SCLC Treatment Landscape

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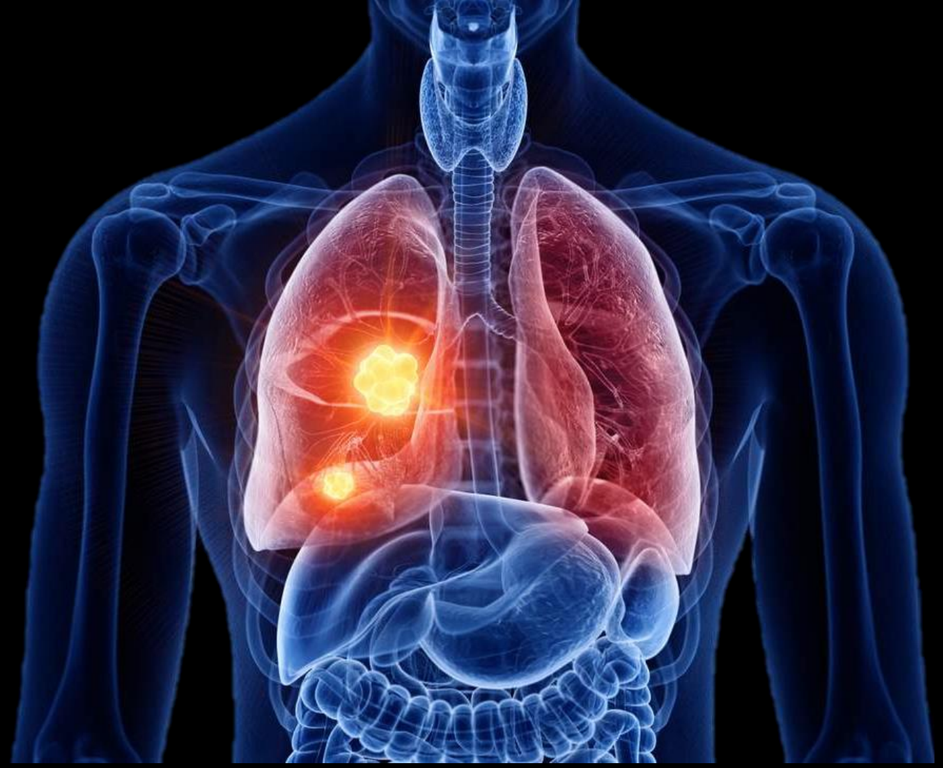
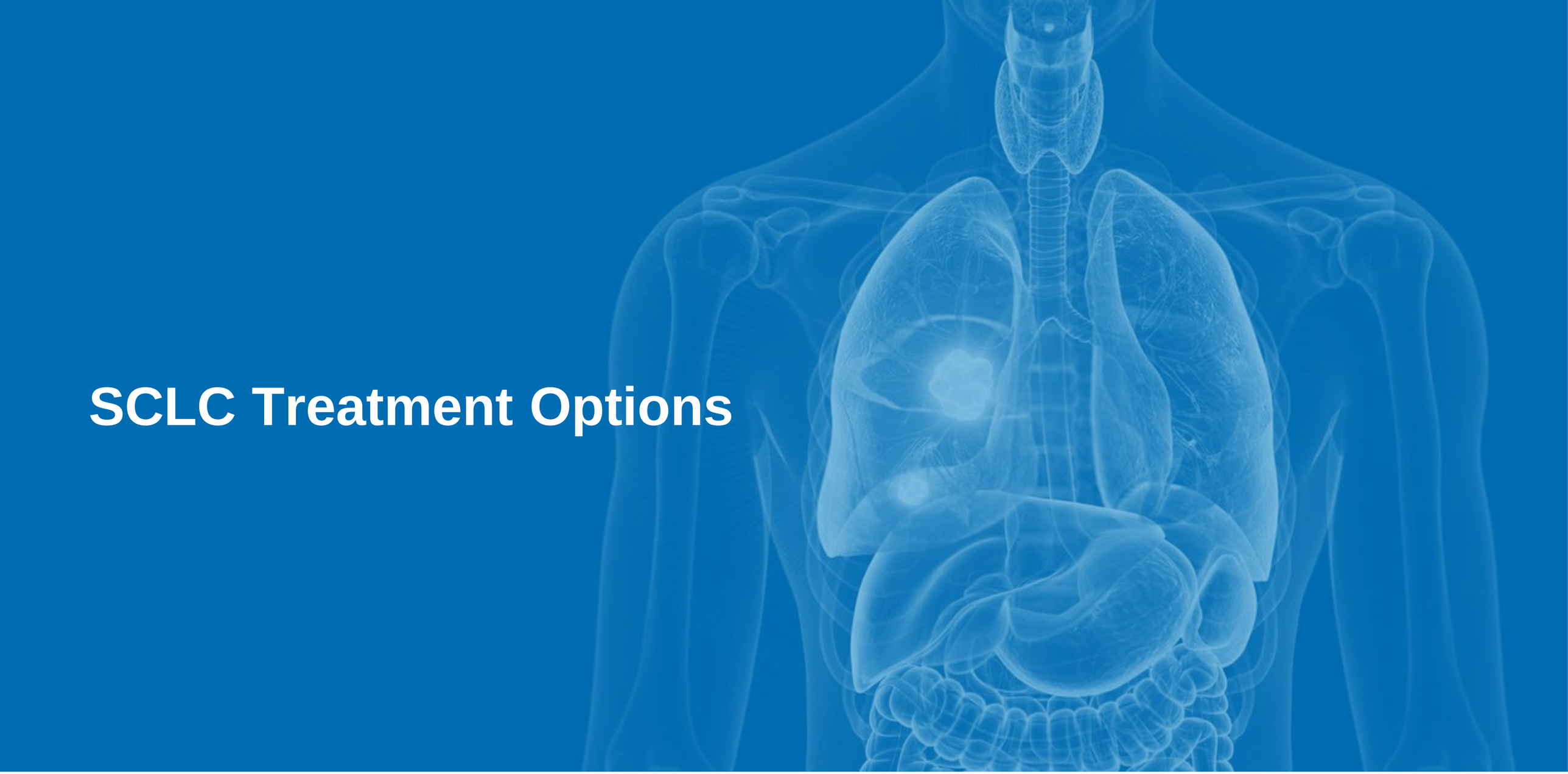


Learning Objectives

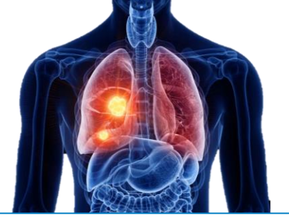
Upon completion of this module, you will be able to:

- ✓ Discuss the roles of surgery and radiation therapy in small cell lung cancer (SCLC)
- ✓ Summarize the mechanisms of action and list the indications of the chemotherapeutic agents used in SCLC
- ✓ Summarize the mechanisms of action and list the immunotherapies used in SCLC
- ✓ Summarize the National Comprehensive Cancer Network (NCCN) guidelines regarding the use of systemic therapy in patients with SCLC

