Egyptian National Guidelines for Small Cell Lung Cancer

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➢ Abbreviations

AJCC	American joint commission on cancer
BSC	Best supportive care
CBC	Complete blood count
CCRT	Concomitant radio-chemo-therapy
CT	Computed Tomography
EHC	Egyptian Health Council
G-CSF	Granulocyte colony stimulating factor

IHC	Immunohistochemistry
KFTs	Kidney function tests
LFTs	Liver function tests
MRI	Magnetic resonance imaging
OS	Overall Survival
PCI	Prophylactic cranial irradiation
PET/ CT	Positron emission tomography/Computed Tomography
PS	Performance Status
SCLC	Small-cell lung cancer
ULN	Upper limit of normal

- **Executive Summary**

This guidance provides a data-supported approach to diagnosis, staging, treatment and follow up of patients diagnosed with SCLC.

Recommendation	Strength of recommendation
Diagnosis and Risk Assessment	
Initial assessment should include smoking history, physical examination, complete blood count, liver enzymes, sodium, potassium, calcium, glucose, LDH and creatinine (pulmonary function tests if localized disease).	**Good practice statement**
Attention drawn towards potential autoimmune-mediated paraneoplastic symptoms is advised .	**Conditional**

Combined approach of using the AJCC TNM staging system (9th edition) and the older Veterans Administration (VA) Lung Study Group's 2-stage classification VA scheme for SCLC staging should be used (appendix 1).	**Good practice statement**
The effusion should be excluded as a staging element if: 1) multiple cytopathologic examinations of the pleural fluid are negative for cancer; 2) the fluid is not bloody and not an exudate; and 3) clinical judgment concludes that the effusion is not directly related to the cancer.	**Good practice statement**
Pericardial effusions are classified using the same criteria mentioned above.	**Good practice statement**
A contrast-enhanced CT of the chest and abdomen is recommended.	**Strong**
Brain MRI is recommended for all patients. However, contrast enhanced CT is an option when MRI is not available.	**Strong**
FDG–PET–CT is optional for staging in limited-stage disease, and FDG–PET findings that modify treatment decisions should be pathologically confirmed.	**Conditional**
FDG–PET–CT is advised to assist in RT volume delineation.	**Conditional**
In limited-stage disease, additional bone scintigraphy is recommended when no FDG–PET–CT has been carried out.	**Strong**
In limited-stage disease, a bone marrow aspiration and biopsy are advised in the case of abnormal blood counts suggesting bone marrow involvement only if it changes clinical management.	**Conditional**
The workup for SCLC should not delay the onset of treatment for >1 week because of the aggressive nature of SCLC.	**Good practice statement**
Tobacco smoking cessation counseling and intervention should be strongly promoted in patients with SCLC and patients who previously smoked tobacco should be strongly encouraged to remain abstinent.	**Good practice statement**
Treatment	

Management of limited-stage disease (i.e. stages I-III SCLC eligible for treatment of curative intent)	
Surgery should be considered in patients with clinical stages I and II (cT1-2N0) SCLC in the context of a multimodal treatment concept and following a multidisciplinary board decision.	**Strong**
The aim of surgical treatment should be achieving an R0 resection.	**Strong**
When considering surgical treatment for SCLC, pathological mediastinal staging should be done.	**Strong**
Sublobular resection is not recommended for SCLC.	**Conditional**
After surgical resection, in case of pT1-2N0-1, R0 resection, adjuvant chemotherapy should be given.	**Strong**
After surgical resection, in case of R1-R2 resection or positive mediastinal lymph nodes (N2), adjuvant chemotherapy should be combined with RT, preferably concurrently.	**Strong**
The preferred Chemotherapy for patients with limited-stage (stage I-III) SCLC is platinum plus etoposide.	**Strong**
G-CSF is a treatment option to prevent haematological toxicity.	**Good practice statement**
Patients with T1-4N0-3M0 tumours and a good PS (0-1) should be treated with concurrent platinum-salt based chemotherapy and thoracic RT.	**Strong**
The recommended dose fractionation schedule is 66 Gy. in 33 fractions or equivalent doses	**Strong**
Thoracic RT should be initiated as early as possible, starting on the first or second cycle of Chemotherapy.	**Strong**
When the patient PS (≥2) or dose to the organs at risk do not allow for the early administration of thoracic RT, it should be postponed until the start of the third cycle of Chemotherapy.	**Strong**

