ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

Oligometastic recurrence during immunotherapy and the role of local therapy

Lung cancer patient case

Johan Vansteenkiste
Respiratory Oncology Unit
Dept. Pulmonology
Univ. Hospital KU Leuven, Belgium
Leuven Lung Cancer Group
www.LLCG.be www.LLCG.eu

Disclosures [update 02/2021, alphabetical]

- **Research funding at University Hospitals KU Leuven**
  - **MSD**

- **Advisory functions**
  - **AstraZeneca, BMS, Boehringer, Daiichi-Sankyo, MSD, Novartis, Pfizer, Roche, Sanofi**

- **Lectures**
  - **AstraZeneca, BMS, Eli-Lilly, MSD, Novartis**

- **Others**
  - **None**

NSCLC immunotherapy

> female patient, born 1952, ex-smoker 25 pack-years

- **Since 2008 relapsing-remitting multiple sclerosis**
  - Clinical trial therapy not tolerated, follow-up only, indolent course
- **06-2019**
  - Persistent cough, chest XR ordered by GP abnormal
  - Adenocarcinoma R upper lobe, stage cT3N2M1c (both adrenals)
  - Molecular: EGFGR/ALK/ROS1 negative. PD-L1 90%. NGS: atypical BRAF ex11 mutation
- **07-2019**
  - Start Pembrolizumab 200 mg q3w
  - 09/2019: PR after 3 cycles [RECIST 123 -> 67 mm]
  - 11/2019: CT after 6 cycles

NSCLC immunotherapy

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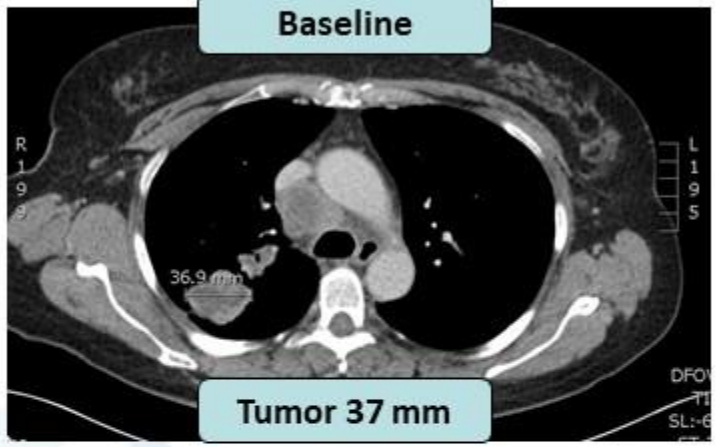
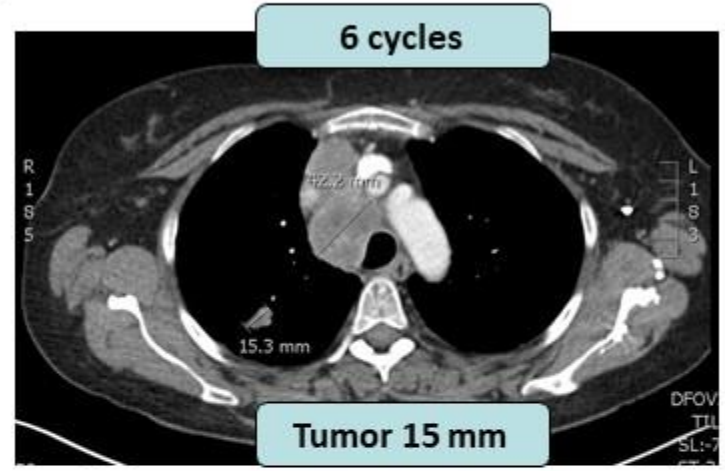
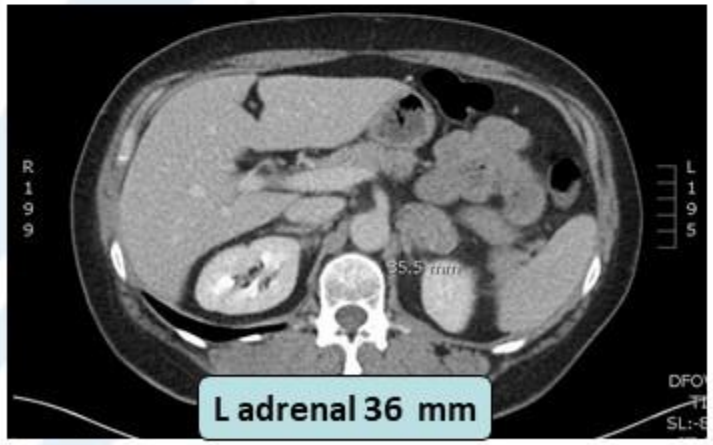