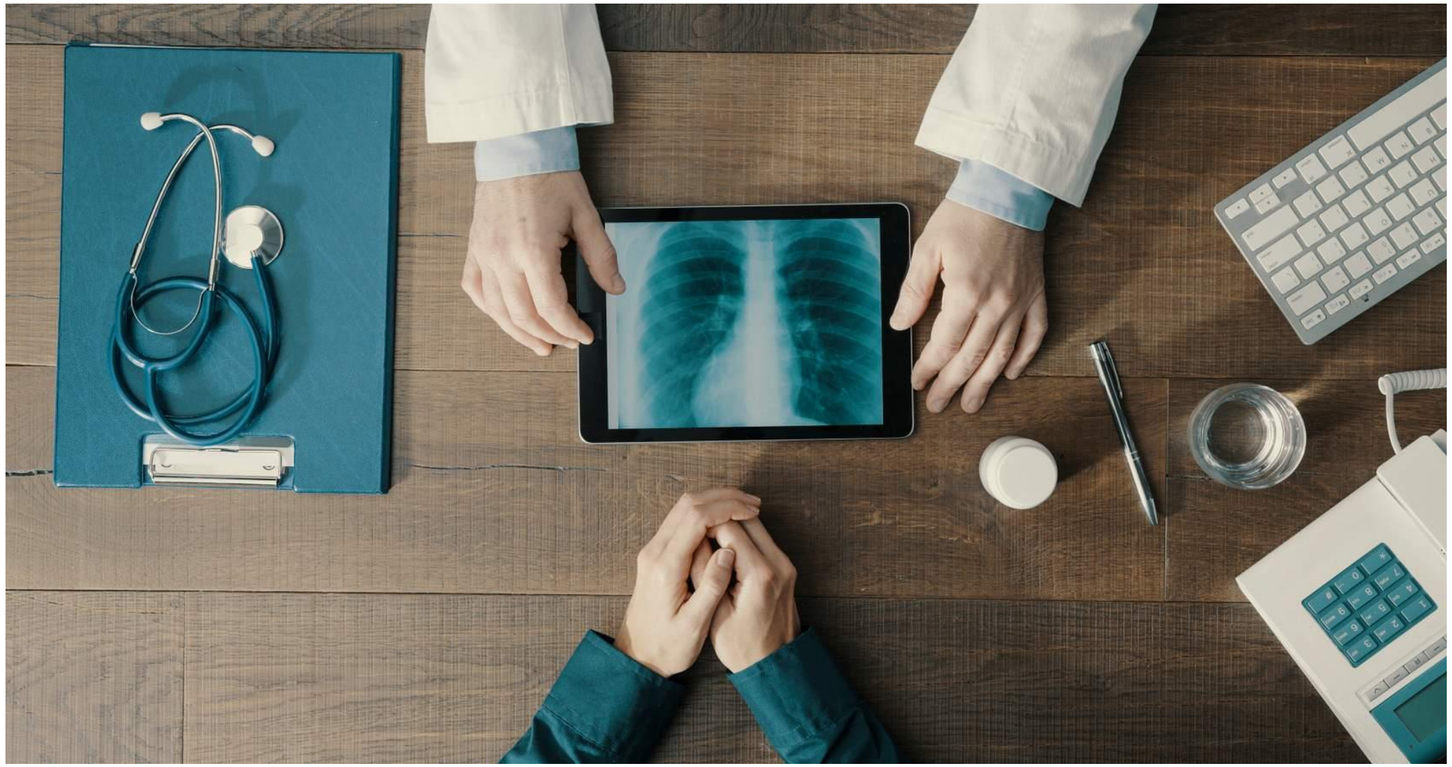
SCLC Treatment Options



SCLC Treatment Options

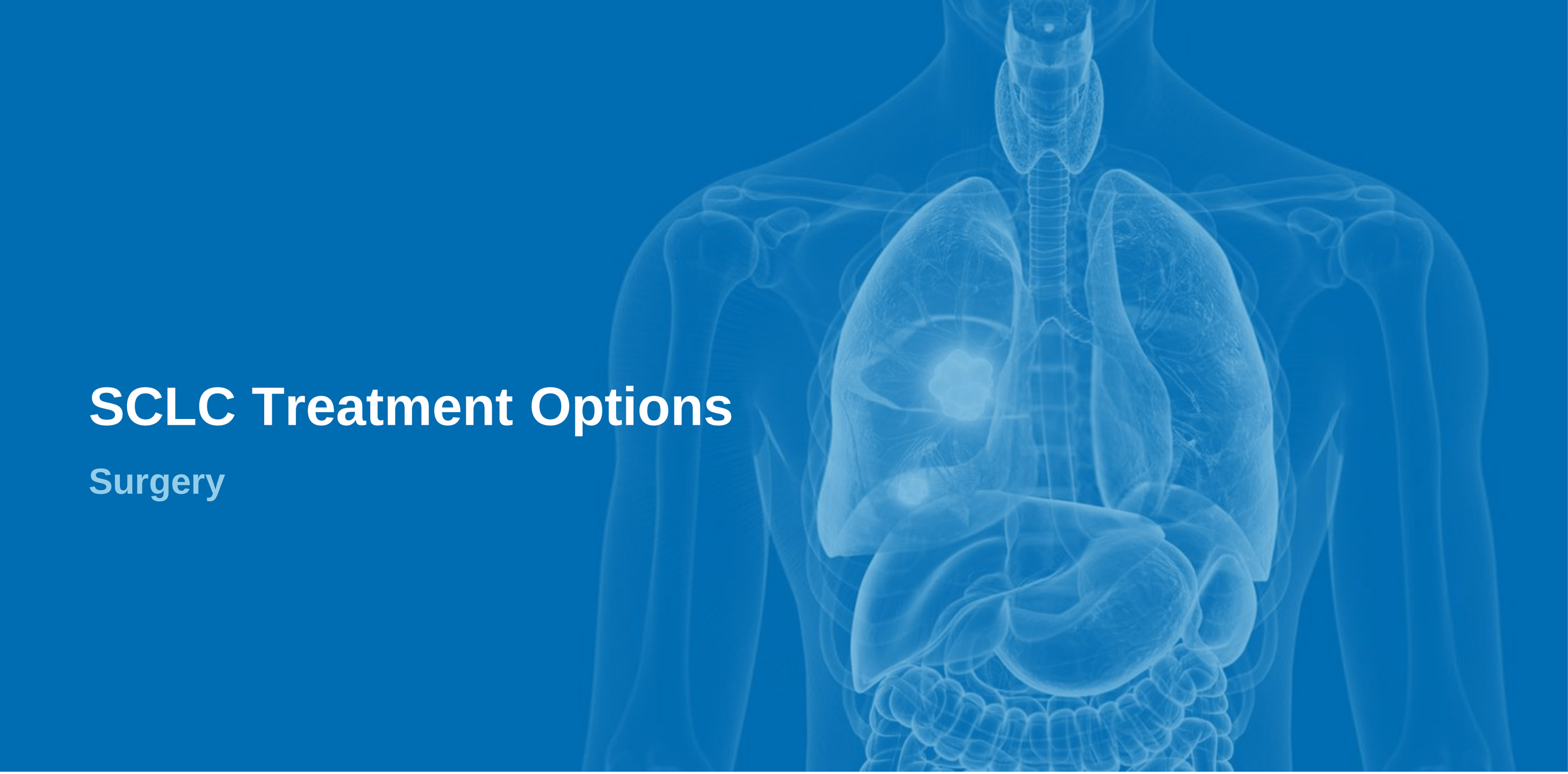


- Surgery
- Radiation therapy
- Systemic therapy



SCLC Treatment Options

Surgery



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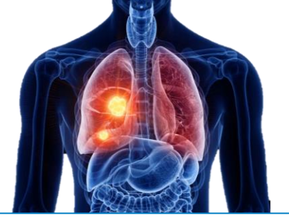
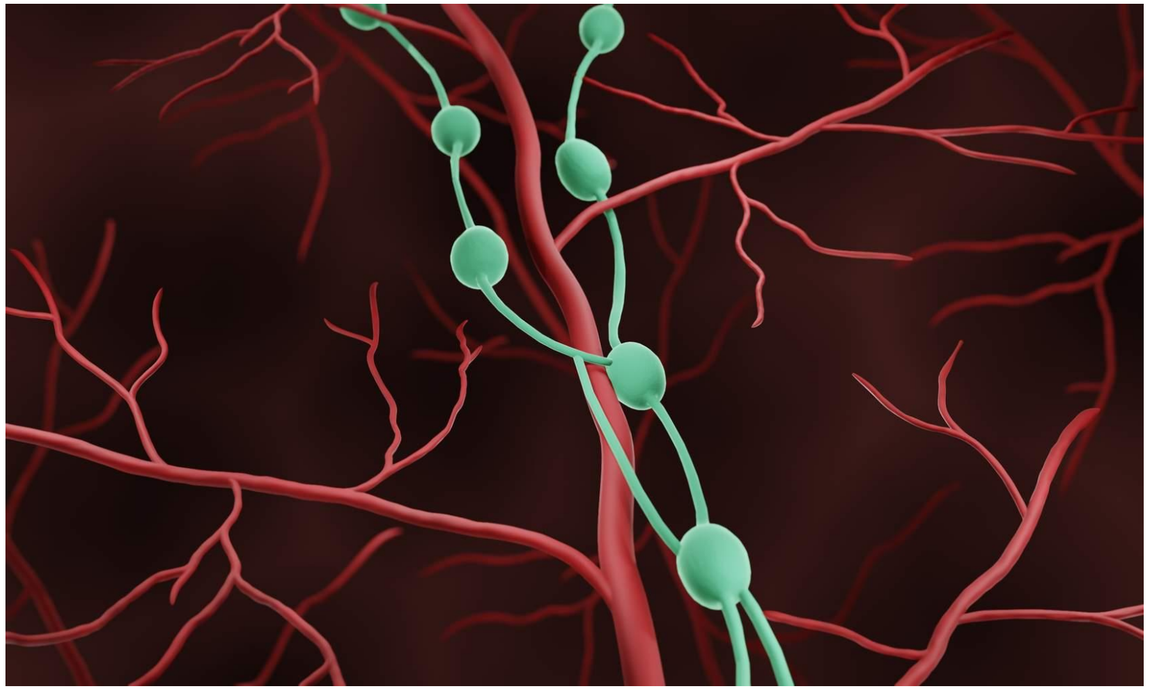
Surgery

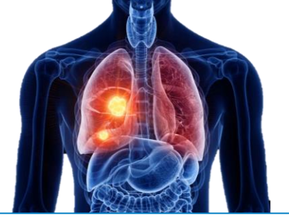




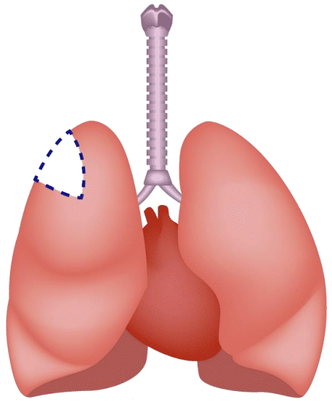
Overview

- Surgery is generally reserved for individuals with limited-stage SCLC (LS-SCLC), ie, clinical stage I-IIA disease[1]
  - This represents only 5% of SCLC patients[1]
- Surgery may also be considered in select patients with T3, N0 SCLC[1]
- During surgery, lymph nodes close to SCLC tumors will also be removed to test if they contain cancer cells and determine if cancer has spread[2]
- Following surgery, patients are usually given adjuvant therapy to rid the body of any remaining cancer cells[1,3]
  - Adjuvant therapy may consist of radiation therapy, systemic therapy, or both[1,3]

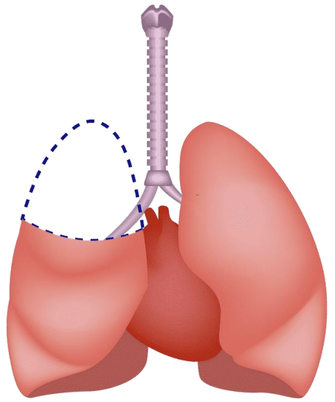
Surgical procedures used in patients with SCLC[2]



Removal of a small wedge of a lung



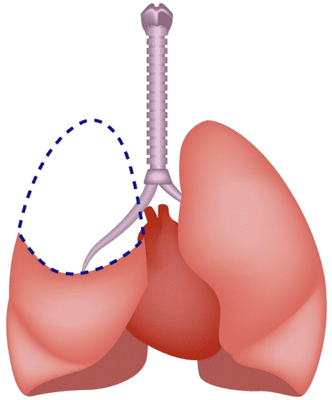
Wedge Resection



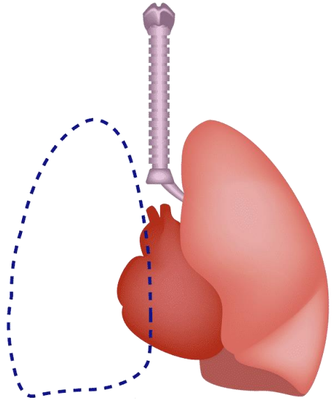
Segmentectomy

Removal of a larger segment of a lung

Removal of an entire lobe of a lung



Lobectomy



Pneumonectomy

Removal of an entire lung

SCLC Treatment Options

Radiation Therapy

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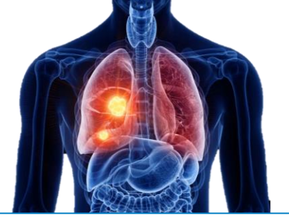
Radiation therapy



