

What has changed with the 8th TNM staging system?

125 - Impact on chemotherapy and multimodality strategies in early and advanced diseases

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#### **Disclosures**

 I attended advisory boards and/or provided lectures for: Roche, Eli Lilly, Boehringer Ingelheim, Astra Zeneca, Pfizer, BMS, Amgen, Astra Zeneca, Novartis, MSD; for which I received honoraria

I declare no conflicts of interest



# Why TNM classification?



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#### TNM staging system

From Wikipedia, the free encyclopedia

The **TNM Classification of Malignant Tumours (TNM)** is a cancer staging notation system that gives codes to describe the stage of a person's cancer, when this originates with a solid tumor.

- T describes the size of the original (primary) tumor and whether it has invaded nearby tissue,
- N describes nearby (regional) lymph nodes that are involved,
- M describes distant metastasis (spread of cancer from one part of the body to another).

The TNM staging system for all solid tumors was devised by Pierre Denoix between 1943 and 1952, using the size and extension of the primary tumor, its lymphatic involvement, and the presence of metastases to classify the progression of cancer. It has gained a wide degree of international acceptance for many solid tumor cancers, but is not applicable to diffused cancers such as leukaemia and is of limited use for other cancers such as diffuse lymphoma and ovarian cancer.

TNM is developed and maintained by the Union for International Cancer Control (UICC) to achieve consensus on one globally recognised standard for classifying the extent of spread of cancer. The TNM classification is also used by the American Joint Committee on Cancer (AJCC) and the International Federation of Gynecology and Obstetrics (FIGO). In 1987, the UICC and AJCC staging systems were unified into a single staging system.

Contents [hide]



# **TNM** staging

Grouping of patients with same pro

# PROGNOSTIC impact

| TABLE 1.  | Study Objectives  |  |  |  |  |
|-----------|---|--|--|--|--|
| Component | Objective   |  |  |  |  |
| T         | Assess the prognostic impact of tumor size.   |  |  |  |  |
|           | Assess the classification capacity of each descriptor defining $\ensuremath{\mathrm{T-status}}.$  |  |  |  |  |
|           | Study new conditions not included in the present T (e.g.,<br>differences between parietal pleura invasion and rib<br>invasion).                               |  |  |  |  |
| N         | Assess the prognostic impact of N-status.   |  |  |  |  |
|           | Explore the prognostic impact of involved lymph node<br>"zones" within N1 and N2 categories.  |  |  |  |  |
|           | Assess the prognostic impact of:  |  |  |  |  |
|           | Nodal extent (single vs. multiple station involvement in<br>N1 and N2 locations),   |  |  |  |  |
|           | Nodal size, i.e., the largest involved node within the<br>relevant N category, and  |  |  |  |  |
|           | Individual nodes being involved in each nodal category.   |  |  |  |  |
|           | Assess the prognostic impact of extracapsular extension.  |  |  |  |  |
|           | Assess the prognostic impact of the N3 nodal location, i.e.,<br>contralateral mediastinum, ipsilateral or contralateral<br>supraclavicular fossa.             |  |  |  |  |
| M         | Assess the prognostic impact of M-status, especially those descriptors now included within the new category of M1a proposed by the IASLC for the 7th edition. |  |  |  |  |
|           | Assess the prognostic impact of:  |  |  |  |  |
|           | Single metastasis in a single organ   |  |  |  |  |
|           | Multiple metastases in a single organ, and  |  |  |  |  |
|           | Multiple metastases in several organs.  |  |  |  |  |
| Other     | Assess the prognostic impact of histologic type and grade.  |  |  |  |  |
|           | Assess the reliability of staging methods utilized in clinical<br>staging (for those tumors with pretreatment and<br>postsurgical classification).            |  |  |  |  |
|           | Assess the prognostic impact of complete, incomplete, and<br>uncertain resections, according to the proposed<br>definitions of the IASLC.                     |  |  |  |  |
|           | Assess the prognostic impact of clinical factors, including   |  |  |  |  |



co-morbidity and pulmonary function tests.

Assess the prognostic impact of maximum standard uptake

#### **TNM: 8th versus 7th version**

- Prospective versus retrospective
- Less variation in treatment
- More T-details (tumor size)
- Number of involved nodes / nodal stations
- Various forms M1 disease
- Pre-treatment T,N,M: use MRI / PET reported
- Data collection 2009-2010;
- follow-up 2011-2012;
- analysis 2013



#### TNM database

- N = 70,967 NSCLC
- 79% patient from Asia, no information on EGFR status
- Treatment not reported

**TABLE 2.** Results of Univariate Analyses of Survival of Pathologically Staged T1–T3 N0M0R0 Cases According to Tumor Size and T2 and T3 Descriptors

|                           |                    | Survival from S   | Surgery |
|---------------------------|--------------------|-------------------|---------|
| Variable                  | n/N (%)            | HR (95% CI)       | P value |
| Other histology vs. adeno | 7064/21,122 (33)   | 2.19 (2.07, 2.32) | < 0.001 |
| Squamous vs. other        | 5237/21,122 (25)   | 1.96 (1.85, 2.07) | < 0.001 |
| Age ≥ 60 vs. <60          | 16,070/21,014 (76) | 2.29 (2.11, 2.49) | < 0.001 |
| Mala va, famala           | 12,457/20,005 (50) | 1.86 (1.75, 1.08) | <0.001  |
| Americas vs. Asia         | 1873/21,123 (9)    | 1.79 (1.64,1.97)  | < 0.001 |
| Europe/Australia vs. Asia | 2361/21,123 (11)   | 2.61 (2.43,2.80)  | < 0.001 |

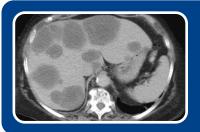
# Chemotherapy in NSCLC, current guidelines