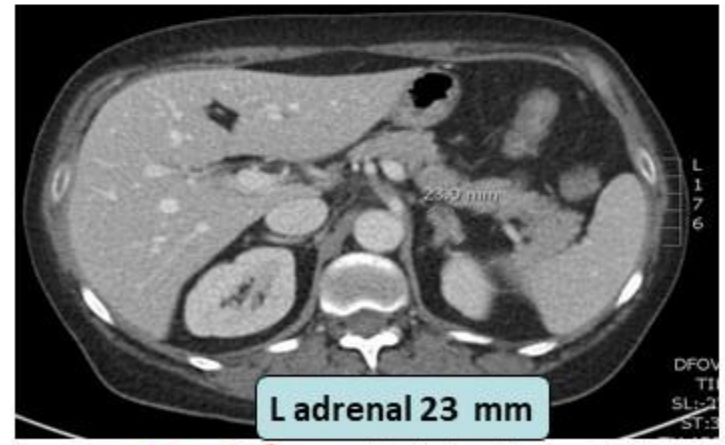


RECIST 123 mm

RECIST 67 mm

RECIST 99 mm





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NSCLC immunotherapy

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RECIST progressive disease.
Oligopression: major increase of mediastinal nodes, but other lesions (e.g. primary tumor and bilateral adrenals) remain well controlled. I will:

1. **Continue immunotherapy, this may be pseudoprogression**
2. **Switch to platinum doublet chemotherapy**
3. **Order locoregional RT to avoid superior v. cava syndrome, and then continue immunotherapy**
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5. **I would not know since I don't treat NSCLC**

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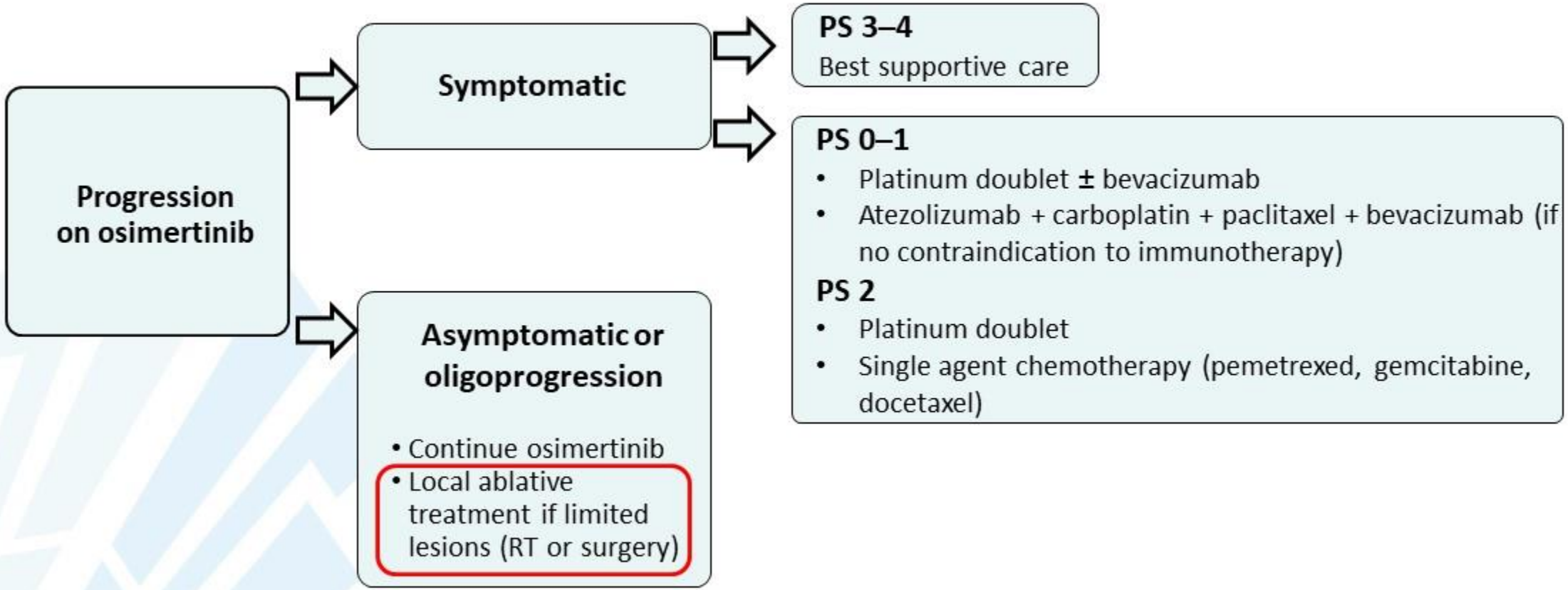
Concept coming from targeted therapies

> e.g. EGFR (TKI response rate 60 to 80%)



Planchard et al, *Ann Oncol* 29 Suppl 4:iv192–237, 2018; updated online 15 September 2020

