

12º SIMPÓSIO  
INTERNACIONAL DE

CÂNCER DE  
PULMÃO

2ª JORNADA ONCONNECTION MULTICARE

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# Como definir irresssecabilidade?

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AC Camargo Cancer

São Paulo - SP

GERENCIAMENTO E PRODUÇÃO



## Como definir irressecabilidade?

### **Conflito de interesses:**

- Speaker AstraZeneca, BMS e MSD.
- Advisory Board MSD.
- Visita à fábrica de grampeadores Lexington Medical.

## Como definir irressecabilidade?

### **Roteiro:**

- Conceito de ressecabilidade.
- Importância atual.
- Quem define?
- Quais os critérios?
- Ferramentas para definir Irressecabilidade.
- Processo decisório.

Como definir irressecabilidade?

## **CONCEITO DE RESSECABILIDADE**

## Como definir irressecabilidade?

**Subjetividade do conceito de ressecabilidade.**

## Como definir irressecabilidade?

### Subjetividade do conceito de ressecabilidade.



## Como definir irressecabilidade?

### Conceito de Ressecabilidade

:

**Operabilidade:** refere-se ao estado do paciente - condições de saúde, comorbidades, risco cirúrgico.

**Ressecabilidade:** refere-se às características do tumor, visando sempre a Ressecção R0.

## Como definir irressecabilidade?

### Conceito de Ressecabilidade

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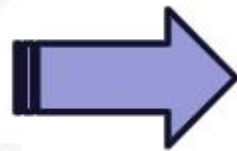


Como definir irressecabilidade?

## Ressecção R0

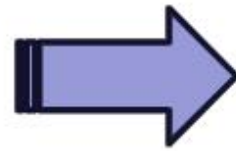
- Margens microscópicas livres.
- Linfadenectomia sistemática ou lobo-específica.
- LN comprometidos sem extravasamento extracapsular.
- LN mediastinal mais alto removido negativo.

Como definir irressecabilidade?



**Linfadenectomia regional adequada**

Como definir irressecabilidade?



**Linfadenectomia regional adequada**

Como definir irresssecabilidade?

**IMPORTÂNCIA ATUAL**

## Como definir irressecabilidade?

### PACIFIC trial: Study design

NCT02125461

- Phase III, randomized, double-blind, placebo-controlled, multicenter, global study (26 countries)

Patients with locally advanced  
unresectable NSCLC (stage III)  
in a consolidation setting (n = 702)

Absence of progression following  
at least 2 cycles of platinum-based chemo  
concomitant with radiation therapy

R 2:1

Arm 1 (n = 468):  
**Durvalumab** iv. 10 mg/kg q2w  
for up to 12 months

Arm 2 (n = 234):  
**Placebo** iv. q2w

#### Primary endpoints

- PFS, OS

#### Secondary endpoints

- ORR, DoR, DSR
- Safety/tolerability
- PK, immunogenicity, QoL

## Como definir irresssecabilidade?

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### METHODS

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#### **PATIENTS**

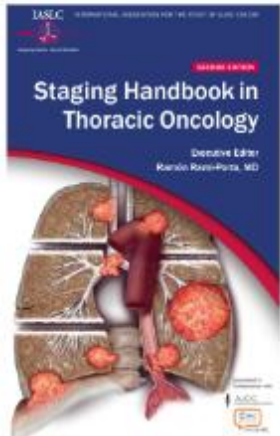
Eligibility criteria, as reported previously,<sup>18</sup> included histologically or cytologically documented stage III, unresectable NSCLC according to the *Staging Manual in Thoracic Oncology*, version 7, of the International Association for the Study of Lung Cancer.<sup>21</sup> Patients also had to have received at least two cycles of platinum-based chemotherapy (con-

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## Como definir irressecabilidade?

