TECENTRIQ + CARBOPLATIN/ETOPOSIDE

A PROVEN CONNECTION IN 1L ES-SCLC

The first FDA-approved cancer immunotherapy combination to advance the standard of care in 1L ES-SCLC

TECENTRIQ®
atezolizumab 840 mg / 1200 mg INJECTION FOR IV USE
CONNECT WITH PURPOSE

Pivotal data and exploratory analysis with 2 years of follow-up inside

- Median OS was 12.3 months with TECENTRIQ + carbo/etop vs 10.3 months with placebo + carbo/etop (HR=0.70; 95% CI, 0.54, 0.91; *P*=0.0069) with a median follow-up of 13.9 months[1,2*]

*Based on OS interim analysis.

NCCN CATEGORY 1, PREFERRED

Atezolizumab (TECENTRIQ) + carbo/etop is a preferred immunotherapy/chemotherapy option (Category 1) for first-line treatment of patients with ES-SCLC in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).[3†‡]

† 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. See the NCCN Guidelines® for detailed recommendations, including other preferred options.

‡ Category 1: based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

1L=first line; carbo/etop=carboplatin/etoposide; CI=confidence interval; ES-SCLC=extensive-stage small cell lung cancer; HR=hazard ratio; NCCN=National Comprehensive Cancer Network; OS=overall survival.

Indication

TECENTRIQ, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Select Important Safety Information

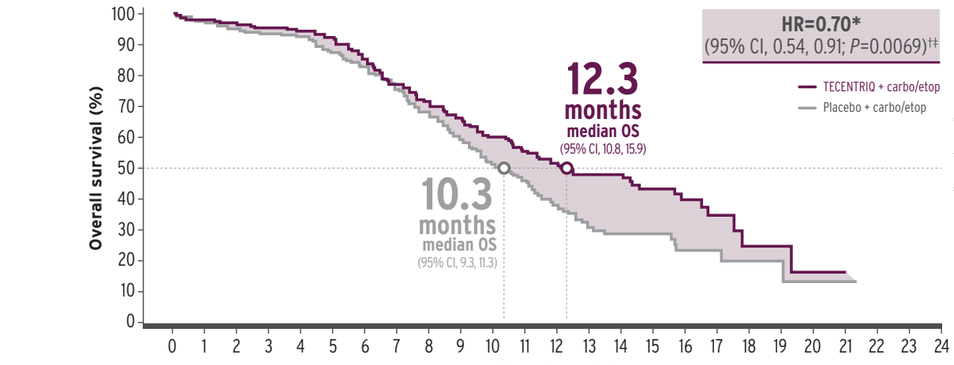
Serious and sometimes fatal adverse reactions occurred with TECENTRIQ treatment. Warnings and precautions include immune-mediated serious adverse reactions, including pneumonitis, hepatitis, colitis, endocrinopathies, and other immune-mediated adverse reactions. Other warnings and precautions include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

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

Median follow-up of 13.9 months

THE FIRST COMBINATION TO SHOW SUPERIOR OS IN 20 YEARS[2,4]

30% reduction in the risk of death vs placebo + carbo/etop[1,2]



AUC=area under the concentration-time curve; CNS=central nervous system; ECOG=Eastern Cooperative Oncology Group; PFS=progression-free survival; PS=performance status.

*Analyses were stratified by gender and ECOG PS only.

†Based on the stratified log-rank test.

‡Based on OS interim analysis.

Number at risk																							
TECENTRIQ + carbo/etop	201	191	187	182	180	174	159	142	130	121	108	92	74	58	46	33	21	11	5	3	2	1	
Placebo + carbo/etop	202	194	189	186	183	171	160	146	131	114	96	81	59	36	27	21	13	8	3	3	2	2	

Adding TECENTRIQ to carbo/etop significantly improved median PFS[1]

- 5.2 months median PFS vs 4.3 months with placebo + carbo/etop (HR=0.77; 95% CI, 0.62, 0.96; *P*=0.0170)
- The most common grade 3 or 4 treatment-related adverse reactions were neutropenia, anemia, and decreased neutrophil count[2]