- Radiation therapy involves the use of high-energy radiation to shrink and kill cancerous tumors[3]
- For patients with SCLC, radiation therapy may be given at any disease stage[1]
- Radiation therapy is usually given in conjunction with systemic therapy, most commonly chemotherapy—this is called chemoradiation[4]

Fast Fact

Compared with other types of lung cancer, SCLC is more responsive to radiation therapy. Nevertheless, a cure is difficult to achieve since SCLC tends to be widely disseminated in the body at the time of diagnosis.[5]

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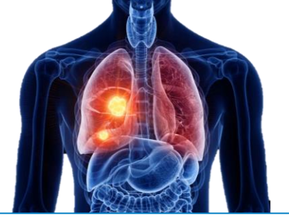
Thoracic radiation



- Most common type given to patients with SCLC: external-beam radiation therapy (EBRT)[4]
  - Involves delivery of radiation beams from a source located outside of the body[4]
- Accurate determination of the radiation target is required to maximize tumor control and minimize toxicities[4]
  - Achieved with 3-dimensional conformal radiation therapy (3D-CRT), which uses computers to precisely map tumors[4]

Timing of thoracic radiation

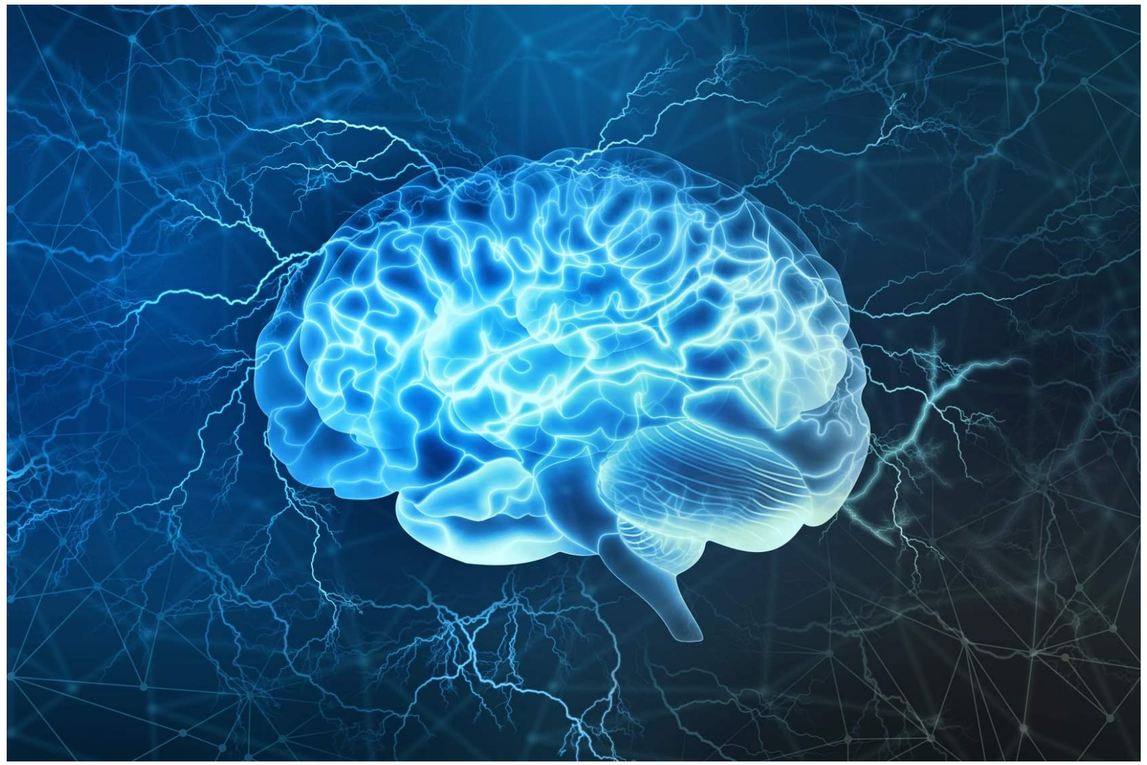
LS-SCLC

- Thoracic radiation given as the standard of care in conjunction with chemotherapy[1]

ES-SCLC

- Thoracic radiation reserved for patients who have responded to first-line systemic therapy[1]

Cranial radiation



- Prophylactic cranial radiation (PCI): Radiation given to the brain in some patients with SCLC to reduce the risk of cancer spread to the brain[1]
- PCI more commonly given to patients with LS-SCLC than to patients with ES-SCLC[4]
- The use of PCI in SCLC is associated with a risk of neurotoxicity, particularly in patients above the age of 60 years[1]

SCLC Treatment Options

Systemic Therapy

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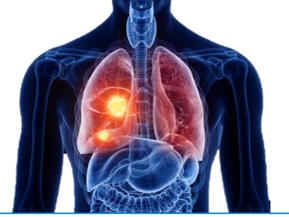
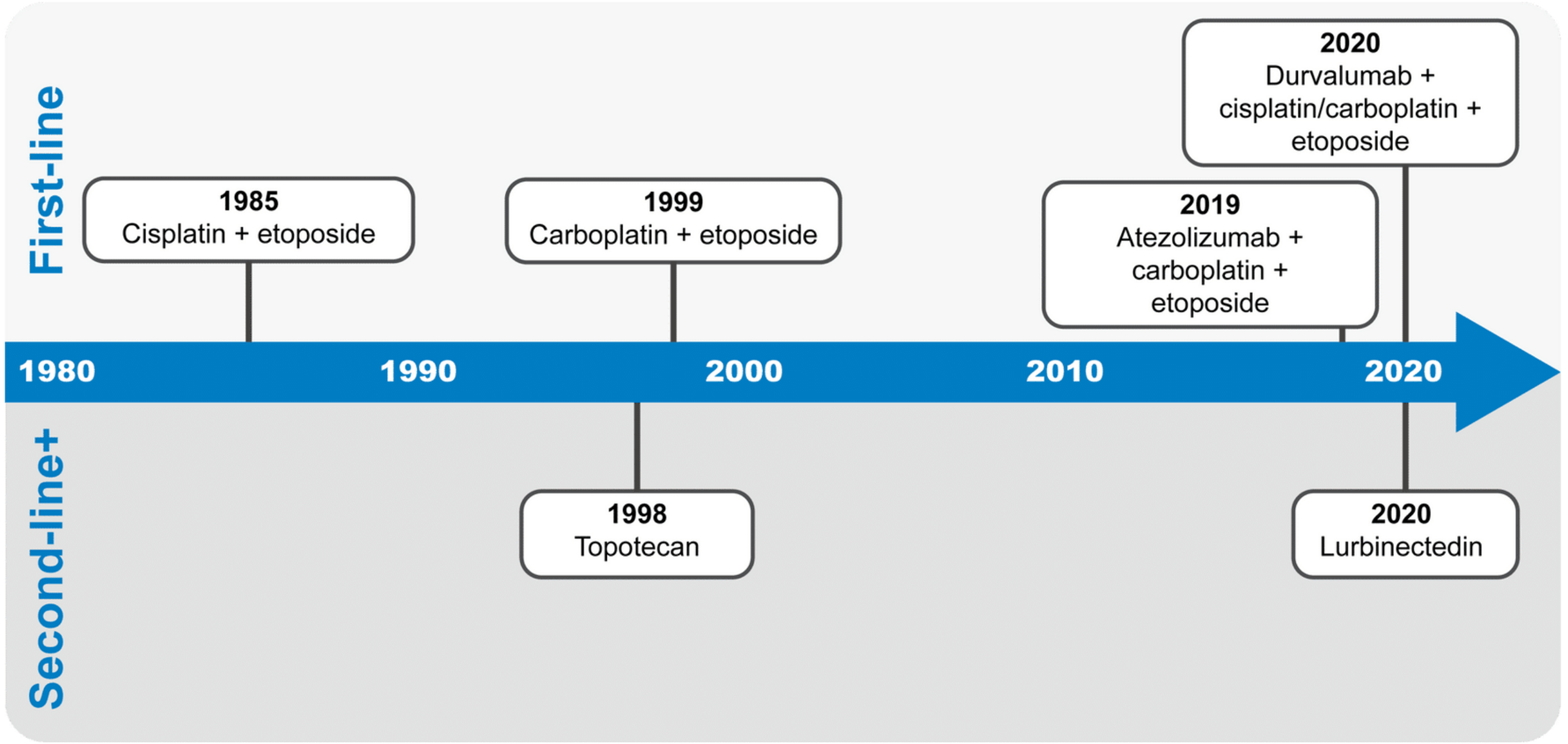
Overview of systemic therapy



- Systemic therapy consists of the administration of medications through the bloodstream, enabling them to reach cells throughout the body[3]
- As shown in the timeline, limited advances have been made in the SCLC treatment landscape over the past few decades[7-12]



