Het onderste uit de kan…

Paul E. Van Schil

Dienst thorax- en vaatheelkunde

UZ Antwerpen

conflicts of interest: geen

Salvage surgery

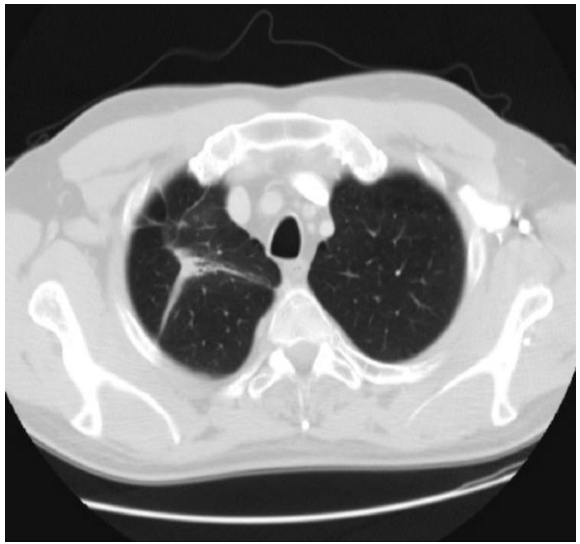
52-year ♂

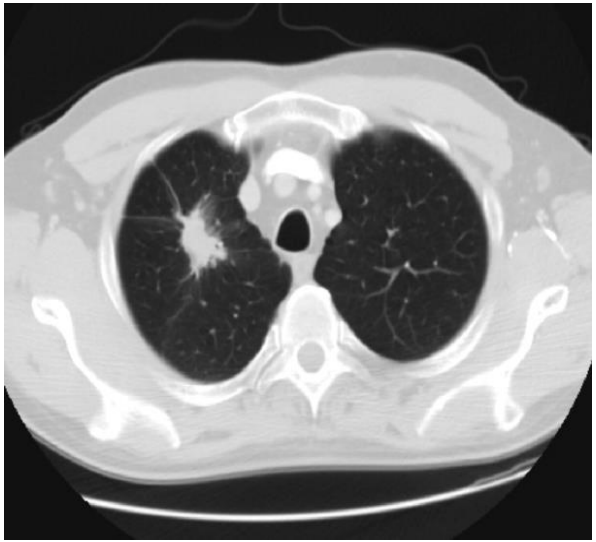
2006 NSCLC RUL + bone met L femur

stabilisation + RT L leg + 6 cycles CT - RT RUL

X-ray
300407

Salvage operation for oligometastatic lung cancer



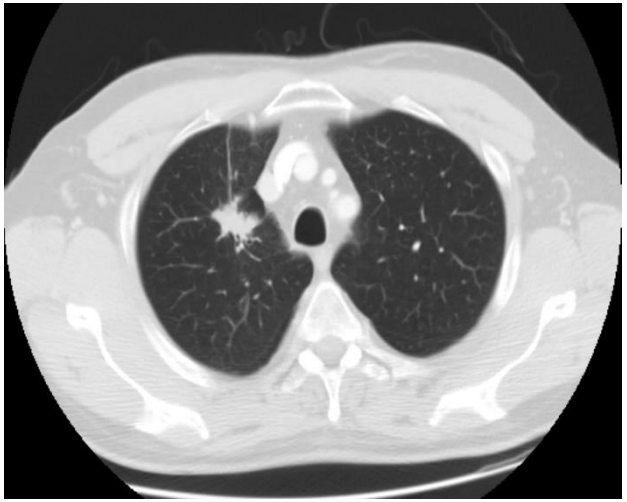