Sequential CRT is the preferred option for patients who are not candidates for concurrent CRT due to poor PS, comorbidities and/or disease volume.	**Strong**
In case of response to Chemotherapy, the post-Chemotherapy primary tumour should be included in the radiation field.	**Strong**
In case of response to Chemotherapy, the pre-Chemotherapy nodal stations should be included in the radiation field.	**Strong**
Selective node irradiation is recommended (i.e. involved nodes defined as FDG avid on PET–CT, enlarged on CT and/or biopsy-positive).	**Strong**
Patients with stage III SCLC with a response after treatment (CRT) and a PS of 0-1 should be offered PCI.	**Strong**
PCI can be considered in patients with a PS of 2.	**Conditional**
The role of PCI is not as well defined in patients with stage I-II SCLC or in those >70 years of age or who are frail. In such cases, shared decision making is advised.	**Conditional**
The recommended PCI regimen is 25 Gy/10 fractions.	**Strong**
Management of extensive-stage disease (i.e. stage IV or stage III SCLC not eligible for treatment of curative intent)	
The preferred first-line treatment of extensive-stage SCLC (PS 0-2) is four to six cycles of a platinum plus etoposide	**Strong**
Cisplatin with irinotecan or topotecan are alternative treatment options.	**Conditional**
In poor prognosis patients, gemcitabine plus carboplatin is an alternative treatment option.	**Conditional**
In patients achieving a response after Chemotherapy and a PS of 0-2, RT to the residual primary tumour and lymph nodes (30 Gy/10 fractions) is a treatment option.	**Conditional**

PCI (20 Gy/5 fractions and 25 Gy/10 fractions) is justified without prior MRI staging or follow-up in patients <75 years of age and a PS of 0-2 who achieved a response after Chemotherapy.	**Strong**
In patients with extensive-stage SCLC without brain metastases on brain MRI after Chemotherapy and who can be followed-up with regular brain MRI, PCI may be omitted.	**Strong**
Patients with platinum-refractory SCLC have a poor prognosis and BSC is recommended.	**Conditional**
Topotecan is recommended for patients with platinum-resistant or -sensitive relapse; CAV , texans, gemcitabine, and oral etoposide are alternative options.	**Strong**
In patients with platinum-sensitive SCLC, rechallenge with first-line platinum plus etoposide can be considered.	**Strong**

➢ Introduction

Small-cell lung cancer (SCLC) is the most aggressive form of lung cancer. Although SCLC is characterized by rapid responses to chemotherapy and sensitivity to radiotherapy, due to early treatment resistance, the 5-year overall survival (OS) is <10%. The incidence of SCLC has decreased in recent decades, and with a prevalence of 1-5 per 10 000 people in the European community (1-4). In Egypt, there was an estimated 375 new cases of SCLC and 335 deaths occurred because of this disease based on GLOBOCAN 2022. (5)

➢ Purpose and scope

These guidelines are developed to improve the quality of care for SCLC cancer via providing a uniform standard of care across the country to help in early diagnosis, treatment and follow up for SCL cancer so more optimal treatment options and improved clinical outcomes.

➢ Target audience

Clinicians who are involved in the care and treatment of patients with SCLC, include medical oncologists, radiation oncologists, clinical oncologist, surgeons, clinical dietitian , intervention radiologists, radiologists, pathologists, and palliative care specialists.

➢ Methodology

A comprehensive search for guidelines was undertaken to identify the most relevant guidelines to consider for adaptation.