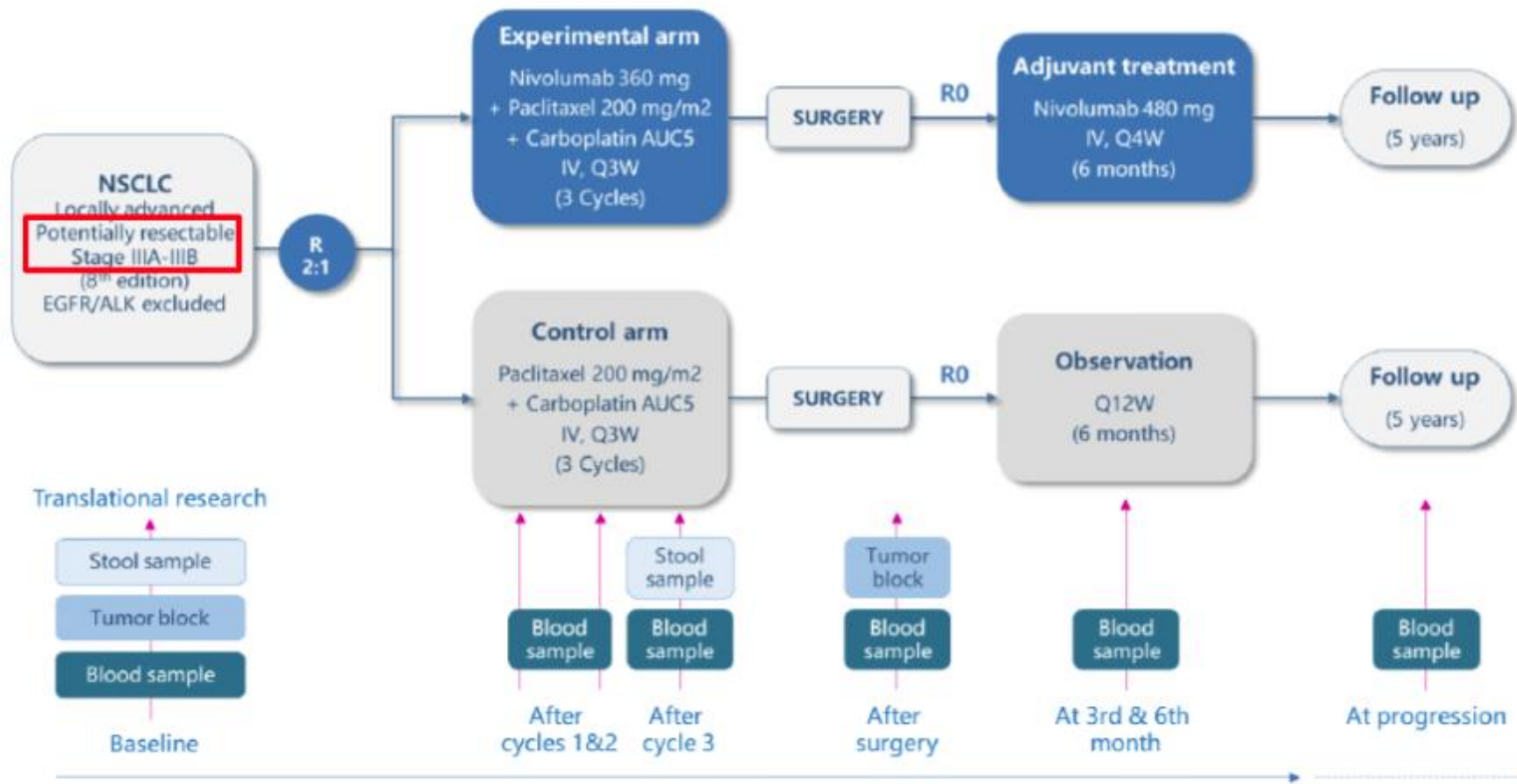


Figure S1. Study design. NADIM II (NCT03838159) is a randomized, phase 2, open-label, multicenter study evaluating nivolumab + chemotherapy *versus* chemotherapy alone as a neoadjuvant treatment for potentially resectable NSCLC.