SCLC Treatment Options

Systemic Therapy: Chemotherapy

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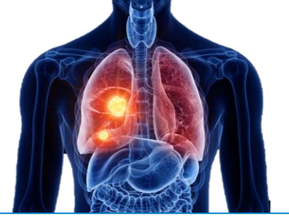
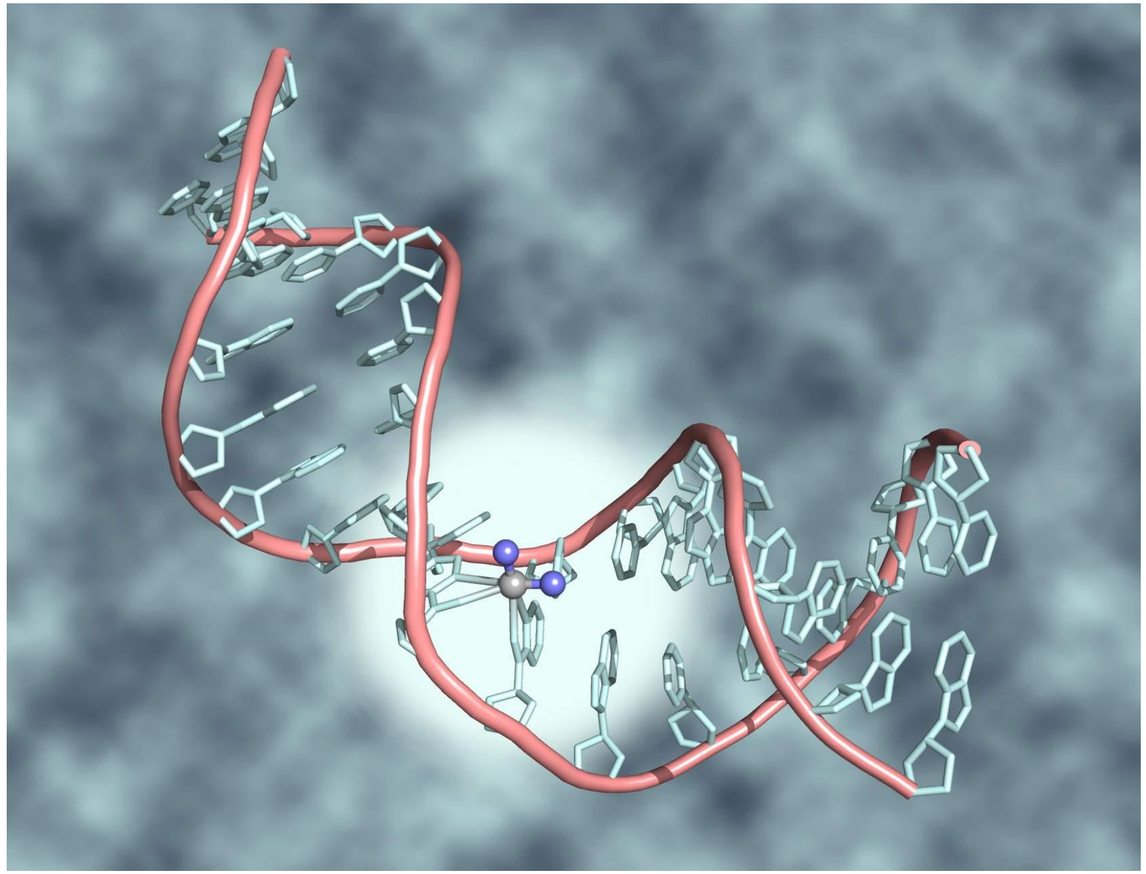
Chemotherapy



- Chemotherapy involves the administration of medications that stop cancer cell growth, either by killing the cancer cells or by preventing them from proliferating[3]

- Major classes of chemotherapeutic agents used in SCLC:
  - Platinum agents
  - Topoisomerase inhibitors
  - Alkylating agents



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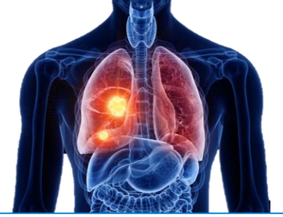
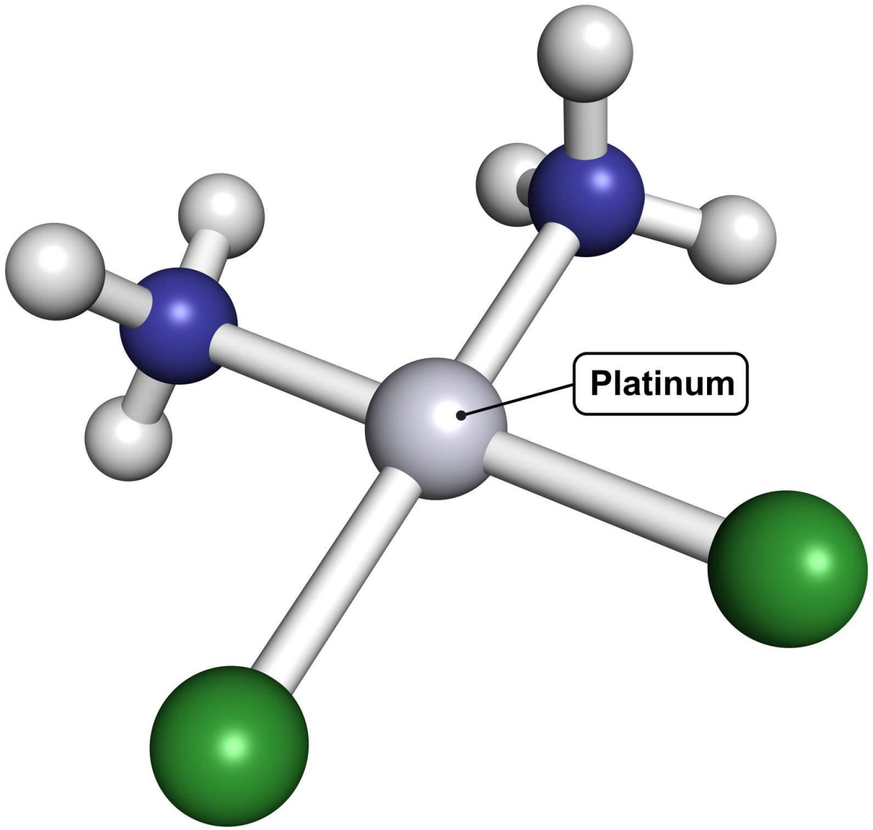
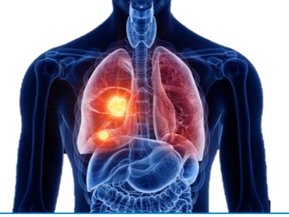
Platinum agents





- Platinum agents derive their name from the platinum atom they contain[13,14]
- Platinum agents form complexes called cross-links with DNA, which inhibit cell growth and lead to apoptosis (programmed cell death)[14,15]
- Platinum agent-based regimens have been used for the treatment of SCLC since 1985[8]
  - They are considered standards of care for first-line treatment of both LS-SCLC and ES-SCLC[8]

Cisplatin (Platinol®)



OVERVIEW

- Cisplatin was first used for the treatment of SCLC in 1985, in combination with etoposide[8]

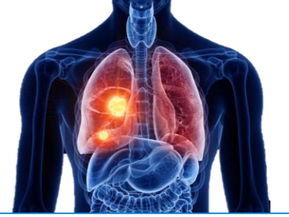
- The FDA-approved indication for cisplatin in SCLC is included in the etoposide prescribing information (PI) but not in the cisplatin PI[11]

INDICATIONS

Cisplatin is FDA-approved for the treatment of:[13]

- Metastatic testicular tumors
- Metastatic ovarian tumors
- Advanced bladder cancer

Cisplatin (continued)



BOXED WARNING[13,16]

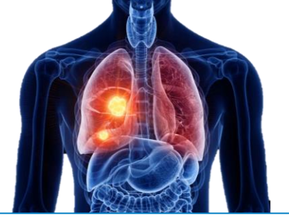
The cisplatin PI includes a boxed warning about:

- Renal toxicity
- Ototoxicity (damage to the ears)
- Anaphylactic-like reactions

COMMONLY REPORTED ADVERSE REACTIONS[13,16]

- Renal toxicity
- Ototoxicity
- Myelosuppression
- Gastrointestinal (GI) toxicity, including nausea, vomiting, and diarrhea
- Cardiovascular toxicities
- Serum electrolyte disturbances
- Hyperuricemia
- Neurotoxicity
- Ocular toxicity (damage to the eyes)
- Anaphylactic-like reactions
- Hepatotoxicity (damage to the liver)

Carboplatin (Paraplatin®)



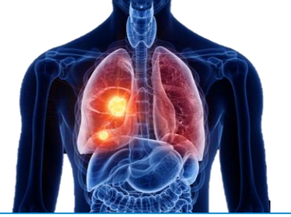
INDICATIONS[14]

- Carboplatin is FDA-approved for first- and second-line treatment of ovarian cancer

OVERVIEW

- Carboplatin is a platinum agent that has been used to treat patients with SCLC since 1999, also in combination with etoposide[8]
- Although carboplatin + etoposide regimens are not specifically included in either of the agent's PIs, older versions of the etoposide PI state that it may be used in combination with "other approved chemotherapeutic agents"[17]
- Clinicians often substitute carboplatin for cisplatin due to concerns about vomiting, neurotoxicity, and renal toxicity[1]
  - However, carboplatin is associated with a higher risk of myelosuppression[1]

Carboplatin (continued)



BOXED WARNINGS[14]

- The carboplatin PI includes a boxed warning about myelosuppression and anaphylactic-like reactions

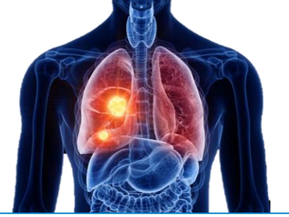
Did you know?[1,14]

- Carboplatin is dosed in a unique way; dosing is calculated according to 2 parameters:
  (1) how well a patient's kidneys are functioning, measured in terms of the glomerular filtration rate (GFR), and
  (2) the desired amount of carboplatin that the body is exposed to (target exposure), represented by the area under the curve (AUC)
- A target exposure that corresponds to an AUC of 4-6 mg/mL·min is generally considered an appropriate dose range for most cancer patients
- Carboplatin doses are expressed as AUC values, without the units (eg, AUC 5)

COMMONLY REPORTED ADVERSE REACTIONS[14]