Inclusion/exclusion criteria followed in the search and retrieval of guidelines to be adapted:

- Selecting only evidence-based guidelines (guidelines must include a report on systematic literature searches and explicit links between individual recommendations and their supporting evidence). - Selecting only national and/or international guidelines.
- Specific range of dates for publication (using Guidelines published or updated 2020 and later).
- Selecting peer reviewed publications only.
- Selecting guidelines written in English language.
- Excluding guidelines written by a single author not on behalf of an organization to be valid and comprehensive, a guideline ideally requires multidisciplinary input.
- Excluding guidelines published without references as the panel needs to know whether a thorough literature review was conducted and whether current evidence was used in the preparation of the recommendations.

All retrieved Guidelines were screened and appraised using AGREE II instrument (www.agreetrust.org) by at least two members. the panel decided a cutoff point or rank the guidelines (any guideline scoring above 50% on the rigor dimension was retained)

The NCCN, ESMO, NICE guidelines are the main sources used while formulating the national guidelines for SCLC (6-8).

- **Evidence assessment**

According to WHO handbook for Guidelines we used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to assess the quality of a body of evidence, develop and report recommendations. GRADE methods are used by WHO because these represent internationally agreed standards for making transparent recommendations. Detailed information on GRADE is available through the on the following sites:

- GRADE working group: https://www.gradeworkinggroup.org/
- GRADE online training modules: http://cebgrade.mcmaster.ca/

Table 1: Quality of evidence in GRADE

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

GRADE: Grading of Recommendations Assessment, Development and Evaluation.

Table 2: Significance of the four levels of evidence

Quality	Definition	Implications
High	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change confidence in the estimate of effect
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Any estimate of effect is very uncertain

Table 3: Factors that determine How to upgrade or downgrade the quality of evidence

Downgrade in presence of	Upgrade in presence of
Study limitations -1 Serious limitations -2 Very serious limitations	Dose-response gradient +1 Evidence of a dose-response gradient
Consistency -1 Important inconsistency	Direction of plausible bias +1 All plausible confounders would have reduced the effect
Directness -1 Some uncertainty -2 Major uncertainty	Magnitude of the effect +1 Strong, no plausible confounders, consistent and direct evidence
Precision -1 Imprecise data	+2 Very strong, no major threats to validity and direct evidence
Reporting bias -1 High probability of reporting bias	

➢ The strength of the recommendation

The strength of a recommendation communicates the importance of adherence to the recommendation:

Strong recommendations: With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted as policy.

Conditional recommendations: These are made when there is greater uncertainty about the four factors above (Table 2) or if local adaptation must account for a greater variety in values and preferences, or when resource use makes the intervention suitable for some, but not for other locations. This means that there is a need for substantial debate and involvement of stakeholders before this recommendation can be adopted as policy.

When not to make recommendations; when there is lack of evidence on the effectiveness of an intervention, it may be appropriate not to make a recommendation.

➢ Recommendations

Diagnosis and Risk Assessment

- Initial assessment should include smoking history, physical examination, complete blood count, liver enzymes, sodium, potassium, calcium, glucose, LDH and creatinine (pulmonary function tests if localized disease).

Good practice statement

- Attention drawn towards potential autoimmune-mediated paraneoplastic symptoms is advised.

Conditional recommendation, low grade evidence (9)

- Combined approach of using the AJCC TNM staging system (9th edition) and the older Veterans Administration (VA) Lung Study Group's 2-stage classification VA scheme for SCLC staging should be used (appendix 1).

Good practice statement

- The effusion should be excluded as a staging element if: 1) multiple cytopathologic examinations of the pleural fluid are negative for cancer; 2) the fluid is not bloody and not an exudate; and 3) clinical judgment concludes that the effusion is not directly related to the cancer.

Good practice statement

- Pericardial effusions are classified using the same criteria mentioned in the above recommendation.

Good practice statement

- A contrast-enhanced CT of the chest and abdomen is recommended.

Strong recommendation, very low grade evidence (10)

- Brain MRI is recommended for all patients. However, contrast enhanced CT is an option when MRI is not available.

Strong recommendation, low grade evidence (10)

- FDG–PET–CT is optional for staging in limited-stage disease, and FDG–PET findings that modify treatment decisions should be pathologically confirmed.