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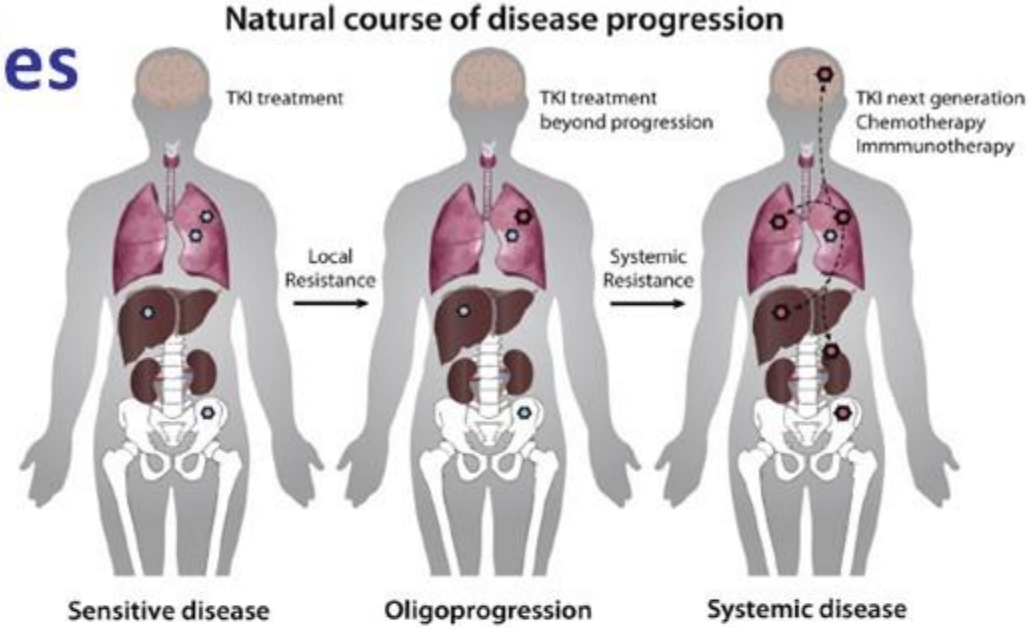
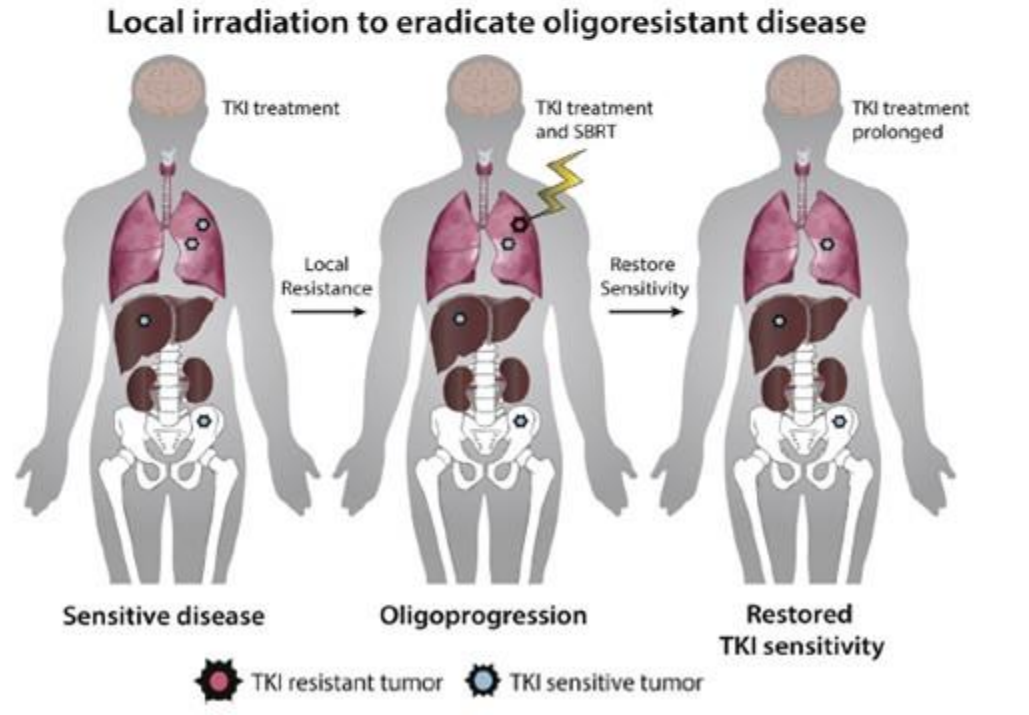
Concept coming from targeted therapies
> e.g. EGFR (TKI response rate 60 to 80%)

- **Largely based on retrospective case series !**
- **Ongoing non-controlled ph2 studies**
- **UK/EORTC HALT phase 2R/3 trial** (Targeted therapy with or without dose intensified radiot**H**erapy for oligo-progressive disease in oncogene-**A**ddicted **L**ung **T**umors)