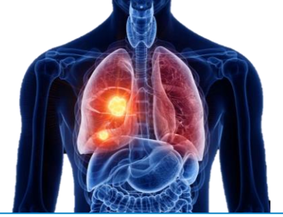
- Myelosuppression
- GI toxicity, notably nausea and vomiting
- Neurotoxicity, particularly peripheral neuropathy
- Renal toxicity
- Hepatotoxicity
- Electrolyte changes
- Allergic reactions
- Injection site reactions

Topoisomerases



- During normal cell functioning, DNA strands can become very tightly wound[18]
- Enzymes called topoisomerases make small cuts, or nicks, in the DNA strands to relieve that tension[18]
- The topoisomerases then reseal the nicks to restore normal DNA structure[18]
- By inhibiting topoisomerase activity, topoisomerase inhibitors induce breaks in the DNA structure, ultimately inhibiting cell proliferation and causing cell death[11]
- Human cells have 2 types of topoisomerases:[19]
  - Type I topoisomerases bind to double-stranded DNA and create a nick in one of the strands
  - Type II topoisomerases bind to double-stranded DNA and cleave both strands

Irinotecan (Camptosar®)



OVERVIEW

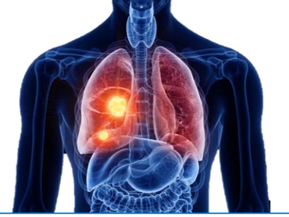
- Irinotecan is a topoisomerase I inhibitor that has been used for patients with relapsed or refractory SCLC since 1992[18]

- Note that irinotecan is not approved by the FDA for SCLC[8]

INDICATION[18]

- Irinotecan is FDA-approved for the treatment of metastatic colorectal cancer

Irinotecan (continued)



BOXED WARNING[18]

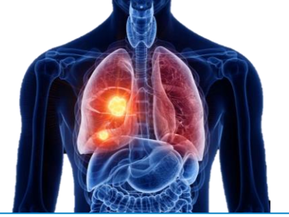
- The irinotecan PI includes a boxed warning about diarrhea and myelosuppression

COMMONLY REPORTED ADVERSE REACTIONS

Common adverse reactions observed in ≥30% of patients treated with irinotecan monotherapy include:[18]

- Nausea
- Vomiting
- Abdominal pain
- Diarrhea
- Constipation
- Anorexia
- Neutropenia
- Leukopenia
- Anemia
- Asthenia
- Fever
- Decreased body weight
- Alopecia

Topotecan (Hycamtin®)



OVERVIEW

- Topotecan is a topoisomerase I inhibitor that is available in 2 formulations:,
  - Topotecan for intravenous (IV) infusion, FDA-approved for the treatment of SCLC in 1998[7,20]
  - Oral formulation of topotecan, approved for SCLC in 2007[21,22]

INDICATIONS

- The IV formulation of topotecan is indicated as a single agent for the treatment of patients with SCLC with platinum-sensitive disease who progressed at least 60 days after initiation of first-line chemotherapy[20]
  - It is also approved for use in ovarian cancer and cervical cancer[20]
- The oral formulation of topotecan is indicated for the treatment of relapsed SCLC in patients with a prior complete or partial response, and who are at least 45 days from the end of first-line chemotherapy[22]

Fast Fact

Topotecan was the first agent to be approved by the FDA for second-line treatment of ES-SCLC, and was the only agent indicated in this setting until 2020.[8,9]

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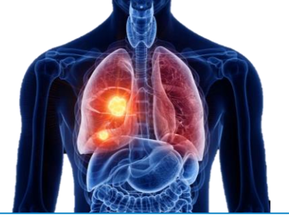
Topotecan (continued)



BOXED WARNING[20,22]

- Both the IV and oral topotecan PIs have a boxed warning about myelosuppression

COMMON ADVERSE REACTIONS—IV FORMULATION

Common Grade 3-4 hematologic adverse reactions observed in >5% of patients treated with IV topotecan include:[20]

- Neutropenia
- Anemia
- Thrombocytopenia
- Febrile neutropenia

Common all-grade adverse reactions observed in >5% of patients treated with IV topotecan include:[20]

- Asthenia
- Dyspnea
- Nausea
- Pneumonia
- Abdominal pain
- Fatigue

COMMON ADVERSE REACTIONS—ORAL FORMULATION

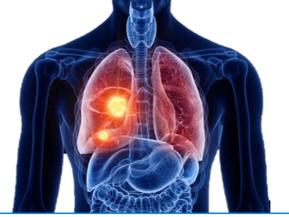
Common Grade 3-4 hematologic adverse reactions observed in >20% of patients treated with oral topotecan include:[22]

- Neutropenia
- Anemia
- Thrombocytopenia

Common all-grade adverse reactions observed in >10% of patients treated with oral topotecan include:[22]

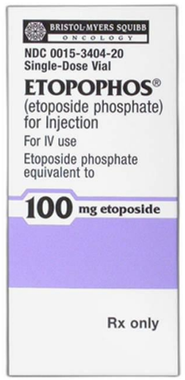
- Nausea
- Diarrhea
- Vomiting
- Alopecia
- Fatigue
- Anorexia

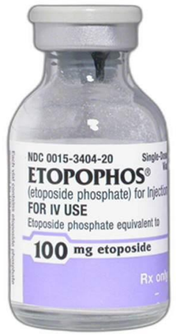
Etoposide (Etopophos®, VePesid®)

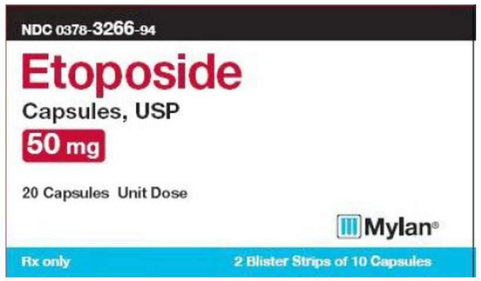


OVERVIEW

- The topoisomerase II inhibitor etoposide has been used for the treatment of SCLC in combination with other agents since 1985[8,17]
- Two formulations of etoposide are available:
  - IV formulation approved in the 1990s under the brand name Etopophos[11]
  - Oral formulation approved in 2001 under the brand name VePesid, although currently it is only available as a generic agent in the United States[23]



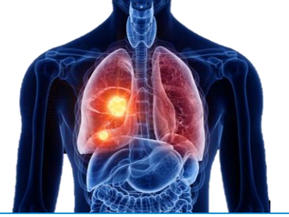




INDICATIONS

- Etoposide is indicated in combination with cisplatin as first-line treatment in patients with SCLC[11]
  - Note that older versions of the etoposide PI, as well as the oral etoposide PI, state that etoposide is indicated in combination with other approved chemotherapeutic agents as first-line treatment in patients with SCLC[17,24]
- The IV formulation of etoposide is also indicated for the treatment of testicular tumors[17]

Etoposide (continued)



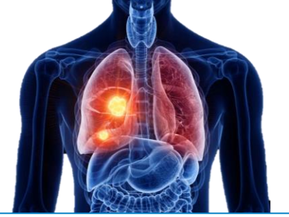
BOXED WARNING [17,24]

- Both the IV and oral etoposide PIs include a boxed warning about myelosuppression

NOTABLE ADVERSE REACTIONS[16,17,24]

- Myelosuppression
- GI toxicity, including nausea and vomiting
- Blood pressure increases (hypertension; IV formulation only) and decreases (hypotension; both formulations)
- Allergic reactions, including anaphylactic-like reactions and rash, urticaria (hives), and pruritus (itching)
- Alopecia

Alkylating agents: Lurbinectedin (Zepzelca®)



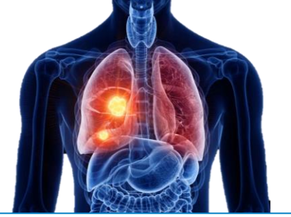
OVERVIEW OF ALKYLATING AGENTS

- Alkylating agents directly bind to DNA and introduce a chemical group called an alkyl group[9]
  - This triggers a series of cellular events, eventually leading to inhibition of cell group and subsequent cell death[16]
- Lurbinectedin is an alkylating agent that was initially approved by the FDA in 2020[9]

INDICATION[9]

- Lurbinectedin is indicated for the treatment of adult patients with metastatic 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 confirmatory trial(s)

Lurbinectedin (continued)



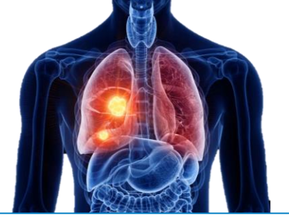
MOST COMMON (≥20%) ADVERSE REACTIONS[9]

- Leukopenia
- Lymphopenia
- Fatigue
- Anemia
- Neutropenia
- Increased creatinine
- Increased alanine aminotransferase (ALT)
- Increased glucose
- Thrombocytopenia
- Nausea
- Decreased appetite
- Musculoskeletal pain
- Decreased albumin
- Constipation
- Dyspnea
- Decreased sodium
- Increased aspartate aminotransferase (AST)
- Vomiting
- Cough
- Decreased magnesium levels
- Diarrhea

Did you know?