Conditional recommendation, moderate grade evidence (11,12)

- FDG–PET–CT is advised to assist in RT volume delineation.

Conditional recommendation, low grade evidence (11,12)

- In limited-stage disease, additional bone scintigraphy is recommended when no FDG–PET–CT has been carried out.

Strong recommendation, very low grade evidence (11,12)

- In limited-stage disease, a bone marrow aspiration and biopsy are advised in the case of abnormal blood counts suggesting bone marrow involvement only if it changes clinical management..

Conditional recommendation, low grade evidence (11)

- The workup for SCLC should not delay the onset of treatment for >1 week because of the aggressive nature of SCLC.

Good practice statement

- Tobacco smoking cessation counseling and intervention should be strongly promoted in patients with SCLC.

Good practice statement

Treatment

- The WHO classification recognizes two types of SCLC: pure and combined SCLC, patients with combined SCLC should treated using regimens for SCLC, because it is the more aggressive cancer.

Strong recommendation, strong grade evidence (13)

Management of limited-stage disease (i.e. stage I-III SCLC eligible for treatment of curative intent)

- Surgery should be considered in patients with clinical stages I and II (cT1-2N0) SCLC in the context of a multimodal treatment concept and following a multidisciplinary board decision.

Strong recommendation, low grade evidence (14)

- The aim of surgical treatment should be achieving an R0 resection.

Strong recommendation, low grade evidence (15)

- When considering surgical treatment for SCLC, pathological mediastinal staging should be done.

Strong recommendation, very low grade evidence (16,17)

- Sublobular resection is not recommended for SCLC.

Conditional recommendation, low grade evidence (15)

- After surgical resection, in case of pT1-2N0-1, R0 resection, adjuvant chemotherapy should be given.

Strong recommendation, very low grade evidence (18)

- After surgical resection, in case of R1-R2 resection or positive mediastinal lymph nodes (N2), adjuvant chemotherapy should be combined with RT, preferably concurrently.

Strong recommendation, very low grade evidence (16)

- The preferred Chemotherapy for patients with limited-stage (stage I-III) SCLC is cisplatin plus etoposide.

Strong recommendation, high grade evidence (19)

- When cisplatin is contraindicated because of comorbidities, carboplatin plus etoposide is recommended.

Strong recommendation, high grade evidence (20)

- G-CSF is a treatment option to prevent haematological toxicity.

Good practice statement

- Patients with T1-4N0-3M0 tumours and a good PS (0-1) should be treated with concurrent platinum-salt based chemotherapy and thoracic RT.

Strong recommendation, high grade evidence (21,22)

- The recommended fractionation schedule is 66 Gy in 33 fractions or equivalent doses.

Strong recommendation, high grade evidence (21)

- Thoracic RT should be initiated as early as possible, starting on the first or second cycle of Chemotherapy.

Strong recommendation, high grade evidence (23)

- When the patient PS (≥2) or dose to the organs at risk do not allow for the early administration of thoracic RT, it should be postponed until the start of the third cycle of Chemotherapy.

Strong recommendation, high grade evidence (24,25)

- Sequential CRT is a preferred option for patients who are not candidates for concurrent CRT due to poor PS, comorbidities and/or disease volume.

Strong recommendation, low grade evidence (26)

- In case of response to Chemotherapy, the post-Chemotherapy primary tumour should be included in the radiation field.

Strong recommendation, low grade evidence (26)

- In case of response to Chemotherapy, the pre-Chemotherapy nodal stations should be included in the radiation field.

Strong recommendation, low grade evidence (26)

- In case of stable disease, surveillance is recommended until progression.
  Good practice statement
- In case of disease progression treatment of extensive disease is recommended
  Good practice statement

- Selective node irradiation is recommended (i.e. involved nodes defined as FDG avid on PET–CT, enlarged on CT and/or biopsy-positive).

Strong recommendation, high grade evidence (24)

- Patients with stage III SCLC with a response after treatment (CRT) and a PS of 0-1 should be offered PCI.

  Strong recommendation, low grade evidence (27)

- PCI can be considered in patients with a PS of 2.