Adjuvant cisplatin-based chemotherapy



(conc) platinum based chemotherapy



Palliative cisplatin based chemotherapy

# No chemotherapy in NSCLC

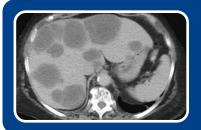


Adjuvant cisplatin-based chemotherapy

Stage I

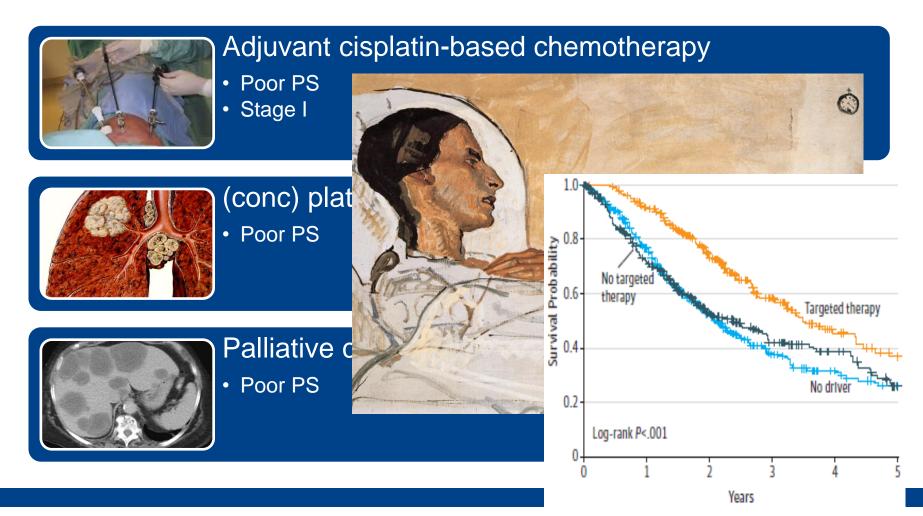


(conc) platinum based chemotherapy



Palliative cisplatin based chemotherapy

# No chemotherapy in NSCLC





# **Chemotherapy in NSCLC, TNM 8**



Adjuvant cisplatin-based chemotherapy



(conc) platinum based chemotherapy

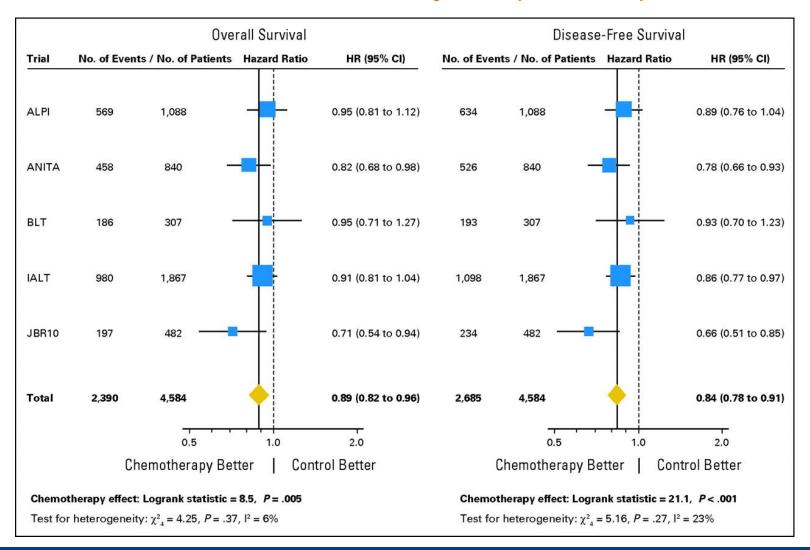


Palliative cisplatin based chemotherapy

# Adjuvant chemotherapy: ESMO guideline

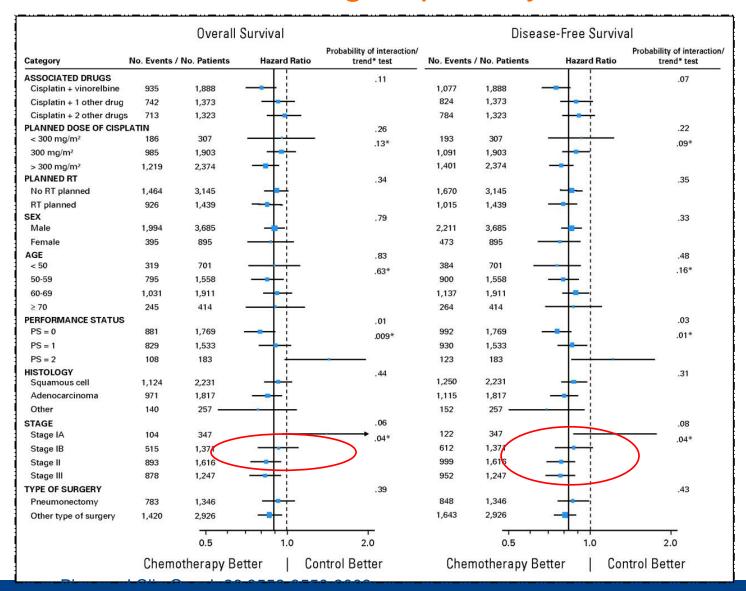
Adjuvant chemotherapy should be offered to patients with resected stage II and III NSCLC [I, A] and can be considered in patients with resected
stage IB disease and a primary tumour >4 cm [II, B]. Pre-existing comorbidity, time from surgery and postoperative recovery need to be taken into
account in this decision taken in a multidisciplinary tumour board [V, A].