Lurbinectedin was initially approved through the FDA's Accelerated Approval program. This program enables approval of agents via surrogate endpoints, which are thought to indicate clinical benefit but are not actual measures of clinical benefit. Accelerated Approval can result in a shorter time to approval compared to traditional approval. However, the sponsor must conduct a follow-up study to confirm that the agent does indeed provide clinical benefit. If confirmatory trials demonstrate clinical benefit, the FDA grants traditional approval. The confirmatory trial for lurbinectedin failed to meet its primary endpoint. However, although the FDA usually rescinds approvals in such situations, it did not do so for lurbinectedin—it remains under accelerated approval status.[1,25,26]

Additional chemotherapy agents



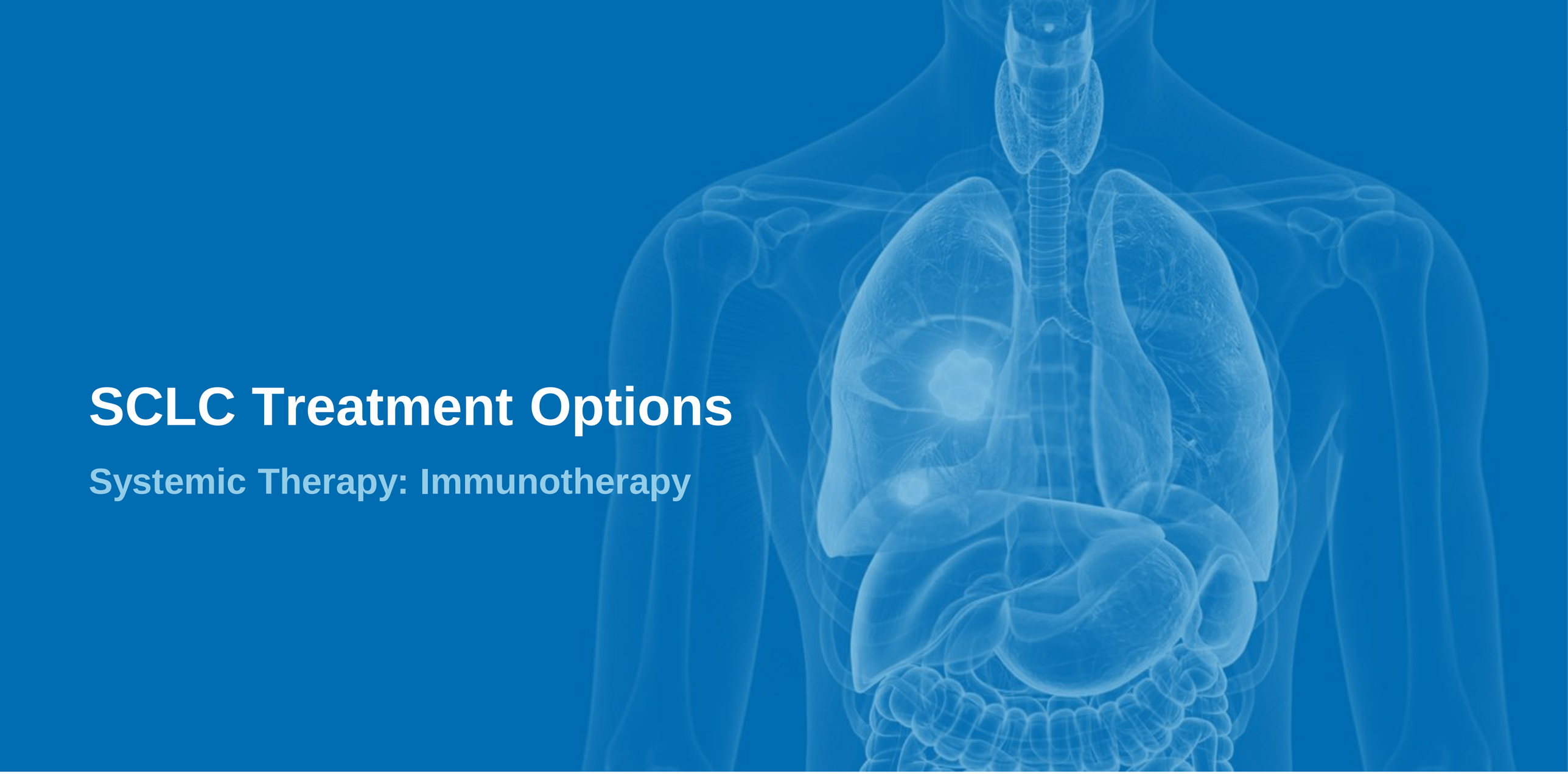
Additional chemotherapy agents that may be used in the treatment of relapsed or refractory SCLC[a]

Agent	Class	Indication(s)
Bendamustine (Bendeka®)[15,27]	Alkylating agent	Chronic lymphocytic leukemia (CLL), non-Hodgkin lymphoma (NHL)
Cyclophosphamide[15,28]	Alkylating agent	Lymphomas (NHL, Hodgkin lymphoma [HL]), multiple myeloma, leukemia (CLL, chronic granulocytic leukemia, acute myelogenous/monocytic leukemia [AML], acute lymphoblastic leukemia [ALL]), mycosis fungoides, neuroblastoma, ovarian cancer, retinoblastoma, breast cancer
Docetaxel (Taxotere®)[29]	Antimicrotubule agent	Breast cancer, NSCLC, prostate cancer, gastric cancer, head and neck cancer
Doxorubicin[15,30]	Topoisomerase II inhibitor	Breast cancer, leukemia (ALL, AML), lymphoma (NHL, HL), Wilms' tumor, neuroblastoma, soft tissue sarcoma, bone sarcoma, ovarian cancer, transitional cell bladder cancer, thyroid cancer, gastric cancer, bronchogenic carcinoma
Gemcitabine (Gemzar®)[15,31]	Nucleoside analog	Ovarian cancer, breast cancer, NSCLC, pancreatic cancer
Paclitaxel (Taxol®)[32]	Antimicrotubule agent	Ovarian cancer, breast cancer, NSCLC, AIDS-related Kaposi sarcoma
Temozolomide (Temodar®)[33]	Alkylating agent	Anaplastic astrocytoma, glioblastoma
Vincristine[34]	Antimicrotubule agent	Acute leukemia
Vinorelbine (Navelbine®)[35]	Antimicrotubule agent	NSCLC

[a]None of these agents are FDA-approved for SCLC; however, they are included as subsequent systemic therapy options in the NCCN guidelines[1]

SCLC Treatment Options

Systemic Therapy: Immunotherapy



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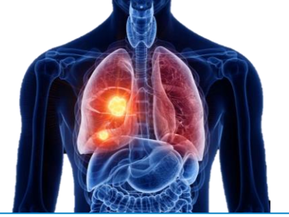
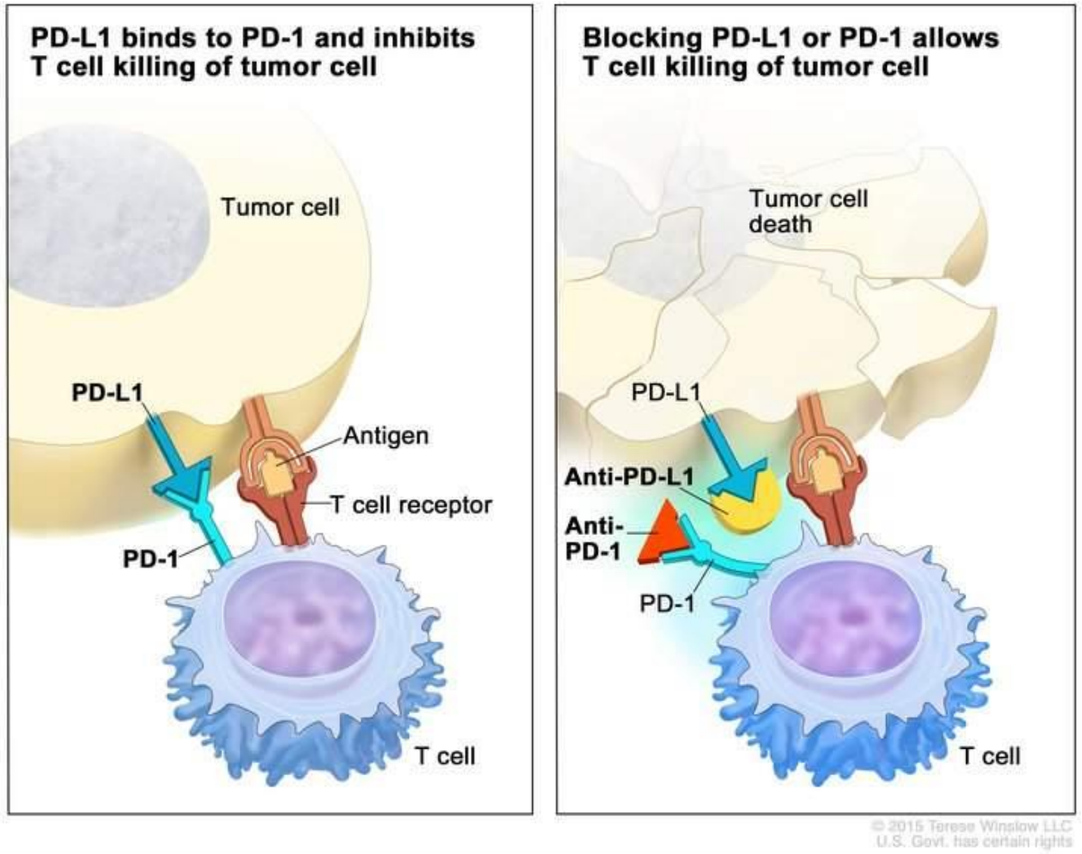
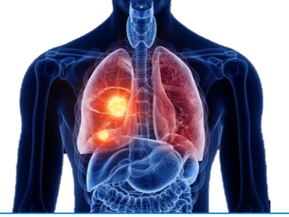
Overview of immunotherapy[1]



- Immunotherapy involves the use of medications that stimulate the immune system to help the body fight cancer[3]
- The type of immunotherapies used in SCLC are called checkpoint inhibitors[36]
- Immune checkpoints are normally used by the body to regulate the intensity of immune responses[37]
  - Cancers take advantage of a key checkpoint, which involves the molecules PD-1 and PD-L1, using it to suppress immune responses directed against tumor cells[37]
  - Checkpoint inhibitors, specifically anti–PD-1 and anti–PD-L1 agents, block the interactions between PD-L1 on tumor cells and PD-1 on T cells, thereby restoring the body's ability to launch an anti-tumor immune response and kill tumor cells[37]



Atezolizumab (Tecentriq®)



OVERVIEW

- Atezolizumab is a monoclonal antibody (mAb) directed against PD-L1[38]
- It was approved by the FDA for the treatment of ES-SCLC in March 2019[10]

INDICATIONS

- Atezolizumab, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with ES-SCLC[38]
- Atezolizumab is also indicated for the treatment of urothelial carcinoma, NSCLC, hepatocellular carcinoma, and melanoma[38]

MOST COMMON ADVERSE REACTIONS (≥20% OF PATIENTS)[38,a]

