

MEET THE EXPERTS

SMALL CELL LUNG CANCER

ISSUE 10

FEATURING

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“Drug development for ES-SCLC has been challenging, so it’s encouraging to finally see additional treatments emerging that may extend patients’ lives.”

—Laura Macke

“It’s not only the clinical aspect—we have to think of the operational and financial aspects too... Different fields have to come together as a team to care for the patient.”

—Minhee Kang

OPTIMIZING THE POST-INDUCTION PHASE IN SCLC: THE ROLE OF CHEMOIMMUNOTHERAPY IN 1L MAINTENANCE

INSIDE THIS ISSUE:

- ◆ Importance of communication among the multidisciplinary team in the care of patients with SCLC
- ◆ Expert perspectives on 1L maintenance chemoimmunotherapy
- ◆ Practical guidance on the management of treatment-related adverse events

1L=first-line; ES-SCLC=extensive-stage small cell lung cancer; SCLC=small cell lung cancer.

*Laura Macke and Minhee Kang are paid consultants of Jazz Pharmaceuticals. This content is intended for informational purposes only and is not a substitute for your clinical knowledge or professional judgment. The views and opinions expressed in this article are those of the authors and Jazz Pharmaceuticals and do not necessarily reflect the opinions of Lombardi Comprehensive Cancer Center.

THE ROLE OF APPs WITHIN A MULTIDISCIPLINARY TEAM MANAGING THE CARE OF SCLC PATIENTS

Q. Can you describe the typical patient with SCLC you see in your practice?

LM. SCLC is a very aggressive disease. When patients present initially, they're usually quite ill. They typically have shortness of breath, cough, fatigue, and possibly pain, to the point where they often need to be admitted to start chemotherapy induction as quickly as possible.¹ The good news is, SCLC is a very chemoresponsive disease, so we do see patients start to feel better very quickly after starting induction therapy.²

MK. SCLC patients represent 10% of lung cancer patients who come to our clinic.² I agree that it is a very aggressive cancer, and I say they need to be treated as aggressively as possible.¹ The good part is that chemotherapy works well in this population, despite having a limited number of established regimens available.^{2,3}

“ When we are talking about ES-SCLC, we are talking about a disease that we don’t yet have a cure for. We talk about what our goals are from both the patients’ and provider’s perspectives. ”

—Laura Macke

Q. How would you describe your role as an APP in treating patients with SCLC?

LM. I work very closely with the medical oncologist and nursing team to help manage these patients. I meet the patients early on in their course, if possible, in order to establish a solid baseline assessment and plan. My role includes closely monitoring patients’ symptoms and scans, and evaluating their response to treatment. Proactive monitoring is vital here; because SCLC moves fast, catching small changes early helps us better support our patients.

MK. My role in the multidisciplinary team includes managing drug inventory and procurement, as well as patient education at the bedside. From my own experience here, even though patients receive treatment-related education from providers, nurse practitioners, or other team members, they still

appreciate having the information reinforced in certain situations. For example, when a patient is just starting chemotherapy, or when there is an issue in the middle of a treatment cycle, I discuss with the patient what the issue is, why it happened, and what they can do to prevent it from happening again in the future.

Q. What are your key relationships within the multidisciplinary team, and what is their importance?

MK. I believe we have a strong relationship among providers, pharmacists, and the nursing team at our cancer center, where we trust and rely on each other. Effective patient care requires strong team collaboration and the integration of multiple perspectives—clinical, operational, and financial—and that is what we strive for at our institution.

LM. We maintain strong, collaborative communication across the team, with a shared approach to mutual oversight to ensure optimal patient care. Having an extra set of eyes and ears on what’s happening with our patients is always an advantage. We are all human and going to miss something here or there along the way: whether an order isn’t in, or a prescription doesn’t go through. I enjoy working alongside our pharmacy and nursing teams, keeping the lines of communication open so we can provide the best care possible for our patients. Being part of a multidisciplinary team allows us to connect our patients with resources that meet their needs, whether that’s symptom control, nutritional support, or social issues like transportation assistance. I think that there’s a nice balance of all of us working together to support the patient.

APP=advanced practice provider.



HELPING PATIENTS NAVIGATE TREATMENT OPTIONS: FROM TRIAL DATA TO REAL-WORLD DECISIONS

Q. How does clinical research impact your perspective when caring for patients with SCLC?

MK. At our cancer center, we have an oncology team and a research team that work as one; we see the same patients who were previously enrolled in a clinical trial in the research infusion setting transition to the oncology infusion setting. We witness the continuation of their treatment journey, which is truly remarkable. As a clinical pharmacist involved in both research and oncology, I am familiar with the extent to which a dose was tolerated during the trial, the side effects to monitor, and how the real-world experience would match the trial experience. In this way, my role allows me to bridge the ideal world of a clinical trial with the real world of oncology practice.

“ I stay very connected to our patients through frequent check-ins and care coordination, but it’s the multidisciplinary team’s collective efforts and balance that really make it all work. ”

—Laura Macke

LM. I could go on and on about the importance of clinical research. It has been my passion and my career for over 10 years now, working in various clinical trials that examine different disease types. I always explain to patients that every drug that’s approved has started with clinical trials. I would say these trials are what’s driving the future of cancer care, and we are constantly learning, evolving, and trying to find better treatments for our patients to help them live longer.

