NOW WITH 5 APPROVALS IN LUNG CANCER
A NEW MONOTHERAPY OPTION FOR 1L PD-L1-HIGH mNSCLC

TECENTRIQ®
atezolizumab 840 mg / 1200 mg INJECTION FOR IV USE

Approved May 18, 2020

Dear Healthcare Provider,

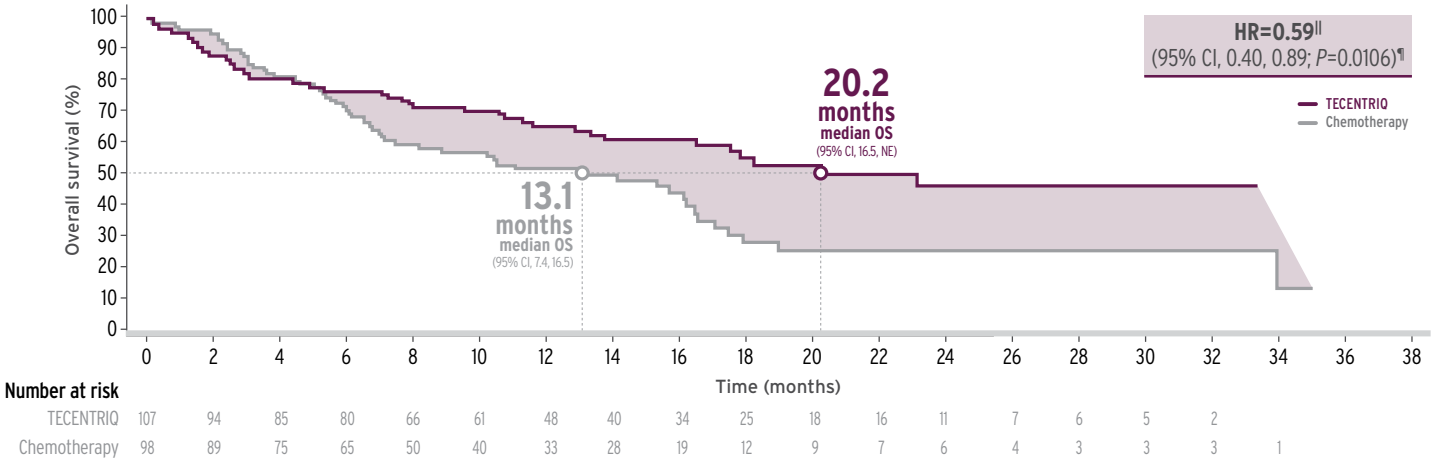
Genentech is pleased to announce a **new TECENTRIQ monotherapy approval in lung cancer, expanding your options when treating patients with both squamous and non-squamous, previously untreated, PD-L1-high metastatic non-small cell lung cancer (mNSCLC)**. TECENTRIQ, as a single agent, is indicated for the first-line treatment of adult patients with mNSCLC whose tumors have high PD-L1 expression (PD-L1–stained ≥50% of tumor cells [TC ≥50%] or PD-L1–stained tumor-infiltrating immune cells [IC] covering ≥10% of the tumor area [IC ≥10%]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

IMPOWER110: A PIVOTAL STUDY EVALUATING TECENTRIQ IN PD-L1–SELECTED PATIENTS WITH 1L mNSCLC[1,2]

The IMpower110 study was a Phase III, multicenter, international, randomized (1:1), open-label trial evaluating TECENTRIQ in patients with stage IV NSCLC, who had received no prior chemotherapy for metastatic disease and whose tumors expressed PD-L1* (N=572, of whom 554 were in the ITT-WT population†). The primary endpoint was OS in PD-L1–selected subgroups of the ITT-WT population. Randomization was stratified by ECOG performance status, histology (non-squamous vs squamous), PD-L1 expression status,‡ and gender.

