**Transcript Details**
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/patient-case-study-a-first-line-treatment-approach-in-extensive-stage-small-cell-lung-cancer/12474/

**ReachMD**
www.reachmd.com
info@reachmd.com
(866) 423-7849

---

Patient Case Study: A First-Line Treatment Approach in Extensive-Stage Small Cell Lung Cancer

**Announcer:**
Welcome to ReachMD.

This medical industry feature, titled “Patient Case Study: A First-Line Treatment Approach in Extensive Stage Small Cell Lung Cancer” is presented on behalf of Genentech, and the information presented is intended for physicians and consistent with FDA guidelines.

**Dr. Evans:**
Before we start our discussion, let’s go over some important disclosure information. First, this program is presented on behalf of Genentech and is consistent with FDA guidelines. I, along with Dr. Mudad have been compensated by Genentech to serve as speakers for this program.

Now, about the program, itself, it’s intended to provide general information about TECENTRIQ, or atezolizumab, and is not intended to be medical advice for any particular patient. Any adverse events included in this presentation today, have already been reported to Genentech drug safety, so no action is required by any member of the audience.

Lastly, this program may be monitored by Genentech to ensure adherence to program requirements and all materials are the property of Genentech and my not be recorded, photographed, copied, or reproduced.

**Dr. Evans:**
This is ReachMD and I’m Dr. Tracey Evans, the Director of Thoracic Oncology Research at Lankenau Institute for Medical Research.

Joining me is Dr. Raja Mudad, a Thoracic Medical Oncologist and founding partner at Florida Precision Oncology. Dr. Mudad, thanks for being here, today.

**Dr. Mudad:**
Thanks for having me.

**Dr. Evans:**
Before we begin, let’s briefly review the indication, warnings, and precautions for TECENTRIQ.

**Announcer:**
TECENTRIQ (atezolizumab) is a programmed death-ligand 1 (PD-L1) blocking antibody indicated in combination with carboplatin and etoposide for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Serious and sometimes fatal adverse reactions occurred with TECENTRIQ treatment. Warnings and precautions include severe and fatal immune-mediated adverse reactions, including pneumonitis, colitis, hepatitis, endocrinopathies, dermatologic adverse reactions, nephritis and renal dysfunction, and solid organ transplant rejection. Other warnings and precautions include infusion-related reactions, complications of allogeneic HSCT, and embryo-fetal toxicity.

Please see full Prescribing Information for additional Important Safety Information.

**Dr. Evans:**
Great. And now, Dr. Mudad, let’s examine a patient case to get a better sense of appropriate candidates for this treatment path. Can you set the stage for us with this patient?

**Dr. Mudad:**
So, this is a hypothetical case. Richard is a 66-year-old male who presented with cough, shortness of breath, right upper quadrant pain, and weight loss over the past eight to twelve weeks. He has a performance status of 1. His past medical history is significant for hypertension and coronary artery disease, both well-controlled. The patient was a smoker of two packs a day for forty-five years and had no family history of lung cancer.

**Dr. Evans:**
So, with this background in mind, what steps are taken next to establish a baseline assessment and diagnosis for Richard and what are the findings in this case?

**Dr. Mudad:**
So, hematologic and renal function tests were within normal limit. His liver function tests were slightly elevated; AST and ALT over 2.5 times upper limit of normal. His alkaline phosphatase was normal. Richard underwent a CT scan of the chest that revealed a right hilar mass extending to the chest wall. Further imaging showed that Richard has metastatic liver disease. He underwent a CT-guided biopsy of the right lung mass and the pathology revealed extensive stage small cell lung cancer.

**Dr. Evans:**
Given these findings and resulting diagnosis, what's the initial therapy for Richard?

**Dr. Mudad:**
Our patient has been diagnosed with extensive stage small cell lung cancer and he has an excellent performance status. Initial therapy: Based on the IMpower133 data and Richard's profile, TECENTRIQ plus carboplatin and etoposide is an appropriate therapy. PDL1 testing in extensive stage small cell lung cancer is not required to prescribe TECENTRIQ. PD-L1 testing in ES-SCLC is not required to prescribe TECENTRIQ.

I would add that once starting therapy for Richard, if he completes the four cycles of TECENTRIQ with chemotherapy, which can be administered together as Q3 weeks, I might consider changing the administration schedule of TECENTRIQ to Q4 weeks, since TECENTRIQ can be administered at 1680 mg every four weeks, 1200 mg every three weeks, or 840 mg every two weeks.