IMpower133 was a Phase III, multicenter, randomized, double-blind, placebo-controlled trial in patients who had received no prior chemotherapy for ES-SCLC (N=403). Patients were randomized 1:1 to receive TECENTRIQ or placebo with carbo/etop. The major efficacy outcome measures were OS and investigator-assessed PFS. Select secondary efficacy measures included 12-month OS rate. During induction, patients were assigned to receive carboplatin AUC 5 mg/mL/min on Day 1 and etoposide 100 mg/m^2 on Days 1 to 3 of each 21-day cycle for a maximum of 4 cycles, with either TECENTRIQ 1200 mg or placebo intravenously (IV) on Day 1 of each cycle. The induction phase was followed by a maintenance phase during which patients received either TECENTRIQ or placebo every 3 weeks until disease progression or unacceptable toxicity. Randomization was stratified by gender, ECOG PS, and the presence of brain metastases; analyses were stratified by gender and ECOG PS only. This study excluded patients who had active or untreated CNS metastases; history of autoimmune disease; administration of a live, attenuated vaccine within 4 weeks prior to randomization; or administration of systemic immunosuppressive medications within 1 week prior to randomization. Prophylactic cranial irradiation was permitted during maintenance phase, but thoracic radiation therapy was not.[1,2]

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

- TECENTRIQ can cause immune-mediated pneumonitis or interstitial lung disease, defined as requiring use of corticosteroids, including fatal cases
- In clinical studies of TECENTRIQ as a single agent (N=2616), pneumonitis occurred in 2.5% of patients, including Grade 3 (0.6%), Grade 4 (0.1%), and Grade 5 (<0.1%) events. The median time to onset of pneumonitis was 3.6 months (range, 3 days to 20.5 months) and the median duration of pneumonitis was 1.4 months (range, 1 day to 15.1 months). Pneumonitis led to discontinuation of TECENTRIQ in 0.4% of patients
- In clinical studies of TECENTRIQ in combination with platinum-based chemotherapy (N=2421) for NSCLC and SCLC, pneumonitis occurred in 5.5% of patients, including Grades 3 to 4 (1.4%) events
- Monitor patients for signs and symptoms of pneumonitis. Evaluate patients with suspected pneumonitis with radiographic imaging. Administer corticosteroids at a dose of 1–2 mg/kg/day prednisone or equivalents, followed by a taper for Grade 2 or higher pneumonitis
- Withhold TECENTRIQ for Grade 2 and permanently discontinue for Grade 3 or 4 pneumonitis

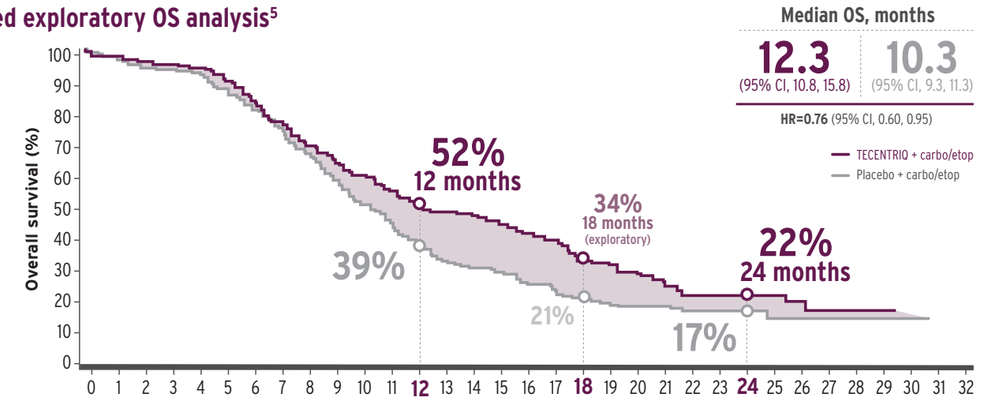
Immune-Mediated Hepatitis

- TECENTRIQ can cause liver test abnormalities and immune-mediated hepatitis, defined as requiring use of corticosteroids. Fatal cases have been reported
- In clinical studies of TECENTRIQ as a single agent (N=2616), hepatitis occurred in 9% of patients, including Grade 3 (2.3%), Grade 4 (0.6%), and Grade 5 (<0.1%) events. The median time to onset of hepatitis was 1.4 months (range, 1 day to 25.8 months) and the median duration was 24 days (range, 1 day to 13 months). Hepatitis led to discontinuation of TECENTRIQ in 0.4% of patients
- In clinical studies of TECENTRIQ in combination with platinum-based chemotherapy (N=2421) for NSCLC and SCLC, hepatitis occurred in 14% of patients, including Grades 3 to 4 (4.1%) events
- Monitor patients for signs and symptoms of hepatitis, during and after discontinuation of TECENTRIQ, including clinical chemistry monitoring. Administer corticosteroids at a dose of 1–2 mg/kg/day prednisone or equivalents, followed by a taper for Grade 2 or higher elevations of ALT, AST and/or total bilirubin
- Withhold TECENTRIQ for AST or ALT >3–8 × ULN or total bilirubin >1.5–3 × ULN. Permanently discontinue TECENTRIQ for AST or ALT >8 × ULN or total bilirubin >3 × ULN