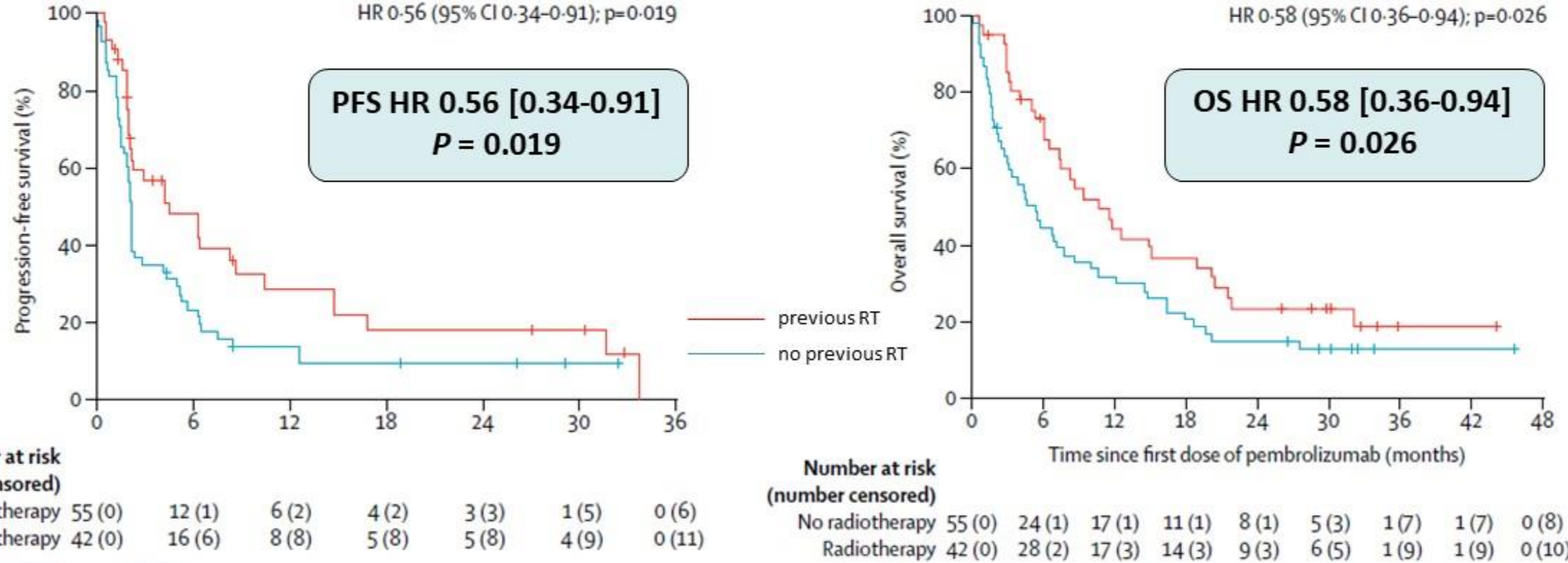
Basler et al, Lung Cancer 106:50-57, 2017

NSCLC immunotherapy

> IO and radiotherapy: retrospective analysis of ph1 pembrolizumab (KN-001)

Previous radiotherapy and the clinical activity and toxicity of pembrolizumab in the treatment of non-small-cell lung cancer: a secondary analysis of the KEYNOTE-001 phase 1 trial

Narek Shaverdian*, Aaron E Lisberg*, Krikor Bornazyan, Darlene Veruttipong, Jonathan W Goldman, Silvia C Formenti, Edward B Garon†, Percy Lee†



Number at risk (number censored)

No radiotherapy	55 (0)	12 (1)	6 (2)	4 (2)	3 (3)	1 (5)	0 (6)
Radiotherapy	42 (0)	16 (6)	8 (8)	5 (8)	5 (8)	4 (9)	0 (11)

Number at risk (number censored)

No radiotherapy	55 (0)	24 (1)	17 (1)	11 (1)	8 (1)	5 (3)	1 (7)	1 (7)	0 (8)
Radiotherapy	42 (0)	28 (2)	17 (3)	14 (3)	9 (3)	6 (5)	1 (9)	1 (9)	0 (10)