**Dr. Evans:**
Dr. Mudad, can you tell us about Richard's experience with treatment?

**Dr. Mudad:**
So, Richard was started on TECENTRIQ plus carbo and etoposide. During treatment he developed immune-mediated hepatitis. So, let's take a moment to review some important safety information on this.

TECENTRIQ can cause immune-mediated hepatitis. In over 2,000 patients receiving TECENTRIQ as a single agent, immune-mediated hepatitis occurred in 1.8%, including fatal in less than 0.1%, grade 4, 0.2%, grade 3, 0.5% and grade 2, 0.5%.

So, in our patient, TECENTRIQ was withheld. He was treated with prednisone at 1 mg/kg per day with a taper. Once the side effect was reduced to less than grade 1, TECENTRIQ was resumed.

**Dr. Evans:**
Taking this treatment-specific side effect and management into account, talk to us about the next steps for Richard.

**Dr. Mudad:**
So, if you recall, uh, his initial CT scan showed a large, right hilar mass, extending to the chest wall. Richard had a repeat CT scan after two cycles and that showed a response. I would certainly repeat scans after four cycles, also. And in his case, there was no further change in the CT scan, so Richard was continued on TECENTRIQ. And the plan is to continue TECENTRIQ until disease progression or unacceptable toxicity.

**Dr. Evans:**
So, taking the therapeutic decisions from this case in mind, Dr. Mudad, what are some key take-aways you think we should know regarding TECENTRIQ's role in first line treatment for extensive stage small cell lung cancer?

**Dr. Mudad:**
IMpower133 is a phase 3, multi-center, randomized, double-blind, placebo-controlled trial in extensive stage small cell lung cancer patients who had received no prior chemotherapy for extensive stage disease and with an ECOG performance status of 0 or 1.

Let's walk you through a summary of IMpower133 efficacy and select safety data. Increased survival was demonstrated with addition of TECENTRIQ to carbo and etoposide in first line extensive stage small cell lung cancer patients. The median overall survival was 12.3

months with TECENTRIQ with carbo and etoposide versus 10.3 months with placebo and carbo and etoposide. The median progression-free survival was 5.2 months with TECENTRIQ and carbo/etoposide versus 4.3 months with placebo and carbo/etoposide. The overall response rate was similar between both treatment arms; 60% with TECENTRIQ and carbo/etoposide versus 64% with placebo and carbo/etoposide.

The most common serious adverse reactions were pneumonia, neutropenia, febrile neutropenia, and thrombocytopenia. Something to keep in mind, TECENTRIQ can be administered in three flexible dosing options.

**Dr. Evans:**
Well, with these practical insights in mind, I want to thank my guest, Dr. Mudad for reviewing a patient case with us to help us better understand the role of TECENTRIQ in first line combination treatment for extensive stage small cell lung cancer. Dr. Mudad, it was great speaking with you, today.

**Dr. Mudad:**
Thanks so much for having me.

**Dr. Evans:**
For ReachMD, I'm Dr. Tracey Evans. Now, before we close, let's review some important safety information.

**Announcer:**
**Serious Adverse Reactions**
Please refer to the full Prescribing Information for important dose management information specific to adverse reactions.

**Severe and Fatal Immune-Mediated Adverse Reactions**
TECENTRIQ is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death-receptor 1 (PD-1) or the PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. The following immune-mediated adverse reactions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions can occur in any organ system or tissue and at any time after starting a PD-1/PD-L1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, they can also manifest after discontinuation of treatment.

Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue TECENTRIQ depending on severity. In general, if TECENTRIQ requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less, then initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

**Immune-Mediated Pneumonitis**
TECENTRIQ can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

Immune-mediated pneumonitis occurred in 3% (83/2616) of patients receiving TECENTRIQ as a single agent, including fatal (<0.1%), Grade 4 (0.2%), Grade 3 (0.8%), and Grade 2 (1.1%) adverse reactions Pneumonitis led to permanent discontinuation of TECENTRIQ in 0.5% and withholding of TECENTRIQ in 1.5% of patients. Systemic corticosteroids were required in 55% (46/83) of patients with pneumonitis.

