MEET THE EXPERT

ISSUE 3

SMALL CELL LUNG CANCER

INSIDE THIS ISSUE:

- Patient experience and treatment strategies in second-line small cell lung cancer
- Efficacy and safety considerations in treatment selection
- Importance of the platinum-free interval
- Considering patient lifestyle and dosing schedule when choosing a treatment

FEATURING

Jason Porter, MD*

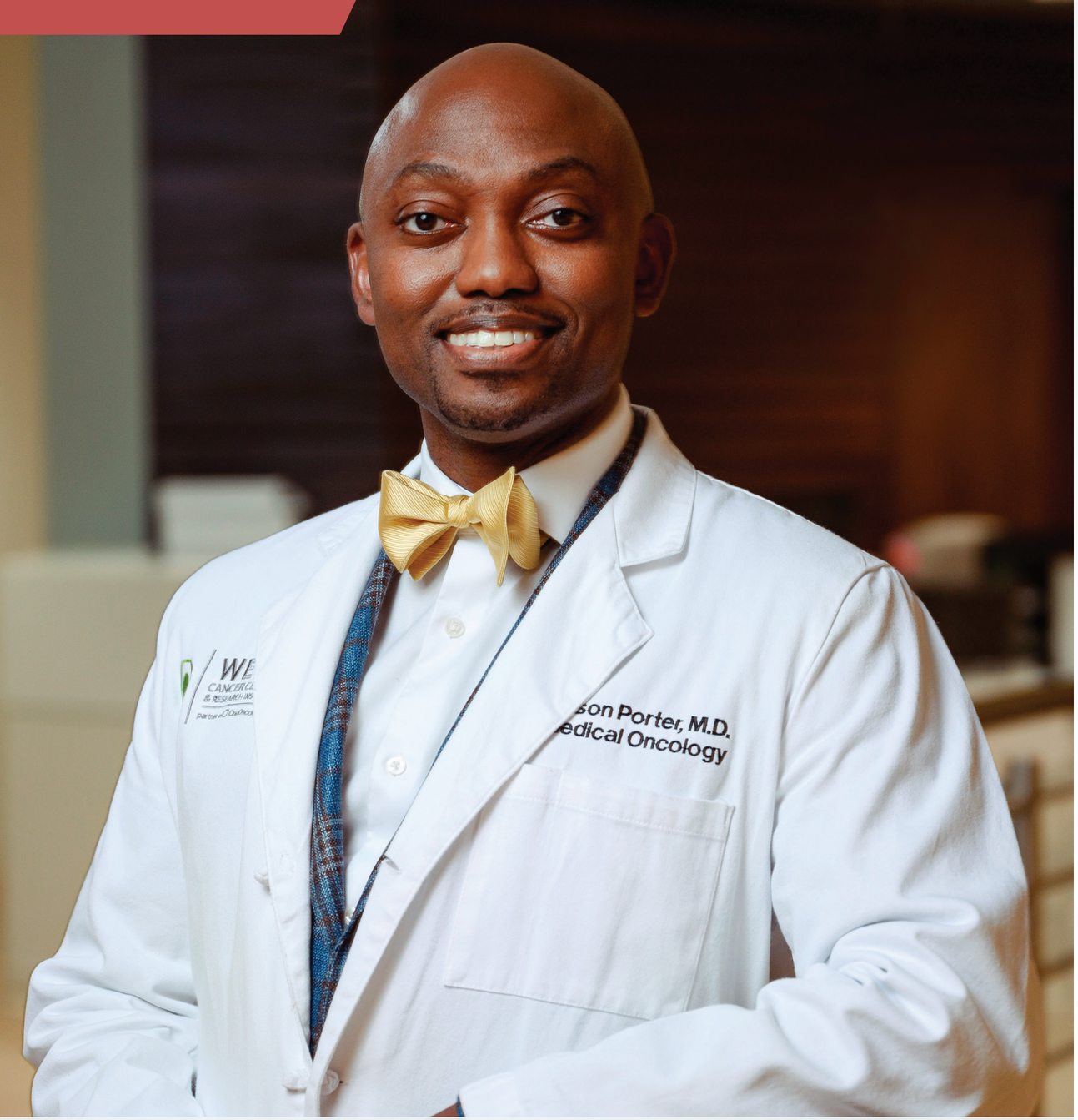
West Cancer Center and Research Institute

