Cáncer de Pulmón

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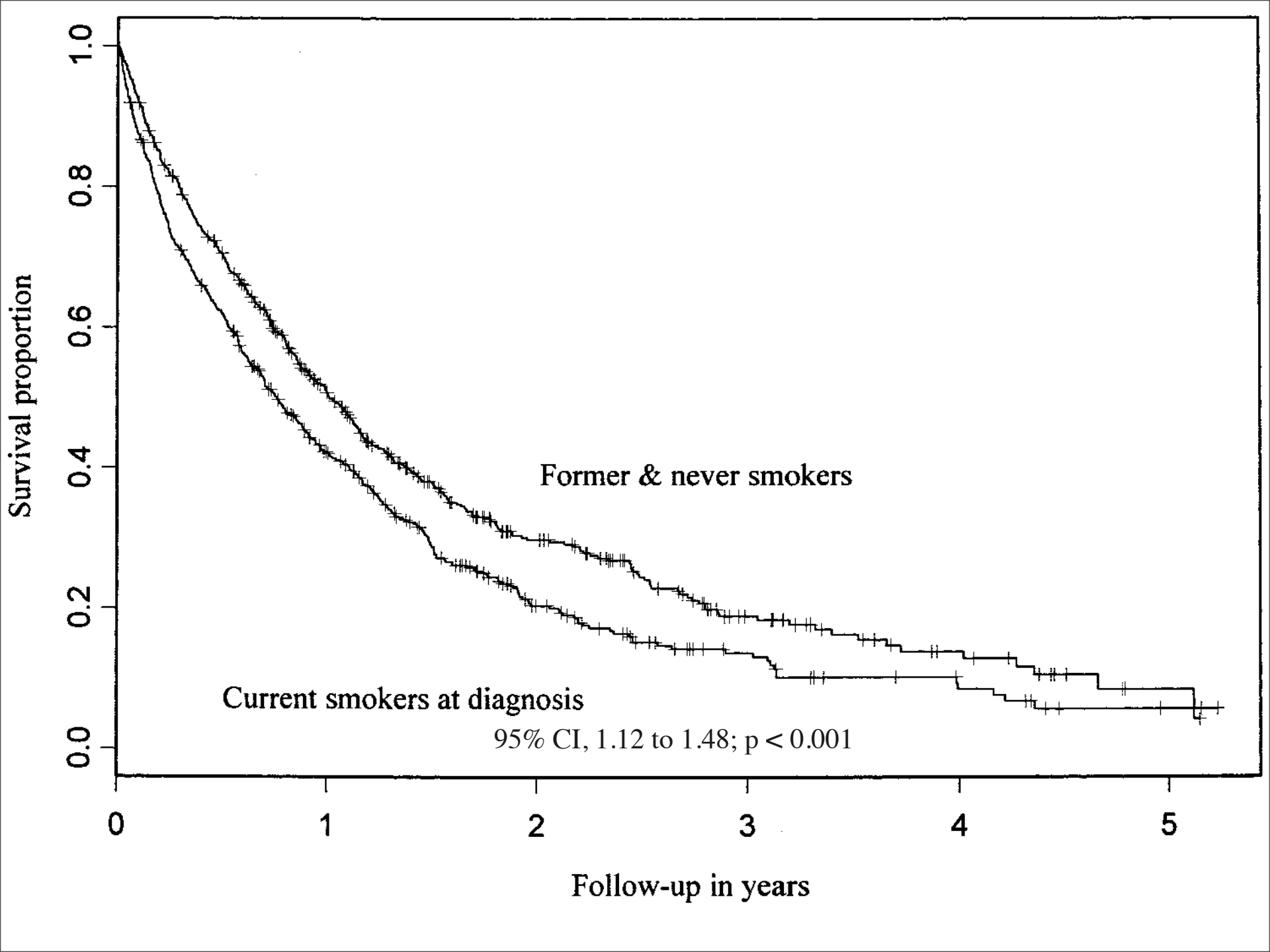
Oncología Clínica