## Como definir irressecabilidade?

### 1. Tumor Resectability Assessment

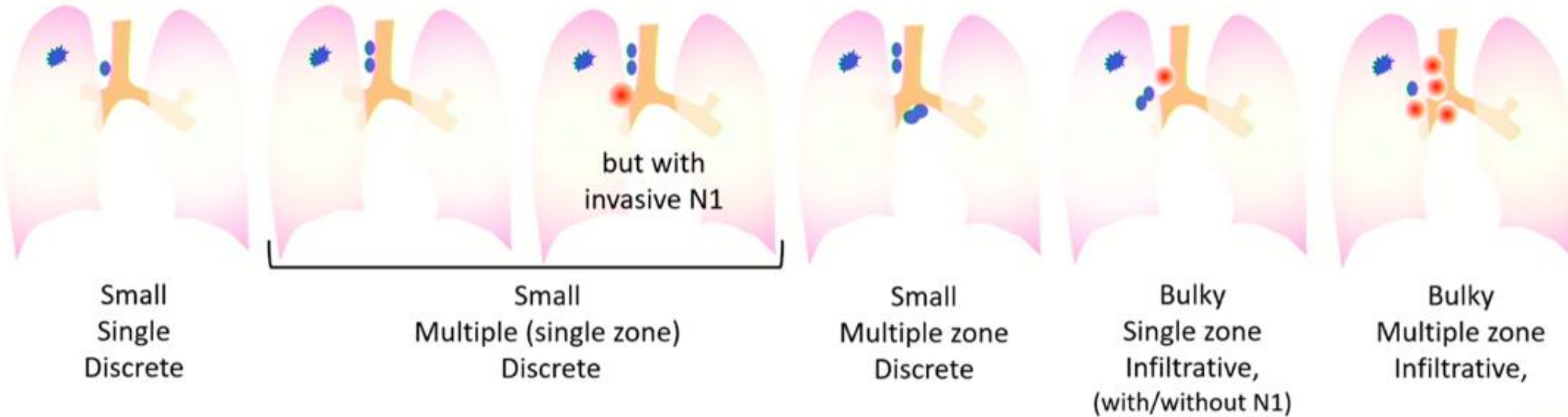
the lesion. Tumor resectability was re-assessed after neoadjuvant treatment by a Multidisciplinary Tumor Board based on the possibility of obtaining R0 surgery regardless of the type of surgery to be performed. R0 was defined as no residual tumor according to IASLC R0 criteria<sup>1,2</sup>. A CT-scan after neoadjuvant treatment and before surgery was required for all patients. Patients left the study if there was evidence of tumor progression. N2 persistence after

## Como definir irressecabilidade?



Technically resectable

Technically difficult / unresectable

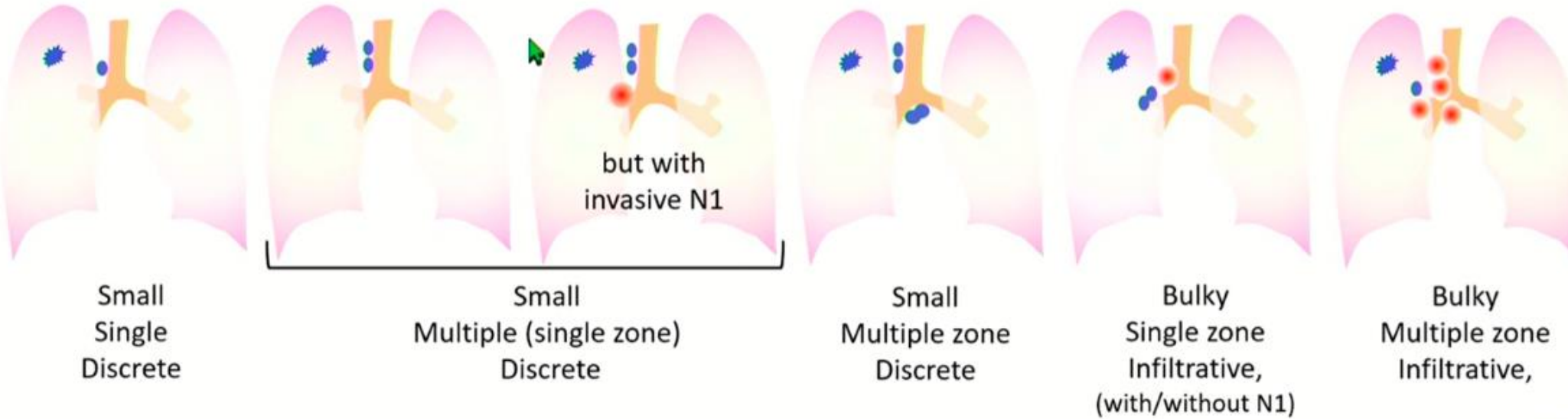


Other considerations

- PS, Age, co-morbidity, organ function
- Possibility of pneumonectomy (esp. right)
- Patient preference



## Como definir irressecabilidade?



- Other considerations
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  - Possibility of pneumonectomy (esp. right)
  - Patient preference



Como definir irressecabilidade?