Median follow-up of 22.9 months

ADDITIONAL SURVIVAL DATA BASED ON NEARLY 2 YEARS OF FOLLOW-UP

Updated exploratory OS analysis[5]



Number at risk																													
TECENTRIQ + carbo/etop	201	191	187	182	180	174	159	142	130	121	109	101	93	87	86	81	75	71	61	57	51	39	28	25	21	13	8	2	1	1
Placebo + carbo/etop	202	194	189	186	183	171	160	146	131	114	97	88	74	63	58	55	49	45	39	35	33	26	20	12	8	6	3	2	2	2	2

Landmark analyses were not powered to demonstrate statistically significant differences and no conclusions can be drawn from these analyses. The 12- and 24-month OS rates were prespecified secondary endpoints. The 18-month OS rate was not prespecified and is considered exploratory. The 24-month OS rates may be subject to change with longer follow-up.

The safety observed in the updated analysis was generally consistent with the safety observed in the initial analysis.

Important Safety Information (cont'd)

Immune-Mediated Colitis

- TECENTRIQ can cause immune-mediated diarrhea or colitis, defined as requiring use of corticosteroids
- In clinical studies of TECENTRIQ as a single agent (N=2616), diarrhea or colitis occurred in 20% of patients, including Grade 3 (1.4%) events. The median time to onset of diarrhea or colitis was 1.5 months (range, 1 day to 41 months). Diarrhea or colitis led to discontinuation of TECENTRIQ in 0.2% of patients
- In clinical studies of TECENTRIQ in combination with platinum-based chemotherapy (N=2421) for NSCLC and SCLC, diarrhea or colitis occurred in 29% of patients, including Grades 3 to 4 (4.3%) events
- Monitor patients for signs and symptoms of diarrhea or colitis. If symptoms persist for longer than 5 days or recur, administer corticosteroids at a dose of 1–2 mg/kg/day prednisone or equivalents, followed by a taper for Grade 2 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 until Grade 1 or resolved and clinically stable on hormone replacement therapy
- Thyroid Disorders
  - In clinical studies of TECENTRIQ as a single agent (N=2616), hypothyroidism occurred in 4.6% of patients and hyperthyroidism occurred in 1.6% of patients. One patient experienced acute thyroiditis
  - In clinical studies of TECENTRIQ in combination with platinum-based chemotherapy (N=2421) for NSCLC and SCLC, hypothyroidism occurred in 11% of patients, including Grades 3 to 4 (0.3%) events
  - Monitor thyroid function prior to and periodically during treatment with TECENTRIQ. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated. Continue TECENTRIQ for hypothyroidism and interrupt for hyperthyroidism based on the severity
- Adrenal Insufficiency
  - In clinical studies of TECENTRIQ as a single agent (N=2616), adrenal insufficiency occurred in 0.4% of patients, including Grade 3 (<0.1%) events. The median time to onset was 5.7 months (range, 3 days to 19 months)
  - Monitor patients for clinical signs and symptoms of adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate prednisone 1–2 mg/kg/day or equivalents, followed by corticosteroid taper and hormone replacement therapy as clinically indicated
- Type 1 Diabetes Mellitus
  - In clinical studies of TECENTRIQ as a single agent (N=2616), 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

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

IMPORTANT SAFETY INFORMATION (CONT'D)

Immune-Mediated Endocrinopathies (cont'd)

- Hypophysitis
  - In clinical studies of TECENTRIQ as a single agent (N=2616), Grade 2 hypophysitis occurred in <0.1% of patients
  - For Grade 2 or higher hypophysitis, initiate prednisone 1–2 mg/kg/day or equivalents, followed by corticosteroid taper and hormone replacement therapy as clinically indicated
- The frequency and severity of hyperthyroidism, thyroiditis, adrenal insufficiency, diabetes mellitus, and hypophysitis were similar whether TECENTRIQ was given as a single agent or in combination with other antineoplastic drugs in NSCLC and SCLC