Shaverdian et al, Lancet Oncol 18:895-903, 2017

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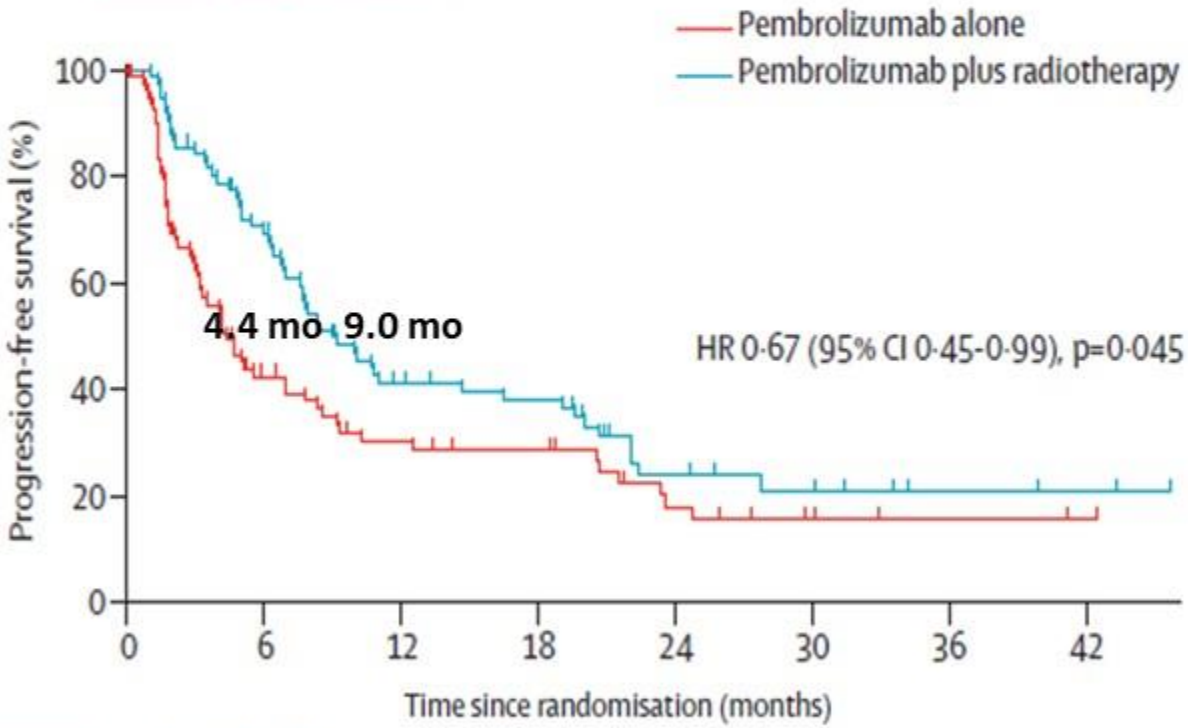
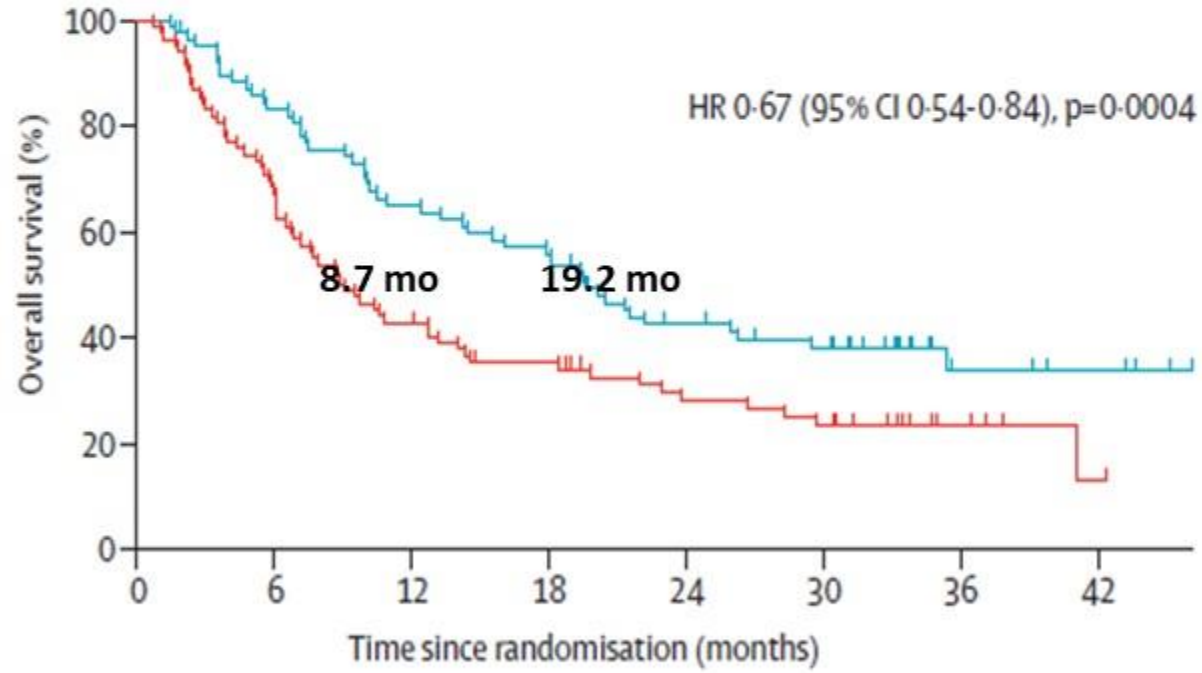
NSCLC immunotherapy

> IO and radiotherapy: RCT evidence (pooled analysis)

Pembrolizumab with or without radiotherapy for metastatic non-small-cell lung cancer: a pooled analysis of two randomised trials

Willemijn S M E Theelen, Dawei Chen*, Vivek Verma, Brian P Hobbs, Heike M U Peulen, Joachim G J V Aerts, Idris Bahce, Anna Larissa N Niemeijer, Joe Y Chang, Patricia M de Groot, Quynh-Nhu Nguyen, Nathan I Comeaux, George R Simon, Ferdinandos Skoulidis, Steven H Lin, Kewen He, Roshal Patel, John Heymach†, Paul Baas†, James W Welsh†*





Theelen et al, Lancet Oncol online October 20, 2020

- **Best ARR: 19.7% (15/76) with pembro vs. 41.7% (30/72) with pembro plus RT (OR 2.96, 95%CI 1.42-6.20; p=0.0039)**

