Latest Clinical Evidence in Extensive-Stage Small Cell Lung Cancer Treatment

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Presenters' disclosures of conflicts of interest are found at the end of this article.

https://doi.org/10.6004/jadpro.2026.17.2.10

Abstract

Extensive-stage small cell lung cancer is an aggressive malignancy with historically poor survival outcomes. At JADPRO Live, presenters highlighted recent advances that are reshaping the management of this disease. Practical guidance focused on recognizing and managing oncologic emergencies, chemotherapy-related toxicities, immune-related adverse events, and novel toxicities associated with bispecific T-cell engagers, with a focus on patient and caregiver education.

At JADPRO Live, the session "Latest Clinical Evidence in Extensive-Stage Small Cell Lung Cancer (ES-SCLC) Treatment," led by **Stephanie McDonald, FNP-BC, AOCNP,** and **Elizabeth Castronovo, AGNP-C,** both nurse practitioners in the Thoracic Oncology Program at Dana-Farber Cancer Institute in Boston, provided updates in managing this challenging disease. Ms. McDonald and Ms. Castronovo covered recently approved agents, efficacy and safety data from pivotal trials, and practical approaches to monitoring and managing treatment-related adverse events. They also highlighted strategies for supportive care, reinforcing the advanced practitioner's (AP's) role in monitoring, education, triage, and supportive care coordination.

BACKGROUND ON ES-SCLC

Ms. Castronovo began with an overview of the disease. "Small cell lung cancer is known to be one of the most aggressive and challenging cancers we face," she stated. She cited poor historical outcomes, explaining that "the 5-year overall survival is only 5% to 10%" and that for patients treated palliatively with metastatic or extensive-stage disease, "the median survival is only 6 to 12 months (Okamoto et al., 2007)."

While non–small cell lung cancer (NSCLC) makes up around 77% of all lung cancers, SCLC is only about 13%. Ms. Castronovo commented, "Small cell also has a high mitotic rate, which leads to the aggressive nature of the disease."

Staging uses the Veterans Administration Lung Study Group system. Limited-stage disease is confined to the hemithorax and fits

J Adv Pract Oncol 2026;17(suppl 1):22–26

within a tolerable radiation field, while extensive-stage disease is metastatic, "anywhere beyond the hemithorax," and cannot be safely encompassed by a radiation field.

ONCOLOGIC EMERGENCIES

Many patients with small cell lung cancer present with paraneoplastic syndrome. "Paraneoplastic syndrome is not from the actual tumor spread or invasion, but is in fact a clinical condition that is caused by substances or proteins excreted from neuroendocrine cells," stated Ms. Castronovo.

These include hyponatremia of malignancy or syndrome of inappropriate antidiuretic hormone (SIADH) and hypercalcemia of malignancy, which are considered oncologic emergencies.

"If you're not sure if a patient has SIADH and they have a diagnosis of small cell lung cancer, you want to be careful and not give them large boluses of saline. That further dilutes the sodium and can make it worse," cautioned Ms. Castronovo. "Instead, while I'm waiting for urine studies, sometimes I'll hang a very small bolus of saline and then recheck the sodium. If it goes up, they're a little dehydrated. If it goes down, consider starting sodium tablets."

Another oncologic emergency, tumor lysis syndrome (TLS), occurs with rapid tumor cell death following treatment, causing tumor cells to excrete uric acid, potassium, and phosphorus.

"At Dana-Farber, we start patients on allopurinol at 300 mg daily at cycle one to make sure this doesn't happen," noted Ms. Castronovo.

THERAPIES

First Line

The standard first-line approach remains carboplatin and etoposide plus an immune checkpoint inhibitor (durvalumab [Imfinzi] or atezolizumab [Tecentriq]), followed by maintenance immunotherapy.

IMpower133 showed a median overall survival of 12.3 months with atezolizumab compared with 10.3 months with chemotherapy alone and a median progression-free survival of 5 months with atezolizumab vs. 4 months with chemotherapy alone (Horn et al., 2018). CASPIAN was a similar study looking at durvalumab as the immunotherapy agent. There was a median overall survival of about 13 months compared with 10.3 months with chemotherapy alone (Paz-Ares et al., 2019).

"You can recommend either of these drugs with chemotherapy, as they have a similar side effect profile," commented Ms. McDonald.

Updated long-term follow-up from the CASPIAN and IMpower-133 trials confirmed that adding immunotherapy to platinum–etoposide chemotherapy provides a durable survival benefit for patients with extensive-stage small cell lung cancer. In the updated CASPIAN analysis, the 3-year overall survival rate increased from 5.8% to nearly 18% with the addition of durvalumab (Paz-Ares et al., 2022). The 5-year follow-up data from IMpower-133 demonstrated a 12% 5-year survival rate when atezolizumab was combined with chemotherapy (Liu et al., 2023).

"Prior to this, the average patient who was only receiving chemotherapy was living less than 2 years," Ms. McDonald said. "Now, a subset can have this longer-term control."

Recently, the FDA approved the addition of lurbinectedin (Zepzelca) to atezolizumab in the maintenance phase based on the IMforte study. After four cycles of induction platinum/etoposide plus immunotherapy, lurbinectedin is added during maintenance with atezolizumab given every three weeks. The addition of lurbinectedin to atezolizumab showed an increase of 3 months in both overall and progression-free survival (Paz-Ares et al., 2025).

"Three months might not seem like a lot, but in a disease that can be so aggressive, it can be meaningful," commented Ms. McDonald.

One consideration is that central venous access is recommended for lurbinectedin; therefore, APs should anticipate the need for port placement early to avoid delays in initiating maintenance therapy.