Memphis, TN

> *"It's really important to treat SCLC patients every chance you can."*
>
> — Jason Porter, MD

THE IMPORTANCE OF SECOND-LINE TREATMENT OPTIONS IN SMALL CELL LUNG CANCER

*Dr Porter is a paid consultant 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 author and Jazz Pharmaceuticals and do not necessarily reflect the opinions of West Cancer Center and Research Institute.



A LOOK AT SECOND-LINE **SCLC PATIENT EXPERIENCE** AND TREATMENT STRATEGIES

with **Dr Jason Porter**

"I think it's really important for SCLC patients to stay on treatment. Without therapy, this disease is going to progress; with therapy, there is a chance that we can control it a little longer."

— Jason Porter, MD

Q. What are the biggest challenges when it comes to treating small cell lung cancer (SCLC)?

A. With SCLC, the problem often is that it grows so fast[1]: you're asymptomatic one day, and the next day you can't breathe. You're having seizures from hyponatremia.[2] Many of the patients I see are hospitalized at diagnosis. The disease itself can have varied presentations; in a few instances these "SCLCs" don't actually start in the lung. Maybe they started in the GI tract or in the bladder or prostate, but there is a lung nodule, and they get classified as SCLC.[3] Despite how heterogeneous the disease is, we're limited to the same treatments for all these different manifestations.[4] With these limited options, it's really important to treat these patients every chance that you can.

Q. What are some of the important points practitioners should keep in mind regarding relapse after first-line therapy in SCLC?

A. SCLC doesn't discriminate; it doesn't care how much money a patient has or how health literate they are. Some patients, often those with less health education, may not understand that the side effects or symptoms they are having are related to their disease or to progression,[3] so they don't always come in for treatment. SCLC is one of those diseases where you can fall off the scale of "treatable" really quickly, so it's important to keep relapse in mind before it happens. That means having low threshold to repeat imaging for new, even seemingly vague, symptoms. I think setting the stage up front that there's a high chance for relapse is really important[5]; that way, when you get to the point of needing second-line therapy, your patient isn't devastated and not willing to do more therapy.

Q. How many of your patients with SCLC require a second-line treatment option and how important is it for these patients to stay on treatment?

A. Most patients are going to relapse, unfortunately.[5] In the time that I've been practicing, I can count on my hands the number of patients I've treated who are still on their primary immune therapy maintenance and haven't progressed. I tell all my patients that there is a high chance of them having a great response to first-line therapy. After their first 2 cycles, we'll do a CT scan, and it's going to look beautiful and I want them to be encouraged because not long after that we will probably see the disease start to progress again[3]—then they won't be surprised when I tell them that we need a second-line therapy.

Q. What patient characteristics or medical criteria do you keep in mind when you're considering a second-line option?

A. I see how the patients responded to platinum—are they platinum-sensitive or not? Usually, the longer I can keep my patients off of chemotherapy and platinum before I rechallenge, the better.[6] I also try to think of the patient's needs: do they have family support to help with their treatment schedule? Both of my parents were diagnosed with cancer; my dad had brain metastases at diagnosis and couldn't drive himself because he was having seizures. Without family support to drive him back and forth to appointments, he wouldn't have been able to receive his therapy. So, support and dosing schedules in many ways can be a big part of treatment considerations; that's something I work with the patient on.

CT=computed tomography; SCLC=small cell lung cancer.

"Most patients are going to relapse, unfortunately. In the time that I've been practicing, I can count on my fingers the number of patients I've treated who are still on their primary immune therapy maintenance and haven't progressed."

