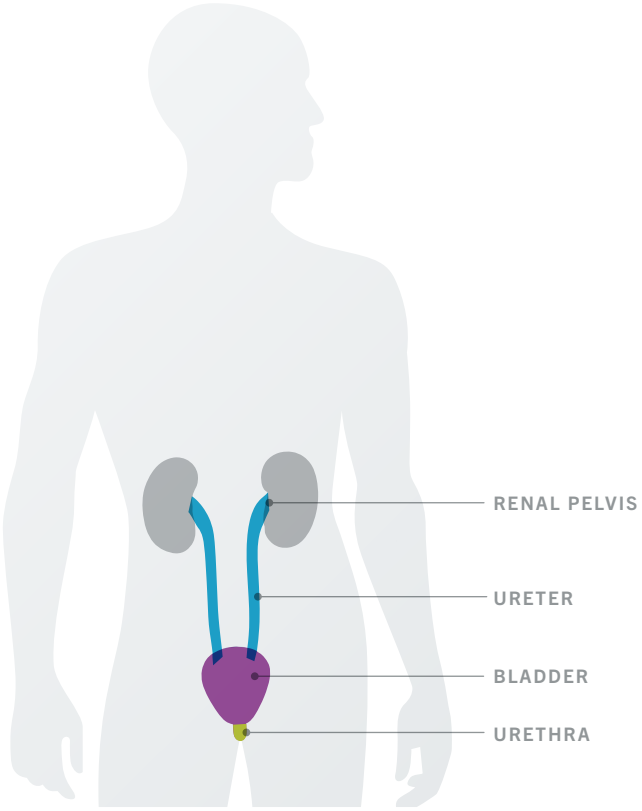
Urothelial carcinoma accounts for **90%** of all bladder cancers and can also be found in the renal pelvis, ureter and urethra.[5]

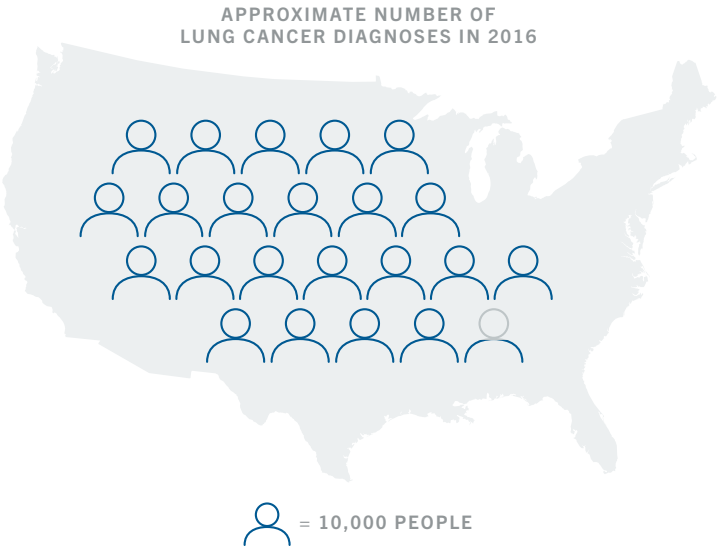
APPROXIMATELY 76,000

people in the U.S. will be diagnosed with bladder cancer in 2016.[6]

11%

new diagnoses are made when bladder cancer is in advanced stages.[6]





About Lung Cancer

Approximately **224,000** people in the U.S. will be diagnosed with lung cancer in 2016.[7]

ABOUT 6 IN 10

of lung cancer diagnoses are made when the disease is in advanced stages.[8]

UP TO 85%

of all lung cancers are classified as non-small cell lung cancer.[7]

Important Safety Information (continued)

Getting medical treatment right away may help keep these problems from becoming more serious. A healthcare provider may treat a patient with corticosteroid or hormone replacement medicines. A healthcare provider may delay or completely stop treatment with TECENTRIQ if a patient has severe side effects.

Patients should call or see their healthcare provider right away if they get any symptoms of the following problems or these symptoms get worse.