Q. What changes in patient outcomes have you observed with the availability of additional treatment options for patients with ES-SCLC, and what unmet needs remain?

LM. Drug development for ES-SCLC has been challenging, so it’s encouraging to finally see

additional treatments emerging that may extend patients’ lives.^{4,5} We’re certainly not in the space where we are able to cure people yet, but that will always be our goal. In the meantime, learning about these new drugs coming to market that give patients a chance to prolong their lives in a clinically meaningful way has been very exciting to see.

We want our patients to feel supported by their treatment, not burdened by it. Tolerability and efficacy are key considerations to help patients stay the course. Our goal is always to give our patients the “best-case scenario,” whatever that means to them.

MK. Beyond the inherent challenge of limited treatment options for this aggressive disease, financial concerns and logistical barriers often impede

access and adherence to care. Managing treatment-related adverse events, particularly the profound impact of fatigue, remains critical for maintaining patient treatment continuation. Furthermore, there’s a pressing need to bridge the gap between clinical trial findings and real-world outcomes to reflect a broader, more diverse patient population.

Q. How do you explain the difference between induction and maintenance treatment to patients?

LM. I would explain that the induction phase is where we’re giving what some might consider “the heavier hitting chemotherapy drugs” that work very well, but are not sustainable for a long period of time. I tell patients that, unfortunately, relapse is essentially inevitable if we stop treatment after



these initial drugs. I explain that, in addition to the 2 chemotherapy drugs, they will also be getting an immunotherapy drug, which would continue into the maintenance phase. I think that by describing the first 3 drugs you get, and the fact that you’re keeping one of them to continue beyond 4 cycles, is a good starting point for the conversation.

When you talk about adding a different medication in the maintenance phase, I could see how that can be a little bit confusing for patients thinking: “Now there’s a new drug being added; I wasn’t getting this before. How is this different?” In that situation, I would focus on the idea that this is intended to help prolong the response that we’ve seen from the induction therapy.⁶ I would also tell patients that this is a drug that we

have been giving in later-line settings, and we want to bring it forward to the maintenance setting with the immunotherapy they have already been getting as a way for us to ensure they get a drug that we think could help prolong their life.^{3,7}

MK. Personally, I don’t usually use the terms “induction” and “maintenance.” Instead, I focus on helping patients understand the underlying concept by explaining that we need to attack this aggressively with as much force as possible, and then the goal is to break down what remains and continue to manage the disease. This approach helps patients grasp the concept of induction and maintenance and understand why the medication regimen might change between the 2 phases.

IMPORTANT SAFETY INFORMATION (continued)

Myelosuppression (continued)

Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm³ and platelet count of at least 100,000/mm³. To reduce the risk of febrile neutropenia during treatment with ZEPZELCA in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, administer granulocyte colony-stimulating factor (G-CSF).

Monitor blood counts including neutrophils, red blood cells and platelets prior to each ZEPZELCA administration. For neutrophil count less than 500 cells/mm³ or any value less than lower limit of normal, administer G-CSF. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

In the IMforte study, primary prophylaxis of G-CSF was administered to 84% of patients. Based on laboratory values, decreased neutrophils occurred in 36%, including 18% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased neutrophil cells was 31 days and a median duration of 10 days. Febrile neutropenia occurred in 1.7%. Sepsis occurred in 1%. There were 7 fatal infections: pneumonia (n=3), sepsis (n=3), and febrile neutropenia (n=1).

Based on laboratory values, decreased platelets occurred in 54%, including 15% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased platelet cells was 31 days and a median duration of 12 days.

Based on laboratory values, decreased hemoglobin occurred in 51%, including 13% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased hemoglobin was 64 days and a median duration of 8 days.



INDICATION

ZEPZELCA (lurbinectedin) for injection 4 mg, in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, is indicated for the maintenance treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab or atezolizumab and hyaluronidase-tqjs, carboplatin and etoposide.

IMPORTANT SAFETY INFORMATION

Myelosuppression

ZEPZELCA can cause severe and fatal myelosuppression including febrile neutropenia and sepsis, thrombocytopenia and anemia.

APP PERSPECTIVES: EFFICACY DATA WITH ZEPZELCA® (lurbinectedin) + atezolizumab

Q. What was your impression of the IMforte clinical trial results and the subsequent FDA approval of the regimen?

LM. The first thing that was notable to me was that there were no new or unexpected safety findings for ZEPZELCA and atezolizumab in IMforte.⁷⁻⁹ To me, that was the first big impression, because as APPs in the clinic managing these toxicities, day-to-day tolerability of treatment is our utmost concern. In terms of the efficacy data, we observed a favorable response with a median overall survival of 13.2 months in the combination arm compared with 10.6 months in the monotherapy arm, with a statistically significant hazard ratio of 0.73*. Notably, this did not include the 3.2-month induction period.^{7,9} Additionally, we saw longer periods for progression-free survival: a median of 5.4 months in the combination arm compared with 2.1 months in the atezolizumab monotherapy arm, not including the 3.2-month induction period**.^{7,9} Patients were going longer without having progression, and they were living longer. These are both endpoints we certainly hope will translate into real-world clinical practice. The other interesting thing was that the patients on the combination arm received almost twice as many doses of these drugs as those on the monotherapy arm.⁹ I would say it's an exciting time for our patients with ES-SCLC. We have a new

first-line maintenance option that not only improves progression-free survival but also overall survival.⁷

MK. Regarding the IMforte clinical trial, I found the overall survival data particularly important, along with the observed discontinuation rate, which is a key consideration in the post-induction phase. In a disease setting historically marked by limited options, data like these offer meaningful hope for patients.

