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Multidisciplinary treatment approach of a patient with lung cancer
Diagnosis:
Right upper lobe lung cancer stage II B (cT3N0M0G3)

**Anamnesis**
Clinical examination

- Male, 44 years old
- Heavy smoker
- PS 1
- Cough
- Right shoulder pain (VAS=4)

**Imaging**
- Thorax CT scan:
  - tumor 52/55/52 mm → posterior segments of the right upper lobe of lung
  - invasion of the right second rib
- Head MRI:
  - No mets

**Right minithoracotomy biopsy of tumor**

Pathology
- Pulmonary adenocarcinoma G3

Diagnosis:
Right upper lobe lung cancer stage II B (cT3N0M0G3)
June 2013 - July 2013
- Neoadjuvant treatment -

Concurrent external radiotherapy
Total dose = 45 Gy/25 fr/ 38 days
On tumoral PTV + right supraclavicular LNs

Concurrent Chemotherapy - mEP regimen, 2x2 cycles

- Cisplatin 50 mg/m2/day (TD = 180 mg/cycle) day 1, 8, 29, 36
- Etoposide 50 mg/m2/day (TD = 450 mg/cycle) days 1-5, 29-33

Well tolerated
- hematologic toxicity – grade 1
- esophagitis – grade 1

Rusch et al. J Clin Oncol 25: 313-318
**August 2013**
Thorax, abdomen and head CT scan:
tumor (RUL) of 44/53/50 mm
**STABLE DISEASE (RECIST 1.1)**

**September 2013**
Right upper lobectomy, lymphadenectomy and

Head CT scan: left frontal lobe tumor

Surgery → pathology: cerebral metastasis of adenocarcinoma of lung G3
**August 2014**
PS 2, severe right spastic hemiparesis
Thorax, abdomen and head CT scan: without signs of disease recurrence
Whole brain radiotherapy: TD=30Gy/10fr/12 days
*Treatment well tolerated*

**September 2014- Present (at 42 months after diagnosis)**
PS 1, right spastic hemiparesis
Blood tests: normal
Thorax, abdomen and head CT scan: without signs of disease recurrence

**Conclusions**
- Neoadjuvant RT/CTx can obtain in some cases pCR, nevertheless imaging complete responses are very rare
- Although the patient was noncompliant, he had a good outcome after treatment
- Tumor heterogeneity and the biology of cancer played an important role in the good evolution of this case
potentially operable IIIA(N2) disease and selected IIIB disease—
but at high risk of incomplete resection

Recommendation 4.2.2: In potentially resectable superior sulcus tumours, concurrent chemoradiotherapy induction followed by definitive surgery is the treatment of choice [III, A]. The same strategy may be applied for potentially resectable T3 or T4 central tumours in highly selected cases and experienced centres [III, B]. In both situations, surgery should be carried out within 4 weeks after the end of radiotherapy [III, B].

For potentially resectable superior sulcus tumours, concurrent chemoradiotherapy induction followed by surgery has become the standard of care [81] (Table 2, Figure 1). As randomised trials are difficult to perform because of rarity of these tumours, this recommendation is based on a multicentre prospective phase II Southwest Oncology Group (SWOG) trial in North America, which demonstrated an excellent complete resection rate and markedly improved 5-year survival rates [81]. A com-

years [hazard ration (HR) 0.84; P = 0.004]. These trials were carried out with presently outdated staging methods and mostly 2D radiotherapy techniques.

Patients who are considered to be unfit for concurrent chemotheraphy and radiotherapy can be treated with induction chemotherapy and high-dose radiotherapy with curative intent [87–90]. Accelerated radiotherapy may be beneficial in this situation [91–93] as it has shown superior results [90, 92]. Also, the results of an individual-patient-data-based meta-analysis for non-concurrent chemoradiotherapy further support this individualised strategy [92].

Few groups have piloted surgery after combined-modality approaches in N3-disease patients—mostly chemoradiotherapy. There is old phase II data from SWOG and from the West German Cancer Centre Group and from several other investigations looking at this subset [65, 67–69]. In the ESPATÜ trial presented at ASCO 2014, one-third of the patient group included patients with T1–3N3 disease with N3 proven and found at staging mediastinoscopy [82]. Long-term survival was
Induction Chemoradiation and Surgical Resection for Superior Sulcus Non–Small-Cell Lung Carcinomas: Long-Term Results of Southwest Oncology Group Trial 9416 (Intergroup Trial 0160)

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ABSTRACT

Purpose
Traditional treatment for superior sulcus non–small-cell lung cancers (SS NSCLC), radiation plus surgery, yields a 50% rate of complete resection and a 30% 5-year survival. On the basis of improved outcomes in other subsets of stage III NSCLC, this trial tested the feasibility of induction chemoradiotherapy for SS NSCLC.

Patients and Methods
Patients with T3-4, N0-1 SS NSCLC received two cycles of cisplatin and etoposide concurrently with radiation (45 Gy). Patients with stable or responding disease underwent thoracotomy. All patients received two more cycles of chemotherapy. Survival was calculated by the Kaplan-Meier method and prognostic factors were assessed by Cox regression analysis.