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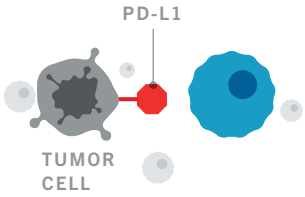
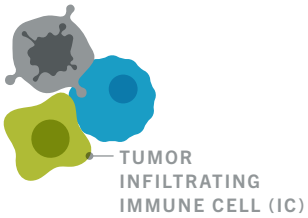
What is PD-L1?[9, 10, 11]

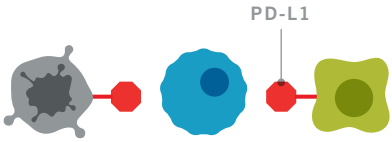
The immune system can help protect the body against cancer by sending T cells – a type of white blood cell – to attack tumor cells.



However, tumor cells can produce a protein called **PD-L1** that works like a "stop sign" to inactivate T cells.

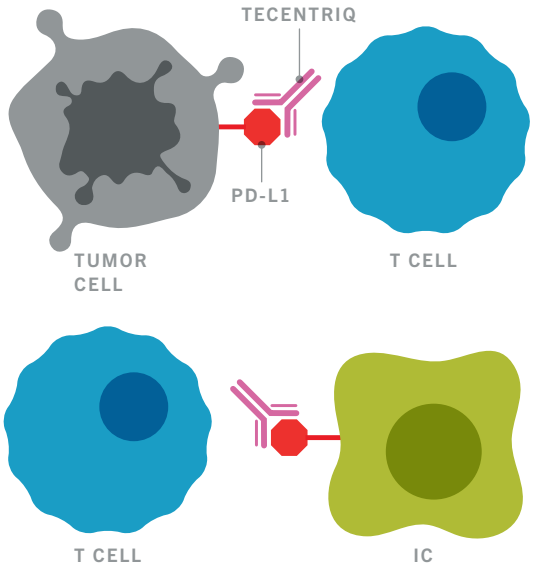


As a tumor grows, many other cells can join and interact with it.

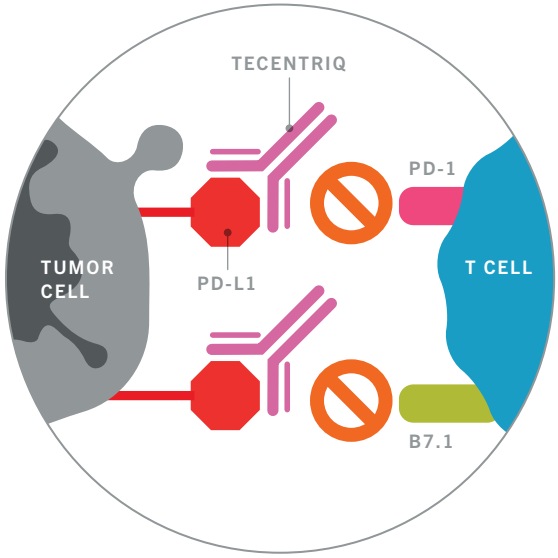


Some of these cells, called tumor-infiltrating immune cells, can also express PD-L1 and inactivate T cells.

How TECENTRIQ May Work[1] (Proposed Mechanism of Action)



TECENTRIQ is designed to bind to PD-L1 expressed on tumor cells and tumor-infiltrating immune cells. TECENTRIQ may also affect normal cells.



TECENTRIQ may prevent PD-L1 from binding to other proteins called PD-1 and B7.1, which may remove the "stop sign" which signals to inactivate T-cells.

Important Safety Information (continued)

TECENTRIQ can cause serious side effects, including:

- **Lung Problems (pneumonitis)** – Signs and symptoms of pneumonitis may include new or worsening cough, shortness of breath, and chest pain
- **Liver Problems (hepatitis)** – Signs and symptoms of hepatitis may include yellowing of the skin or the whites of the eyes, severe nausea or vomiting, pain on the right side of the stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal and feeling less hungry than usual

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Please see the following pages and TECENTRIQ full Prescribing Information including Most Serious Side Effects for Important Safety Information.