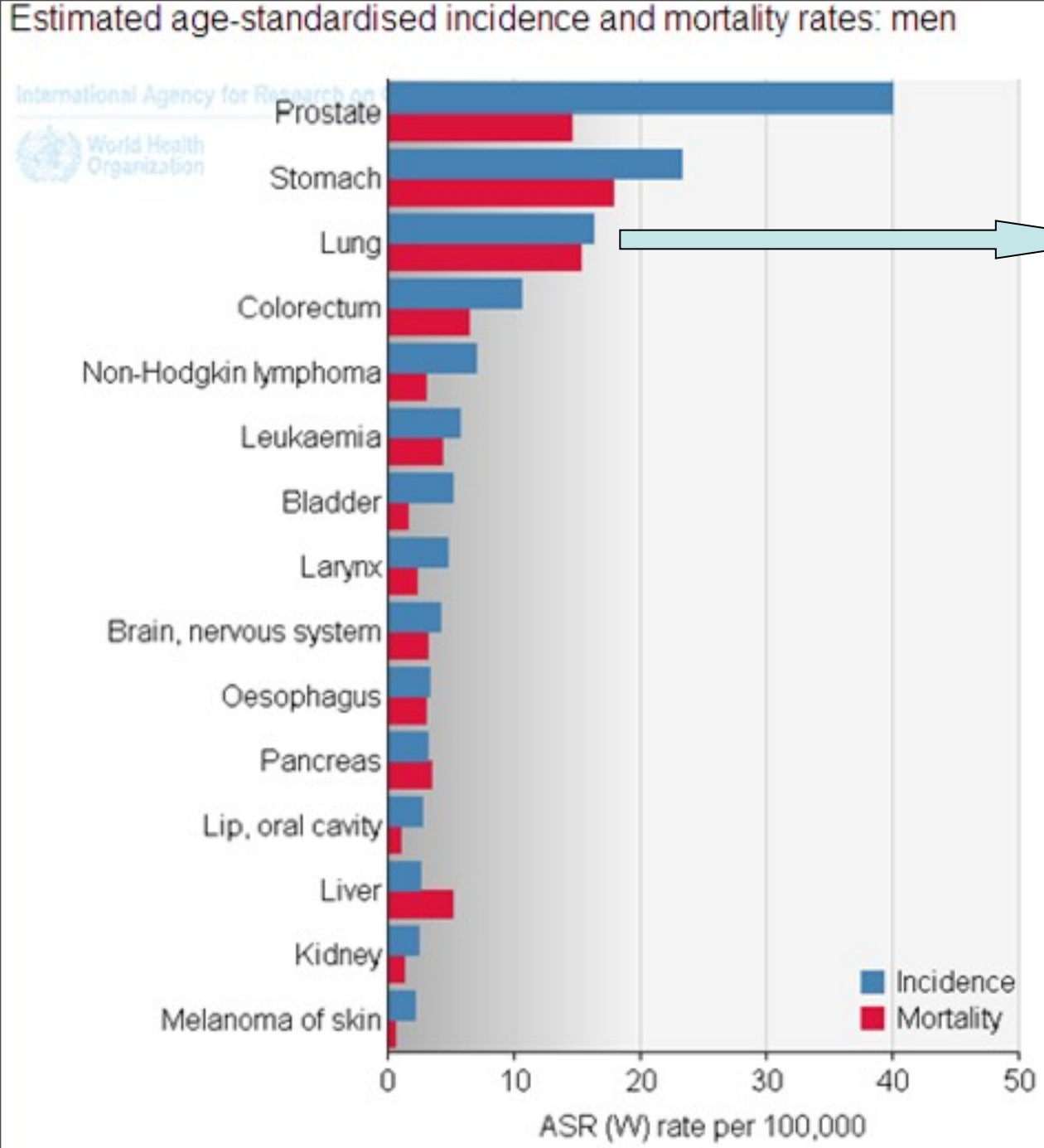
Smoking and Lung Cancer Survival*

The Role of Comorbidity and Treatment

- Experiencia de un centro
- 1155 pacientes diagnosticados
- Evaluacion del impacto del habito de fumar
- Ajuste por comorbilidades y edad
- Mayor probabilidades de recibir tratamiento en fumadores