# LACE meta analysis (TNM 6)



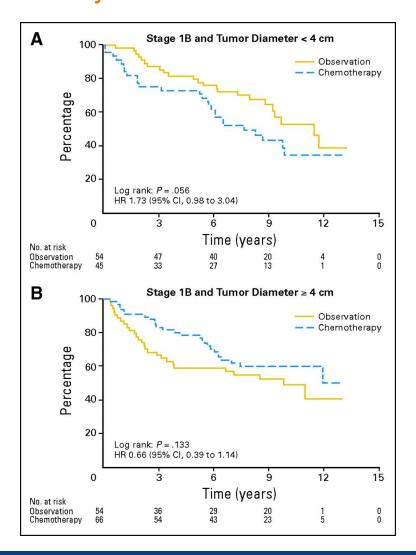


# LACE: subgroup analysis





# Survival comparison for stage IB (TNM6) patients with primary tumor ≥ 4 cm by treatment arm: JBR-10





#### From TNM 6 to TNM 7

**TABLE 4.** Descriptors, Proposed T and M Categories, and Proposed Stage Groupings

| Sixth Edition<br>T/M Descriptor | Proposed<br>T/M | N0  | N1   | N2   | N3   |
|---------------------------------|-----------------|-----|------|------|------|
| T1 (≤2 cm)                      | Tla             | IA  | IIA  | IIIA | IIIB |
| T1 (>2-3 cm)                    | T1b             | IA  | IIA  | IIIA | IIIB |
| 12 (≤5 cm)                      | T2a             | IB  | IIA  | IIIA | IIIB |
| T2 (>5-7 cm)                    | T2b             | IIA | ИB   | IIIA | IIIB |
| T2 (>7 cm)                      | T3              | IIB | ША   | ША   | IIIB |
| T3 invasion                     |                 | IIB | IIIA | IIIA | IIIB |
| T4 (same lobe nodules)          |                 | IIB | ША   | ША   | IIIB |
| T4 (extension)                  | T4              | ША  | ША   | IIIB | IIIB |
| M1 (ipsilateral lung)           |                 | ША  | IIIA | IIIB | IIIB |
| T4 (pleural effusion)           | Mla             | IV  | IV   | IV   | IV   |
| M1 (contralateral lung)         |                 | IV  | IV   | IV   | IV   |
| M1 (distant)                    | Mlb             | IV  | IV   | IV   | IV   |

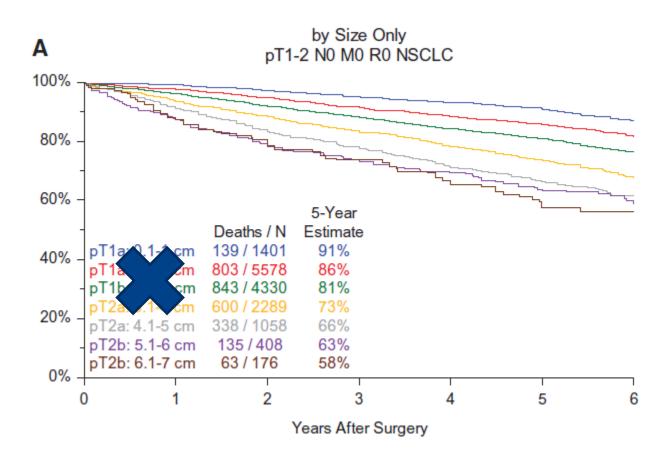
Cells in bold indicate a change from the sixth edition for a particular TNM category.



# Adjuvant chemotherapy: ESMO guideline TNM 7

Adjuvant chemotherapy 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]. Pre-existing comorbidity, time from surgery and postoperative recovery need to be taken into
account in this decision taken in a multidisciplinary tumour board [V, A].

## **TNM 8 T-descriptor: size matters!**





### 8th TNM system

Table 5. Descriptors and T and M categories in the seventh edition and as proposed for the eighth edition<sup>a</sup>

|   |              | N categories Overall stage |            |             |             |  |
|---|--------------|----------------------------|------------|-------------|-------------|--|
|   |              |                            |            |             |             |  |
| Descriptor in 7th edition                     | Proposed T/M | NO                         | N1         | N2          | N3          |  |
| T1 ≤ 1 cm                                     | T1a          | IA1 (IA)                   | IIB (IIA)  | IIIA        | IIIB        |  |
| T1 > 1-2 cm                                   | T1b          | IA2 (IA)                   | IIB (IIA)  | IIIA        | IIIB        |  |
| T1 > 2-3 cm                                   | T1c          | IA3 (IA)                   | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 3-4 cm                                   | T2a          | IB                         | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 4-5 cm                                   | T2b          | IIA (IB)                   | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 5-7 cm                                   | T3           | IIB (IIA)                  | IIIA (IIB) | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 structures                                 | T3           | IIB                        | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 > 7 cm                                     | T4           | IIIA (IIB)                 | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 diaphragm                                  | T4           | IIIA (IIB)                 | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 endobronchial: location/atelectasis 3-4 cm | T2a          | IB (IIB)                   | IIB (IIIA) | IIIA        | IIIB        |  |
| T3 endobronchial: location/atelectasis 4-5 cm | T2b          | IIA (IIB)                  | IIB (IIIA) | IIIA        | IIIB        |  |
| T4  | T4           | IIIA                       | IIIA       | IIIB        | IIIC (IIIB) |  |
| M1a   | M1a          | IVA (IV)                   | IVA (IV)   | IVA (IV)    | IVA (IV)    |  |
| M1b single lesion                             | M1b          | IVA (IV)                   | IVA (IV)   | IVA (IV)    | IVA (IV)    |  |
| M1c multiple lesions                          | M1c          | IVB (IV)                   | IVB (IV)   | IVB (IV)    | IVB (IV)    |  |

Where there is a change, the resultant stage groupings proposed for the eighth edition are in bold, and the stage in the seventh edition is given in parenthesis.