# An International EORTC Survey on Resectability of Stage III Non-small Cell Lung Cancer

I. Houda<sup>1</sup>, I. Bahce<sup>1</sup>, C. Dickhoff<sup>1</sup>, T.E. Kroese<sup>2</sup>, S.G.C. Kroeze<sup>3</sup>, A.V. Mariolo<sup>4</sup>, M. Tagliamento<sup>5</sup>, L. Moliner<sup>6</sup>, M. Brandao<sup>7</sup>, J. Edwards<sup>8</sup>, I. Opitz<sup>2</sup>, C. Faivre-Finn<sup>9</sup>, D. de Ruysscher<sup>10</sup>, J. Remon<sup>11</sup>, T. Berghmans<sup>7</sup>, A-M.C. Dingemans<sup>12</sup>, B. Besse<sup>5</sup>, L.E.L. Hendriks<sup>10</sup>

<sup>1</sup>Amsterdam University Medical Centers, location VU Medical Center, Amsterdam/NL ,<sup>2</sup>Universitätsspital Zürich, Zürich/CH ,<sup>3</sup>Kantonsspital Aarau AG, Aarau/CH ,<sup>4</sup>Curie-MontsourisThoracic Institute, Paris/FR ,<sup>5</sup>Gustave Roussy, Villejuif/FR ,<sup>6</sup>Institut Catala d'Oncologia, Barcelona/ES ,<sup>7</sup>Institut Jules Bordet, Bruxelles/BE ,<sup>8</sup>Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield/GB ,<sup>9</sup>The Christie NHS Foundation Trust, Manchester/GB ,<sup>10</sup>Maastricht University Medical Center, Maastricht/NL ,<sup>11</sup>Centro Integral Oncológico Clara Campal HM Nou Delfos, Barcelona/ES ,<sup>12</sup>Erasmus University Medical Center, Rotterdam/NL



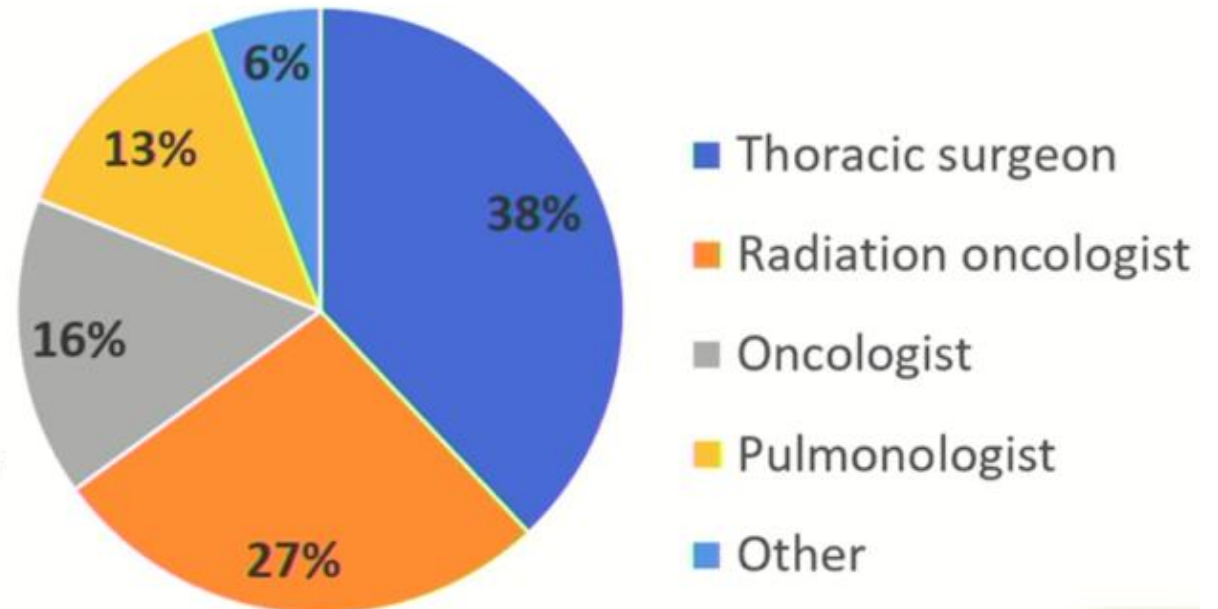
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## RESULTS