- Fatigue/asthenia
- Nausea
- Alopecia
- Constipation
- Diarrhea
- Decreased appetite

[a]In patients with lung cancer who received atezolizumab in combination with other agents

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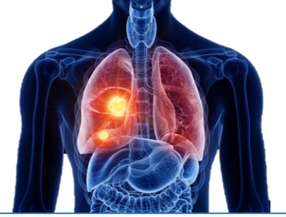
Durvalumab (Imfinzi®)



OVERVIEW

- Durvalumab is an mAb directed against PD-L1[37]
- It was approved by the FDA for the treatment of ES-SCLC in March 2020[12]

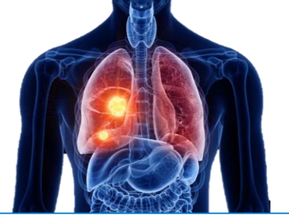
INDICATIONS[37]

- Durvalumab, in combination with etoposide and either carboplatin or cisplatin, is indicated for the first-line treatment of adult patients with ES-SCLC
- Durvalumab is also indicated for the treatment of NSCLC and biliary tract cancers

MOST COMMON ADVERSE REACTIONS (≥20% OF PATIENTS)[37]

- Nausea
- Fatigue/asthenia
- Alopecia

Additional immunotherapy agents



Additional immunotherapy agents that may be used in the treatment of relapsed or refractory SCLC[a]

Agent	Description	Indications
Nivolumab (Opdivo®)	mAb directed against PD-1	Melanoma, NSCLC, mesothelioma, renal cell carcinoma, HL, head and neck cancer, urothelial cancer, microsatellite instability (MSI)-high or mismatch repair deficient (MMR) colorectal cancer, hepatocellular carcinoma, esophageal cancer, gastric cancer, gastroesophageal junction cancer, esophageal cancer[39]
Pembrolizumab (Keytruda®)	mAb directed against PD-1	Melanoma, NSCLC, head and neck cancer, HL, mediastinal large B-cell lymphoma, urothelial cancer, MSI-high or MMR cancer, MSI-high or MMR colorectal cancer, gastric cancer, esophageal cancer, cervical cancer, hepatocellular carcinoma, Merkel cell cancer, renal cell carcinoma, endometrial cancer, tumor mutational burden (TMB)-high cancer, cutaneous squamous cell carcinoma, triple-negative breast cancer[40]

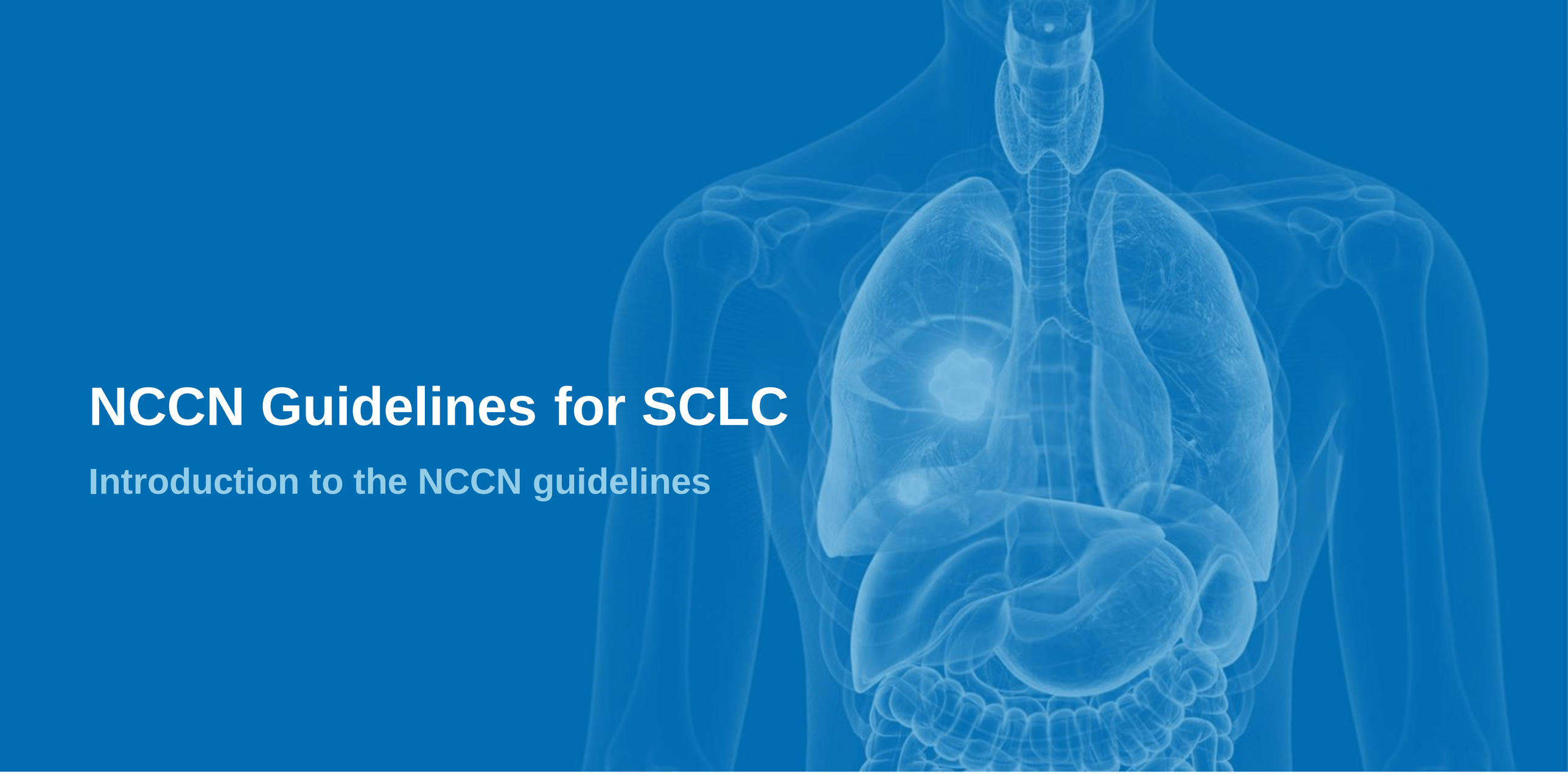
Fast Fact

Both nivolumab and pembrolizumab were at one time FDA-approved for third-line treatment of SCLC, through the FDA's accelerated approval process. However, the SCLC indications for both agents were withdrawn in 2021, based on the failure of convincing confirmatory trials.[41]

[a]Neither of these agents are FDA-approved for SCLC; however, they are included as subsequent systemic therapy options in the NCCN guidelines[1]

NCCN Guidelines for SCLC

Introduction to the NCCN guidelines



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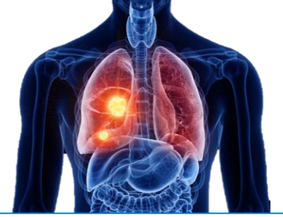
NCCN guidelines

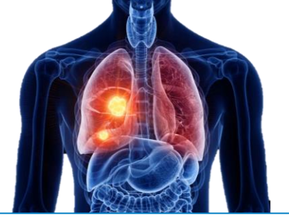


- The purpose of the NCCN guidelines is to provide insight on optimal treatment strategies for complex, fatal diseases; NCCN guidelines are considered a guiding authority in this regard[42]

- NCCN recommendations are based on robust, scientific evidence and/or clinical expertise that is beyond FDA-approved indications; this is often referred to as off-label use, which is the use of an approved drug for an indication that is not supported by the product label[42]

- In the treatment of complex and fatal cancers in the United States, off-label use of drugs is common. The reason is multifaceted, but generally based on the fact that FDA-approved indications are narrowly defined, high-quality data are rapidly evolving, and there is a high need to provide effective treatments to patients with fatal diseases who otherwise might not have access[42]

NCCN recommendation categories



NCCN CATEGORIES OF EVIDENCE AND CONSENSUS[1]

Category	Description
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate
Category 2C	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Note that all recommendations are category 2A unless otherwise indicated.

NCCN CATEGORIES OF PREFERENCE[1]

Category	Description
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes
Useful in certain circumstances	Other interventions that may be used for selected patient populations (defined with recommendation)

Note that the NCCN considers all their listed recommendations to be appropriate.

NCCN Guidelines for SCLC

LS-SCLC

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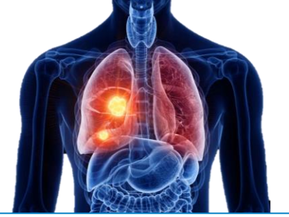
NCCN-recommended primary or adjuvant therapy regiments for LS-SCLC[1]



- All recommended regimens are doublets consisting of a platinum agent and etoposide
- The guidelines recommend four treatment cycles, each 21 to 28 days in length
- In this setting, systemic therapy is given concurrently with radiation therapy

NCCN-PREFERRED REGIMENS FOR LS-SCLC

- Cisplatin 75 mg/m^2 day 1 and etoposide 100 mg/m^2 days 1, 2, 3 (category 2A)
- Cisplatin 60 mg/m^2 day 1 and etoposide 120 mg/m^2 days 1, 2, 3 (category 2A)

OTHER NCCN-RECOMMENDED REGIMENS

- Cisplatin 25 mg/m^2 days 1, 2, 3 and etoposide 100 mg/m^2 days 1, 2, 3 (category 2A)
- Carboplatin AUC 5–6 day 1 and etoposide 100 mg/m^2 days 1, 2, 3 (if cisplatin is contraindicated or not tolerated; category 2A)

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NCCN Guidelines for SCLC

ES-SCLC

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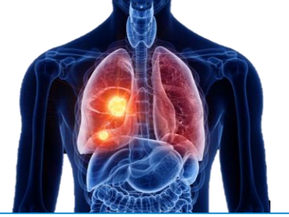
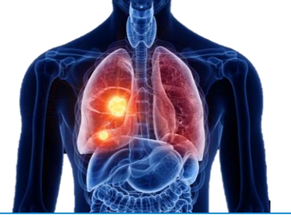
Primary therapy regimens: overview[1]