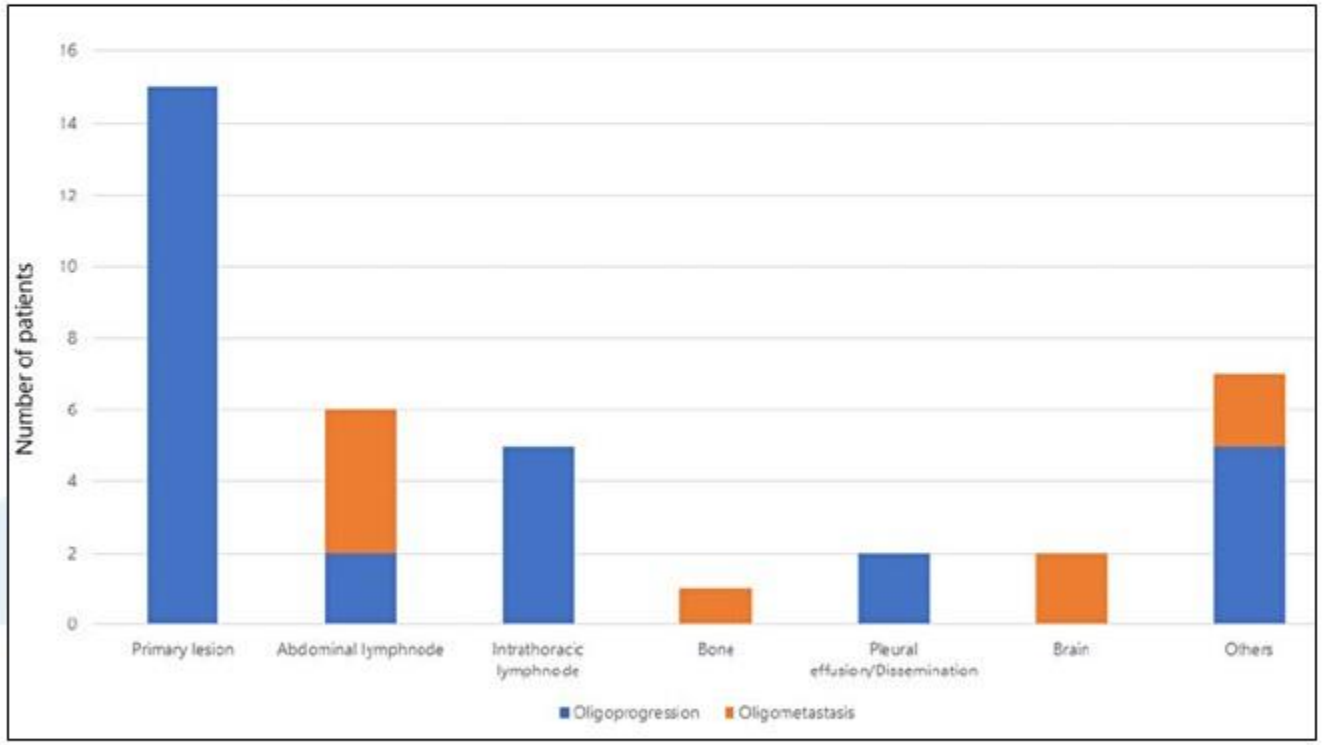
NSCLC immunotherapy

> oligoprogression: sites

ORIGINAL ARTICLE

Cancer Science WILEY

Efficacy of local therapy for oligoprogressive disease after programmed cell death 1 blockade in advanced non-small cell lung cancer



Kagawa et al, Cancer Sci 111:4442-4452, 2020 (table adapted)