**Immune-Mediated Colitis**
TECENTRIQ can cause immune-mediated colitis. Colitis can present with diarrhea, abdominal pain, and lower gastrointestinal (GI) bleeding. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 1% (26/2616) of patients receiving TECENTRIQ as a single agent, including Grade 3 (0.5%) and Grade 2 (0.3%) adverse reactions. Colitis led to permanent discontinuation of TECENTRIQ in 0.2% and withholding of TECENTRIQ in 0.5% of patients. Systemic corticosteroids were required in 50% (13/26) of patients with colitis. Colitis resolved in 73% of the 26

patients. Of the 12 patients in whom TECENTRIQ was withheld for colitis, 8 reinitiated treatment with TECENTRIQ after symptom improvement; of these, 25% had recurrence of colitis.

**Immune-Mediated Hepatitis**

TECENTRIQ can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 1.8% (48/2616) of patients receiving TECENTRIQ as a single agent, including fatal (<0.1%), Grade 4 (0.2%), Grade 3 (0.5%), and Grade 2 (0.5%) adverse reactions. Hepatitis led to permanent discontinuation of TECENTRIQ in 0.2% and withholding of TECENTRIQ in 0.2% of patients. Systemic corticosteroids were required in 25% (12/48) of patients with hepatitis. Hepatitis resolved in 50% of the 48 patients. Of the 6 patients in whom TECENTRIQ was withheld for hepatitis, 4 reinitiated treatment with TECENTRIQ after symptom improvement; of these, none had recurrence of hepatitis.

**Immune-Mediated Endocrinopathies**

***Adrenal Insufficiency***

TECENTRIQ can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated.

Adrenal insufficiency occurred in 0.4% (11/2616) of patients receiving TECENTRIQ as a single agent, including Grade 3 (<0.1%) and Grade 2 (0.2%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of TECENTRIQ in 1 patient and withholding of TECENTRIQ in 1 patient. Systemic corticosteroids were required in 81% (9/11) of patients with adrenal insufficiency; of these, 3 patients remained on systemic corticosteroids. The single patient in whom TECENTRIQ was withheld for adrenal insufficiency did not reinitiate TECENTRIQ.

***Hypophysitis***

TECENTRIQ can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated.

Hypophysitis occurred in <0.1% (2/2616) of patients receiving TECENTRIQ as a single agent, including Grade 2 (1 patient, <0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of TECENTRIQ in 1 patient and no patients required withholding of TECENTRIQ. Systemic corticosteroids were required in 50% (1/2) of patients with hypophysitis. Hypophysitis did not resolve in these 2 patients.

**Immune-Mediated Endocrinopathies (cont'd)**

***Thyroid Disorders***

TECENTRIQ can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or medical management for hyperthyroidism as clinically indicated.

Thyroiditis occurred in 0.2% (4/2616) of patients receiving TECENTRIQ as a single agent, including Grade 2 (<0.1%) adverse reactions. Thyroiditis did not lead to permanent discontinuation of TECENTRIQ in any of these patients, but led to withholding of TECENTRIQ in 1 patient. Hormone replacement therapy was required in 75% (3/4) of patients with thyroiditis. Systemic corticosteroids were required in 25% (1/4) of patients with thyroiditis. Thyroiditis resolved in 50% of patients. The single patient in whom TECENTRIQ was withheld for thyroiditis reinitiated TECENTRIQ, this patient did not have recurrence of thyroiditis.

Hyperthyroidism occurred in 0.8% (21/2616) of patients receiving TECENTRIQ as a single agent, including Grade 2 (0.4%) adverse reactions. Hyperthyroidism did not lead to permanent discontinuation of TECENTRIQ in any of these patients, but led to withholding of TECENTRIQ in 0.1% of patients. Antithyroid therapy was required in 29% (6/21) of patients with hyperthyroidism. Of these 6 patients, the majority remained on antithyroid treatment. Of the 3 patients in whom TECENTRIQ was withheld for hyperthyroidism, 1 patient reinitiated TECENTRIQ; this patient did not have recurrence of hyperthyroidism.

Hypothyroidism occurred in 4.9% (128/2616) of patients receiving TECENTRIQ as a single agent, including Grade 3 (0.2%) and Grade 2 (3.4%) adverse reactions. Hypothyroidism did not lead to permanent discontinuation of TECENTRIQ in any of these patients, but led to withholding of TECENTRIQ in 0.6% of patients. Hormone replacement therapy was required in 81% (104/128) of patients with hypothyroidism. The majority of patients with hypothyroidism remained on thyroid hormone replacement. Of the 17 patients in whom TECENTRIQ was withheld for hypothyroidism, 8 reinitiated TECENTRIQ after symptom improvement.