TECENTRIQ Efficacy Profiles

mUC[1]

SECOND-LINE (OR HIGHER) TREATMENT

TECENTRIQ* **shrank tumors in 14.8 percent** of people with mUC whose disease worsened after initial treatment (95% CI: 11.1, 19.3)

IMvigor 210 STUDY - COHORT 2	Patients N=310	Low PD-L1 Expression (<5% in tumor-infiltrating immune cells) n=210	High PD-L1 Expression (≥5% in tumor-infiltrating immune cells) n=100
OBJECTIVE RESPONSE RATE (ORR) (PRIMARY ENDPOINT)	14.8% (95% CI: 11.1, 19.3)	9.5% (95% CI: 5.9, 14.3)	26.0% (95% CI: 17.7, 35.7)
MEDIAN DURATION OF RESPONSE (DOR) (KEY SECONDARY ENDPOINT)	Median DOR was not reached in all patients and patients with high PD-L1 expression. In patients with low PD-L1 expression, median DOR was 12.7 months.		

* 1200 mg IV every 3 weeks

NSCLC

SECOND-LINE (OR HIGHER) TREATMENT

TECENTRIQ* **helped people live a median of 13.8 months**, 4.2 months longer than those treated with docetaxel chemotherapy (95% CI: 0.63, 0.87)

OAK STUDY (PRIMARY ANALYSIS POPULATION)	TECENTRIQ n=425	Docetaxel n=425	Hazard Ratio 95% CI
MEDIAN OVERALL SURVIVAL (OS), MONTHS (PRIMARY ENDPOINT)	13.8 (95% CI: 11.8, 15.7)	9.6 (95% CI: 8.6, 11.2)	0.74 (95% CI: 0.63, 0.87)

POPLAR STUDY	TECENTRIQ n=144	Docetaxel n=143	Hazard Ratio 95% CI
MEDIAN OS, MONTHS (PRIMARY ENDPOINT)	12.6 (95% CI: 9.7, 16.0)	9.7 (95% CI: 8.6, 12.0)	0.69 (95% CI: 0.52, 0.92)

* 1200 mg IV every 3 weeks

IMvigor 210 STUDY

The FDA's accelerated approval of TECENTRIQ for mUC was based on the results of IMvigor210, a Phase II, open-label, multicenter, two-cohort study that evaluated TECENTRIQ in a cohort of 310 people previously treated for locally advanced or mUC. Eligible patients had progressed during or following previous treatment with a platinum-based chemotherapy regimen or had disease progression within 12 months of receiving a platinum-based neoadjuvant or adjuvant chemotherapy regimen. Outcomes were evaluated in all patients and in subgroups based on PD-L1 expression. The median follow-up time for this cohort was 14.4 months.[1]

OAK AND POPLAR STUDIES

The approval of TECENTRIQ for NSCLC was based on results from the global, multicenter, open-label, randomized Phase III OAK and Phase II POPLAR studies that evaluated TECENTRIQ compared with docetaxel in patients with metastatic NSCLC whose disease had progressed after platinum-containing chemotherapy. Patients were randomized 1:1 to receive either docetaxel (75 mg/m2 intravenous infusion) or TECENTRIQ (1200 mg intravenous infusion) every three weeks. OAK enrolled people regardless of their PD-L1 status and included both squamous and non-squamous disease types.