TECENTRIQ monotherapy significantly improved OS in PD-L1–high (TC ≥50% or IC ≥10%) patients vs chemotherapy[1§]

41% reduction in the risk of death



In the study, patients received either TECENTRIQ 1200 mg intravenously on Day 1 of each 21-day cycle, until disease progression or unacceptable toxicity, or platinum-based chemotherapy consisting of carboplatin or cisplatin on Day 1 with either pemetrexed on Day 1 (non-squamous disease) or gemcitabine on Days 1 and 8 (squamous disease) of each 21-day cycle for 4 or 6 cycles, followed by pemetrexed (non-squamous disease) or best supportive care (squamous disease) until disease progression or unacceptable toxicity. Randomization was stratified by ECOG PS, histology (non-squamous vs squamous), PD-L1 expression on TC and IC, and gender; analyses were stratified by ECOG PS and gender only. The trial excluded patients with a history of autoimmune disease; administration of live, attenuated vaccine within 28 days prior to randomization; active or untreated CNS metastases; and/or administration of systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2 weeks prior to randomization.

- Median follow-up in PD-L1–high patients: 15.7 months

Progression-free survival (PFS) in PD-L1–high patients[1,2#]

- 8.1 months median PFS vs 5.0 months with platinum-based chemotherapy (HR=0.63‖; 95% CI, 0.45, 0.88)

First and only single-agent immunotherapy in 1L mNSCLC with flexible q2w, q3w, and q4w dosing options[1]**

1L=first line; ALK=anaplastic lymphoma kinase; CI=confidence interval; CNS=central nervous system; ECOG=Eastern Cooperative Oncology Group; EGFR=epidermal growth factor receptor; HR=hazard ratio; ITT=intent to treat; NE=not estimable; OS=overall survival; PD-L1=programmed death-ligand 1; PS=performance status; q2w=every 2 weeks; q3w=every 3 weeks; q4w=every 4 weeks; RECIST=Response Evaluation Criteria In Solid Tumors; WT=wild-type.

*TC or IC ≥1%.
†ITT-WT refers to patients who did not have EGFR or ALK genomic tumor aberrations.
‡TC ≥1% and any IC vs TC <1% and IC ≥1%.
§Based on OS interim analysis.
‖Stratified by gender and ECOG performance status.
¶Based on the stratified log-rank test.
#Investigator-assessed PFS per RECIST v1.1.
**TECENTRIQ can be administered at 840 mg q2w, 1200 mg q3w, or 1680 mg q4w, until disease progression or unacceptable toxicity. TECENTRIQ was administered q3w in the IMpower110 trial.

Select Important Safety Information

Serious and sometimes fatal adverse reactions occurred with TECENTRIQ treatment. Warnings and precautions include immune-mediated serious adverse reactions, including pneumonitis, hepatitis, colitis, endocrinopathies, and other immune-mediated adverse reactions. Other warnings and precautions include infections, infusion-related reactions, and embryo-fetal toxicity.

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

Confirmed objective response rate (ORR) and duration of response (DoR) in PD-L1–high patients[1-3]

	TECENTRIQ	Platinum-based chemotherapy
ORR*	n=107	n=98
Number of responders (%)	**41 (38%)**	**28 (29%)**
(95% CI)	(29, 48)	(20, 39)
DoR*	n=41	n=28
Median (months)	**NE**	**6.7**
(95% CI)	(11.8, NE)	(5.5, 17.3)

Adverse reactions (ARs) occurring in ≥10% of patients receiving TECENTRIQ monotherapy[1]

	TECENTRIQ (n=286)		Platinum-based chemotherapy (n=263)	
Adverse reaction	**All grades† (%)**	**Grades 3-4† (%)**	**All grades† (%)**	**Grades 3-4† (%)**
Fatigue/asthenia	25	1.4	34	4.2
Decreased appetite	15	0.7	19	0
Dyspnea	14	0.7	10	0
Nausea	14	0.3	34	1.9
Pyrexia	14	0	9	0.4
Constipation	12	1.0	22	0.8
Cough	12	0.3	10	0
Diarrhea	11	0	12	0.8