“ Adding lurbinectedin to atezolizumab in this regimen makes sense based off the aggressive nature of ES-SCLC. The data supports the important role of chemotherapy. ”

—Minhee Kang

Q. What does an approximately 3-month improvement in survival mean to you and your patients with ES-SCLC?

MK. Speaking from both a clinical and personal standpoint, I believe an additional 3 months could be very meaningful for patients and their families. This perspective is deeply personal for me, having witnessed its impact firsthand with a family member. For aggressive cancers like SCLC, this improvement is truly an impactful outcome. The fact that the IMforte trial demonstrated an improvement in overall survival, rather than just progression-free or disease-free survival, speaks to the strength of the data.⁷

LM. Statistics are a big part of the conversation in oncology, and I've noticed that for some patients, seeing the data helps them feel more informed and

*95% CI for HR: 0.57, 0.95; P=0.0174.⁷
**HR, 0.54; 95% CI for HR: 0.43, 0.67; P<0.0001.⁷

CI=confidence interval; FDA=US Food and Drug Administration; HR=hazard ratio.

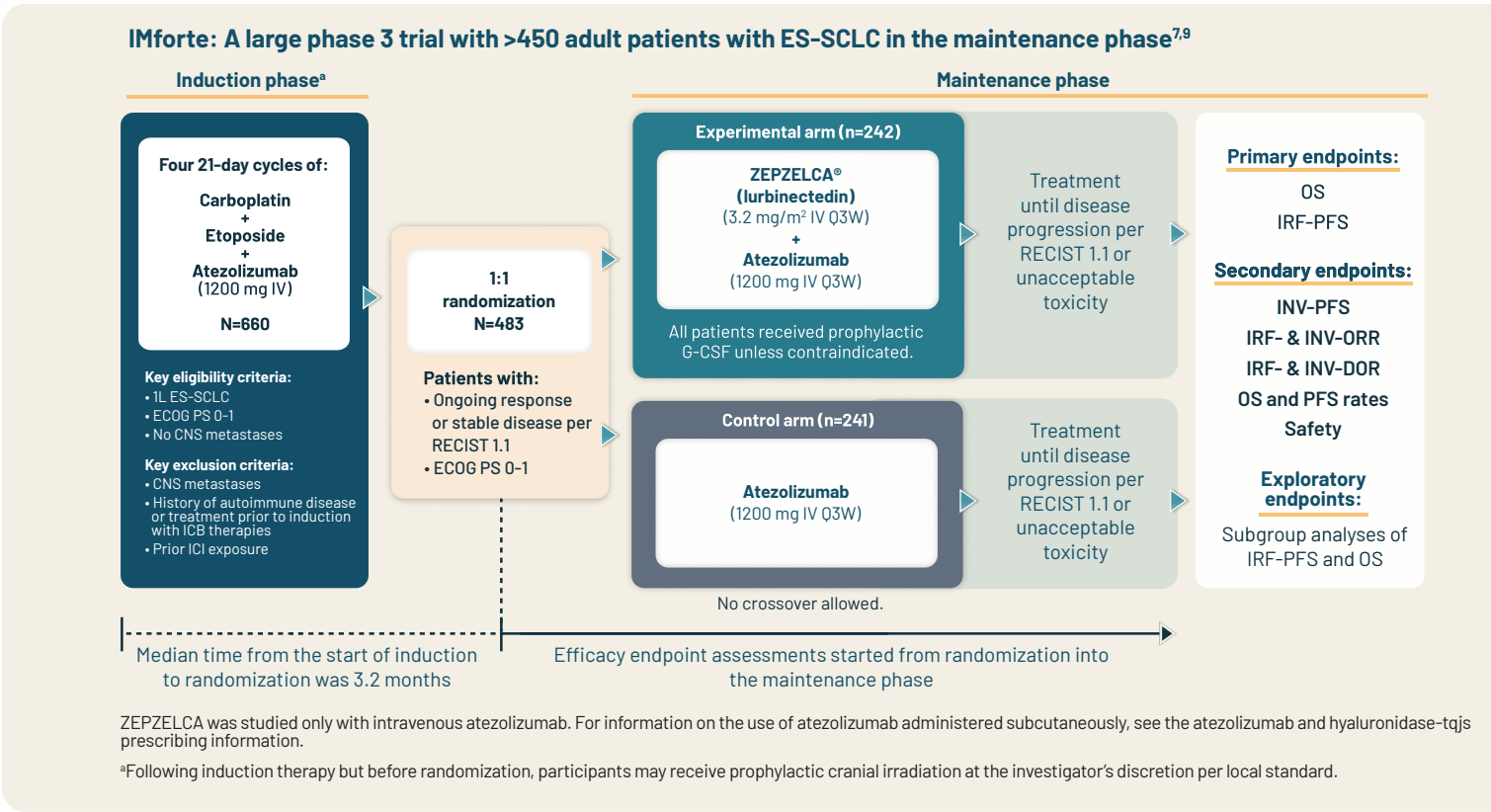
IMPORTANT SAFETY INFORMATION (continued)

Hepatotoxicity

ZEPZELCA can cause hepatotoxicity which may be severe.

