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

Exploring First-Line Treatment in Extensive-Stage Small Cell Lung Cancer

Announcer:
You're listening to ReachMD. This medical industry feature, titled "Exploring First-Line Treatment in Extensive-Stage Small Cell Lung Cancer," is sponsored by AstraZeneca. This program is intended for physicians. Here's your host Dr Jennifer Caudle.

Dr. Caudle:
In the treatment landscape for extensive-stage small cell lung cancer, therapeutic options have remained virtually unchanged for more than three decades, but could the introduction of immunotherapy agents lead to meaningful advancements against this devastating disease? Coming to you from the ReachMD studios, I'm your host, Dr. Jennifer Caudle, and joining me to discuss extensive-stage small cell lung cancer and recent data from the phase III CASPIAN clinical trial is Dr. Suma Satti, Lung Cancer Specialist and Director of Chemo Infusion at Ochsner Medical Center in New Orleans. Dr. Satti, welcome to you.

Dr. Satti:
Hello, everyone. Thank you for having me. I'm very happy to be here.

Dr. Caudle:
Before we get started, let's review some select important safety information about IMFINZI in extensive-stage small cell lung cancer

Announcer:
Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated dermatologic adverse reactions, immune-mediated nephritis and renal dysfunction, and solid organ transplant rejection. IMFINZI can cause severe or life-threatening infusion-related reactions. 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.

Advise women not to become pregnant or breastfeed during treatment with IMFINZI and for at least 3 months after the last dose.

In the CASPIAN trial, the most frequent serious adverse reactions reported in at least 1% of patients were febrile neutropenia (4.5%), pneumonia (2.3%), anemia (1.9%), pancytopenia (1.5%), pneumonitis (1.1%) and COPD (1.1%).

The most common adverse reactions (≥20%) were nausea, fatigue/asthenia and alopecia.

The safety and effectiveness of IMFINZI have not been established in pediatric patients

Please refer to the Important Safety Information during this feature and the full Prescribing Information for important dosage modification and management information specific to adverse reactions.

Dr. Caudle:
So, let's start, Dr. Satti, by considering some of the challenges associated with the treatment and management of small cell lung cancer. What can you tell us about that?

Dr. Satti:
Small cell lung cancer is an aggressive form of lung cancer with a particularly poor prognosis. It's less common than non-small cell lung cancer, but it tends to grow more rapidly than non-small cell lung cancer. Because of its rapid progression and the fact that the symptoms are not recognizable early enough, patients tend to present in the later stage of the disease, and pretty much two-thirds of

them present when the disease has advanced to an extensive-stage, which would mean, like, the disease has spread from the lung to the other parts of the body, and that could be bone, brain, fluid around the lungs, etc. Treatment, unfortunately, is very limited. For years, we have had really nothing for small cell lung cancer, so with the introduction of immunotherapy, there is definitely new hope for the patients.

Dr. Caudle:
Well, that's a great segway into our next focus point because in the past couple of years we've seen the approval of several immunotherapy drugs in combination with chemotherapy for the first-line treatment of extensive-stage small cell lung cancer, most recently durvalumab, which was approved by the FDA in March 2020. So, Dr. Satti, can you tell us what this approval means for small cell lung cancer?

Dr. Satti:
Durvalumab was approved based on positive results from a planned interim analysis of the phase III CASPIAN trial showing that durvalumab in combination with etoposide and either carboplatin or cisplatin demonstrated a significant improvement in overall survival versus the standard of care. The median overall survival was 13 months for durvalumab plus chemotherapy versus 10.3 months for chemotherapy alone. These positive findings have been further reinforced by updated data presented at the 2020 ASCO annual meeting. For two-thirds of the patients diagnosed with extensive-stage disease, only 3 percent will be alive five years after diagnosis, so there is an urgent need for new treatment options in these patients.

Dr. Caudle:
And what's the significance of durvalumab being approved for use with carboplatin or cisplatin?

Dr. Satti:
So, in the phase III CASPIAN study, durvalumab demonstrated improved overall survival in combination with either cisplatin or carboplatin plus etoposide. Because of this flexibility, it enables physicians to choose their preferred regimen as a backbone when treating with durvalumab, and that allows us to tailor treatment to the needs of that particular patient.

Dr. Caudle:
If we take a look at the updated data shared at the 2020 ASCO annual meeting, what can you tell us about those findings?

Dr. Satti:
After a median follow-up of more than two years, durvalumab plus chemotherapy continues to show consistent improvements in overall survival for patients with extensive-stage small cell lung cancer. The updated median overall survival was 12.9 months for durvalumab plus chemotherapy versus 10.5 months with chemotherapy alone. A post hoc analysis found that 22.2 percent of patients treated with durvalumab plus chemotherapy remained alive at 24 months versus 14.4 percent for chemotherapy alone.