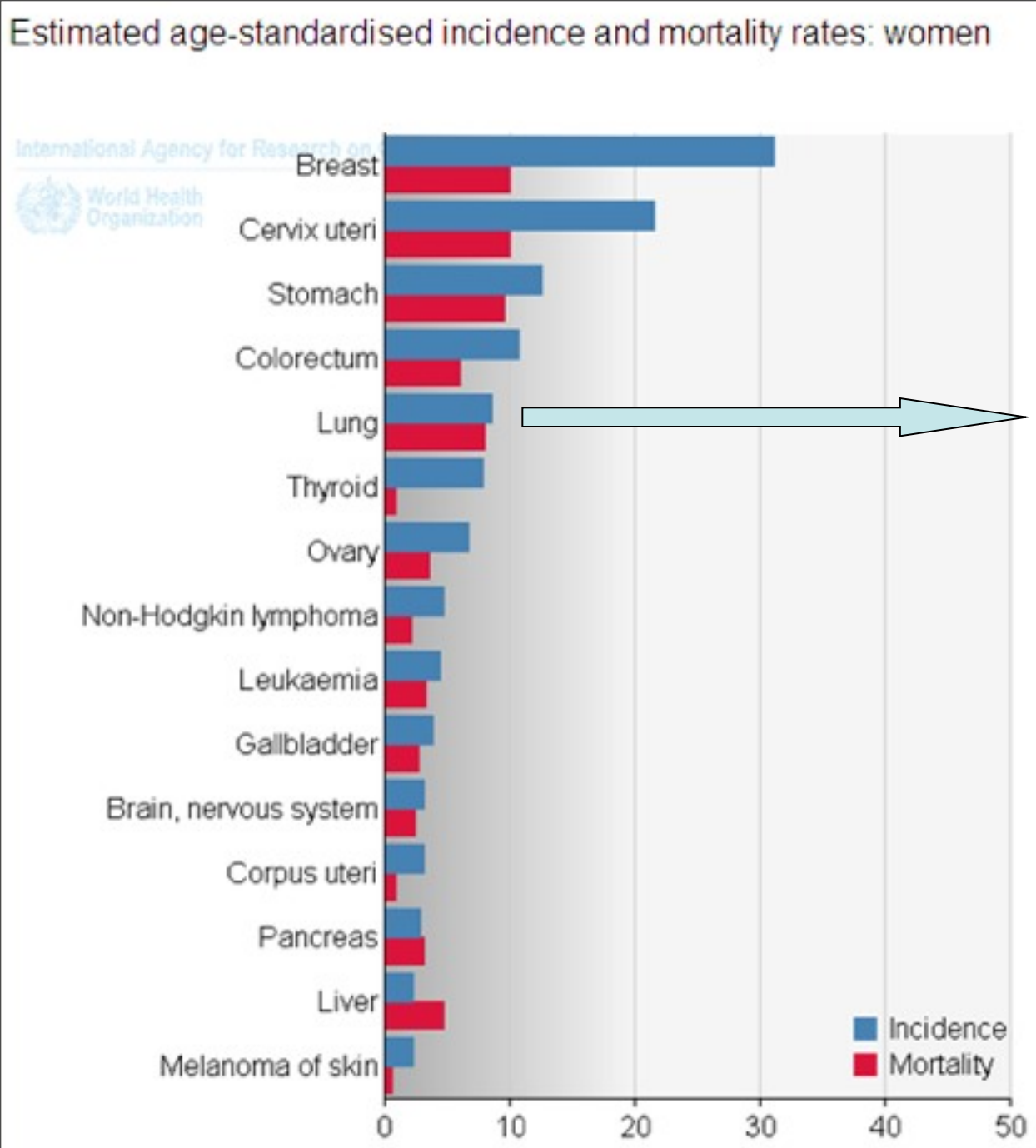
CHEST 2004; 125:27–37


Survival proportion
1.0
0.8
0.6
0.4
0.2
0.0
Former & never smokers
Current smokers at diagnosis
95% CI, 1.12 to 1.48; p < 0.001
0
1
2
3
4
5
Follow-up in years