**558** respondents

- 80% **>5 years** of experience
- 81% **Specialized** center
- 72% **Europe**
- 77% **Treat >20 pts** stage III NSCLC annually



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## SURVEY - CONSENSUS SUMMARY

### AREAS OF CONTROVERSY IN RESECTABLE STAGE III NSCLC

	NO	N1	N2 SINGLE	N2 MULTI	N2 BULKY	N2 INVASIVE	N3
<b>T1-2</b>	NOT STAGE III DISEASE	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	?	UNRESECTABLE <sup>2</sup>	UNRESECTABLE	UNRESECTABLE
<b>T3 size</b>	NOT STAGE III DISEASE	RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE	UNRESECTABLE	
<b>T3 satellite</b>	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE	UNRESECTABLE	
<b>T3 invasion</b>	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	? <sup>1</sup>	?	UNRESECTABLE	UNRESECTABLE	
<b>T4 size</b>	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE <sup>2</sup>	UNRESECTABLE	UNRESECTABLE	
<b>T4 satellite</b>	POTENTIALLY RESECTABLE	? <sup>1</sup>	?	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE	
<b>T4 invasion</b>	? <sup>1</sup>	? <sup>1</sup>	?	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE	

- TN-subgroups for stage III NSCLC; Some results may deviate from the results in the final consensus; ?, no consensus achieved; 1, no consensus achieved but considered as potentially resectable by thoracic surgeons; 2, consensus unresectable but no consensus in the group of thoracic surgeons.

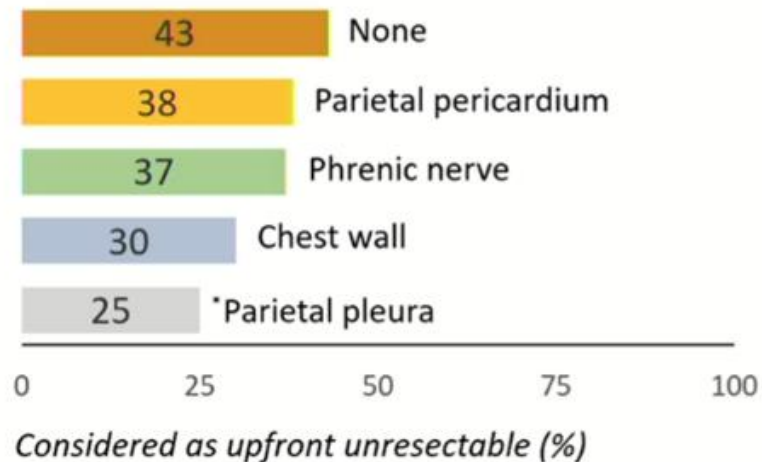


## Como definir irresseccabilidade?



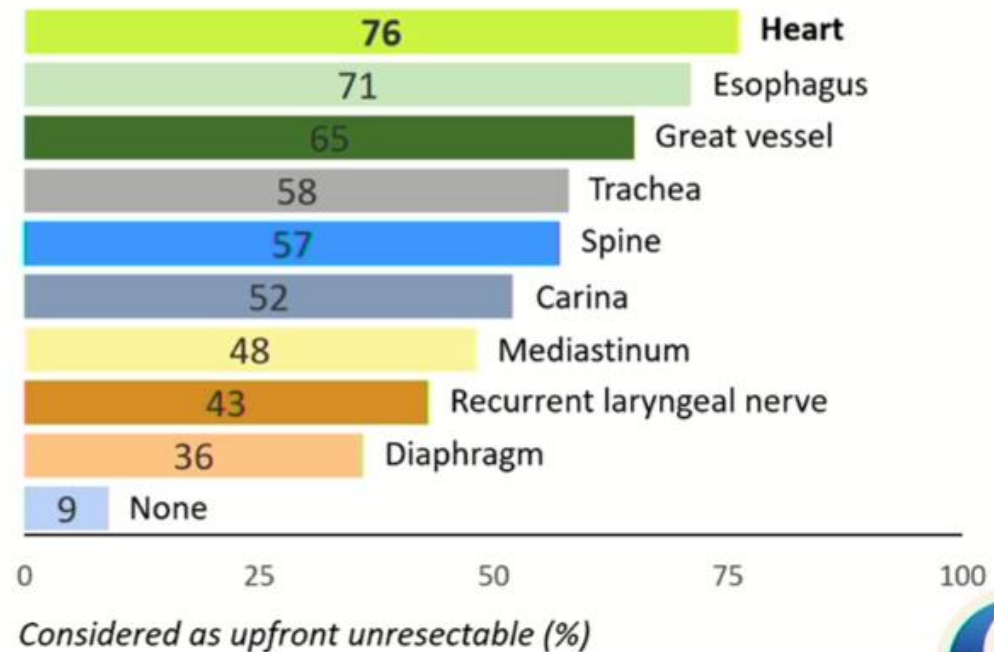
# RESECTABILITY OF INVASIVE T3 AND T4 TUMORS

