



## SURGERY FOR SMALL CELL LUNG CANCER: INDICATIONS AND RESULTS

Michael Dusmet

*Royal Brompton Hospital, London, UK and Sanjay Popat (Royal Marsden Hospital, London, UK)*

Small cell lung cancer (SCLC) is a high-grade neuroendocrine tumour that accounts for approximately 15 % of all cases of lung cancer. It almost exclusively occurs in smokers, often heavy smokers, and typically at a late age so this is a very challenging patient population, often with a high co-morbidity burden. For practical reasons (the body of evidence and most treatment protocols) it is conventionally staged as limited stage disease (disease which can be encompassed in a tolerable radiotherapy field – so a definition that varies from one institution to another) and extensive stage disease. However, it should always also be staged using the TNM staging system. SCLC is characterised by a rapid doubling time, a propensity for early dissemination, sensitivity to chemotherapy and radiotherapy with initial excellent response but a profound tendency to relapse. It also has a high frequency of aberrations in both oncogenes and tumour suppressors. It is a highly lethal cancer with often short survival and also quite poor overall survival, even when treated radically (which is only appropriate in a minority of patients).

Surgery only has a limited role in the treatment of this disease, and this has shrunk over time. Firstly, there are patients who undergo surgery without a tissue diagnosis, and SCLC is the final pathological diagnosis. Patients with true stage I (T1-2, N0, M0) disease have been known to benefit from surgery for many decades, with typical survival in the 50% range, albeit in a highly selected patient cohort (good performance status, acceptable lung function and co-morbidity burden). Many surgeons have tried to argue for a role for surgery in stage II, and indeed IIIa, SCLC on the basis of weak evidence – retrospective reviews of very highly selected patient populations, often including many patients operated on without a tissue diagnosis, and many of the stage II and IIIa patients were actually lower clinical stage patients upstaged by the surgery. Radiotherapy has undergone radical transformation over these decades so now radical concurrent twice-daily chemo-radiotherapy offers, in the prospective trial setting (CONVERT trial), survival that is superior to the results of the highly biased entirely retrospective surgical literature. This is why all the current guidelines on SCLC (ESMO, ASCO, ACCP, NICE) recommend concurrent twice-daily chemo-radiation therapy for stage II and IIIa patients.

At present surgery is thus reserved for true stage I patients. All the guidelines concur that the staging of these patients must be thorough and include CT of the chest and abdomen, PET-CT, MRI brain as well as the customary fitness for surgery evaluation. The mediastinum must be

staged invasively, preferably surgically (and we would go further and suggest that VAMLA is mandatory in this patient population).

Surgery should be followed with adjuvant chemotherapy (platinum-based agent + etoposide), although the evidence for this recommendation is weak. As noted above 50% 5-year survival after surgery was achieved in the older reports when platinum-based chemotherapy was not available. The role of immunotherapy in the limited stage setting is currently being investigated.

If surgery does not achieve an R0 resection or surgical staging shows N2 disease adjuvant chemo-radiotherapy should be offered instead of chemotherapy.

Prophylactic cranial irradiation (PCI) is a slightly contentious subject in these patients, often being recommended, but it carries the risk of neurotoxicity which can have a detrimental impact on quality of life. Regular surveillance with MRI, and treatment for early detected lesions with brain radiotherapy offers the same outcome as PCI and may defer brain radiotherapy for the majority of patients and spare a minority altogether.

Key references:

- 1) Recent Developments in the Treatment of Small Cell Lung Cancer. Hiddinga BI et al. Eur Resp Rev 2021;30:210079 [DOI: 10.1183/16000617.0079-2021]
- 2) Current Diagnosis and Management of Small-Cell Lung Cancer. Wang s et al. Mayo Clin Proc 2019;94:1599-1622
- 3) Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. Ann Oncol 2021;32:839-853
- 4) Concurrent Once-Daily Versus Twice-Daily Chemoradiotherapy in Patients with Limited-Stage Small-Cell Lung Cancer (CONVERT): An Open-Label, Phase 3, Randomised Superiority Trial. Lancet Oncol 2017;18:1116-25

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