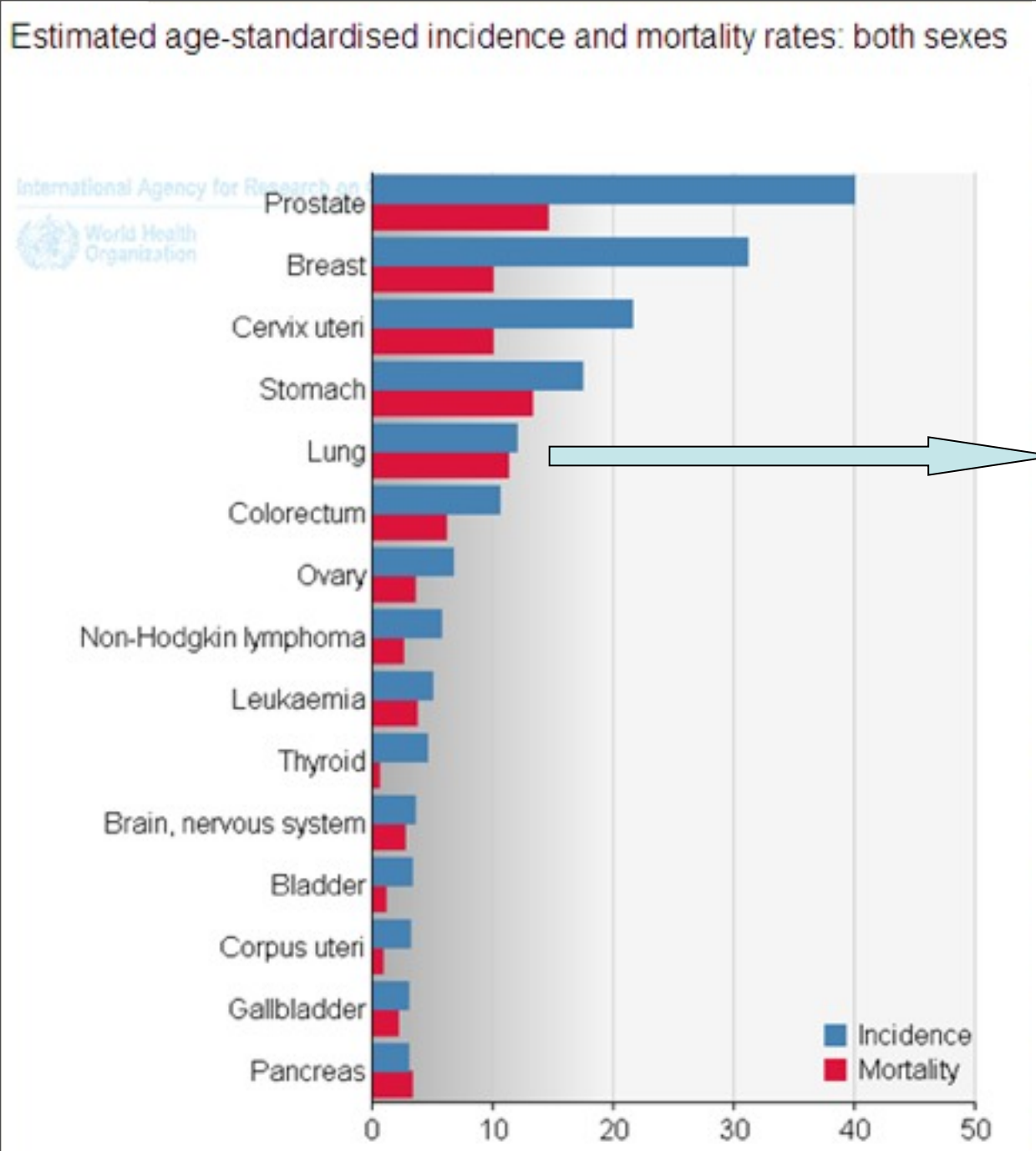
2697 casos (9,8%)
2524 muertes
(15.1%)