Monitor liver function tests prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

In the IMforte study, based on laboratory values, increased alanine aminotransferase (ALT) occurred in 25%, including 3% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. Increased aspartate aminotransferase (AST) occurred in 24% including 3% Grade 3 or Grade 4. The median time to onset of Grade ≥3 elevation in transaminases was 52 days (range: 6 to 337).



empowered. But I've also learned that survival could mean something very different to patients. I can tell a patient about a median overall survival of 13.2 months instead of 10.6 months, and they may start wondering:

What do 13 months look like? While the efficacy data are significant, we also think beyond the numbers. Our goal is to provide therapies that give our patients more time and meet their treatment goals.

“ Personally, I believe an additional 3 months could be very meaningful for patients and their families... For aggressive cancers like SCLC, this improvement is truly an impactful outcome. ”

—Minhee Kang

CNS=central nervous system; DOR=duration of response; ECOG PS=Eastern Cooperative Oncology Group performance status; G-CSF=granulocyte colony-stimulating factor; ICB=immune checkpoint blockade; ICI=immune checkpoint inhibitor; INV=investigator-assessed; IRF=independent review facility-assessed; IV=intravenous; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; Q3W=every 3 weeks; RECIST=Response Evaluation Criteria in Solid Tumors.

IMPORTANT SAFETY INFORMATION (continued)

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA can cause skin and soft tissue injury, including necrosis requiring debridement. Consider use of a central venous catheter to reduce the risk of extravasation, particularly in patients with limited venous access. Monitor patients for signs and symptoms of extravasation during the ZEPZELCA infusion. If extravasation occurs, immediately discontinue the infusion, remove the infusion catheter, and monitor for signs and symptoms of tissue necrosis. The time to onset of necrosis after extravasation may vary.

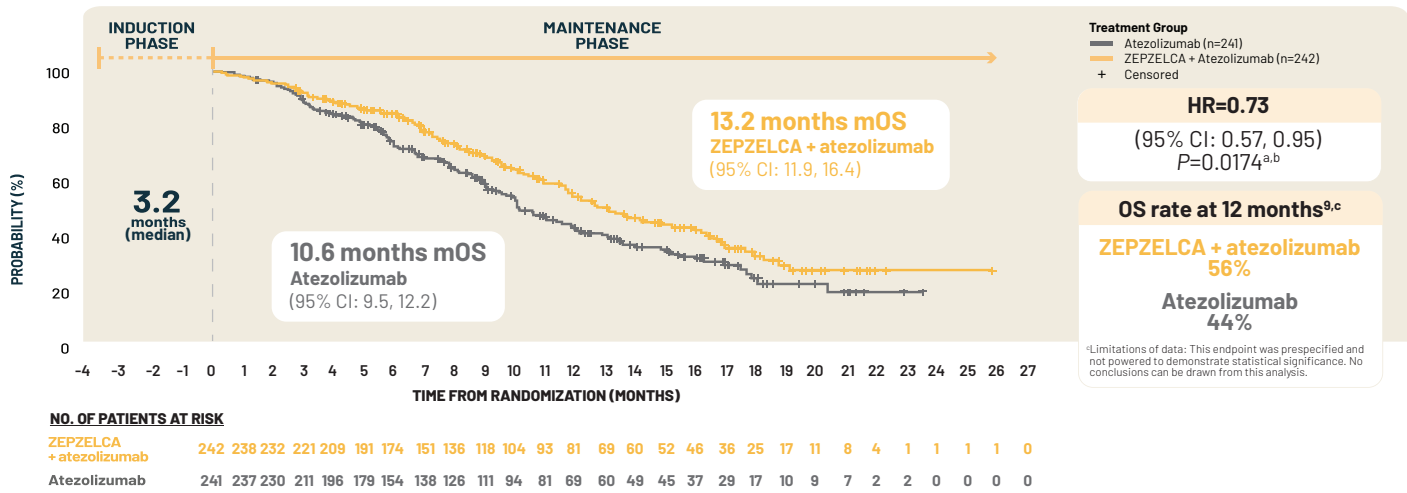
In the IMforte study, extravasation resulting in skin necrosis occurred in one patient who received ZEPZELCA in combination with atezolizumab.

Administer supportive care and consult with an appropriate medical specialist as needed for signs and symptoms of extravasation. Administer subsequent infusions at a site that was not affected by extravasation.