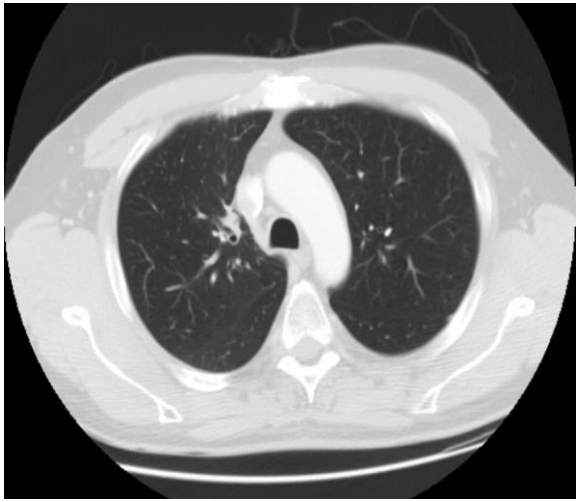
CT 281106

Salvage operation for oligometastatic lung cancer

chest CT 0807 : partial response, stable disease

CT
130807

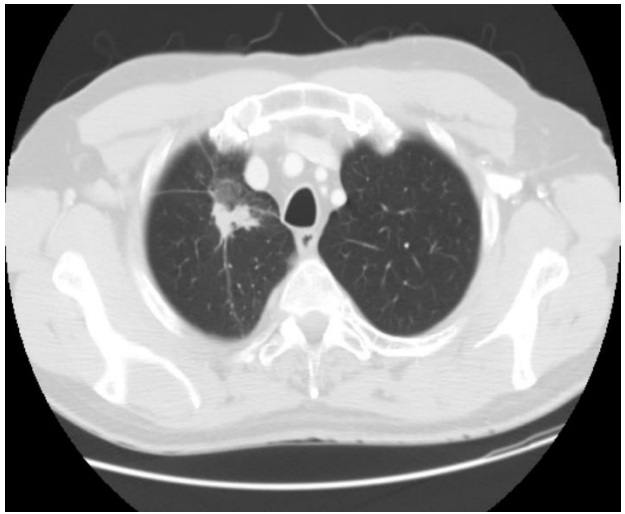


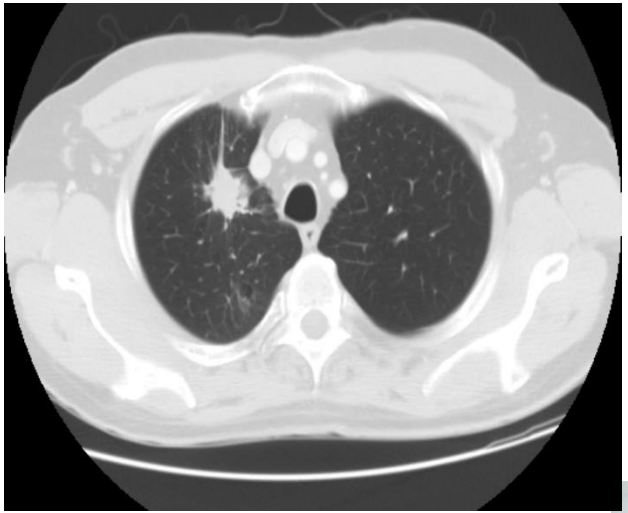


Salvage operation for oligometastatic lung cancer

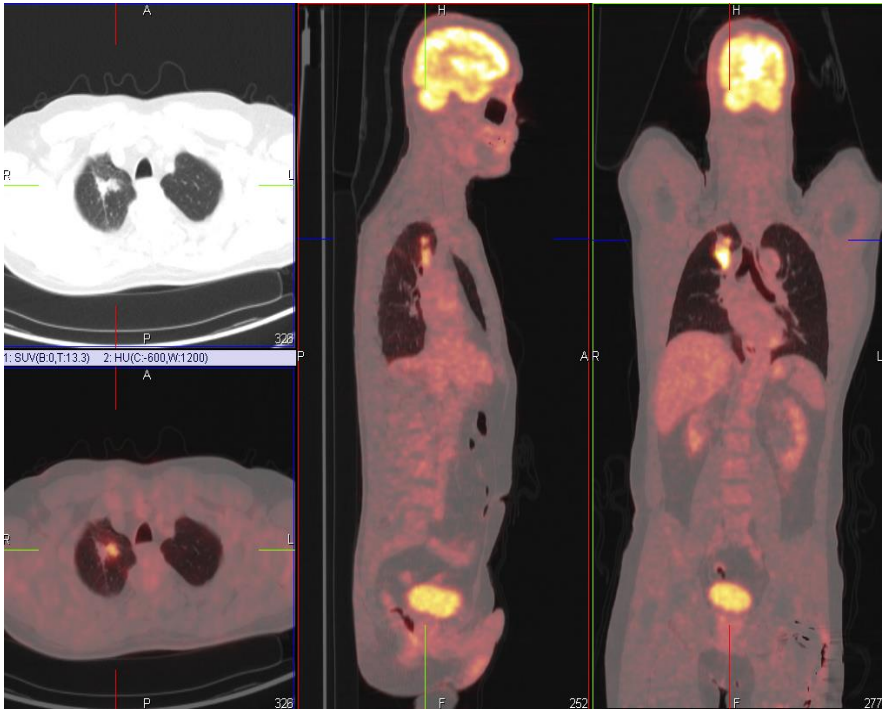
chest CT 1207 : progressive disease (locally)