Second-Line and Later

Tarlatamab (Imdelltra) was added as an NCCN Guidelines category 1 preferred second-line therapy following platinum-based chemotherapy, based on the DeLLphi-304 trial demonstrating superior overall survival compared with standard chemotherapy (Mountzios et al., 2025).

Tarlatamab is a bispecific T-cell engager. It targets delta-like ligand 3 (DLL3), which is abnormally expressed on approximately 85% of SCLC tumor cells, and CD3 on T cells, physically linking immune cells to malignant cells and inducing tumor cell lysis (Figure 1).

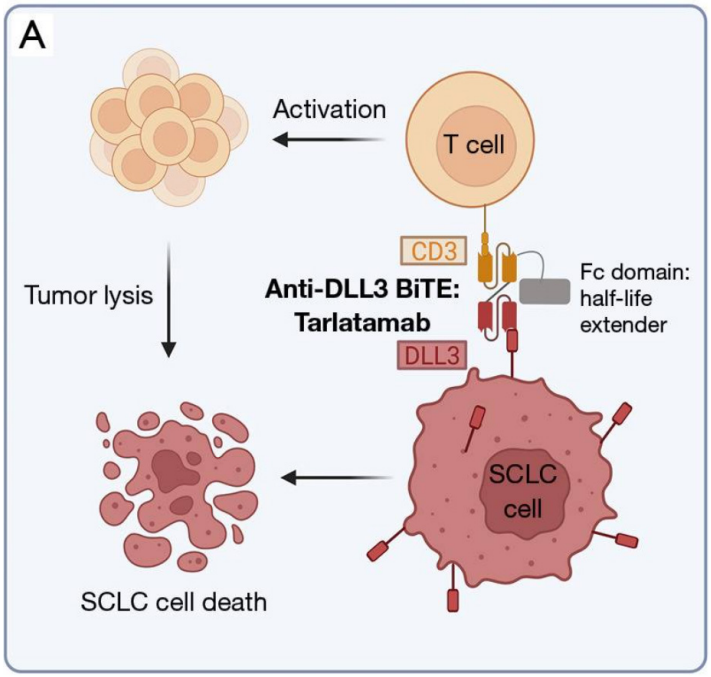

Figure 1. Antitumor activity of tarlatamab in SCLC. Adapted from Apaydin & Sage (2023).

In the second-line setting, cytotoxic agents include irinotecan, which has largely replaced topotecan in practice, lurbinectedin if not previously used in earlier lines, and taxanes such as docetaxel or paclitaxel in patients with an ECOG performance status of 2 or less.

Temozolomide was also highlighted as an option. "This is an oral chemotherapy that we don't often see but is good for patients if they are later in their disease and it is harder for them to get to clinic," explained Ms. Castronovo. It also has blood–brain barrier penetration.

Platinum rechallenge remains an option in select patients with platinum-sensitive disease, defined by progression occurring at least 6 months after completion of first-line platinum-based therapy. Lurbinectedin can also be used in the relapsed setting when not used in maintenance.

TOXICITY MANAGEMENT

With platinum-based chemotherapy with etoposide, cytopenias are common but usually grade 1 or 2. Growth factor support can be implemented for these patients. Nausea is generally well controlled with antiemetic regimens, including ondansetron and prochlorperazine, post-treatment dexamethasone for delayed nausea, and olanzapine in patients receiving cisplatin or those at higher risk.

Fatigue tends to be cumulative, while constipation is most prominent during the first week of treatment and is typically manageable with stool softeners and gentle laxatives.

"I think the most distressing part for some patients, which we may overlook, is hair loss," commented Ms. McDonald. "Providing that extra emotional support for patients during this time can go a long way."

"Immunotherapy toxicity can be unique and differ from chemotherapy," noted Ms. McDonald. A typical onset window is about 5 to 12 weeks, but it can also be seen a year or two after a patient has completed immunotherapy.

The most common immune-related adverse events (irAEs) include hypothyroidism, which is often identified through routine laboratory monitoring and managed with levothyroxine without discontinuing therapy, as well as rash and pruritus, typically controlled with antihistamines,

emollients, and topical corticosteroids. Less common but potentially life-threatening events include pneumonitis, colitis, and myocarditis. CTCAE is used to grade immunotherapy toxicity.

Ms. McDonald recommended "maintaining a high level of suspicion when a new symptom develops. We want to be getting these patients seen sooner to work up and diagnose the toxicity sooner."

Trilaciclib (Cosela) is indicated to decrease the incidence of chemotherapy-induced myelosuppression in patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen. It is a CDK4/6 inhibitor administered over 30 minutes each day chemotherapy is administered.

Pooled data from three phase II randomized trials demonstrated significant reductions in severe cytopenias, including grade 3 anemia and grade 4 neutropenia, as well as lower rates of hospitalization and sepsis (Weiss et al., 2021).

"This is something we should definitely consider for our high-risk patients," said Ms. McDonald.

Adverse event management with tarlatamab focuses on early recognition and patient education, particularly for cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS). Cytokine release syndrome most commonly occurs early in treatment and is generally low grade (grade 1–2), predictable, and manageable with step-up dosing, inpatient observation during initial doses, and supportive care.

Immune effector cell–associated neurotoxicity syndrome is less frequent but requires vigilance. Patients and caregivers are educated before treatment to recognize early neurologic changes using at-home cognitive assessments.

"This is an encouraging and exciting time for managing these patients," concluded Ms. McDonald. "We all play a pivotal role in bridging this novel science with the compassionate, patient-centered care that patients deserve." ●

Disclosure

Ms. McDonald has received consulting fees from Amgen, AstraZeneca, BMS, and Pfizer. Ms. Castronovo has received consulting fees from Pfizer.

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