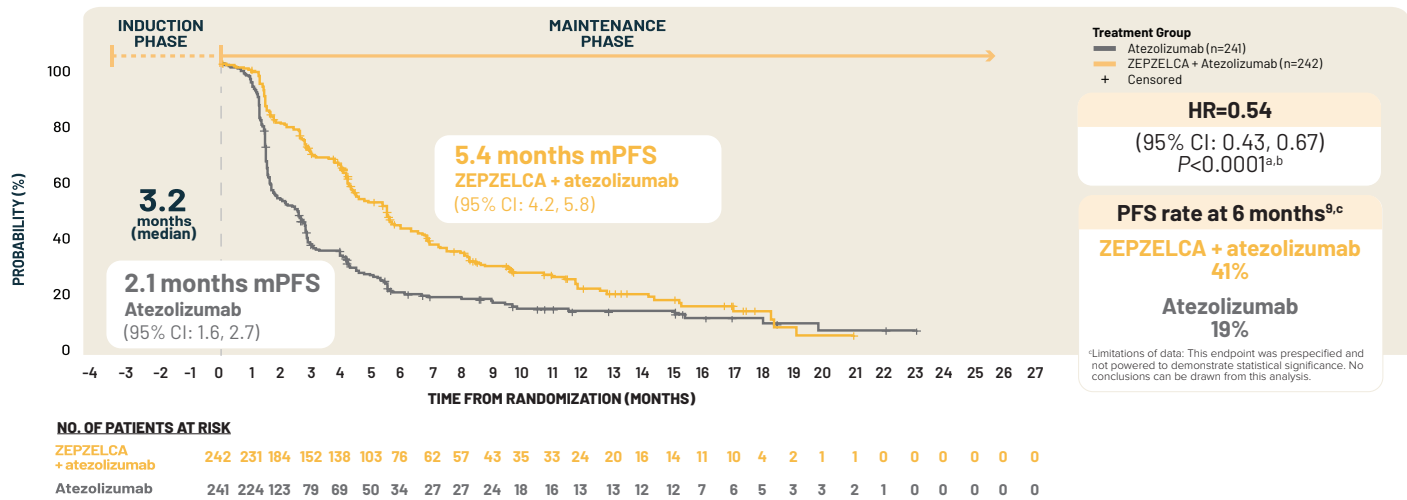
APP PERSPECTIVES: EFFICACY DATA WITH ZEPZELCA® (lurbinectedin) + atezolizumab (continued)

Kaplan–Meier estimates of IRF overall survival in the full analysis set^{7,9}



mOS=median overall survival.
^aBased on the 2-sided stratified log-rank test.
^cCompared to the allocated alpha of 0.0313 (2-sided) for this interim OS analysis.

Kaplan–Meier estimates of IRF progression-free survival in the full analysis set^{7,9}



mPFS=median progression-free survival.
^aBased on the 2-sided stratified log-rank test.
^cCompared to the allocated alpha of 0.001 (2-sided) for this final PFS analysis.

IMPORTANT SAFETY INFORMATION (continued)

Rhabdomyolysis

Rhabdomyolysis has been reported in patients treated with ZEPZELCA.

Monitor creatine phosphokinase (CPK) prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold or reduce the dose based on severity.

APP PERSPECTIVES: SAFETY AND TOLERABILITY OF ZEPZELCA® (lurbinectedin) + atezolizumab

Q. What are your thoughts on the safety and tolerability of ZEPZELCA + atezolizumab based on the IMforte trial results?

LM. We often use terms such as “manageable” when we talk about adverse events, but these are very subjective. A more objective way to look at it is the proportion of patients who had to discontinue the drug due to toxicity. In the IMforte trial, only 5% of patients needed to permanently discontinue treatment with ZEPZELCA due to toxicity, and most of the adverse events that we saw in the ZEPZELCA plus atezolizumab arm were Grade 1 or 2.^{7,9} Some patients did require

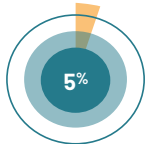
“ In the IMforte trial, only about 5% of patients needed to discontinue treatment due to toxicity, and most of the adverse events that we saw were Grade 1 or 2. ”

—Laura Macke

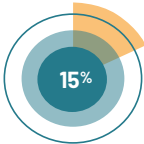
dose interruptions or dose reductions, but importantly, they were able to stay on their treatment regimen.⁷

MK. Initially, I did have some concerns about the potential for increased toxicities given it’s a 2-drug regimen, particularly regarding myelosuppression and fatigue, which are common with cytotoxic agents.⁷ However, reviewing the IMforte data was quite reassuring. The side effects were able to be managed with the proactive use of growth factors, as reflected within the data, and the low discontinuation rate. We still continue to monitor for potential issues like thrombocytopenia.

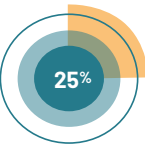
Most adverse reactions were Grade 1 or 2^{7,a}



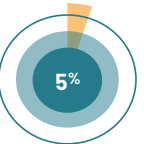
Discontinuation
Low discontinuation rate of ZEPZELCA (5%) due to adverse reactions in patients receiving ZEPZELCA + atezolizumab⁷
The adverse reaction resulting in permanent discontinuation in ≥1% of patients who received ZEPZELCA was decreased neutrophil count



Dose reduction
15% of patients receiving ZEPZELCA + atezolizumab had dose reductions of ZEPZELCA due to an adverse reaction⁷
Adverse reactions which required dosage reduction in ≥2% of patients included decreased platelet count, fatigue, nausea, and vomiting



Interruption
25% of patients receiving ZEPZELCA + atezolizumab had an adverse reaction leading to interruption of ZEPZELCA⁷
Adverse reactions which required dosage interruption in ≥2% of patients included anemia, fatigue, decreased neutrophil count, and decreased platelet count



Adverse reactions
Fatal adverse reactions occurred in 5% of patients receiving ZEPZELCA + atezolizumab⁷
These included pneumonia (3 patients), sepsis (3 patients), cardio-respiratory arrest (2 patients), myocardial infarction (2 patients), and febrile neutropenia (1 patient)

^a242 patients in the ZEPZELCA + atezolizumab group and 240 patients in the atezolizumab group were included in the safety analysis set.