Dr. Caudle:
For those who are just joining us, this is ReachMD, and I'm your host, Dr. Jennifer Caudle. Today I'm speaking with Dr. Suma Satti about the treatment landscape for extensive-stage small cell lung cancer and recent data from the phase III CASPIAN clinical trial. So, Dr. Satti, earlier you mentioned some interesting findings from a prespecified CASPIAN subanalysis. On that line of thought, can you tell us more about the survival rates in patients taking durvalumab plus chemotherapy versus standard chemotherapy alone?

Dr. Satti:
Small cell lung cancer is a devastating disease where improving outcomes has been a challenge. There's an urgent need for new medicines to improve survival in extensive-stage disease, as the prognosis is especially poor with only 3 percent of patients alive five years after diagnosis. Despite the historically short survival for these patients, durvalumab in combination with standard of care chemotherapy demonstrated overall survival for 22 percent patients after median follow-up of more than two years compared to 14 percent of patients receiving chemotherapy alone. Durvalumab plus chemotherapy has demonstrated a sustained 25 percent reduction in the risk of death versus chemotherapy alone with a hazard ratio of .75, 95 percent confidence interval of .62 to .91.

Dr. Caudle:
And Dr. Satti, based on your own clinical experience, can you speak to the impact of COVID-19 on small cell lung cancer patients who aren't receiving a timely diagnosis? And what steps can be taken to address that?

Dr. Satti:
So, unfortunately, what has happened in the pandemic is patients were not diagnosed early enough. These patients are very sick, and when we see a small cell lung cancer patient, whether it's limited or extended, our mind is automatically saying that these patients need treatment – they should have started treatment two months ago. So, with the pandemic and things slowing down, especially here in New Orleans, Louisiana, we did not have a lot of elective procedures being done in March and April, and patients were also afraid to

seek medical care in the middle of the pandemic, result of which we have seen a lot of sicker patients coming in May and June, um, way more sicker than they would have if they came in March and April. So, there's a significant delay in the diagnosis in seeking care, leading to very poor outcomes, all the more reason that if we see a small cell lung cancer patient, that patient has to be started, like, immediately. Typically, insurance companies have been very, um, accommodating with, uh, these type of requests of expediting small cell lung cancers, and so oftentimes when somebody calls me that there's a small cell, I see the patient on the same day and get started in the next day or two. This is the only population where we sometimes treat in the hospital, chemotherapy in the hospital if the patient is very sick, so it's very important that these patients are diagnosed and treated on time. Now, we have, in the advent of immunotherapy, we have treatment options that we can actually give a survival benefit for our patients, which for those of us who have been treating small cell for a very long time, we have not had that luxury where, where patients will die very quickly. So, that's very important but all the more reason to get started as soon as you see.

Dr. Caudle:
There can be a lot of points of entry for cancer patients depending on the symptoms they present with and the setting in which they are diagnosed, and this can impact the trajectory of their care. How are you seeing this play out in small cell lung cancer?

Dr. Satti:
So, yes, we do get patients from different sources – primary care, pulmonologist, emergency room – a lot of times patients, there's a delay in getting a diagnosis, but once the diagnosis has been made, they need to see the medical oncologist right away. What we do at our hospital system, especially, is we have a navigator system, and we communicate very well with our pulmonologists and primary care providers. So, they know that they have to pick up a phone, and we get the patient in on the same day. It's very important to have a system built in so that these patients, you know, once you find out it is small cell, there is no time. You're already playing catch-up, so they need to be seen immediately. We do have a system of Multi-D conferences, so that helps out, but they're once a week, and we all know that if we see a small cell, it's almost like a ripple in the system. A patient has to be seen immediately and has to be started, so communicating with the pulmonologists, primary cares, talking to them about the advances in treatment will also help tremendously if, in your individual hospital settings.

Dr. Caudle:
Lastly, Dr. Satti, are there any final thoughts you would like to share with our audience today?

Dr. Satti:
Yes. Um, after decades of not having any treatment options for extensive-stage small cell lung cancer, we have finally a treatment option that will prolong the overall survival. So, essentially, immunotherapy in combination with chemotherapy will be the first-line standard of option of care for these patients who face such a poor prognosis. Uh, it should be standard practice in institutions, and, uh, there should really be no doubt about what's the first-line treatment for these patients, and, uh, uh, every patient should be, who qualifies, should be offered this treatment.

Dr. Caudle:
Well, with those important thoughts in mind, we've come to the end of today's program, and I'd really like to thank my guest, Dr. Suma Satti, for helping us better understand the current treatment landscape for extensive-stage small cell lung cancer with recent data from the phase III CASPIAN clinical trial. Dr. Satti, it was great speaking with you today.

Dr. Satti:
Thank you for having me. The pleasure is all mine. Um, this is very exciting field we are in right now, so I'm, I'm wishing more and more success in the future.

Dr Caudle:
And now let's review some important safety information about IMFINZI.

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI® (durvalumab).