6% of patients discontinued treatment with TECENTRIQ due to ARs[1]

- The most common ARs (≥2 patients) leading to discontinuation were peripheral neuropathy and pneumonitis

Additional ARs reported in IMpower110[1]

- Fatal ARs occurred in 3.8% of patients; these included death (reported as unexplained death and death of unknown cause), aspiration, chronic obstructive pulmonary disease, pulmonary embolism, acute myocardial infarction, cardiac arrest, mechanical ileus, sepsis, cerebral infarction, and device occlusion (1 patient each)
- Serious ARs occurred in 28% of patients
  - The most frequent (>2%) were pneumonia, chronic obstructive pulmonary disease, and pneumonitis
- ARs leading to the interruption of TECENTRIQ occurred in 26% of patients
  - The most common (>1%) were increased ALT, increased AST, pneumonitis, pyrexia, pneumonia, and upper respiratory tract infection
- Of all grade laboratory abnormalities that worsened from baseline in ≥20% of patients receiving TECENTRIQ in IMpower110, grade 3 or 4 abnormalities with TECENTRIQ vs platinum-based chemotherapy included anemia (1.8% vs 20%), lymphopenia (9% vs 17%), hypoalbuminemia (0.4% vs 2%), increased alkaline phosphatase (2.5% vs 1.2%), hyponatremia (9% vs 7%), increased ALT (3.2% vs 0.8%), increased AST (3.2% vs 0.8%), hyperkalemia (3.9% vs 2.7%), hypocalcemia (1.4% vs 2.7%), increased blood creatinine (0.7% vs 1.5%)‡, and hypophosphatemia (3.6% vs 2%)†§

ALT=alanine aminotransferase; AST=aspartate aminotransferase.

*Investigator-assessed per RECIST v1.1.
†Graded per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.
‡Increased blood creatinine only includes patients with test results above the normal range.
§Each test incidence is based on the number of patients who had at least 1 on-study laboratory measurement available: TECENTRIQ (range: 278-281); platinum-based chemotherapy (range: 256-260).

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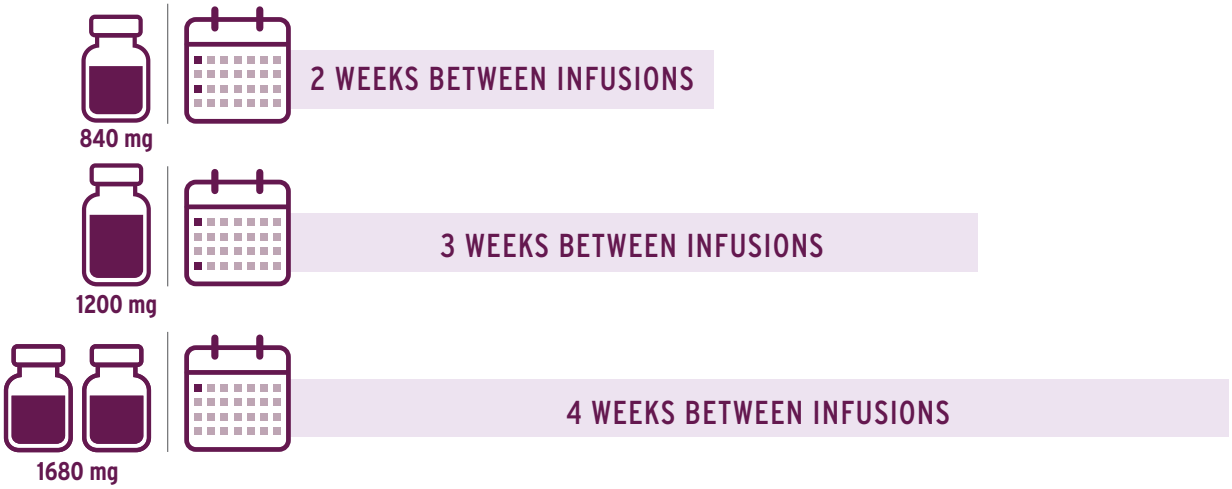
TECENTRIQ offers flexible dosing options when used as a single agent