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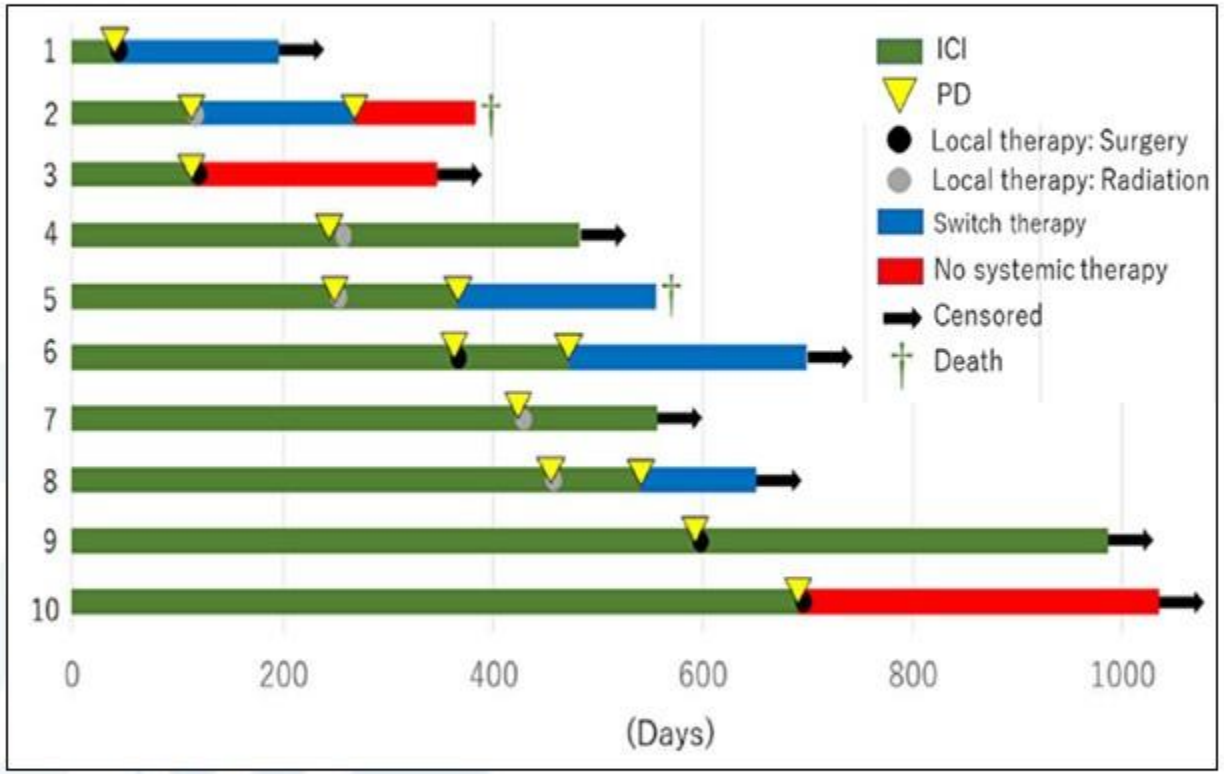
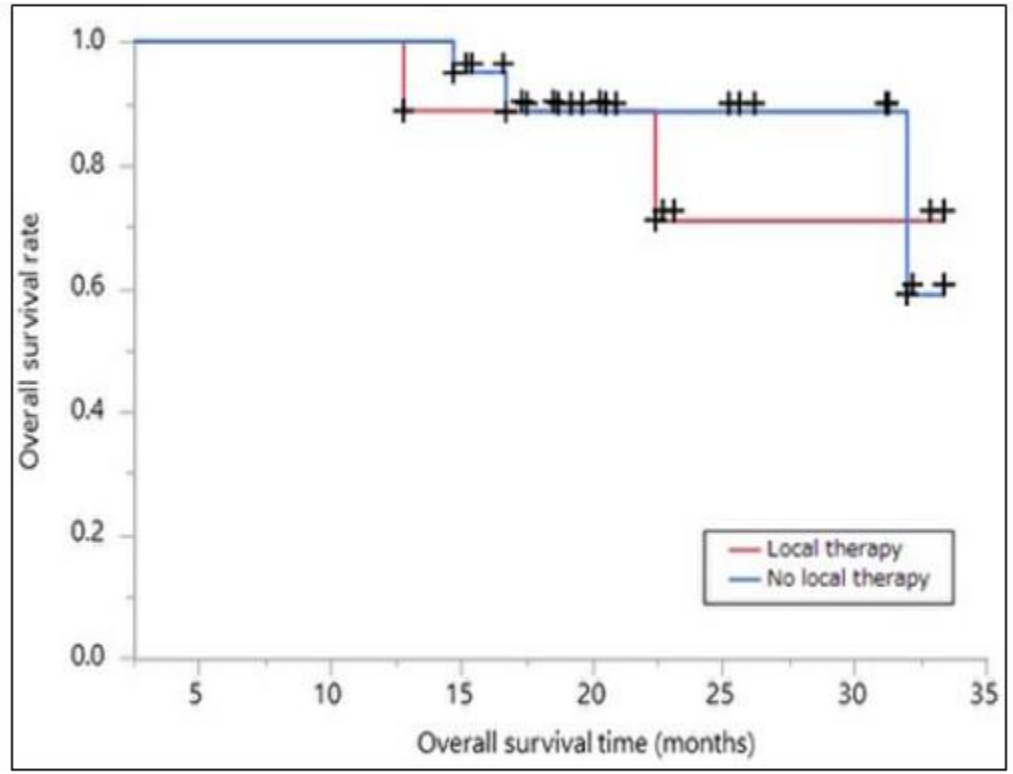
NSCLC immunotherapy

> local ablative therapy for oligoprogression: course and OS effect





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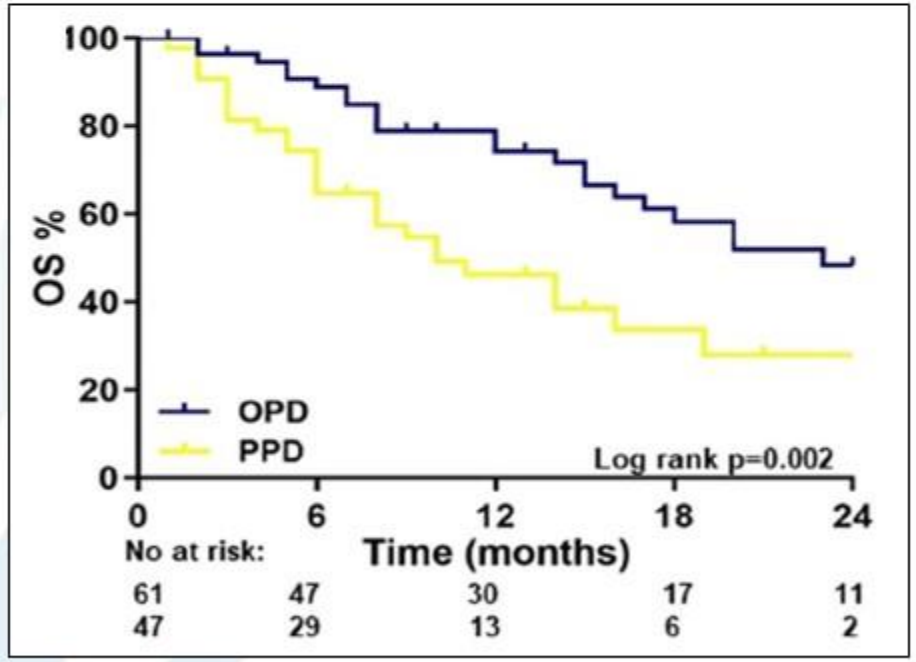
> local ablative therapy for oligoprogression