Immune-Mediated Adverse Reactions

Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment or after discontinuation. 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 IMFINZI depending on severity. See Dosing and Administration for specific details. In general, if IMFINZI requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, 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

IMFINZI can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation. In patients who did not receive recent prior radiation, the incidence of immune-mediated pneumonitis was 2.0% (28/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. In patients who received recent prior radiation, the incidence of pneumonitis (including radiation pneumonitis) in patients with unresectable Stage III NSCLC following definitive chemoradiation within 42 days prior to initiation of IMFINZI in PACIFIC was 16.6% (79/475) in patients receiving IMFINZI and 13.2% (31/234) in patients receiving placebo. Of the 79 patients who received IMFINZI, 1.1% were fatal and 2.5% were Grade 3-4 adverse reactions. The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar in patients who received IMFINZI as a single agent or with ES-SCLC when in combination with chemotherapy.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis that is frequently associated with diarrhea. 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 1.6% (31/1889) of patients receiving IMFINZI, including Grade 4 (0.1%) and Grade 3 (0.3%) adverse reactions.

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 1.0% (19/1889) of patients receiving IMFINZI, including fatal (<0.1%) and Grade 3 (0.6%) adverse reactions.

Immune-Mediated Endocrinopathies

- ***Adrenal Insufficiency***:IMFINZI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Immune-mediated adrenal insufficiency occurred in 0.4% (7/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- ***Hypophysitis***:IMFINZI 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 symptomatic treatment including hormone replacement as clinically indicated. Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) of patients who received IMFINZI.
- ***Thyroid Disorders***:IMFINZI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement therapy for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated.
- ***Thyroiditis***: Immune-mediated thyroiditis occurred in 0.4% (7/1889) of patients receiving IMFINZI.
- ***Hyperthyroidism:*** Immune-mediated hyperthyroidism occurred in 1.4% (27/1889) of patients receiving IMFINZI.
- ***Hypothyroidism***:Immune-mediated hypothyroidism occurred in 7.3% (137/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- ***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. Grade 3 immune-mediated type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI.

Immune-Mediated Nephritis with Renal Dysfunction

IMFINZI can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (5/1889) of patients receiving IMFINZI, including Grade 3 (0.1%) adverse reactions.

Immune-Mediated Dermatology Reactions

IMFINZI can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), have occurred with PD-1/L-1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Immune-mediated rash or dermatitis occurred in 1.6% (30/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions.

Other Immune-Mediated Adverse Reactions

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in patients who received IMFINZI 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 to include 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 including increases in serum amylase and lipase levels, gastritis, duodenitis.
- ***Musculoskeletal and connective tissue disorders***: 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 thrombocytopenia, solid organ transplant rejection.

Infusion-Related Reactions

IMFINZI 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 IMFINZI based on the severity. See Dosing and Administration for specific details. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses. Infusion-related reactions occurred in 2.2% (42/1889) of patients receiving IMFINZI, including Grade 3 (0.3%) adverse reactions.

Complications of Allogeneic HSCT after IMFINZI

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/L-1 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/L-1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMFINZI and for at least 3 months after the last dose of IMFINZI.

Lactation

There is no information regarding the presence of IMFINZI in human milk; however, because of the potential for adverse reactions in breastfed infants from IMFINZI, advise women not to breastfeed during treatment and for at least 3 months after the last dose.

Adverse Reactions

- In patients with extensive-stage SCLC in the CASPIAN study receiving IMFINZI plus chemotherapy (n=265), the most common adverse reactions (≥20%) were nausea, fatigue/asthenia, and alopecia. The most common Grade 3 or 4 adverse reaction (≥3%) was fatigue/asthenia (3.4%)
- In patients with extensive-stage SCLC in the CASPIAN study receiving IMFINZI plus chemotherapy (n=265), IMFINZI was discontinued due to adverse reactions in 7% of the patients receiving IMFINZI plus chemotherapy. Serious adverse reactions occurred in 31% of patients receiving IMFINZI plus chemotherapy. The most frequent serious adverse reactions reported in at least 1% of patients were febrile neutropenia (4.5%), pneumonia (2.3%), anemia (1.9%), pancytopenia (1.5%), pneumonitis (1.1%), and COPD (1.1%). Fatal adverse reactions occurred in 4.9% of patients receiving IMFINZI plus chemotherapy

The safety and effectiveness of IMFINZI have not been established in pediatric patients.

Indications:

IMFINZI, in combination with etoposide and either carboplatin or cisplatin, is indicated for the first-line treatment of adult patients

with extensive-stage small cell lung cancer (ES-SCLC).

Please see complete Prescribing Information, including Medication Guide.

Announcer:
This program was sponsored by AstraZeneca. For more information on durvalumab also known as IMFINZI, including safety and prescribing information, visit imfinzi-h-c-p-dot-com. If you missed any part of this discussion, visit reach-m-d-dot-com. This is ReachMD. Be part of the knowledge.