IMPORTANT SAFETY INFORMATION (continued)

Rhabdomyolysis (continued)

In the IMforte study, among 235 patients who had a creatine phosphokinase laboratory evaluation, increased creatine phosphokinase occurred in 9% who received ZEPZELCA in combination with atezolizumab.

Embryo-Fetal Toxicity

ZEPZELCA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 7 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the last dose.



APP PERSPECTIVES: SAFETY AND TOLERABILITY OF ZEPZELCA® (lurbinectedin) + atezolizumab (continued)

Q. Do you utilize G-CSF prophylaxis for the management of ZEPZELCA + atezolizumab-related myelosuppression in your practice? In which patients, and why?

LM. Unless the patient has a contraindication, they receive G-CSF prophylactically prior to their

ZEPZELCA doses during the maintenance phase. At that point, they have already received 4 cycles of induction chemotherapy, which can have a significant impact on their blood counts.⁸ We know that ZEPZELCA can cause more myelosuppression, so we want to stay ahead of it and give G-CSF prior

The safety profile of ZEPZELCA + atezolizumab was established in IMforte^{7,9}

Adverse reactions (≥10% of patients receiving ZEPZELCA® (lurbinectedin) + atezolizumab) ⁷					Select lab abnormalities (≥20% of patients receiving ZEPZELCA® (lurbinectedin) + atezolizumab) worsening from baseline ⁷				
	ZEPZELCA + Atezolizumab (n=242)		Atezolizumab (n=240)			ZEPZELCA + Atezolizumab (n=242)		Atezolizumab (n=240)	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)		All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
Gastrointestinal disorders					Hematology				
Nausea	36	3	4	1	Decreased lymphocytes	55	17	31	11
Diarrhea ^a	15	0	8	0	Decreased platelets	54	15	15	3
Vomiting	14	1	3	0	Decreased hemoglobin	51	13	12	3
Constipation	12	0	6	1	Decreased neutrophils	36	18	7	4
General disorders and administration site conditions					Chemistry				
Fatigue ^b	32	5	13	2	Increased alkaline phosphatase	29	1	14	0
Musculoskeletal and connective tissue disorders					Decreased sodium	27	4	30	5
Musculoskeletal pain ^c	19	2	16	1	Increased ALT	25	3	18	2
Metabolism and nutrition disorders					Increased AST	24	3	22	1
Decreased appetite	17	0	7	0	Decreased calcium	24	3	8	1
Respiratory, thoracic, and mediastinal disorders					Increased creatinine	21	3	14	0
Cough ^d	12	0	8	0					
Dyspnea ^e	11	2	10	2					

Graded per NCI CTCAE v5.0.
ALT=alanine aminotransferase; AST=aspartate aminotransferase; NCI CTCAE= National Cancer Institute Common Terminology Criteria for Adverse Events.

^aIncludes diarrhea and colitis. ^bIncludes fatigue and asthenia. ^cIncludes arthralgia, arthritis, back pain, bone pain, musculoskeletal chest pain, musculoskeletal discomfort, musculoskeletal pain, myalgia, neck pain, non-cardiac chest pain, and pain in extremity. ^dIncludes cough, productive cough, and upper-airway cough syndrome. ^eIncludes dyspnea and dyspnea exertional.

IMPORTANT SAFETY INFORMATION (continued) ADVERSE REACTIONS

Serious adverse reactions occurred in 31% of patients receiving ZEPZELCA in combination with atezolizumab. Serious adverse reactions occurring in >2% were pneumonia (2.5%), respiratory tract infection (2.1%), dyspnea (2.1%), and decreased platelet count (2.1%). Fatal adverse reactions occurred in 5% of patients receiving ZEPZELCA with atezolizumab including pneumonia (3 patients), sepsis (3 patients), cardio-respiratory arrest (2 patients), myocardial infarction (2 patients), and febrile neutropenia (1 patient).

The most common adverse reactions (≥15%), including laboratory abnormalities, in patients who received ZEPZELCA with atezolizumab were decreased lymphocytes, decreased platelets, decreased hemoglobin, decreased neutrophils, nausea, fatigue, increased alkaline phosphatase, decreased sodium, increased ALT, increased AST, decreased calcium, increased creatinine, musculoskeletal pain, decreased appetite and diarrhea.