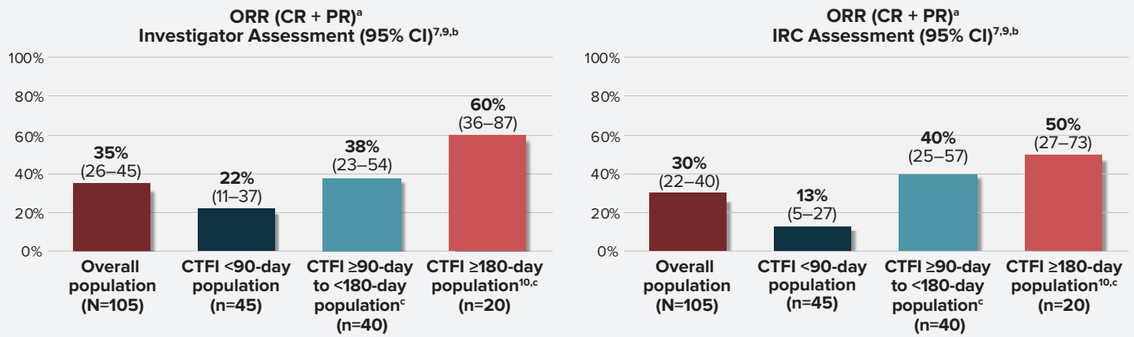
— Jason Porter, MD

CLINICAL EXPERIENCE: SECOND-LINE TREATMENT FOR SCLC WITH ZEPZELCA® (lurbinectedin)

Q. Why do you consider prescribing ZEPZELCA for your patients with SCLC who have relapsed?

A. ZEPZELCA has done well in my practice. The safety and efficacy data from the ZEPZELCA pivotal phase 2 trial closely align with the experience I have had with my patients. In the phase 2 trial in adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy, ZEPZELCA provided an ORR of 35% by IA and 30% by IRC.[7,8] The median DoR was 5.3 months by IA and 5.1 months by IRC.[7,8] The DCR was 69% by IA and 62% by IRC.[8,9] Similar results were seen within subgroups by CTFI.[9] I use ZEPZELCA as second-line treatment for both my platinum-sensitive and platinum-resistant patients. I keep them on ZEPZELCA for as long as possible, allowing for discussions regarding future treatment options.

For adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy,
ZEPZELCA PROVIDED SUBSTANTIAL EFFICACY IN BOTH PLATINUM-RESISTANT AND PLATINUM-SENSITIVE PATIENTS[7]



[a]**CR + PR breakdowns are shown on opposite page. Please see DCR bar chart titled Exploratory Analysis of Disease Control With ZEPZELCA.**

[b]According to RECIST v1.1. CR: Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to <10 mm. PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.[11]

[c]**Limitations of subgroup analyses: These subgroup exploratory analyses were not powered to determine statistical significance. Results are descriptive only.[10]**

CI=confidence interval; CTFI=chemotherapy-free interval; CR=complete response; DCR=disease control rate; DoR=duration of response; IA=investigator assessment; IRC=independent review committee; ORR=overall response rate; PR=partial response; RECIST=Response Evaluation Criteria in Solid Tumors.

INDICATION

ZEPZELCA® (lurbinectedin) is indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

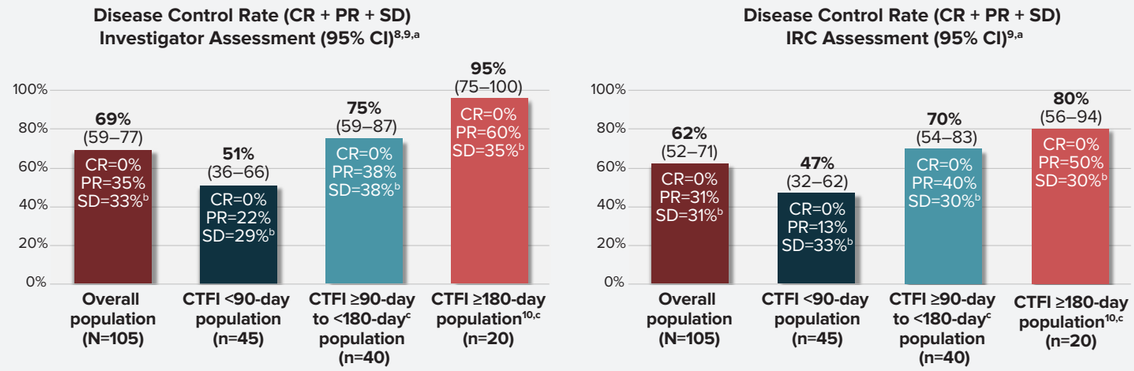
"Disease control rate is very important to me, especially with a disease like SCLC where you're talking weeks to months of survival."