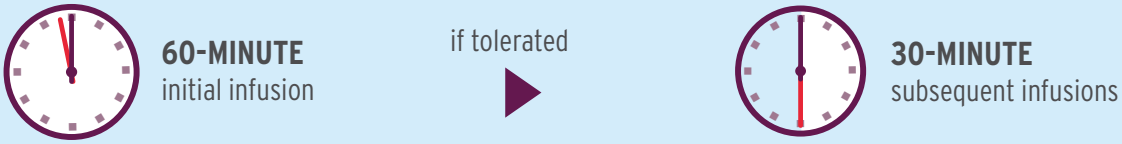
Choose the most suitable infusion schedule for your patients

FLEXIBLE DOSING OPTIONS



Until disease progression or unacceptable toxicity

INFUSION TIME



TECENTRIQ was administered q3w in IMpower110. Visualization of vials is illustrative and does not represent actual vial usage.

IV=intravenous; q3w=every 3 weeks.

- Do not administer TECENTRIQ as an IV push or bolus
- Do not co-administer other drugs through the same IV line

With this 5th lung approval, TECENTRIQ monotherapy for 1L PD-L1–high mNSCLC represents Genentech's continued commitment to provide more options for patients with lung cancer

IMPORTANT SAFETY INFORMATION

Serious Adverse Reactions

Please refer to the full Prescribing Information for important dose management information specific to adverse reactions.

Immune-Mediated Pneumonitis

- Immune-mediated pneumonitis or interstitial lung disease, including fatal cases, have occurred with TECENTRIQ treatment
- In clinical studies of TECENTRIQ as a single agent, 2.5% of patients developed pneumonitis, including Grade 3 (0.6%), Grade 4 (0.1%), and Grade 5 (<0.1%) events
- Monitor patients for signs and symptoms of pneumonitis. Evaluate patients with suspected pneumonitis with radiographic imaging. Administer corticosteroids followed by a taper. Withhold TECENTRIQ for Grade 2 and permanently discontinue for Grade 3 or 4 pneumonitis

Immune-Mediated Hepatitis

- Liver test abnormalities and immune-mediated hepatitis, including fatal cases, have occurred with TECENTRIQ treatment
- In clinical studies of TECENTRIQ as a single agent, hepatitis occurred in 9% of patients, including Grade 3 (2.3%), Grade 4 (0.6%), and Grade 5 (<0.1%) events
- Monitor patients for signs and symptoms of hepatitis, during and after discontinuation of TECENTRIQ, including clinical chemistry monitoring. Administer corticosteroids followed by a taper for immune-mediated hepatitis. Withhold TECENTRIQ for AST or ALT elevations more than 3 and up to 8 times the upper limit of normal or total bilirubin more than 1.5 and up to 3 times the upper limit of normal. Permanently discontinue TECENTRIQ for AST or ALT elevations more than 8 times the upper limit of normal or total bilirubin more than 3 times the upper limit of normal

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Immune-Mediated Colitis

- Immune-mediated diarrhea or colitis have occurred with TECENTRIQ treatment
- In clinical studies of TECENTRIQ as a single agent, diarrhea or colitis occurred in 20% of patients, including Grade 3 (1.4%) events
- Monitor patients for signs and symptoms of diarrhea or colitis. Withhold TECENTRIQ for Grade 2 or 3 and permanently discontinue for Grade 4 diarrhea or colitis