T, tumor; M, metastasis



# **Chemotherapy in NSCLC, TNM 8**

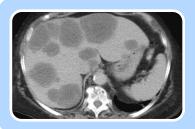


Adjuvant cisplatin-based chemotherapy

• in resected stage II-III NSCLC patients



(conc) platinum based chemotherapy



Palliative cisplatin based chemotherapy

# **Chemotherapy in NSCLC, TNM 8**



Adjuvant cisplatin-based chemotherapy

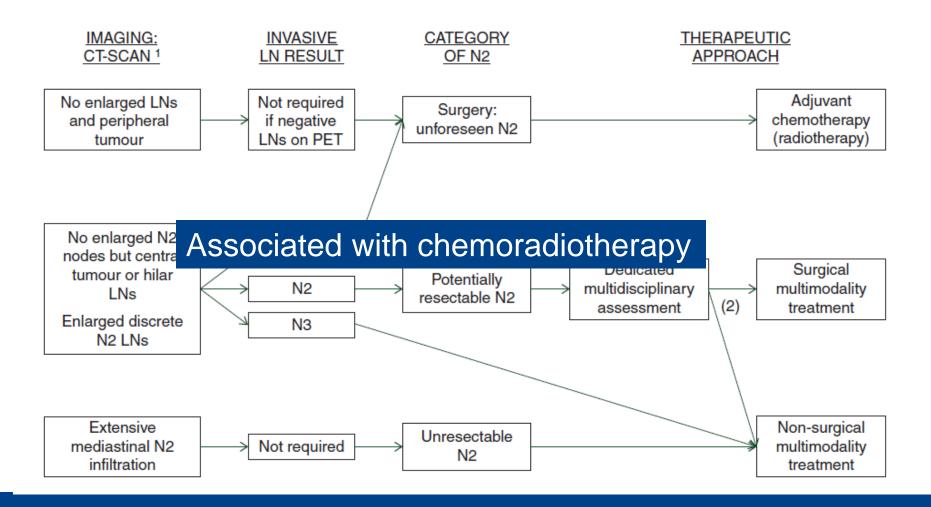


(conc) platinum based chemotherapy



Palliative cisplatin based chemotherapy

# ESMO guideline: Stage III, a heterogeneous disease



# 8th TNM system

Table 5. Descriptors and T and M categories in the seventh edition and as proposed for the eighth edition<sup>a</sup>

|   |              | N categories Overall stage |            |             |             |  |
|---|--------------|----------------------------|------------|-------------|-------------|--|
|   |              |                            |            |             |             |  |
| Descriptor in 7th edition                     | Proposed T/M | NO                         | N1         | N2          | N3          |  |
| T1 ≤ 1 cm                                     | T1a          | IA1 (IA)                   | IIB (IIA)  | IIIA        | IIIB        |  |
| T1 > 1-2 cm                                   | T1b          | IA2 (IA)                   | IIB (IIA)  | IIIA        | IIIB        |  |
| T1 > 2-3 cm                                   | T1c          | IA3 (IA)                   | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 3-4 cm                                   | T2a          | IB                         | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 4-5 cm                                   | T2b          | IIA (IB)                   | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 5-7 cm                                   | T3           | IIB (IIA)                  | IIIA (IIB) | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 structures                                 | T3           | IIB                        | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 > 7 cm                                     | T4           | IIIA (IIB)                 | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 diaphragm                                  | T4           | IIIA (IIB)                 | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 endobronchial: location/atelectasis 3-4 cm | T2a          | IB (IIB)                   | IIB (IIIA) | IIIA        | IIIB        |  |
| T3 endobronchial: location/atelectasis 4-5 cm | T2b          | IIA (IIB)                  | IIB (IIIA) | IIIA        | IIIB        |  |
| T4  | T4           | IIIA                       | IIIA       | IIIB        | IIIC (IIIB) |  |
| M1a   | M1a          | IVA (IV)                   | IVA (IV)   | IVA (IV)    | IVA (IV)    |  |
| M1b single lesion                             | M1b          | IVA (IV)                   | IVA (IV)   | IVA (IV)    | IVA (IV)    |  |
| M1c multiple lesions                          | M1c          | IVB (IV)                   | IVB (IV)   | IVB (IV)    | IVB (IV)    |  |

Where there is a change, the resultant stage groupings proposed for the eighth edition are in bold, and the stage in the seventh edition is given in parenthesis.

T, tumor; M, metastasis



# **Stage III according to TNM 8**

- Includes T3 T4 = IIIa
- tumors > 7 cm
- Includes diafragm invasion

No change in N descriptors



# **TNM 8 ≠ changing treatment**

As it was the case after the 7<sup>th</sup> edition was published, many specialists managing lung cancer patients used the changes in the classification to modify therapy. If the proposed IASLC recommendations are eventually introduced in the 8th edition of the TNM classification, they should not be interpreted as basis for changing treatment. They imply a taxonomic refinement and not new indications of already established treatment protocols that should ideally be derived from clinical trials.33,34 So, for the T component, upstaging invasion of the diaphragm or tumors greater than 7 cm from T3 to T4 does not imply that these tumors should not be resected if they are amenable to complete resection.

### Stage III = IIIA - IIIB - IIIC

Table 5. Descriptors and T and M categories in the seventh edition and as proposed for the eighth edition

|   |              | N categori    | es         |             |             |  |
|---|--------------|---------------|------------|-------------|-------------|--|
|   |              | Overall stage |            |             |             |  |
| Descriptor in 7th edition                     | Proposed T/M | N0            | N1         | N2          | N3          |  |
| T1 ≤ 1 cm                                     | T1a          | IA1 (IA)      | IIB (IIA)  | IIIA        | IIIB        |  |
| T1 > 1-2 cm                                   | T1b          | IA2 (IA)      | IIB (IIA)  | IIIA        | IIIB        |  |
| T1 > 2-3 cm                                   | T1c          | IA3 (IA)      | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 3-4  cm                                  | T2a          | IB            | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 4-5  cm                                  | T2b          | IIA (IB)      | IIB (IIA)  | IIIA        | IIIB        |  |
| T2 > 5-7  cm                                  | T3           | IIB (IIA)     | IIIA (IIB) | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 structures                                 | T3           | IIB           | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 > 7  cm                                    | T4           | IIIA (IIB)    | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 diaphragm                                  | T4           | IIIA (IIB)    | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |
| T3 endobronchial: location/atelectasis 3-4 cm | T2a          | IB (IIB)      | IIB (IIIA) | IIIA        | IIIB        |  |
| T3 endobronchial: location/atelectasis 4-5 cm | T2b          | IIA (IIB)     | IIB (IIIA) | IIIA        | IIIB        |  |
| T4  | T4           | IIIA          | IIIA       | IIIB        | IIIC (IIIB) |  |
| M1a   | M1a          | IVA (IV)      | IVA (IV)   | IVA (IV)    | IVA (IV)    |  |
| M1b single lesion                             | M1b          | IVA (IV)      | IVA (IV)   | IVA (IV)    | IVA (IV)    |  |
| M1c multiple lesions                          | M1c          | IVB (IV)      | IVB (IV)   | IVB (IV)    | IVB (IV)    |  |

<sup>a</sup>Where there is a change, the resultant stage groupings proposed for the eighth edition are in bold, and the stage in the seventh edition is given in parenthesis.