— Jason Porter, MD

Q. Can you explain further about DCR and why it matters to you and your patients?

A. Disease control rate is very important to me. SCLC grows; it doesn't just hang out most times.[1] So, if it's not growing, I tell my patients that a stable scan is actually a really good thing. If I can control the disease for a period of time, that is meaningful to patients. To me, that's a relevant motivation. During that time, the patient can focus on loving their family and doing the things that matter to them.

For adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy,
EXPLORATORY ANALYSIS OF DISEASE CONTROL WITH ZEPZELCA[8]



[a]According to RECIST v1.1. CR: Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to <10 mm. PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum diameters while on study.[11]

[b]Includes 5 patients with partial response not confirmed.[8,9]

[c]These subgroup exploratory analyses were not powered to determine statistical significance. Results are descriptive only.[10]

Limitations of DCR data: No conclusions about efficacy can be drawn from these descriptive data because they are results from exploratory end points in a phase 2, single-arm study.[9]

STUDY DESIGN

The phase 2 trial was a multicenter, open-label, multi-cohort trial evaluating ZEPZELCA as a single agent in 105 adult patients with advanced or metastatic SCLC with disease progression on or after platinum-based chemotherapy. Patients received ZEPZELCA 3.2 mg/m^2 by intravenous infusion every 21 days (one cycle) for a median of 4 cycles (range: 1 to 24 cycles). The median age was 60 years (range: 40 to 83 years). Baseline ECOG PS was 0–1 in 92% of patients. The primary efficacy outcome was confirmed ORR by IA. Additional efficacy outcome measures included DoR and an IRC-assessed ORR using RECIST version 1.1.[7,8]

ECOG PS=Eastern Cooperative Oncology Group Performance Status; SD=stable disease.

IMPORTANT SAFETY INFORMATION

Myelosuppression

ZEPZELCA can cause myelosuppression. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 or 4 neutropenia occurred in 41% of patients, with a median time to onset of 15 days and a median duration of 7 days. Febrile neutropenia occurred in 7% of patients.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Please see page 7 for Important Safety Information and accompanying full Prescribing Information.

CLINICAL EXPERIENCE: SECOND-LINE TREATMENT FOR SCLC WITH ZEPZELCA® (lurbinectedin)

"The dosing and administration schedule is nice, both in terms of the time it takes to give ZEPZELCA and the minimal infusion visits."

— Jason Porter, MD

Q. What do the safety results from the clinical trial tell you about ZEPZELCA as a monotherapy?

A. In my patients, ZEPZELCA has been generally well tolerated. It's all about selecting the right patient for the therapy. The permanent discontinuation rate in the trial due to an adverse reaction was 1.9%; ARs include peripheral neuropathy and myelosuppression.[7] Twenty-nine percent of patients were on ZEPZELCA for ≥6 months, and 6% were on it for >1 year.[7] There were 11 patients (10.5%) who had an SAE, and in 9 of these it was related to hematological events; all SAEs resolved.[9]

AR=adverse reaction; SAE=serious adverse event.

Q. How do you feel ZEPZELCA fits into the treatment landscape?

A. Looking at the clinical trial data, ZEPZELCA provided efficacy in both platinum-resistant and platinum-sensitive patients.[10] The dosing and administration schedule is nice, both in terms of the time it takes to give ZEPZELCA and the minimal infusion visits. You can tell a patient, "I'm going to give you a treatment every 3 weeks, and you're not going to be in the clinic that long." I had a patient who wanted to go on trips, so 1 day versus 3 to 5 days was important[7]; with the short infusion time, she could finish the treatment and then visit her sister's home in another state.

Please see Important Safety Information below and on the opposite page.