GLOBOCAN 2008 (IARC) *Section of Cancer Information* *(28/2/2012)*



1172 casos (5.7%)
1656 muertes (9.6%)

GLOBOCAN 2008 (IARC) *Section of Cancer Information (28/2/2012)*



4469 casos (7.6%)
4180 muertes (12.3%)

GLOBOCAN 2008 (IARC) *Section of Cancer Information* *(28/2/2012)*

TABLE 1. Estimated New Cancer Cases and Deaths by Sex, United States, 2012*

	ESTIMATED NEW CASES			ESTIMATED DEATHS		
	BOTH SEXES	MALE	FEMALE	BOTH SEXES	MALE	FEMALE
All Sites	**1,638,910**	**848,170**	**790,740**	**577,190**	**301,820**	**275,370**
Oral cavity & pharynx	**40,250**	**28,540**	**11,710**	**7,850**	**5,440**	**2,410**
Tongue	12,770	9,040	3,730	2,050	1,360	690
Mouth	11,620	7,030	4,590	1,790	1,070	720
Pharynx	13,510	10,790	2,720	2,330	1,730	600
Other oral cavity	2,350	1,680	670	1,680	1,280	400
Digestive system	**284,680**	**156,760**	**127,920**	**142,510**	**80,560**	**61,950**
Esophagus	17,460	13,950	3,510	15,070	12,040	3,030
Stomach	21,320	13,020	8,300	10,540	6,190	4,350
Small intestine	8,070	4,380	3,690	1,150	610	540
Colon†	103,170	49,920	53,250	51,690	26,470	25,220
Rectum	40,290	23,500	16,790			
Anus, anal canal, & anorectum	6,230	2,250	3,980	780	300	480
Liver & intrahepatic bile duct	28,720	21,370	7,350	20,550	13,980	6,570
Gallbladder & other biliary	9,810	4,480	5,330	3,200	1,240	1,960
Pancreas	43,920	22,090	21,830	37,390	18,850	18,540
Other digestive organs	5,690	1,800	3,890	2,140	880	1,260
Respiratory system	**244,180**	**130,270**	**113,910**	**164,770**	**91,110**	**73,660**
Larynx	12,360	9,840	2,520	3,650	2,880	770
Lung & bronchus	226,160	116,470	109,690	160,340	87,750	72,590
Other respiratory organs	5,660	3,960	1,700	780	480	300
Bones & joints	**2,890**	**1,600**	**1,290**	**1,410**	**790**	**620**
Soft tissue (including heart)	**11,280**	**6,110**	**5,170**	**3,900**	**2,050**	**1,850**
Skin (excluding basal & squamous)	**81,240**	**46,890**	**34,350**	**12,190**	**8,210**	**3,980**
Melanoma-skin	76,250	44,250	32,000	9,180	6,060	3,120
Other nonepithelial skin	4,990	2,640	2,350	3,010	2,150	860
Breast	**229,060**	**2,190**	**226,870**	**39,920**	**410**	**39,510**
Genital system	**340,650**	**251,900**	**88,750**	**58,360**	**28,840**	**29,520**
Uterine cervix	12,170		12,170	4,220		4,220
Uterine corpus	47,130		47,130	8,010		8,010
Ovary	22,280		22,280	15,500		15,500
Vulva	4,490		4,490	950		950
Vagina & other genital, female	2,680		2,680	840		840
Prostate	241,740	241,740		28,170	28,170	
Testis	8,590	8,590		360	360	
Penis & other genital, male	1,570	1,570		310	310	
Urinary system	**141,140**	**97,610**	**43,530**	**29,330**	**19,670**	**9,660**
Urinary bladder	73,510	55,600	17,910	14,880	10,510	4,370
Kidney & renal pelvis	64,770	40,250	24,520	13,570	8,650	4,920
Ureter & other urinary organs	2,860	1,760	1,100	880	510	370
Eye & orbit	**2,610**	**1,310**	**1,300**	**270**	**120**	**150**
Brain & other nervous system	**22,910**	**12,630**	**10,280**	**13,700**	**7,720**	**5,980**
Endocrine system	**58,980**	**14,600**	**44,380**	**2,700**	**1,240**	**1,460**
Thyroid	56,460	13,250	43,210	1,780	780	1,000
Other endocrine	2,520	1,350	1,170	920	460	460
Lymphoma	**79,190**	**43,120**	**36,070**	**20,130**	**10,990**	**9,140**
Hodgkin lymphoma	9,060	4,960	4,100	1,190	670	520
Non-Hodgkin lymphoma	70,130	38,160	31,970	18,940	10,320	8,620
Myeloma	**21,700**	**12,190**	**9,510**	**10,710**	**6,020**	**4,690**
Leukemia	**47,150**	**26,830**	**20,320**	**23,540**	**13,500**	**10,040**
Acute lymphocytic leukemia	6,050	3,450	2,600	1,440	820	620
Chronic lymphocytic leukemia	16,060	9,490	6,570	4,580	2,730	1,850
Acute myeloid leukemia	13,780	7,350	6,430	10,200	5,790	4,410
Chronic myeloid leukemia	5,430	3,210	2,220	610	370	240
Other leukemia‡	5,830	3,330	2,500	6,710	3,790	2,920
Other & unspecified primary sites‡	31,000	15,620	15,380	45,900	25,150	20,750