T, tumor; M, metastasis.



# **Chemotherapy in NSCLC, TNM 8**

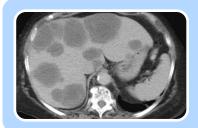


Adjuvant cisplatin-based chemotherapy



(conc) platinum based chemotherapy

More surgery



Palliative cisplatin based chemotherapy

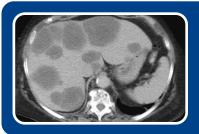
# **Chemotherapy in NSCLC, TNM 8**



Adjuvant cisplatin-based chemotherapy



(conc) platinum based chemotherapy



Palliative cisplatin based chemotherapy

# **ESMO** guideline: Stage IV

# treatment of stage IV NSCLC

The treatment strategy should take into account histology, molecular pathology, age, PS, comorbidities, and patient's preferences. Treatment decisions should ideally be discussed within a multidisciplinary tumour board. Systemic therapy should be offered to all stage IV NSCLC patients with a PS 0–2 [I, A].

# ESMO guideline: Oligometastatic disease

- Stage IV NSCLC patients with oligometastases in the brain: See recommendations for brain metastases treatment.
- Stage IV patients with one to three synchronous metastases may experience long-term disease-free survival (DFS) after systemic therapy and a radical local treatment (high-dose radiotherapy or surgery) [II, B].
   Because only one non-randomised phase II trial is available, inclusion in trials is preferred.
- Stage IV patients with a few metachronous metastases may be treated with a radical local treatment and experience long-term DFS [III, B]. However, this is based only on retrospective data.
- Solitary lesions in the contralateral lung should, in most cases, be considered as synchronous secondary primary tumours and, if possible, treated with radical intent [IV, B].

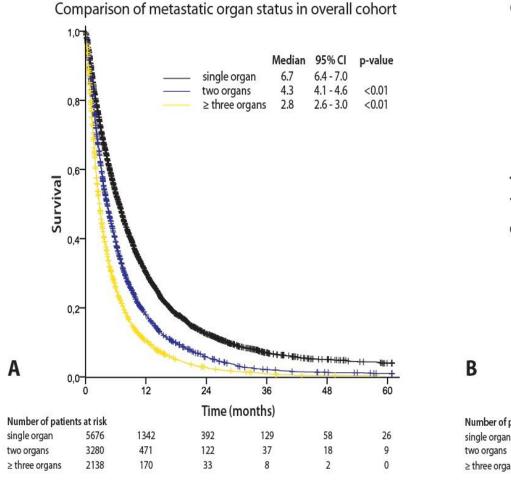
# Oligometastatic disease

 $\leq$  5 metastatic lesions

Single organ?



# Dutch Cancer Registry, population based OS – number of organs affected



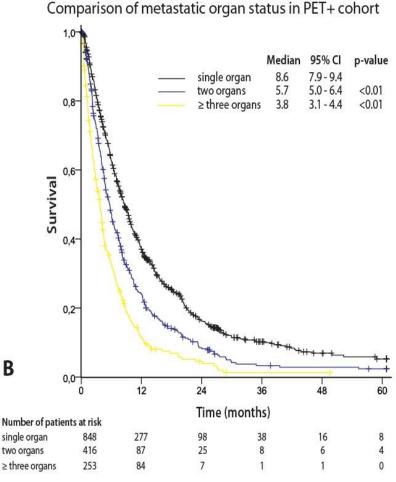




TABLE 1. Subject Counts by Data Source and 7th edition M Category

|                                 |                                |  | 7th Editio | n M Category |
|---------------------------------|--------------------------------|--|------------|--------------|
| Database Type                   | Country                        | Institution                                  | M1a        | M1b          |
| EDC Argentina                   | Argentina                      | Hospital Británico de Buenos Aires           | 2          | 4            |
|                                 | Hospital Universitario Austral | 2  | 2          |              |
|                                 |                                | Hospital Universitario-Fundación Favalor     |            | 7            |
| Australia                       |                                | Hospital de Rehabilitación Respiratoria      | 3          | 1            |
|                                 |                                | Peter MacCallum Cancer Institute             |            | 2            |
|                                 | Belgium                        | University Hospital Antwerp                  | 15         | 51           |
|                                 |                                | University Hospital Ghent                    | 6          | 18           |
|                                 | China                          | Currendone Constral Hespital                 | 83         | 188          |
|                                 | China                          | Guangdong General Hospital                   | 83         | 100          |
|                                 | Greece                         | Athens School of Medicine                    | 6          | 15           |
|                                 | Spain                          | Complejo Hospitalario de Ourense             | 41         | 83           |
|                                 | Span                           | Complejo Hospitalario La Mancha Centro       | 9          | 31           |
|                                 |                                | Fundación Jiménez Díaz                       | 18         | 45           |
|                                 |                                | Htal, de la Plana Vila-Real                  | 12         | 28           |
|                                 |                                | Htal. General Universitario de Valencia      | 1          |              |
| Soloctic                        | on bias?                       | Htal. General Universitario Gregorio Mar     | i          |              |
| SCICCIIC                        | ni Dias:                       | Htal. General Universitario de Albacete      | 14         | 42           |
|                                 |                                | Htal. Meixoeiro                              | 3          | 26           |
|                                 |                                | Htal. Nuestra Señora de Sonsoles             | 2          | 8            |
|                                 |                                | Htal. San Pedro Alcántara                    | 12         | 24           |
|                                 |                                | Htal. Severo Ochoa                           | 10         | 13           |
|                                 |                                | Htal. Sierrallana, Sección de Neumología     | 9          | 23           |
|                                 |                                | Htal. Universitari Joan XXIII                | 13         | 10           |
|                                 |                                | Htal. Universitario Central de Asturias      | 6          | 5            |
|                                 |                                | Htal. Universitario La Fe                    | 12         | 28           |
|                                 |                                | Htal. Universitario de Canarias              | 10         | 15           |
|                                 |                                | Htal. de Sagunto                             |            | 4            |
|                                 | United States                  | Mayo Clinic Rochester                        |            | 13           |
|                                 |                                | NYU Langone Medical Center and Cancer Center | 29         | 37           |
|                                 |                                | Penrose Cancer Center                        | 2          | 5            |
| Subtotal—EDC cases by 7th ed    | lition M category              |  | 324        | 735          |
| Subtotal—EDC cases              |                                |  | 1          | 1059         |
| Consortium                      | Turkey                         | Turkish Thoracic Society                     | 81         | 1215         |
| Institutional registry          | Australia                      | Prince Charles Hospital                      | 2          | 54           |
| Subtotal—All institutions by 7t | h edition M category           |  | 407        | 2004         |