  Conditional recommendation, low grade evidence (27)

- The role of PCI is not as well defined in patients with stage I-II SCLC or in those >70 years of age or who are frail. In such cases, shared decision making is advised.

Conditional recommendation, very low grade evidence (28)

- The recommended PCI regimen is 25 Gy/10 fractions.

Strong recommendation, high grade evidence (29)

Management of extensive-stage disease (i.e. stage IV or stage III SCLC not eligible for treatment of curative intent)

- The preferred first-line treatment of extensive-stage SCLC (PS 0-2) is four to six cycles of a platinum plus etoposide.

Strong recommendation, high grade evidence (19)

- Cisplatin with irinotecan or topotecan are alternative treatment options.

Conditional recommendation, moderate grade evidence (30,31)

- In poor prognosis patients, gemcitabine plus carboplatin is an alternative treatment option.

Conditional recommendation, moderate grade evidence (32)

- In patients achieving a response after Chemotherapy and a PS of 0-2, RT to the residual primary tumour and lymph nodes (30 Gy/10 fractions) is a treatment option.

Conditional recommendation, moderate grade evidence (33)

- PCI (20 Gy/5 fractions and 25 Gy/10 fractions) is justified without prior MRI staging or follow-up in patients <75 years of age and a PS of 0-2 who achieved a response after Chemotherapy.

Strong recommendation, high grade evidence (34)

- In patients with extensive-stage SCLC without brain metastases on brain MRI after Chemotherapy and who can be followed-up with regular brain MRI, PCI may be omitted.

Conditional recommendation, high grade evidence (35)

- Patients with platinum-refractory SCLC have a poor prognosis and BSC is recommended.

Strong recommendation, moderate grade evidence (36)

- Topotecan is recommended for patients with platinum-resistant or -sensitive relapse; CAV , Texans, Gemcitabine, oral etoposide are alternative options.

Strong recommendation, moderate grade evidence (37)

- In patients with platinum-sensitive SCLC, rechallenge with first-line platinum plus etoposide can be considered.

Strong recommendation, high grade evidence (38)

➢ Clinical indicators for monitoring

For patients newly diagnosed with SCL cancer:

- laboratory evaluation (CBC, LFT, and KFT)
- imaging
- tissue biopsy for pathological confirmation and IHC

➢ Research gaps

- Address the leading cause of lung cancer, such as smoking.
- Systematically incorporate cost-benefit analyses into clinical trials, including health economic measures such as the incremental cost-effectiveness ratio, to support clinical decision-making (e.g., ultra-low-dose immunotherapy).
- Identify predictive biomarkers for response to specific targeted therapies and immunotherapy.
- Improve preclinical models for testing novel drugs.
- Identify tools for assessing quality of life in clinical trials.

➢ Update of this guideline

- This guideline will be updated whenever there is new evidence.

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➢ Annexes

1-TNM Classification

T		Primary Tumor
TX		Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0		No evidence of primary tumor
Tis		Carcinoma *in situ* Squamous cell carcinoma *in situ* (SCIS) Adenocarcinoma *in situ* (AIS): adenocarcinoma with pure lepidic pattern, ≤3 cm in greatest dimension
T1		Tumor ≤3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)
	T1mi	Minimally invasive adenocarcinoma: adenocarcinoma (≤3 cm in greatest dimension) with a predominantly lepidic pattern and ≤5 mm invasion in greatest dimension
	T1a	Tumor ≤1 cm in greatest dimension. A superficial, spreading tumor of any size whose invasive component is limited to the bronchial wall and may extend proximal to the main bronchus also is classified as T1a, but these tumors are uncommon.
	T1b	Tumor >1 cm but ≤2 cm in greatest dimension
	T1c	Tumor >2 cm but ≤3 cm in greatest dimension
T2		Tumor >3 cm but ≤5 cm or having any of the following features: (1) Involves the main bronchus, regardless of distance to the carina, but without involvement of the carina; (2) Invades visceral pleura (PL1 or PL2); (3) Associated with atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung. T2 tumors with these features are classified as T2a if ≤4 cm or if the size cannot be determined and T2b if >4 cm but ≤5 cm.
	T2a	Tumor >3 cm but ≤4 cm in greatest dimension
	T2b	Tumor >4 cm but ≤5 cm in greatest dimension
T3		Tumor >5 cm but ≤7 cm in greatest dimension or directly invading any of the following: parietal pleura (PL3), chest wall (including superior sulcus tumors), phrenic nerve, parietal pericardium; or separate tumor nodule(s) in the same lobe as the primary
T4		Tumor >7 cm or tumor of any size invading one or more of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, or carina; separate tumor nodule(s) in an ipsilateral lobe different from that of the primary