STUDY ADVERSE EVENTS IN mUC

Most common side effects (≥ 20%) in patients with locally advanced or mUC were fatigue, decreased appetite, nausea, urinary tract infection, pyrexia (fever), and constipation. Three people (0.9%) who were treated with TECENTRIQ experienced either sepsis, pneumonitis (lung problems) or intestinal obstruction, which led to death. TECENTRIQ was discontinued for adverse reactions in 3.2% (10) of the 310 patients.[1]

STUDY ADVERSE EVENTS IN NSCLC

Most common side effects (≥ 20%) in patients with metastatic NSCLC were fatigue, decreased appetite, dyspnea (shortness of breath), cough, nausea, musculoskeletal pain, and constipation. Nine people (6.3%) who were treated with TECENTRIQ experienced either pulmonary embolism (2), pneumonia (lung infection, 2), pneumothorax, ulcer hemorrhage (bleeding ulcer), cachexia secondary to dysphagia, myocardial infarction (heart attack), or large intestinal perforation which led to death. TECENTRIQ was discontinued for adverse reactions in 4% (6) of the 142 patients.[1]

Important Safety Information (continued)

- **Intestinal Problems (colitis)** – Signs and symptoms of colitis may include diarrhea (loose stools) or more bowel movements than usual, blood in the stools or dark, tarry, sticky stools, and severe stomach area (abdomen) pain or tenderness

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Please see the following pages and TECENTRIQ full Prescribing Information including Most Serious Side Effects for Important Safety Information.

Important Safety Information (continued)

- **Hormone Gland Problems (especially the pituitary, thyroid, adrenal glands and pancreas)** – Signs and symptoms that the hormone glands are not working properly may include headaches that will not go away or unusual headaches, extreme tiredness, weight gain or weight loss, dizziness or fainting, feeling more hungry or thirsty than usual, hair loss, changes in mood or behavior (such as decreased sex drive, irritability or forgetfulness), feeling cold, constipation, voice gets deeper, urinating more often than usual, nausea or vomiting, and stomach area (abdomen) pain
- **Nervous System Problems (neuropathy, meningitis, encephalitis)** – Signs and symptoms of nervous system problems may include severe muscle weakness, numbness or tingling in hands and feet, fever, confusion, changes in mood or behavior, extreme sensitivity to light, and neck stiffness
- **Inflammation of the Eyes** – Signs and symptoms may include blurry vision, double vision or other vision problems, eye pain or redness
- **Severe Infections** – Signs and symptoms of infection may include fever, cough, frequent urination, flu-like symptoms, and pain when urinating
- **Severe Infusion Reactions** – Signs and symptoms of infusion reactions may include chills or shaking, itching or rash, shortness of breath or wheezing, dizziness, fever, flushing, feeling like passing out, back or neck pain, and swelling of the face or lips

Before receiving TECENTRIQ, patients should tell their healthcare provider about all of their medical conditions, including if they:

- 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 problems; have a condition that affects their nervous system (such as myasthenia gravis or Guillain-Barre syndrome); or are being treated for an infection.
- Are pregnant or plan to become pregnant.
  - o TECENTRIQ can harm an unborn baby.
  - o If patients are able to become pregnant, they should use an effective method of birth control during treatment and for at least 5 months after their last dose of TECENTRIQ.
- Are breastfeeding or plan to breastfeed.
  - o It is not known if TECENTRIQ passes into the breastmilk.
  - o Do not breastfeed during treatment and for at least 5 months after the last dose of TECENTRIQ.

Patients should tell their healthcare provider about all of the medicines they take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

The most common side effects of TECENTRIQ in mUC include:

- feeling tired
- decreased appetite
- nausea
- urinary tract infection
- fever
- constipation

The most common side effects of TECENTRIQ in NSCLC include:

- feeling tired
- decreased appetite
- shortness of breath
- cough
- nausea
- constipation

TECENTRIQ may cause fertility problems in females, which may affect the ability to have children. Patients should talk to their healthcare provider if they have concerns about fertility.

These are not all the possible side effects of TECENTRIQ. Patients should ask their healthcare provider or pharmacist for more information. Patients should call their doctor for medical advice about side effects.

Report side effects to the FDA at (800) FDA-1088, or http://www.fda.gov/medwatch. Report side effects to Genentech at (888) 835-2555.

Please visit http://www.Tecentriq.com for the TECENTRIQ full Prescribing Information for additional Important Safety Information.

1. TECENTRIQ (atezolizumab) Prescribing Information. Genentech, Inc. 2016.
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