CT
101207





Salvage operation for oligometastatic lung cancer



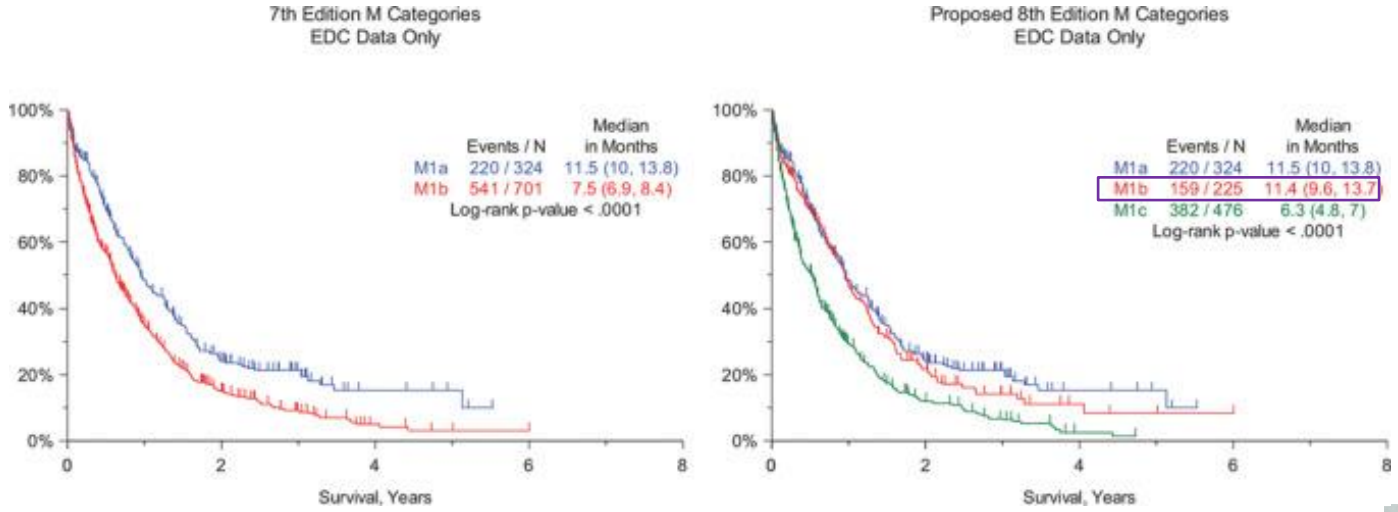
PET 191207

- PET: only RUL +
- 210108 salvage surgery: lobectomy RUL
- pT1N1 R0
- postop.complication: wound infection Staph. aureus
- 2021: NED

M1b

CRAB prospective database – electronic data capture (EDC)

M1b: single metastasis – single organ



Eberhardt W et al. J Thorac Oncol 2015;10:1515-22

Oligometastatic disease
Is there a role for surgery?

- EORTC consensus report
- clinical studies
- ESMO clinical practice guidelines
- conclusions

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EORTC task force OMD

- EORTC consensus meeting 23/01/18
  synchronous oligometastatic disease (OMD)
- low level evidence (survey): *consensus* instead of definition
- prospective data collection / clinical trials
- “common language”
- *not* suggesting how to treat patients
- consensus > 75% agree

Dingemans AM. J Thorac Oncol 2019; 14:2109-2119

EORTC task force OMD

Is number of organs involved important?

Survey 80% yes

Maximum number of organs with metastases excluding primary?

Survey variation ++

Proposal maximum 5 mets and 3 organs

Dingemans AM. J Thorac Oncol 2019; 14:2109-2119

EORTC task force OMD

Are specific organs involved with metastases important?