- All NCCN-recommended primary therapy regimens are platinum-based doublets or triplets
- For these regimens, the guidelines recommend four treatment cycles, although some patients may receive up to 6 cycles based on response and tolerability after the first four cycles

NCCN-preferred regimens for primary treatment of ES-SCLC[1]



Note these are all FDA-approved regimens:

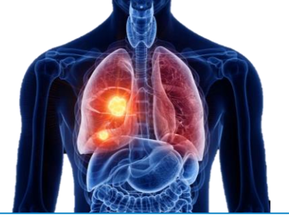
- Carboplatin AUC 5 day 1 and etoposide 100 mg/m^2 days 1, 2, 3 and atezolizumab 1200 mg day 1 every 21 days x 4 cycles followed by maintenance atezolizumab 1200 mg day 1, every 21 days (category 1)[a]
- Carboplatin AUC 5–6 day 1 and etoposide 80–100 mg/m^2 days 1, 2, 3 and durvalumab 1500 mg day 1 every 21 days x 4 cycles followed by maintenance durvalumab 1500 mg day 1 every 28 days (category 1)[a]
- Cisplatin 75–80 mg/m^2 day 1 and etoposide 80–100 mg/m^2 days 1, 2, 3 and durvalumab 1500 mg day 1 every 21 days x 4 cycles followed by maintenance durvalumab 1500 mg day 1 every 28 days (category 1)[a]
- Carboplatin AUC 5 day 1 and etoposide 100 mg/m^2 days 1, 2, 3 and atezolizumab 1200 mg day 1 every 21 days x 4 cycles followed by maintenance atezolizumab 1680 mg day 1, every 28 days (category 2A)[a]

[a]Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or concurrent use of immunosuppressive agents.

Fast Fact

All of the NCCN-preferred regiments for first-line treatment of ES-SCLC are triplets of a platinum agent, etoposide, and a PD-L1 inhibitor.

Addition NCCN-recommended regimens for primary treatment of ES-SCLC[1]



NOTE: These regimens are NOT in the prescribing information

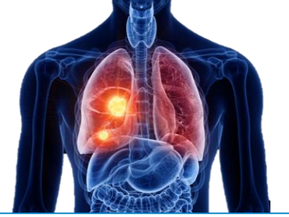
OTHER RECOMMENDED REGIMENS

- Carboplatin AUC 5–6 day 1 and etoposide 100 mg/m2 days 1, 2, 3 (category 2A)
- Cisplatin 75 mg/m^2 day 1 and etoposide 100 mg/m^2 days 1, 2, 3 (category 2A)
- Cisplatin 80 mg/m^2 day 1 and etoposide 80 mg/m^2 days 1, 2, 3 (category 2A)
- Cisplatin 25 mg/m^2 days 1, 2, 3 and etoposide 100 mg/m^2 days 1, 2, 3 (category 2A)

REGIMENS THAT MAY BE USEFUL IN CERTAIN CIRCUMSTANCES

- Carboplatin AUC 5 day 1 and irinotecan 50 mg/m2 days 1, 8, 15 (category 2A)
- Cisplatin 60 mg/m^2 days 1 and irinotecan 60 mg/m^2 days 1, 8, 15 (category 2A)
- Cisplatin 30 mg/m^2 days 1, 8 and irinotecan 65 mg/m^2 days 1, 8 (category 2A)

NCCN-recommended regiments for subsequent therapy[1]



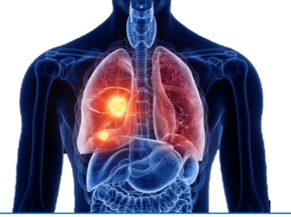
NCCN-preferred subsequent systemic therapy **(Note this is NOT in the prescribing information)**

- Platinum-based doublet (category 2A)
- Clinical trial enrollment (category 2A)

Other NCCN-recommended regiments

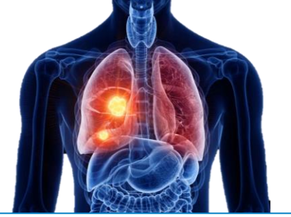
- FDA-approved regimens
  - Topotecan oral or IV (category 2A)[20,22]
  - Lurbinectedin (category 2A)[9]
- Regimens NOT in the prescribing information
  - Cyclophosphamide + doxorubicin + vincristine (category 2A)
  - Docetaxel (category 2A)
  - Oral etoposide (category 2A)
  - Gemcitabine (category 2A)
  - Irinotecan (category 2A)
  - Nivolumab (category 2A)
  - Paclitaxel (category 2A)
  - Pembrolizumab (category 2A)
  - Temozolomide (category 2A)
  - Vinorelbine (category 2A)
  - Bendamustine (category 2B)

References



1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Small cell lung cancer. Version 2.2023—October 28, 2022.
2. American Cancer Society. Surgery for small cell lung cancer treatment. Accessed October 8, 2022. https://www.cancer.org/cancer/lung-cancer/treating-small-cell/surgery.html
3. NCI. Dictionary of cancer terms. Accessed November 16, 2022. https://www.cancer.gov/publications/dictionaries/cancer-terms
4. American Cancer Society. Radiation therapy for small cell lung cancer. Accessed November 22, 2022. https://www.cancer.org/cancer/lung-cancer/treating-small-cell/radiation-therapy.html
5. NCI. Small cell lung cancer treatment (PDQ®)–health professional version. Accessed October 8, 2022. https://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq
6. Mayo Clinic. Image-guided radiation therapy. Accessed November 22, 2022. https://www.mayoclinic.org/tests-procedures/image-guided-radiation-therapy/about/pac-20385267
7. U.S. Food and Drug Administration. Topotecan Letter of Approval. November 30, 1998. Accessed November 16, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/nda/98/20671s004_Hycamtin_appltr.pdf
8. Sabari JK, Lok BH, Laird JH, et al. Unraveling the biology of SCLC: implications for therapy. *Nat Rev Clin Oncol.* 2017;14(9):549-561.
9. Zepzelca (lurbinectedin). Prescribing Information. Jazz Pharmaceuticals, Inc.: April 2022.
10. U.S. Food and Drug Administration. Atezolizumab Letter of Approval. March 18, 2019. Accessed November 21, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/761034Orig1s019ltr.pdf
11. Etopophos (etoposide). Prescribing information. Bristol-Myers Squibb Company: May 2017.
12. U.S. Food and Drug Administration. Durvalumab Letter of Approval. March 27, 2020. Accessed November 21, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/761069Orig1s018ltr.pdf
13. Platinol (cisplatin). Prescribing information. Bristol-Myers Squibb Company: September 2010.
14. Paraplatin (carboplatin). Prescribing information. Bristol-Myers Squibb Company: July 2010.
15. NCI drug dictionary. Accessed November 16, 2022. https://www.cancer.gov/publications/dictionaries/cancer-drug
16. Taber's Medical Dictionary Online. Accessed December 1, 2022. https://www.tabers.com/tabersonline/
17. Etopophos (etoposide). Prescribing information. Bristol-Myers Squibb Company: 2010.
18. Camptosar (irinotecan hydrochloride). Prescribing Information. Pfizer: January 2022.
19. Baker NM, Rajan R, Mondragon A. Structural studies of type I topoisomerases. *Nucleic Acids Res.* 2009;37(3):693-701.
20. Hycamptin (topotecan). Prescribing information. Novartis Pharmaceuticals Corporation: January 2018.
21. U.S. Food and Drug Administration. Topotecan Letter of Approval. October 11, 2007. Accessed November 16, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2008/020981s000ltr.pdf

References



22. Hycamptin (topotecan). Prescribing Information. Novartis Pharmaceuticals Corporation: September 2018.
23. U.S. Food and Drug Administration. Etoposide Letter of Approval. September 19, 2001. Accessed November 16, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2001/75635.ap..pdf
24. Etoposide. Prescribing information. Mylan Pharmaceuticals: April 2016.
25. U.S. Food and Drug Administration. Accelerated approval program. October 26, 2020. Accessed November 21, 2022. https://www.fda.gov/drugs/information-health-care-professionals-drugs/accelerated-approval-program
26. Benjamin DJ, Prasad V. Accelerated approval requirements for lurbinectedin. *Lancet Oncol.* 2022; 23:e206.
27. Bendeka (bendamustine). Prescribing information. Teva Pharmaceuticals: October 2021.
28. Cyclophosphamide. Prescribing information. Baxter Healthcare: May 2013.
29. Taxotere (docetaxel). Prescribing Information. Sanofi-Aventis: December 2013.
30. Doxorubicin. Prescribing information. Pfizer: March 2020.
31. Gemzar (gemcitabine). Prescribing information. Eli Lilly and Company: May 2014.
32. Taxol (paclitaxel). Prescribing information. Bristol-Myers Squibb Company: April 2011.
33. Temodar (temozolomide). Prescribing information. Merck & Co., Inc.: November 2019.
34. Vincristine. Prescribing Information. Hospira: August 2014.
35. Navelbine (vinorelbine). Prescribing information. Pierre Fabre Pharmaceuticals: January 2020.
36. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. *Nat Cancer Rev.* 2012;252(1):252-264.
37. Imfinzi (durvalumab). Prescribing Information. AstraZeneca: September 2022.
38. Tecentriq (atezolizumab). Prescribing Information. Genentech: January 2022.
39. Opdivo (nivolumab). Prescribing information. Bristol-Myers Squibb Company: July 2022.
40. Keytruda (pembrolizumab). Prescribing information. Merck & Co., Inc.: August 2022.
41. Caffery M. After PD-1 inhibitor indications are withdrawn in SCLC, what now? Accessed November 21, 2022. https://www.ajmc.com/view/after-pd-1-inhibitor-indications-are-withdrawn-in-sclc-what-now-
42. Kurzrock R, Gurski LA, Carlson RW, et al. Level of evidence used in recommendations by the National Comprehensive Cancer Network (NCCN) guidelines beyond Food and Drug Administration approvals. *Ann Oncol.* 2019;30(10):1647-1652.

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