Other Immune-Mediated Adverse Reactions

- TECENTRIQ can cause severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system. While immune-mediated reactions usually manifest during treatment with TECENTRIQ, immune-mediated adverse reactions can also manifest after discontinuation of TECENTRIQ
- In clinical studies of TECENTRIQ as a single agent (N=2616) and in combination with platinum-based chemotherapy (N=2421), or were reported in other products in this class, the immune-mediated adverse reactions occurring at an incidence of <1% were cardiac (myocarditis), dermatologic (bullous dermatitis, pemphigoid, erythema multiforme, Stevens Johnson Syndrome/toxic epidermal necrolysis), gastrointestinal (pancreatitis, including increases in serum amylase or lipase levels), general (systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis), hematological (autoimmune hemolytic anemia, immune thrombocytopenic purpura), musculoskeletal (myositis, rhabdomyolysis), neurological (Guillain-Barré syndrome, myasthenia syndrome/myasthenia gravis, demyelination, immune-related meningoencephalitis, aseptic meningitis, encephalitis, facial and abducens nerve paresis, polymyalgia rheumatica, autoimmune neuropathy, and Vogt-Koyanagi-Harada syndrome), ophthalmological (uveitis, iritis), renal (nephrotic syndrome, nephritis), and vascular (vasculitis)
- 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, administer corticosteroids at a dose of 1–2 mg/kg/day prednisone or equivalents, followed by a taper
- If uveitis occurs in combination with other immune-mediated adverse reactions, evaluate for Vogt-Koyanagi-Harada syndrome, which has been observed with other products in this class and may require treatment with systemic steroids to reduce the risk of permanent vision loss
- Permanently discontinue TECENTRIQ for Grade 4 immune-mediated adverse reactions involving a major organ

Infections

- TECENTRIQ can cause severe infections including fatal cases
- In clinical studies of TECENTRIQ as a single agent (N=2616), infections occurred in 42% of patients, including Grade 3 (8.7%), Grade 4 (1.5%), and Grade 5 (1%) events. In patients with UC, the most common Grade 3 or higher infection was urinary tract infections, occurring in 6.5% of patients. In patients with NSCLC, the most common Grade 3 or higher infection was pneumonia, occurring in 3.8% of patients
- The frequency and severity of infections were similar whether TECENTRIQ was given as a single agent or in combination with other antineoplastic drugs in NSCLC and SCLC
- Monitor patients for signs and symptoms of infection. For Grades 3 to 4 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 (N=2616), infusion-related reactions occurred in 1.3% of patients, including Grade 3 (0.2%) events
- The frequency and severity of infusion-related reactions were similar whether TECENTRIQ was given as a single agent or in combination with other antineoplastic drugs in NSCLC and SCLC
- Monitor patients for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue TECENTRIQ based on the severity. For Grade 1 or 2 infusion-related reactions, consider using premedications with subsequent doses. Permanently discontinue TECENTRIQ for 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. There are no available data on the use of TECENTRIQ in pregnant women. Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway can lead to increased risk of immune-related rejection of the developing fetus resulting in fetal death
- 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

Use In Specific Populations

Nursing Mothers

- There is no information regarding the presence of TECENTRIQ in human milk, the effects on the breastfed infant, or the effects on milk production. As human IgG is excreted in human milk, the potential for absorption and harm to the infant is unknown
- Advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months after the last dose

Fertility

- Based on animal studies, TECENTRIQ may impair fertility in females of reproductive potential while receiving treatment

Most Common Adverse Reactions

The most common adverse reactions (rate ≥20%) in patients who received TECENTRIQ in combination with other antineoplastic drugs for NSCLC and SCLC were fatigue/asthenia (49%), nausea (38%), alopecia (35%), constipation (29%), diarrhea (28%), and decreased appetite (27%).

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.

Learn more at **TECENTRIQ-HCP.com/esSCLC**

References: 1. TECENTRIQ Prescribing Information. Genentech, Inc. **2.** Horn L, Mansfield AS, Szczęsna A, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med.* 2018;379:2220-2229. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer V.3.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed February 5, 2020. To view the most recent and complete version of the guideline, go online to www.NCCN.org. **4.** Sabari JK, Lok BH, Laird JH, Poirier JT, Rudin CM. Unravelling the biology of SCLC: implications for therapy. *Nat Rev Clin Oncol.* 2017;14:549-561. **5.** Data on file. Genentech, Inc.

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