Survey yes 73%

Which organs would you *not* involve in your definition of OMD-NSCLC?

Exclude diffuse serosal metastases for meningeal, pericardial, pleural, mesenterial metastases and bone marrow

Special sites: brain and adrenal? publication bias?

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Oligometastases: predictive factors

Meta-analysis

- individual patient data meta-analysis 757 pts
- 1-5 synchronous or metachronous mets
- 3 risk groups:
  - low — metachronous
  - intermediate — synchronous and N0
  - high — synchronous and N+

- adequate lymph node staging required!
- surgery: complete R0 resection

Ashworth AB. Clin Lung Cancer 2014; 15:346-55

Fernandez RA. J Thorac Dis 2019; 11(suppl. 7) : S969-975

Randomised phase II trial

- multicentre, randomised phase II study
- 3 hospitals
- inclusion criteria:
  - stage IV NSCLC
  - ≤ 3 metastatic lesions after standard first-line systemic therapy
  - ECOG PS ≤ 2
  - no progressive disease

Gomez DR. J Clin Oncol 2019; 37:1558-65

Randomised phase II trial

49 pts
- 25 pts → local consolidation
- 24pts → maintenance treatment

- local R/ surgery, radiotherapy or combination
- maintenance: predefined list of approved regimens (EGFR, ALK) or observation

1ary endpoint : PFS

2ary endpoints: OS, safety, tolerability, QOL, TTP, time to appearance of new lesions

Gomez DR. J Clin Oncol 2019; 37:1558-65

Randomised phase II trial

Metastatic location by patient (total 52)

brain	13
bone	10
adrenal gland	8
pleura	7
metastatic lung lesion	6
cervical lymph nodes	4
liver	2
spleen	2

Randomised phase II trial

- median FU 12.4 mos
- median PFS 11.9 mos local consolidation
  3.9 mos maintenance
  HR 0.35 *p= .005*
- 1-year PFS 48% local consolidation
  20% maintenance
- time to appearance of new lesion:
  11.9 mos local consolidation
  5.7 mos maintenance *p= .0497*

