

Diagnosis

- A pretreatment pathological diagnosis is strongly recommended for all patients before SABR, unless a multidisciplinary tumour board is of the opinion that the risk-benefit ratio of the procedure is unacceptable. In such a situation, the predicted likelihood of malignancy should preferably be at least 85%, based upon accepted criteria [III, B] [25].

LLCG/VZN annotation: Instead of reference 25, we use accepted criteria such as Herder model (Herder et al, Chest 2005;128:2490) and/or Brock model (Mc Williams et al, N Engl J Med 2013;369:910).

- FDG-PET may contribute for the selection of patients for anatomical sublobar resections as low SUVmax values of peripheral tumours indicate lack of mediastinal metastases [III, A]. This diagnosis may be made intra-operatively by video-assisted thoracoscopic biopsy and frozen section analysis.

LLCG/VZN annotation: We delete this bullet point on FDG-PET as its contribution still needs to be confirmed by further research. However, we agree that accurate intra-operative frozen section analysis may identify patients for whom an anatomical sublobar resection would be sufficient.

- In isolated cases a diagnostic anatomical sublobar resection may be acceptable.

LLCG/VZN annotation: Isolated cases considered are adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA), lepidic predominant adenocarcinoma (LPA).

Solitary pulmonary nodule

- The diagnostic approach to non-calcified pulmonary nodules should be based on existing standard guidelines [III, A], although new evidence on nodule management is emerging

LLCG/VZN annotation: guidelines/recommendations considered: British Thoracic Society (Callister et al, Thorax 2015;70:ii1), Fleischner Society 2017 (Bankier et al. Radiology 2017;285:584; Mc Mahon et al, Radiology 2017;284:228).

Staging and risk assessment

- If two lung lesions fulfil the criteria for two primaries these should be evaluated and treated accordingly [III, A]

LLCG/VZN annotation: A comprehensive histologic assessment is recommended for distinguishing a second primary lung carcinoma from an intrapulmonary metastasis (Nicholson et al, J Thorac Oncol 2018;13:205).

- For patients with abnormal mediastinal and/or hilar lymph nodes at CT and/or PET imaging, endosonography is recommended over surgical staging [I, A]

LLCG/VZN annotation: add-on: For patients with abnormal hilar lymph nodes at CT and/or PET/CT, and normal mediastinal lymph nodes, surgical mediastinal nodal staging is recommended over endosonography [III, A] (Dooms et al, Chest 2015;147:209; Decaluwe et al, Eur Respir J 2018;online Dec 21, 2017).

- Screening for brain metastases by MRI might be useful in patients considered for curative therapy [III, B]

LLCG/VZN annotation: screening for brain metastases by contrast-enhanced MRI or dedicated CT scan is useful in patients considered for curative therapy.

Treatment of early stages (stages I and II)

- Lobectomy is still considered the standard surgical treatment of tumours ≥ 2 cm in size that have a solid appearance on CT [II, B].

LLCG/VZN annotation: For solid tumours ≤ 2 cm, anatomical segmentectomy seems comparable to lobectomy as long as the surgical margins are larger than the tumour diameter (Moon et al, Respirology 2018;23:695).

- Adjuvant ChT should be offered to patients with resected stage II and III NSCLC [I, A] and can be considered in patients with resected stage IB disease and a primary tumour > 4 cm [II, B]

LLCG/VZN annotation: Within the 8th TNM, resected stage IB based on a primary tumour >4cm did change into a stage IIA classification.

- Even if such patients were not included in RCTs, adjuvant ChT should be considered in patients with R1 resection of stage IB disease and a primary tumour > 4 cm, stage II and III [V, A].

LLCG/VZN annotation: Within the 8th TNM, resected stage IB based on a primary tumour >4cm did change into a stage IIA classification.

Treatment of locally advanced stage (stage III)

- If single station N2 disease can be demonstrated by preoperative pathological nodal analysis, resection followed by adjuvant ChT, ... are options

LLCG/VZN annotation: We don't recommend upfront surgery followed by adjuvant chemotherapy in single station N2 disease. Some surgeons advocate primary surgery for proven single zone N2 disease based on the survival of 34 % In the IASLC paper (Rush et al, J Thorac Oncol 2007;2:603). It is important to keep in mind that these survival analyses were extracted from resected patients with pathologically staged tumours and thus based on lymphadenectomy. Their results cannot be extrapolated to a preoperative clinical staging setting. This is why these data cannot be invoked to propose upfront surgical treatment for patients with clinical presumed single station N2 disease determined by the current clinical staging guidelines. No pretreatment test (CT, PET, EBUS, EUS, mediastinoscopy) can be compared with resectional lymphadenectomy.

- Checkpoint inhibitors are also being evaluated after CRT as consolidation therapy

LLCG/VZN annotation: Since October 2018, durvalumab is approved by EMA as monotherapy for the treatment of locally advanced, unresectable NSCLC in adults whose tumours express PD-L1 on $\geq 1\%$ of tumour cells and whose disease has not progressed following platinum based chemoradiation therapy.

Follow-up, long-term implications and survivorship

- Surveillance every 6 months for 2 years with a visit including history, physical examination and - preferably contrast-enhanced - volume chest CT scan at least at 12 & 24 months is recommended, and thereafter an annual visit including history, physical examination and chest CT scan in order to detect second primary tumours [III, B].

LLCG/VZN annotation: Surveillance with a contrast-enhanced CT scan at 12 and 24 months is recommended, and thereafter an annual low-dose chest CT scan in order to detect second primary tumours [III, B]. After 5 years, yearly low-dose chest CT scan follow-up should continue (Westeel et al, ESMO 2017;abstract 12730).

- For individual patients, follow-up with six-monthly CT scans for 3 years is recommended for patients who are suitable for salvage treatment (e.g. surgery, local ablative therapy) [III, B]. The frequency of the follow-up visits can be tailored to the individual patient for those not suitable for salvage treatment [V, B]

LLCG/VZN annotation: Individual patients considered are defined as 'initially treated for stage I-IIA with SABR' and 'initially treated for stage III with curative intent'.