Radiation Oncology

Metastasis directed stereotactic radiotherapy in NSCLC patients progressing under targeted- or immunotherapy: efficacy and safety reporting from the 'TOaSTT' database

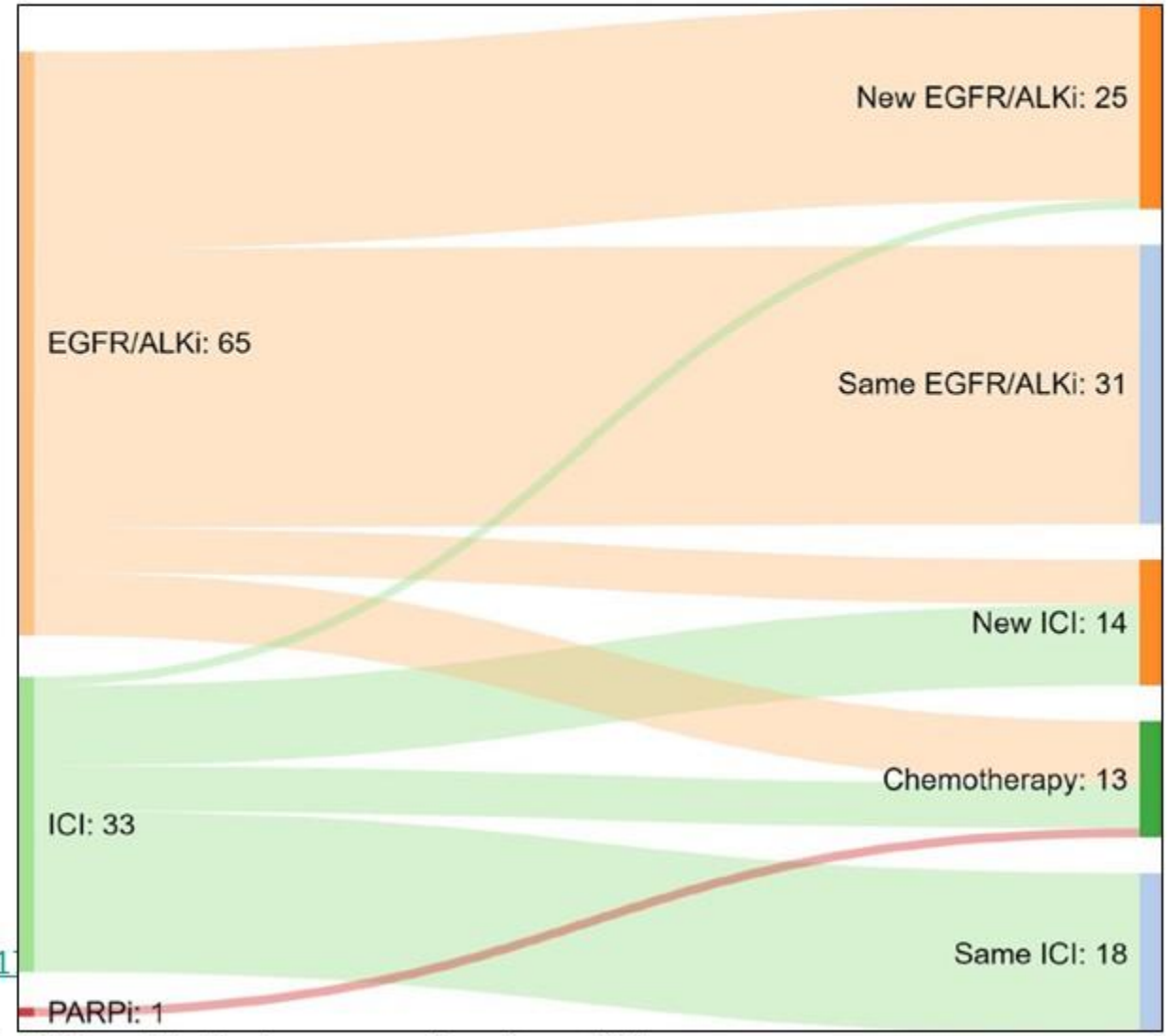
OS of metastatic NSCLCreceiving metastasis directed therapy concurrent to targeted- or immunotherapy



Kroeze et al, Radiat Oncol 2021, https://doi.org/10.1186/s13014-020-01

OPD: oligoprogressive disease; PPD: polyprogressive disease

Flow chart of systemic therapy switch following SRT



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