TABLE 3. Prognostic Impact of Single and Multiple Metastatic Lesions in a Single Organ versus Multiple Metastatic Sites

| Proposed Category |                                    | Overall Survival |                   |         |  |  |
|-------------------|------------------------------------|------------------|-------------------|---------|--|--|
|                   | Variable                           | n/N (%)          | HR (95% CI)       | P Value |  |  |
| M1a               | M1a                                | 324/1025 (32)    | Reference level   |         |  |  |
| M1b               | M1b, single organ/lesion           | 225/1025 (22)    | 1.11 (0.91, 1.36) | 0.308   |  |  |
| M1c               | M1b, single organ/multiple lesions | 229/1025 (22)    | 1.63 (1.34, 1.99) | < 0.001 |  |  |
|                   | M1b, multiple organs               | 247/1025 (24)    | 1.85 (1.52, 2.24) | < 0.001 |  |  |

P value from score χ<sup>2</sup> test in Cox regression. HR, hazard ratio; 95% CI, 95% confidence interval.

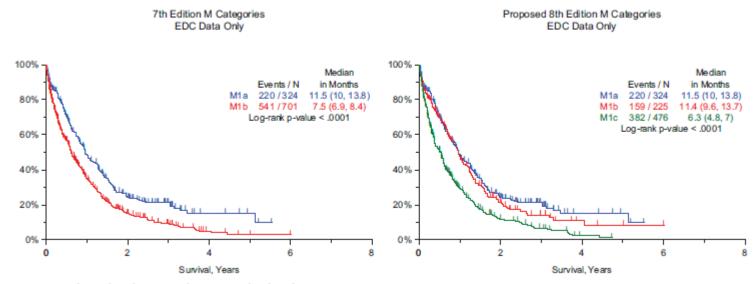


FIGURE 8. The 7th edition and proposed 8th edition M categories.



# Brain and adrenal not superior

7th Edition M1b - Single Lesion at Single Site By Organ EDC Data Only

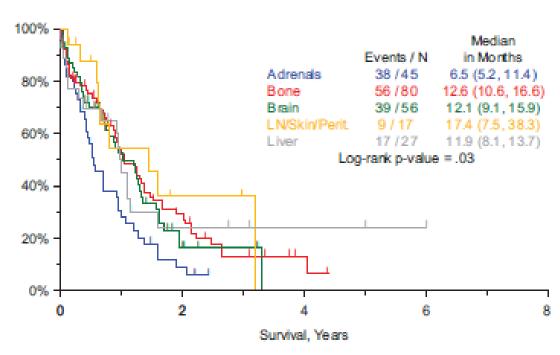


FIGURE 2. Single lesion at single site by organ.

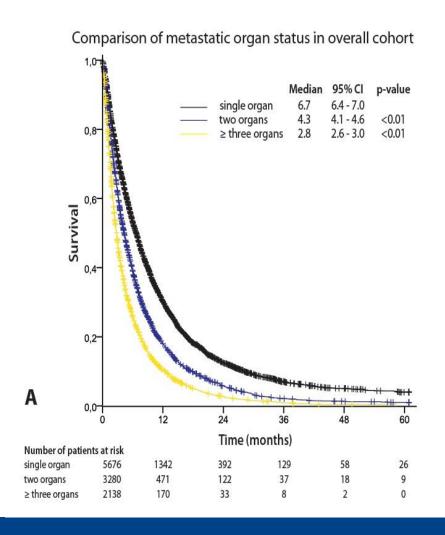


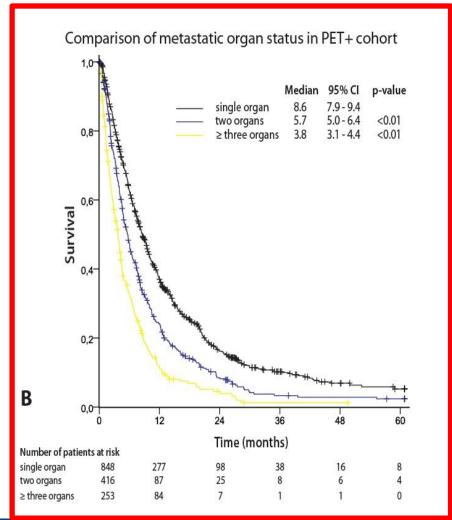
# Single metastasis as separate category

----r----

 Reclassify the current M1b category for patients with a single metastatic lesion in a single organ site, for example: (a) brain, (b) liver, (c) bone, (d) distant lymph node/ skin/peritoneum, and (e) adrenal gland. Categorization of localization of single lesions in a single organ should be prospectively tested based on the individually involved organ.

