

Treatment of metastatic disease

Cytotoxic treatment combined with surgical resection when indicated has been the standard for metastatic bronchial NETs, although the available chemotherapy regimens demonstrate a rather poor effect (III, A).

- For low proliferating tumors treatment with somatostatin analogs and alpha interferon might be an option for functional tumors with clinical symptoms (III, B).
- Treatment with novel agents, such as tyrosine kinase inhibitors (e.g. sunitinib) and the mTOR inhibitor everolimus, have been reported in very small series or in the subgroup analysis of larger studies not designed specifically for lung NET with mainly stabilization of the disease (objective response rates 5%-10%; III, B).
- In nonfunctioning tumors, the use of somatostatin analogs is still controversial, but after the PROMID study indicating antitumor efficacy by octreotide long acting release (LAR) in small intestinal NETs, it is now widely accepted also for nonfunctioning tumors of other origins (III, B).
- Peptide receptor radiotherapy is an option in patients with tumors that present a high content of somatostatin receptors (III, B).
- Available chemotherapy regimens for TC and AC include a combination of streptozotocin plus 5-fluoro-uracil/doxorubicin.
- Temozolomide alone or in combination with capecitabine and sometimes bevacizumab has demonstrated clinical benefit (III, B).
- A combination of cisplatin and etoposide is mainly used in high proliferating tumors (III, B).
- In general chemotherapy, results are discouraging except for temozolomide alone or in combination with capecitabine (III, B).
- The RADIANT-2 trial, which was a randomized trial between everolimus (10 mg) and placebo in NET tumor patients, included 44 of the 429 patients with bronchial NETs. A clear benefit of everolimus compared with placebo was noted (II, A).
- Symptomatic metastatic disease confined to the liver may be treated with embolization, radiofrequency ablation (RFA) and radio-embolization of liver metastases.
- External local irradiation of brain and bone metastases might be beneficial.
- Update 2016: In patients with unresectable or metastatic, well-differentiated (Grade 1 or Grade 2) non-functional neuroendocrine tumours of lung origin with progressive disease, everolimus, as compared with placebo, is associated with a statistically and clinically significant improvement in PFS. In the absence of mature OS and quality of life data, the observed PFS benefit is associated with an ESMO Magnitude of Clinical Benefit Scale (MCBS) score of 3.