### T3 tumors



\*25.3%

### T4 tumors





## Consensual definition of stage III NSCLC Resectability: EORTC-Lung Cancer Group initiative with other scientific societies

A-M. Dingemans<sup>1</sup>, J. Remon<sup>2</sup>, L. Hendriks<sup>3</sup>, J. Edwards<sup>4</sup>, C. Faivre-Finn<sup>5</sup>, N. Reguart<sup>6</sup>, E. Smit<sup>7</sup>, A. Levy<sup>8</sup>, D. Sanchez<sup>9</sup>, J.C. Trujillo<sup>10</sup>, A. Filippi<sup>11</sup>, K. Stathopoulos<sup>12</sup>, T.G. Blum<sup>13</sup>, M. Guckenberger<sup>14</sup>, S. Popat<sup>15</sup>, I. Opitz<sup>14</sup>, A. Brunelli<sup>16</sup>, R. De Angelis<sup>12</sup>, P. Hofman<sup>17</sup>, K. Hartemink<sup>18</sup>, R.H. Petersen<sup>19</sup>, E. Ruffini<sup>20</sup>, C. Dickhoff<sup>21</sup>, E. Prisciandaro<sup>22</sup>, J. Derks<sup>3</sup>, I. Bahce<sup>21</sup>, A. Mariolo<sup>23</sup>, E. Xenophontos<sup>24</sup>, N. Gij Levra<sup>25</sup>, I. Houda<sup>21</sup>, M. Brandão<sup>12</sup>, T. Berghmans<sup>12</sup>

<sup>1</sup>Erasmus MC, Rotterdam/NL, <sup>2</sup>IGR, Paris/FR, <sup>3</sup>MUMC, Maastricht/NL, <sup>4</sup>Sheffield Teaching Hospitals NHS Foundation Trust - Weston Park Hospital, Sheffield/GB, <sup>5</sup>The Christie NHS Foundation Trust, Manchester/GB, <sup>6</sup>Hospital Clinic de Barcelona, Barcelona/ES, <sup>7</sup>LUMC, Leiden/NL, <sup>8</sup>Gustave Roussy, Paris/FR, <sup>9</sup>Hospital Clinic of Barcelona, Barcelona/ES, <sup>10</sup>Hospital de la Santa Creu i Sant Pau, Barcelona/ES, <sup>11</sup>Fondazione IRCCS - Policlinico San Matteo, Pavia/IT, <sup>12</sup>Institut Jules Bordet, Brussels/BE, <sup>13</sup>HELIOS Klinikum Berlin, Berlin/DE, <sup>14</sup>UniversitaetsSpital Zurich, Zurich/CH, <sup>15</sup>Royal Marsden Hospital, London/GB, <sup>16</sup>St. James's University Hospital, Leeds/GB, <sup>17</sup>CHU de Nice - Hopital Pasteur, Nice/FR, <sup>18</sup>NKI-AVL, Amsterdam/NL, <sup>19</sup>Copenhagen University Hospital, Rigshospitalet, Denmark/DK, <sup>20</sup>Universita Di Torino - San Giovanni Battista, Torino/IT, <sup>21</sup>AmsterdamUMC, Amsterdam/NL, <sup>22</sup>U.Z. Leuven - Campus Gasthuisberg, Leuven/BE, <sup>23</sup>Institute Mutualiste Montsouris - Institut du Thorax Curie Montsouris, Paris/FR, <sup>24</sup>EORTC, Brussels/BE, <sup>25</sup>IRCCS Ospedale Sacro Cuore Don Calabria, Verona/IT