# Dutch Cancer Registry, population based PET scan improves outcome!







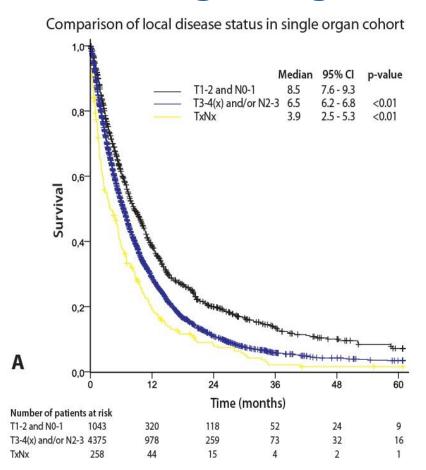
#### **Stage IVA**

|  |                 | N0             |                | N1             |                | N2              |                | N3              |                |
|--|-----------------|----------------|----------------|----------------|----------------|-----------------|----------------|-----------------|----------------|
| Descriptor in seventh edition            | Proposed<br>T/M | Overall stage  | Sample<br>size | Overall stage  | Sample<br>size | Overall stage   | Sample<br>size | Overall stage   | Sample<br>size |
| T1 ≤ 1 cm                                | T1a             | IA ≥ IA1       | 1765           | $IIA \geq IIB$ | 47             | IIIA            | 59             | IIIB            | 4              |
| T1 > 1-2 cm                              | T1b             | $IA \ge IA2$   | 6127           | $IIA \ge IIB$  | 321            | IIIA            | 444            | IIIB            | 20             |
| T1 > 2-3 cm                              | T1c             | $IA \ge IA3$   | 4606           | $IIA \ge IIB$  | 492            | IIIA            | 596            | IIIB            | 37             |
| T2 > 3-4 cm                              | T2a             | IB             | 6382           | $IIA \ge IIB$  | 1250           | IIIA            | 1666           | IIIB            | 89             |
| T2 > 4-5 cm                              | T2b             | $IB \ge IIA$   | 1689           | $IIA \ge IIB$  | 497            | IIIA            | 559            | IIIB            | 35             |
| T2 > 5-7 cm                              | T3              | $IIA \ge IIB$  | 1244           | $IIB \ge IIIA$ | 418            | $IIIA \ge IIIB$ | 455            | $IIIB \ge IIIC$ | 45             |
| T3 structures                            | T3              | IIB            | 1666           | IIIA           | 432            | $IIIA \ge IIIB$ | 736            | $IIIB \ge IIIC$ | 55             |
| T3 > 7 cm                                | T4              | $IIB \ge IIIA$ | 870            | IIIA           | 316            | $IIIA \ge IIIB$ | 320            | $IIIB \ge IIIC$ | 33             |
| T3 diaphragm                             | T4              | $IIB \ge IIIA$ | 47             | IIIA           | 16             | $IIIA \ge IIIB$ | 22             | $IIIB \ge IIIC$ | 0              |
| T3 endobronchial<br>location/atelectasis |                 |                |                |                |                |                 |                |                 |                |
| >3-4 cm                                  | T2a             | $IIB \ge IB$   | 18             | $IIIA \ge IIB$ | 18             | IIIA            | 10             | IIIB            | 1              |
| >4-5 cm                                  | T2b             | $IIB \ge IIA$  | 11             | $IIIA \ge IIB$ | 2              | IIIA            | 9              | IIIB            | 1              |
| T4                                       | T4              | IIIA           | 1862           | IIIA           | 538            | IIIB            | 1770           | $IIIB \ge IIIC$ | 893            |
| M1a                                      | M1a             | $IV \ge IVA$   | 62             | $IV \ge IVA$   | 11             | $IV \ge IVA$    | 100            | $IV \ge IVA$    | 145            |
| M1b single lesion                        | M1b             | $IV \geq IVA$  | 38             | $IV \geq IVA$  | 13             | $IV \ge IVA$    | 68             | $IV \ge IVA$    | 74             |
| M1b multiple lesions                     | M1c             | IV ≥ IVB       | 59             | IV ≥ IVB       | 18             | $IV \ge IVB$    | 128            | $IV \ge IVB$    | 191            |

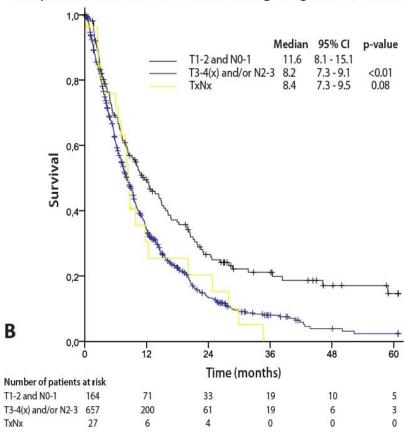


TNM, tumor, node, metastasis.

# OS – single organ & local disease status



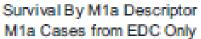
Comparison of local disease status in single organ PET+ cohort



Total single organ cohort, HR low vs high TN-status: 1.40 [1.29-1.51] (p < 0.001) <sup>18</sup>FDG-PET-staged cohort, HR low vs high TN-status: 1.62 [1.41-1.99] (p < 0.001)



# M1a descriptors: same OS



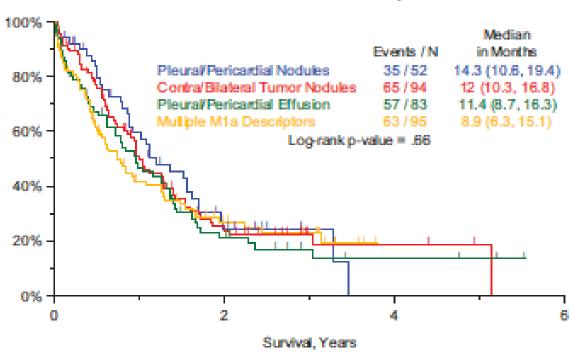


FIGURE 1. Prognostic impact of M1a descriptors.



# ESMO guideline: Oligometastatic disease

- Stage IV NSCLC patients with oligometastases in the brain: See recommendations for brain metastases treatment.
- Stage IV patients with one to three synchronous metastases may experience long-term disease-free survival (DFS) after systemic therapy and a radical local treatment (high-dose radiotherapy or surgery) [II, B].
   Because only one non-randomised phase II trial is available, inclusion in trials is preferred.
- Stage IV patients with a few metachronous metastases may be treated with a radical local treatment and experience long-term DFS [III, B]. However, this is based only on retrospective data.
- Solitary lesions in the contralateral lung should, in most cases, be considered as synchronous secondary primary tumours and, if possible, treated with radical intent [IV, B].