Results
From April 1995 to November 1999, 110 eligible patients (76 men, 34 women) were entered onto the study (78 T3, 32 T4 tumors). Induction therapy was completed by 104 (95%) patients. Of 95 patients eligible for surgery, 89 (92%) underwent thoracotomy, two (2.2%) died postoperatively, and 83 (76%) had complete resection. Pathologic complete response (CR) or minimal microscopic disease was seen in 61 (56%) resection specimens. Five-year survival was 44% for all patients and 54% after complete resection, with no difference between T3 and T4 tumors. Pathologic CR led to better survival than when any residual disease was present ($P = .02$). Disease progression occurred mainly in distant sites.

Conclusion
This combined-modality approach is feasible and is associated with high rates of complete resection and pathologic CR in both T3 and T4 tumors. Local control and overall survival seem markedly improved relative to previous studies of radiation plus resection.

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T 3-4, N 0-1 M0 NSCLC involving the superior sulcus
No pathologic evidence of mediastinal or supraclavicular nodal disease
N = 110

Cisplatin: 50 mg/m², days 1, 8, 29, 36
Etoposide: 50 mg/m², days 1-5, 29-33
Radiation: 180 cGy daily x 5 weeks (45 Gy total)

3 deaths
1 PD
n = 104 (92%)* 2 did not complete therapy

Repeat extent of disease evaluation
(CT scans chest, abdomen, brain and bone scan)
2-4 Weeks after completion of induction treatment

CR, PR or stable
n = 95 (86%)*

Surgical resection
n = 88 (80%)
RO Resection
n = 83 (75%)

Complete or incomplete resection of all gross tumor

2 Additional cycles of chemotherapy
Completed by 49 of 60 patients treated

Follow-up

Disease progression

Medically unfit or refuse surgery
n = 6

Off Protocol

Follow-up
- pCR or minimal microscopic disease – 56% of resection specimens
- 5 OS: 44% for all patients and 54% after complete resection
role of radiotherapy in stage IV NSCLC

Radiotherapy plays a major role in the symptom control of metastases, such as painful chest wall disease, superior vena cava syndrome, soft tissue or neural invasion. Neurological symptoms from spinal cord compression can be relieved by early radiotherapy.

Radiotherapy is indicated in cases of haemoptysis, symptomatic airway obstruction and following surgery for CNS, and, sometimes, bone surgery [II, B].

role of palliative surgery in stage IV NSCLC

Recurrent pleural effusions can be managed by pleurodesis. The preferred sclerosing agent is talc, which is more effective than bleomycin or tetracycline [II, B] [144]; thoracoscopic insufflation with talc (poudrage) is more effective than talc slurry sclerosis [II, B] [145]. If pleurodesis is not possible due to bronchial

In the case of a single metastasis, stereotactic radiosurgery (SRS) or resection is the recommended treatment [II, B] [149, 150]. For two to three metastases, SRS is recommended in patients with RPA class I–II [II, B]. There is currently no evidence that adding upfront whole brain radiotherapy (WBRT) to surgery or to SRS has an impact on OS [I, A] [151].

Data from a prospective observational Japanese study suggested that the use of SRS may have a role in patients with more than three metastases [152]. The observational study enrolled 1194 eligible patients with 1–10 newly diagnosed brain metastases in a 3-year period, with the largest tumour <10 ml in volume and <3 cm in longest diameter; total cumulative volume ≤15 ml, and a KPS score of 70 or higher, with all patients undergoing standard SRS [152]. Median OS after SRS was 13.9 months (95% CI: 12.0–15.6) in the 455 patients with a single metastasis, 10.8 months (95% CI: 9.4–12.4) in the 531 patients with 2–4
Adjuvant Whole-Brain Radiotherapy Versus Observation After Radiosurgery or Surgical Resection of One to Three Cerebral Metastases: Results of the EORTC 22952-26001 Study

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See accompanying editorial on page 121

ABSTRACT

Purpose
This European Organisation for Research and Treatment of Cancer phase III trial assesses whether adjuvant whole-brain radiotherapy (WBRT) increases the duration of functional independence after surgery or radiosurgery of brain metastases.

Patients and Methods
Patients with one to three brain metastases of solid tumors (small-cell lung cancer excluded) with stable systemic disease or asymptomatic primary tumors and WHO performance status (PS) of 0 to 2 were treated with complete surgery or radiosurgery and randomly assigned to adjuvant WBRT (30 Gy in 10 fractions) or observation (OBS). The primary end point was time to WHO PS deterioration to more than 2.

Results
Of 359 patients, 199 underwent radiosurgery, and 160 underwent surgery. In the radiosurgery group, 100 patients were allocated to OBS, and 99 were allocated to WBRT. After surgery, 79 patients were allocated to OBS, and 81 were allocated to adjuvant WBRT. The median time to WHO PS more than 2 was 10.0 months (95% CI, 8.1 to 11.7 months) after OBS and 9.5 months (95% CI, 7.8 to 11.9 months) after WBRT (P = .71). Overall survival was similar in the WBRT and OBS arms (median, 10.9 vs 10.7 months, respectively; P = .89). WBRT reduced the 2-year relapse rate both at initial sites (surgery: 59% to 27%, P < .001; radiosurgery: 31% to 19%, P = .040) and at new sites (surgery: 42% to 23%, P = .008; radiosurgery: 48% to 33%, P = .023). Salvage therapies were used more frequently after OBS than after WBRT. Intracranial progression caused death in 78 (44%) of 179 patients in the OBS arm and in 50 (28%) of 180 patients in the WBRT arm.

Conclusion
After radiosurgery or surgery of a limited number of brain metastases, adjuvant WBRT reduces intracranial relapses and neurologic deaths but fails to improve the duration of functional independence and overall survival.

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