Hypothyroidism occurred in 11% (277/2421) of patients with NSCLC and SCLC receiving TECENTRIQ in combination with platinum-based chemotherapy, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (5.7%) adverse reactions. Hypothyroidism led to permanent discontinuation of TECENTRIQ in 0.1% and withholding of TECENTRIQ in 1.6% of patients. Hormone replacement therapy

was required in 71% (198/277) of patients with hypothyroidism. The majority of patients with hypothyroidism remained on thyroid hormone replacement. Of the 39 patients in whom TECENTRIQ was withheld for hypothyroidism, 9 reinitiated TECENTRIQ after symptom improvement.

**Immune-Mediated Endocrinopathies (cont'd)**

***Type 1 Diabetes Mellitus, Which Can Present With Diabetic Ketoacidosis***

Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated.

Type 1 diabetes mellitus occurred in 0.3% (7/2616) of patients receiving TECENTRIQ as a single agent, including Grade 3 (0.2%) and Grade 2 (<0.1%) adverse reactions. Type 1 diabetes mellitus led to permanent discontinuation of TECENTRIQ in 1 patient and withholding of TECENTRIQ in 2 patients. Treatment with insulin was required for all patients with confirmed Type 1 diabetes mellitus and insulin therapy was continued long-term. Of the 2 patients in whom TECENTRIQ was withheld for Type 1 diabetes mellitus, both re-initiated TECENTRIQ treatment.

**Immune-Mediated Nephritis with Renal Dysfunction**

TECENTRIQ can cause immune-mediated nephritis

Immune-mediated nephritis with renal dysfunction occurred in <0.1% (1/2616) of patients receiving TECENTRIQ as a single agent, and this adverse reaction was a Grade 3 (<0.1%) adverse reaction. Nephritis led to permanent discontinuation of TECENTRIQ in this patient. This patient required systemic corticosteroids. In this patient, nephritis did not resolve.

**Immune-Mediated Dermatologic Adverse Reactions**

TECENTRIQ can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), DRESS, and toxic epidermal necrolysis (TEN), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes.

Immune-mediated dermatologic adverse reactions occurred in 0.6% (15/2616) of patients receiving TECENTRIQ as a single agent, including Grade 3 (<0.1%) and Grade 2 (0.2%) adverse reactions. Dermatologic adverse reactions led to permanent discontinuation of TECENTRIQ in 0.1% and withholding of TECENTRIQ in 0.2% of patients. Systemic corticosteroids were required in 20% (3/15) of patients with dermatologic adverse reactions. Dermatologic adverse reactions resolved in 87% of the 15 patients. Of the 4 patients in whom TECENTRIQ was withheld for immune-mediated dermatologic adverse reactions, none re-initiated TECENTRIQ.

**Other Immune-Mediated Adverse Reactions**

The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received TECENTRIQ or were reported with the use of other PD-1/PD-L1 blocking antibodies

- **Cardiac/Vascular**: Myocarditis, pericarditis, vasculitis
- **Nervous System**: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy
- **Ocular**: Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment, including 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 steroids to reduce the risk of permanent vision loss
- **Gastrointestinal**: Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis
- **Musculoskeletal and Connective Tissue**: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatic
- **Endocrine**: Hypoparathyroidism
- **Other (Hematologic/Immune)**: Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

**Infusion-Related Reactions**

TECENTRIQ can cause severe or life-threatening infusion-related reactions. Monitor 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 pre-medications with subsequent doses.

Infusion-related reactions occurred in 1.3% of patients receiving TECENTRIQ as a single agent, including Grade 3 (0.2%) reactions.

The frequency and severity of infusion-related reactions were similar whether TECENTRIQ was given as a single-agent, in combination with other antineoplastic drugs in NSCLC and SCLC, and across the recommended dose range.

**Complications of Allogeneic HSCT After PD-1/PD-L1 Inhibitors**
Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 blocking antibody.

Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause).

These complications may occur despite intervening therapy between PD-1/PD-L1 blockage and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefits versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

**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 and 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. 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.

**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 full Prescribing Information for additional Important Safety Information.

**Announcer:**
This program was brought to you by Genentech. If you missed any part of this discussion, visit ReachMD.com/industryfeature. This is ReachMD. Be Part of the Knowledge.