APP PERSPECTIVES: MANAGING SIDE EFFECTS OF ZEPZELCA® (lurbinectedin) + atezolizumab

to all the doses.^{7,9} Generally, patients tolerate G-CSF well, though some patients report bone pain, general aches, or feeling a little more tired.¹⁰

MK. In our practice, we widely utilize G-CSF prophylaxis for managing myelosuppression, and our approach is evidence-based. The main side effects observed with G-CSF are fatigue and bone pain, but these are generally manageable and do not typically result in G-CSF discontinuation. The benefit is significant, as it helps patients tolerate myelosuppression and reduces infection risk related to neutropenia.¹⁰ The fact that the IMforte trial design includes prophylactic G-CSF use makes it more applicable to real-world practice and underscores the importance of its use in that setting.⁹ Clinically, I believe in the benefits of G-CSF as it relates to patient safety and treatment continuity.

Q. What are the management protocols in place for the GI adverse events related to treatment with maintenance ZEPZELCA + atezolizumab?

MK. In general, prevention is key. Once nausea starts, it's hard to control, no matter what type of medication we use. That is why, as clinicians, we have to review the emetogenic risk of chemotherapy treatments. We follow the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) when selecting an antiemetic regimen, while considering

individual patient factors as a multidisciplinary team. For example, has the patient experienced nausea or vomiting from different cancers or different medications? If so, we should be proactively managing nausea. When the patient comes to the next cycle after experiencing nausea or vomiting previously, it is advised that they receive an antiemetic, including dexamethasone or ondansetron, for anticipatory nausea/vomiting.⁷ Ultimately, it is not a “one-size-fits-all” approach. We consider multiple patient-specific factors while monitoring the response to antiemetics throughout treatment.

LM. If a patient has both nausea and diarrhea, ondansetron can be particularly helpful, due to its well-known side effect of constipation.^{7,11} On the other hand, some patients struggle with constipation, so perhaps they don't want to be taking ondansetron, in which case we consider other options. We tell

patients upfront that we have options, and that we can switch to another antiemetic if something is not working for them. Sometimes, we do need to involve palliative care in symptom management, if we can. The palliative care team is exceptionally useful in this population that can have not only a heavy symptom burden from cancer but also side effects from medications used to treat their disease. It can be a lot for patients to manage. We do our best to support them.

“**Ultimately, it is not a ‘one-size-fits-all’ type of approach. We consider different factors while monitoring the response to antiemetics throughout treatment.**”
—Minhee Kang

GI=gastrointestinal; NCCN=National Comprehensive Cancer Network.

IMPORTANT SAFETY INFORMATION (continued) DRUG INTERACTIONS

Effect of CYP3A Inhibitors and Inducers

Avoid coadministration with a strong or a moderate CYP3A inhibitor (including grapefruit and Seville oranges) as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration cannot be avoided, reduce the ZEPZELCA dose as appropriate.



APP PERSPECTIVES: MANAGING SIDE EFFECTS OF ZEPZELCA® (lurbinectedin) + atezolizumab (continued)

Q. What are the management protocols in place for fatigue related to treatment with maintenance ZEPZELCA + atezolizumab?

MK. Fatigue management is important because patients cannot really do anything when they experience chemotherapy-related fatigue. In practice, providers either delay the next treatment or reduce the dose of ZEPZELCA. Fatigue is not tangible, but we have to grasp its real impact and act on it. As providers, we must pause and think from the patient’s perspective before we act, taking the time to understand their actual needs. For me, managing adverse events, such as fatigue, has a lot to do with the cadence of communication with our patients. I make it a priority to ensure that a pharmacist follows up with the patient on a continuous basis. Reaching out between cycles to

check on the patient’s status, addressing the side effects they are experiencing, and resolving those concerns promptly rather than waiting from cycle to cycle is essential.

LM. Fatigue is always challenging, even in identifying what is contributing to a patient’s fatigue—is it the cancer? Is it their comorbidities? Is it the treatment? And it’s very hard to tease out what exactly is driving the fatigue. We also don’t have great interventions for fatigue; the only data we have that really support their use for managing fatigue are diet and exercise, which can make a real difference. I tell my patients all the time to stay as active as tolerated. Patients are more likely to be compliant and willing to continue treatment if they feel well.

IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS (continued)

Avoid coadministration with strong CYP3A inducers as it may decrease systemic exposure to lurbinectedin, which may decrease the efficacy of ZEPZELCA.

LACTATION

There are no data on the presence of ZEPZELCA in human milk, however, because of the potential for serious adverse reactions from ZEPZELCA in breastfed children, advise women not to breastfeed during treatment with ZEPZELCA and for 2 weeks after the last dose.

GERIATRIC USE

Of the 242 patients with ES-SCLC treated with ZEPZELCA and atezolizumab in IMforte, 124 (51%) patients were 65 years of age and older, while 29 (12%) patients were 75 years of age and older. No overall differences in effectiveness were observed between older and younger patients. There was no overall difference in the incidence of serious adverse reactions in patients ≥65 years of age and patients <65 years of age (33% vs. 29%, respectively). There was a higher incidence of Grade 3 or 4 adverse reactions in patients ≥65 years of age compared to younger patients (45% vs. 31%, respectively).

HEPATIC IMPAIRMENT

Avoid administration of ZEPZELCA in patients with severe hepatic impairment. If administration cannot be avoided, reduce the dose. Monitor for increased adverse reactions in patients with severe hepatic impairment.

Reduce the dose of ZEPZELCA in patients with moderate hepatic impairment. Monitor for increased adverse reactions in patients with moderate hepatic impairment.