IMPORTANT SAFETY INFORMATION (continued)

Myelosuppression (continued)

Sepsis occurred in 2% of patients and was fatal in 1% (all cases occurred in patients with solid tumors other than SCLC). Grade 3 or 4 thrombocytopenia occurred in 10%, with a median time to onset of 10 days and a median duration of 7 days. Grade 3 or 4 anemia occurred in 17% of patients.

Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm^3 and platelet count of at least 100,000/mm^3.

Monitor blood counts including neutrophil count and platelet count prior to each administration. For neutrophil count less than 500 cells/mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

INDICATION

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Monitor blood counts including neutrophil count and platelet count prior to each administration. For neutrophil count less than 500 cells/mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

Hepatotoxicity

ZEPZELCA can cause hepatotoxicity. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 elevations of ALT and AST were observed in 6% and 3% of patients, respectively, and Grade 4 elevations of ALT and AST were observed in 0.4% and 0.5% of patients, respectively. The median time to onset of Grade ≥3 elevation in transaminases was 8 days (range: 3 to 49), with a median duration of 7 days.

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

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA resulting in skin and soft tissue injury, including necrosis requiring debridement, can occur. 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.

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.

Please see accompanying full Prescribing Information.

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.

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 6 months after the final dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the final dose.

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 final dose.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions, including laboratory abnormalities, (≥20%) are leukopenia (79%), lymphopenia (79%), fatigue (77%), anemia (74%), neutropenia (71%), increased creatinine (69%), increased alanine aminotransferase (66%), increased glucose (52%), thrombocytopenia (37%), nausea (37%), decreased appetite (33%), musculoskeletal pain (33%), decreased albumin (32%), constipation (31%), dyspnea (31%), decreased sodium (31%), increased aspartate aminotransferase (26%), vomiting (22%), decreased magnesium (22%), cough (20%), and diarrhea (20%).

DRUG INTERACTIONS

Strong and Moderate CYP3A Inhibitors

Avoid coadministration with a strong or a moderate CYP3A inhibitor as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration of ZEPZELCA with a moderate CYP3A inhibitor cannot be avoided, consider dose reduction of ZEPZELCA, if clinically indicated.

Strong and Moderate CYP3A Inducers

Avoid coadministration with a strong or moderate CYP3A inducer. Coadministration with a strong CYP3A inducer decreases lurbinectedin systemic exposure which may reduce ZEPZELCA efficacy.

GERIATRIC USE

Of the 105 patients with SCLC administered ZEPZELCA in clinical studies, 37 (35%) patients were 65 years of age and older, while 9 (9%) patients were 75 years of age and older. No overall difference in effectiveness was observed between patients aged 65 and older and younger patients.

There was a higher incidence of serious adverse reactions in patients ≥ 65 years of age than in patients < 65 years of age (49% vs. 26%, respectively). The serious adverse reactions most frequently reported in patients ≥ 65 years of age were related to myelosuppression and consisted of febrile neutropenia (11%), neutropenia (11%), thrombocytopenia (8%), and anemia (8%).

ZEPZELCA® (lurbinectedin) for injection 4 mg

“The most important thing is to be very transparent and let patients know that this is a very aggressive disease, but we will try to control it for as long as possible.”

— Jason Porter, MD

LEARN MORE ABOUT A SECOND-LINE OPTION FOR YOUR PATIENTS WITH RELAPSED SCLC AT

ZEPZELCAPRO.COM

Dr Porter is a leading expert in treating patients with SCLC, both as a physician and researcher.

Jason Porter, MD, is a medical oncologist/hematologist with West Cancer Center and Research Institute and serves as Director of the Lung Cancer Disease Research Group. His specialties are molecularly altered lung cancers and lung cancers with no actionable driver mutation. Dr Porter earned his medical degree at the University of Tennessee Health Science Center, where he also completed his residency in internal medicine. He completed his fellowship at The University of Tennessee Health Science Center/The West Cancer Center in hematology/oncology. Dr Porter has published research on hypertension, advanced lung cancer therapy and side effects, as well as acute leukemia in multiple leading medical journals.

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