N	Regional Lymph Nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

M	Distant Metastasis
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion[a]
M1b	Single extrathoracic metastasis in a single organ (including involvement of a single nonregional node)
M1c	Multiple extrathoracic metastases in a single organ or in multiple organs

	T	N	M
Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	T1mi	N0	M0
	T1a	N0	M0
Stage IA2	T1b	N0	M0
Stage IA3	T1c	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	T1a	N1	M0
	T1b	N1	M0
	T1c	N1	M0
	T2a	N1	M0
	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T1c	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0

	T	N	M
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T1c	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N2	M0
	T4	N2	M0
Stage IIIC	T3	N3	M0
	T4	N3	M0
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	M1a
	Any T	Any N	M1b
Stage IVB	Any T	Any N	M1c

2-Systemic Therapy Doses

PRIMARY OR ADJUVANT THERAPY FOR LIMITED STAGE SCLC

Four cycles of cytotoxic chemotherapy are recommended.

Planned cycle length should be every 21–28 days during concurrent RT.

During cytotoxic chemotherapy + RT, Cisplatin/Etoposide is recommended.

The use of myeloid growth factors is not recommended during concurrent cytotoxic chemotherapy plus RT

- **Cisplatin 75 mg/m, Day 1 and Etoposide 100 mg/m Days 1, 2, 3**
- **Cisplatin 60 mg/m^2 Day 1 and Etoposide 120 mg/m Days 1, 2, 3**
- **Carboplatin area under the curve (AUC) 5–6 Day 1 and Etoposide 100 mg/m Days 1, 2, 3**
- **Cisplatin 25 mg/m^2 Days 1, 2, 3 and Etoposide 100 mg/m Days 1, 2, 3**

PRIMARY THERAPY FOR EXTENSIVE STAGE SCLC
Four cycles of cytotoxic chemotherapy are recommended, **but some patients may receive up to 6 cycles based on response and tolerability after 4 cycles.**
Carboplatin AUC 5–6 Day 1 and Etoposide 80–100 mg/m2 Days 1, 2, 3 **Cisplatin 75–80 mg/m Day 1 and Etoposide 80–100 mg/m2 Days 1, 2, 3** **Carboplatin AUC 5 Day 1 and Irinotecan 50 mg/m2 Days 1, 8, 15** **Cisplatin 60 mg/m2 Day 1 and Irinotecan 60 mg/m2 Days 1, 8, 15** **Cisplatin 30 mg/m2 Days 1, 8 and Irinotecan 65 mg/m2 Days 1, 8**

SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)
Consider dose reduction or growth factor support for patients with PS 2

- **Irinotecan** at a dose of 100 mg/m2 by intravenous 90-minute infusion once a week
- If prolonged disease free time, re-treatment with platinum-based doublet
- Topotecan Oral (PO) or Intravenous (IV) at a dose of 2.3 mg/m2/d, days 1 through 5, every 21 days
- CAV (cyclophosphamide 1,000 mg/m2, doxorubicin 45 mg/m2, and vincristine 2 mg) infused on day 1 every 21 days
- Docetaxel at a dose of 100 mg/m2 of docetaxel in an intravenous infusion given over 1 h every 21 days
- Gemcitabin with 1000 mg/m2 on days 1, 8, and 15 of a four-week cycle.
- Oral Etoposide daily of 50 mg/m
- Paclitaxel (175 mg m(-2) intravenously over 3 h every 3 weeks)