No dose adjustment of ZEPZELCA is recommended for patients with mild hepatic impairment.

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INDICATION

ZEPZELCA (lurbinectedin) for injection 4 mg, in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, is indicated for the maintenance treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab or atezolizumab and hyaluronidase-tqjs, carboplatin and etoposide.

IMPORTANT SAFETY INFORMATION

Myelosuppression

ZEPZELCA can cause severe and fatal myelosuppression including febrile neutropenia and sepsis, thrombocytopenia and anemia.

Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm³ and platelet count of at least 100,000/mm³. To reduce the risk of febrile neutropenia during treatment with ZEPZELCA in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, administer granulocyte colony-stimulating factor (G-CSF).

Monitor blood counts including neutrophils, red blood cells and platelets prior to each ZEPZELCA administration. For neutrophil count less than 500 cells/mm³ or any value less than lower limit of normal, administer G-CSF. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

In the IMforte study, primary prophylaxis of G-CSF was administered to 84% of patients. Based on laboratory values, decreased neutrophils occurred in 36%, including 18% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased neutrophil cells was 31 days and a median duration of 10 days. Febrile neutropenia occurred in 1.7%. Sepsis occurred in 1%. There were 7 fatal infections: pneumonia (n=3), sepsis (n=3), and febrile neutropenia (n=1).

Based on laboratory values, decreased platelets occurred in 54%, including 15% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased platelet cells was 31 days and a median duration of 12 days.

Based on laboratory values, decreased hemoglobin occurred in 51%, including 13% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased hemoglobin was 64 days and a median duration of 8 days.

Hepatotoxicity

ZEPZELCA can cause hepatotoxicity which may be severe.

Monitor liver function tests prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

In the IMforte study, based on laboratory values, increased alanine aminotransferase (ALT) occurred in 25%, including 3% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. Increased aspartate aminotransferase (AST) occurred in 24% including 3% Grade 3 or Grade 4. The median time to onset of Grade ≥3 elevation in transaminases was 52 days (range: 6 to 337).

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA can cause skin and soft tissue injury, including necrosis requiring debridement. Consider use of a central venous catheter to reduce the risk of extravasation, particularly in patients with limited venous access. Monitor patients for signs and symptoms of extravasation during the ZEPZELCA infusion. If extravasation occurs, immediately discontinue the infusion, remove the

infusion catheter, and monitor for signs and symptoms of tissue necrosis. The time to onset of necrosis after extravasation may vary.

In the IMforte study, extravasation resulting in skin necrosis occurred in one patient who received ZEPZELCA in combination with atezolizumab.

Administer supportive care and consult with an appropriate medical specialist as needed for signs and symptoms of extravasation. Administer subsequent infusions at a site that was not affected by extravasation.

Rhabdomyolysis

Rhabdomyolysis has been reported in patients treated with ZEPZELCA.

Monitor creatine phosphokinase (CPK) prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold or reduce the dose based on severity.

In the IMforte study, among 235 patients who had a creatine phosphokinase laboratory evaluation, increased creatine phosphokinase occurred in 9% who received ZEPZELCA in combination with atezolizumab.

Embryo-Fetal Toxicity

ZEPZELCA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 7 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the last dose.

ADVERSE REACTIONS

Serious adverse reactions occurred in 31% of patients receiving ZEPZELCA in combination with atezolizumab. Serious adverse reactions occurring in >2% were pneumonia (2.5%), respiratory tract infection (2.1%), dyspnea (2.1%), and decreased platelet count (2.1%). Fatal adverse reactions occurred in 5% of patients receiving ZEPZELCA with atezolizumab including pneumonia (3 patients), sepsis (3 patients), cardio-respiratory arrest (2 patients), myocardial infarction (2 patients), and febrile neutropenia (1 patient).

The most common adverse reactions (≥15%), including laboratory abnormalities, in patients who received ZEPZELCA with atezolizumab were decreased lymphocytes, decreased platelets, decreased hemoglobin, decreased neutrophils, nausea, fatigue, increased alkaline phosphatase, decreased sodium, increased ALT, increased AST, decreased calcium, increased creatinine, musculoskeletal pain, decreased appetite and diarrhea.

DRUG INTERACTIONS

Effect of CYP3A Inhibitors and Inducers

Avoid coadministration with a strong or a moderate CYP3A inhibitor (including grapefruit and Seville oranges) as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration cannot be avoided, reduce the ZEPZELCA dose as appropriate.

Avoid coadministration with strong CYP3A inducers as it may decrease systemic exposure to lurbinectedin, which may decrease the efficacy of ZEPZELCA.

LACTATION

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“When I saw the IMforte trial data and the safety profile, along with the low discontinuation rate in the ZEPZELCA and atezolizumab arm, I was reassured that this could be a good option for that patient population.”

—Minhee Kang

“I think ZEPZELCA and atezolizumab in the 1L maintenance setting is a great option to offer to our patients. It is still in the early days of seeing this in actual clinical practice, given that it hasn't been available that long. But I think so far, it's going pretty well, and everything I've seen has been consistent with the data we saw in IMforte. So, I'm optimistic.”

—Laura Macke

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