Immune-Mediated Endocrinopathies

- TECENTRIQ can cause immune-mediated endocrinopathies, including thyroid disorders; adrenal insufficiency; type 1 diabetes mellitus, including diabetic ketoacidosis; and hypophysitis/hypopituitarism
- Withhold TECENTRIQ for Grades 2 to 4 endocrinopathies
- Thyroid Disorders
  - In clinical studies of TECENTRIQ as a single agent, hypothyroidism occurred in 4.6% of patients and hyperthyroidism occurred in 1.6% of patients
  - Monitor thyroid function prior to and during treatment with TECENTRIQ. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated
- Adrenal Insufficiency
  - In clinical studies of TECENTRIQ as a single agent, adrenal insufficiency occurred in 0.4% of patients, including Grade 3 (<0.1%) events
  - Monitor patients for clinical signs and symptoms of adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate corticosteroids and hormone replacement therapy as clinically indicated
- Type 1 Diabetes Mellitus
  - In clinical studies of TECENTRIQ as a single agent, type 1 diabetes mellitus occurred in <0.1% of patients
  - Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated
- Hypophysitis
  - In clinical studies of TECENTRIQ as a single agent, Grade 2 hypophysitis occurred in <0.1% of patients
  - For Grades 2 to 4 hypophysitis, initiate corticosteroids and hormone replacement therapy as clinically indicated

Other Immune-Mediated Adverse Reactions

- TECENTRIQ can cause severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system
- In clinical studies of TECENTRIQ as a single agent or were reported in other products in this class, the immune-mediated adverse reactions occurring at an incidence of <1% were cardiac, dermatologic, gastrointestinal, general, hematological, musculoskeletal, neurological, ophthalmological, renal, and vascular
- For suspected Grade 2 immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. For severe (Grade 3 or 4) adverse reactions, withhold TECENTRIQ and administer corticosteroids. Permanently discontinue TECENTRIQ for Grade 4 immune-mediated adverse reactions involving a major organ
- Evaluate for Vogt-Koyanagi-Harada syndrome if uveitis occurs in combination with other immune-mediated adverse reactions

Infections

- TECENTRIQ can cause severe infections including fatal cases
- In clinical studies of TECENTRIQ as a single agent, infections occurred in 42% of patients, including Grade 3 (8.7%), Grade 4 (1.5%), and Grade 5 (1%) events
- Monitor patients for signs and symptoms of infection. For Grade 3 or higher infections, withhold TECENTRIQ and resume once clinically stable

Infusion-Related Reactions

- TECENTRIQ can cause severe or life-threatening infusion-related reactions
- In clinical studies of TECENTRIQ as a single agent, infusion-related reactions occurred in 1.3% of patients, including Grade 3 (0.2%) events
- Monitor patients for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion in patients with Grade 1 or 2 infusion-related reactions. Permanently discontinue TECENTRIQ in patients with Grade 3 or 4 infusion-related reactions

Embryo-Fetal Toxicity

- Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to initiating TECENTRIQ. Advise females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TECENTRIQ and for at least 5 months after the last dose

Nursing Mothers/Fertility

- Because of the potential for serious adverse reactions in breastfed infants from TECENTRIQ, advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months after the last dose
- Based on animal studies, TECENTRIQ may impair fertility in females of reproductive potential while receiving treatment

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Most Common Adverse Reactions

The most common adverse reactions (rate ≥20%) in patients who received TECENTRIQ alone were fatigue/asthenia (48%), decreased appetite (25%), nausea (24%), cough (22%), and dyspnea (22%).

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

Please see accompanying full Prescribing Information for additional Important Safety Information.

For more information, please visit TECENTRIQ-HCP.com/mNSCLC.

Sincerely,

Levi Garraway, MD, PhD
Chief Medical Officer and Head of Global Product Development

References: 1. TECENTRIQ Prescribing Information. Genentech, Inc. **2.** Spigel DR, De Marinis F, Giaccone G, et al. IMpower110: interim OS analysis of a phase III study of atezolizumab (atezo) vs platinum-based chemotherapy (chemo) as 1L treatment (tx) in PD-L1–selected NSCLC. Presented at: ESMO Congress; September 27, 2019; Barcelona, Spain. **3.** Data on file. Genentech, Inc.

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