## INTRODUCTION

- Stage III non-small cell lung cancer (NSCLC) is a highly heterogeneous disease
- Surgical decision on stage III is highly dependent on the relative expertise of thoracic surgeons and radiation oncologists

The aim of this initiative is to provide a **multidisciplinary consensual definition of resectable stage III NSCLC** (according to the 8<sup>th</sup> TNM edition) to be used in clinical trials

- Important considerations:
  - The patient is considered to be medically *operable*
  - All types of surgery from lobectomy up to pneumonectomy can be considered
  - Assessing resectability **upfront**, before any treatment
    - Pancoast tumors are *excluded* from this definition



## METHODS



- **EORTC Lung Cancer Group** members + representatives from the European Thoracic Oncology Platform (**ETOP**), European Society of Thoracic Radiation Oncology (**ESTRO**), European Society of Thoracic Surgery (**ESTS**), European Respiratory Society (**ERS**), International Association for the Study of Lung Cancer (**IASLC**), European Society of Pathology (**ESP**), and the **EORTC Imaging Group**
  - The four main clinical specialties treating people with lung cancer (thoracic surgery, radiation oncology, pneumo-oncology and medical oncology) have been equally represented at each step of the initiative; imaging and pathology specialists have also participated





## Consensus definition

Mandatory Work-up
Contrast enhanced chest CT scan
<sup>18</sup> F-FDG-PET-CT with/without contrast
Brain imaging, preferably a brain MRI
Invasive mediastinal/nodal staging (EBUS, EUS, combined EBUS-EUS and/or mediastinoscopy)
Additional tests may be required if suspicion of invasion of any neighboring structures

Medical specialties involved in the treatment decision:
Thoracic surgeon*
Radiation oncologist
Medical oncologist and/or Pneumo-oncologist
Pulmonologist
Imaging specialist
Pathologist
Decision on technical resectability is made by the thoracic surgeon*, informed by the multidisciplinary team (MDT). The <b>final clinical decision</b> on the local treatment strategy should be placed in the oncological context by the MDT.

\* Criteria for general thoracic surgery are defined in European Guidelines (Eur J Cardiothor Surg 45: 779-86, 2014).



# Como definir irressecabilidade?



**2023 World Conference  
on Lung Cancer**

SEPTEMBER 9-12, 2023 | SINGAPORE



	N0	N1	N2 SINGLE (non-bulky, non-invasive)	N2 MULTI (non-bulky, non-invasive)	N2 BULKY <sup>1</sup>	N2 INVASIVE	N3
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE	RESECTABLE	POTENTIALLY RESECTABLE*	UNCLEAR	UNRESECTABLE	UNRESECTABLE
T3 size / satellite / invasion	NOT STAGE III DISEASE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 size / satellite	RESECTABLE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 invasion	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE* <sup>§</sup>	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE

\*Multiple station N2: case-by-case discussion; the exact number of nodes/stations cannot be defined

<sup>1</sup>Bulky N2: lymph nodes with a short-axis diameter >2.5-3 cm; in specific situations of *highly selected patients*, including those patients in multidisciplinary trials with surgery as local therapy can be discussed

<sup>§</sup>Some T4 tumours by infiltration of major structures are potentially resectable – see Table 1

## Decisão de Irressecabilidade

1

### Estadiamento minucioso

2

T



T3  
T4



- Nódulos satélites.
- Invasão de estruturas adjacentes.

3

N



N1  
N2  
N3



- N2 cadeia única.
- N2 múltiplas cadeias.
- N2 bulky.
- N2 invasão de estruturas adjacentes.

## Decisão de Irressecabilidade

1

### Estadiamento minucioso



## Decisão de Irressecabilidade

### Decisão multidisciplinar



Considerar a preferência do paciente

## Mensagens finais

- Subjetividade do conceito de ressecabilidade:
    - Técnica
    - Oncológica
- Ressecção R0**
- Exames:
    - TC de tórax com contraste / PET-CT / Outros exames de imagem.
    - Estadiamento invasivo do mediastino.
  - Principal parâmetro: Estágio N.
  - Decisão multidisciplinar.