#### Pleural effusion

TNM 6: T4 st IIIb

TNM 7: M1a st IV

TNM 8: M1a st IVa

But: we all know it can not be cured.....



| Table 5. Descriptors and T and M categories in the seventh edition and as proposed for the eighth edition <sup>a</sup> |              |               |            |             |             |  |  |  |  |
|--|--------------|---------------|------------|-------------|-------------|--|--|--|--|
|  |              | N categori    | es         |             |             |  |  |  |  |
|  |              | Overall stage |            |             |             |  |  |  |  |
| Descriptor in 7th edition  | Proposed T/M | NO            | N1         | N2          | N3          |  |  |  |  |
| T1 ≤ 1 cm  | T1a          | IA1 (IA)      | IIB (IIA)  | IIIA        | IIIB        |  |  |  |  |
| T1 > 1-2 cm  | T1b          | IA2 (IA)      | IIB (IIA)  | IIIA        | IIIB        |  |  |  |  |
| T1 > 2-3 cm  | T1c          | IA3 (IA)      | IIB (IIA)  | IIIA        | IIIB        |  |  |  |  |
| T2 > 3-4 cm  | T2a          | IB            | IIB (IIA)  | IIIA        | IIIB        |  |  |  |  |
| T2 > 4-5 cm  | T2b          | IIA (IB)      | IIB (IIA)  | IIIA        | IIIB        |  |  |  |  |
| T2 > 5-7 cm  | T3           | IIB (IIA)     | IIIA (IIB) | IIIB (IIIA) | IIIC (IIIB) |  |  |  |  |
| T3 structures  | T3           | IIB           | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |  |  |  |
| T3 > 7 cm  | T4           | IIIA (IIB)    | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |  |  |  |
| T3 diaphragm   | T4           | IIIA (IIB)    | IIIA       | IIIB (IIIA) | IIIC (IIIB) |  |  |  |  |
| T3 endobronchial: location/atelectasis 3-4 cm  | T2a          | IB (IIB)      | IIB (IIIA) | IIIA        | IIIB        |  |  |  |  |
| T3 endobronchial: location/atelectasis 4-5 cm  | T2b          | IIA (IIB)     | IIB (IIIA) | IIIA        | IIIB        |  |  |  |  |
| T4   | T4           | IIIA          | IIIA       | IIIB        | IIIC (IIIB) |  |  |  |  |

<sup>a</sup>Where there is a change, the resultant stage groupings proposed for the eighth edition are in bold, and the stage in the seventh edition is given in parenthesis.

IVA (IV)

IVA (IV)

IVB (IV)

M<sub>1</sub>a

м1ь

M1c

T, tumor; M, metastasis.

M1b single lesion

M1c multiple lesions

M1a



IVA (IV)

IVA (IV)

IVB (IV)

IVA (IV)

IVA (IV)

IVB (IV)

IVA (IV)

IVA (IV)

IVB (IV)

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- Solitary lesions in the contralateral lung should, in most cases, be considered as synchronous secondary primary M1a
   n radical intent [IV, B].

# **Chemotherapy in NSCLC, TNM 8**



Adjuvant cisplatin-based chemotherapy

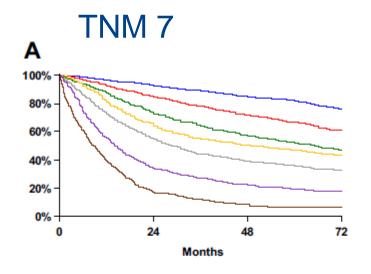


(conc) platinum based chemotherapy



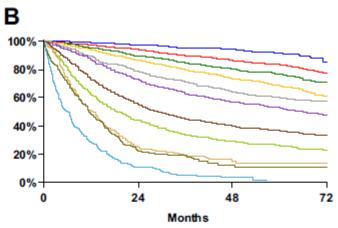
Palliative cisplatin based chemotherapy

Exploration oligometastatic disease



|                     |             |      | 24    | 60    |
|---------------------|-------------|------|-------|-------|
| 7 <sup>th</sup> Ed. | Events / N  | MST  | Month | Month |
| IA                  | 1119 / 6303 | NR   | 93%   | 82%   |
| IB                  | 768 / 2492  | NR   | 85%   | 66%   |
| IIA                 | 424 / 1008  | 66.0 | 74%   | 52%   |
| IIB                 | 382 / 824   | 49.0 | 64%   | 47%   |
| IIIA                | 2139 / 3344 | 29.0 | 55%   | 36%   |
| IIIB                | 2101 / 2624 | 14.1 | 34%   | 19%   |
| IV                  | 664 / 882   | 8.8  | 17%   | 6%    |

#### TNM 8



|          |             |      | 24    | 60    |  |
|----------|-------------|------|-------|-------|--|
| Proposed | Events / N  | MST  | Month | Month |  |
| IA1      | 68 / 781    | NR   | 97%   | 92%   |  |
| IA2      | 505 / 3105  | NR   | 94%   | 83%   |  |
| IA3      | 546 / 2417  | NR   | 90%   | 77%   |  |
| IB       | 560 / 1928  | NR   | 87%   | 68%   |  |
| IIA      | 215 / 585   | NR   | 79%   | 60%   |  |
| IIB      | 605 / 1453  | 66.0 | 72%   | 53%   |  |
| IIIA     | 2052 / 3200 | 29.3 | 55%   | 36%   |  |
| IIIB     | 1551 / 2140 | 19.0 | 44%   | 26%   |  |
| IIIC     | 831 / 986   | 12.6 | 24%   | 13%   |  |
| IVA      | 336 / 484   | 11.5 | 23%   | 10%   |  |
| IVB      | 328 / 398   | 6.0  | 10%   | 0%    |  |
|          |             |      |       |       |  |

#### TNM 8: grouping of patients with same prognosis

stratify in trials "same language"

been moved to a new stage grouping. Although such changes might raise the issue of whether consequent changes to treatment algorithms are needed, it is important to remind ourselves that stage does not dictate treatment. Stage is one, and perhaps the single most important, of several prognostic factors that guide the appropriate treatment option(s) to offer the patient. Any change to established treatment

# **Chemotherapy in NSCLC, TNM 8**



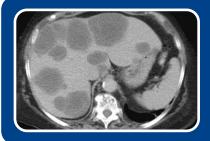
Adjuvant cisplatin-based chemotherapy

Resected stage II-III



(conc) platinum based chemotherapy

- Stage III: more surgery
- Stage IIIc ≠ bulky disease



Palliative cisplatin based chemotherapy
Oligometastatic disease? Further exploration stage M1b