Gomez DR. Lancet Oncol 2016; 17:1672-82

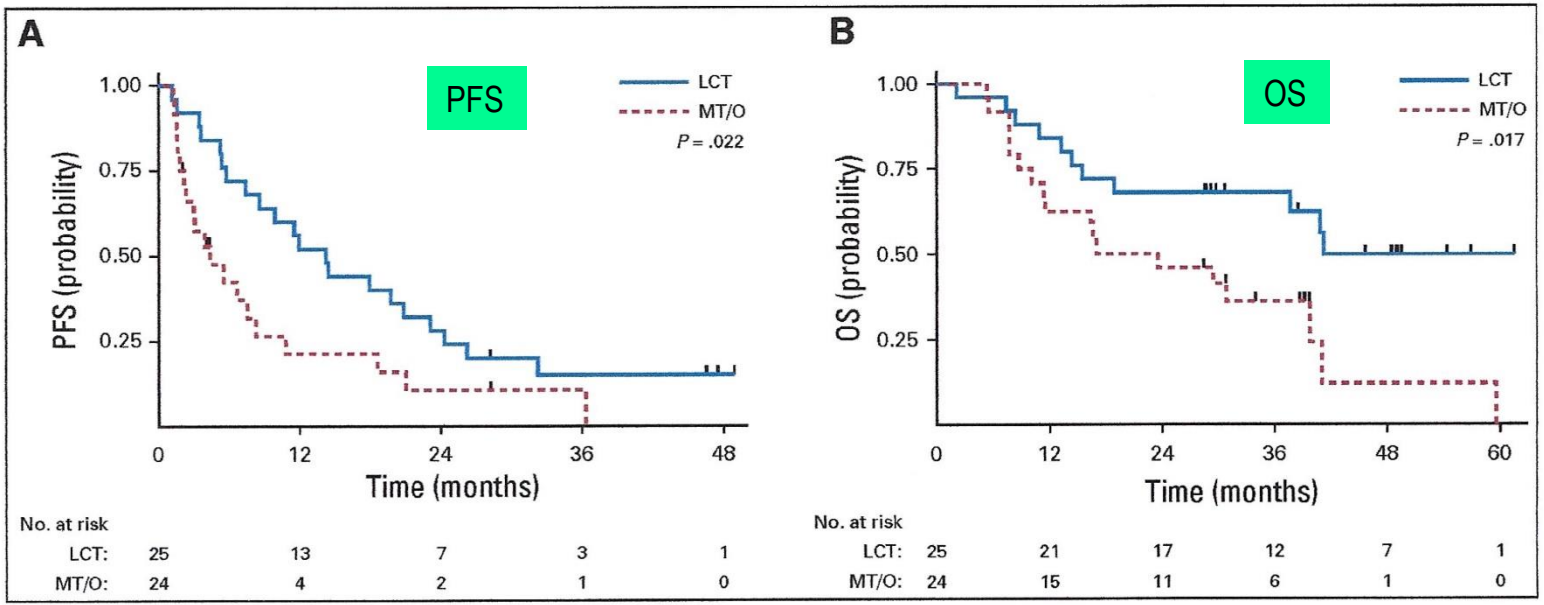

FIG 1. (A) Progression-free survival (PFS) and (B) overall survival (OS) in patients given local consolidative therapy (LCT) or maintenance therapy or observation (MT/O) for oligometastatic non–small-cell lung cancer.

Gomez DR. J Clin Oncol 2019; 37:1558-65

Interpreting the Data for Local Consolidative Therapy in Oligometastatic Disease: Where do we Stand?

Shifting the Oligometastatic Paradigm – Treatment of Patients with the "Four Aces"

Table 2. Major prognostic factors for patients with oligometastatic cancers evident across multiple studies, colloquially termed the "four aces"

Prognostic factor	Common definitions
Young age	Usually defined as <65 or <70, or analyzed as a continuous variable
Patient fitness	Karnofsky performance status ≥70
Slow-growing cancers	Metachronous presentation of oligometastases
	Longer disease-free interval between original tumor and
Minimal disease burden	Presence of fewer metastatic sites
	Single-organ oligometastases
	Lack of extracranial disease

Gomez D. WCLC 19 ES 21.03

Pulmonary resection – oligometastatic lung cancer

- single centre, cT1-3N0-2M1 NSCLC
- period 2000-2017 ≤ 3 synchronous metastases
- local consolidative therapy (LCT) 1ary lesion (surgery, RT)
- 88 pts: 63 (71.6%) radiotherapy – 25 (28.4%) surgery for 1ary lesion
  lobectomy 80%, pneumonectomy 12%, sublobar 8%
- surgical pts. younger, ↓ intrathoracic disease burden
- 90-day ✝ surgery 0% radiotherapy 1.6%

Mitchell K et al. J Thorac Cardiovasc Surg 2020; S0022-5223(20)30633-4

Pulmonary resection – oligometastatic lung cancer

	MST	1-year survival	5-year survival
surgery	55.2 mos	95.7%	48.0%
RT	23.4 mos	74.3%	24.2%

△ disease extent

- no △ in site of first failure, locoregional failures
- pulmonary resection feasible in synchronous oligometastatic NSCLC
- surgery remains a LCT option which should be further considered in clinical trials

Mitchell K et al. J Thorac Cardiovasc Surg 2020; S0022-5223(20)30633-4

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ESMO Clinical Practice Guidelines 2019

- 1-3 *synchronous* metastases:
  long-term DFS may be obtained after systemic therapy and local consolidative therapy – inclusion in clinical trials preferred

- limited *metachronous* metastases:
  long-term DFS may be obtained after radical local treatment – inclusion in clinical trials preferred

- solitary lesions in contralateral lung:
  most cases are synchronous 2nd primary tumours – to be treated with curative-intent therapy

Planchard D. Ann Oncol 2019; 30:863-70

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Oligometastatic disease
Is there a role for surgery?
Conclusions

- oligometastatic disease: relatively new entity – M1b
- every patient to be discussed in MDT
- site of oligometastatic disease: insufficient data, *publication bias towards brain, adrenal gland mets*
- systemic therapy and local consolidative therapy (high-dose radiotherapy or surgery) may provide long-term DFS and OS
- lung resection: lymph node dissection, complete resection
- prospective data needed (IASLC database - EDC)
- inclusion in clinical trials preferred

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