TABLE 1. Estimated New Cancer Cases and Deaths by Sex, United States, 2012*

	ESTIMATED NEW CASES			ESTIMATED DEATHS		
	BOTH SEXES	MALE	FEMALE	BOTH SEXES	MALE	FEMALE
All Sites	**1,638,910**	**848,170**	**790,740**	**577,190**	**301,820**	**275,370**
Oral cavity & pharynx	**40,250**	**28,540**	**11,710**	**7,850**	**5,440**	**2,410**
Tongue	12,770	9,040	3,730	2,050	1,360	690
Mouth	11,620	7,030	4,590	1,790	1,070	720
Pharynx	13,510	10,790	2,720	2,330	1,730	600
Other oral cavity	2,350	1,680	670	1,680	1,280	400
Digestive system	**284,680**	**156,760**	**127,920**	**142,510**	**80,560**	**61,950**
Esophagus	17,460	13,950	3,510	15,070	12,040	3,030
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Colon†	103,170	49,920	53,250	51,690	26,470	25,220
Rectum	40,290	23,500	16,790			
Anus, anal canal, & anorectum	6,230	2,250	3,980	780	300	480
Liver & intrahepatic bile duct	28,720	21,370	7,350	20,550	13,980	6,570
Gallbladder & other biliary	9,810	4,480	5,330	3,200	1,240	1,960
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Respiratory system	**244,180**	**130,270**	**113,910**	**164,770**	**91,110**	**73,660**
Larynx					2,880	770
Lung & bronchus						72,590
Other						300

Respiratory system	244,180	130,270	113,910	164,770	91,110	73,660
Larynx	12,360	9,840	2,520	3,650	2,880	770
Lung & bronchus	226,160	116,470	109,690	160,340	87,750	72,590
Other respiratory organs	5,660	3,960	1,700	780	480	300

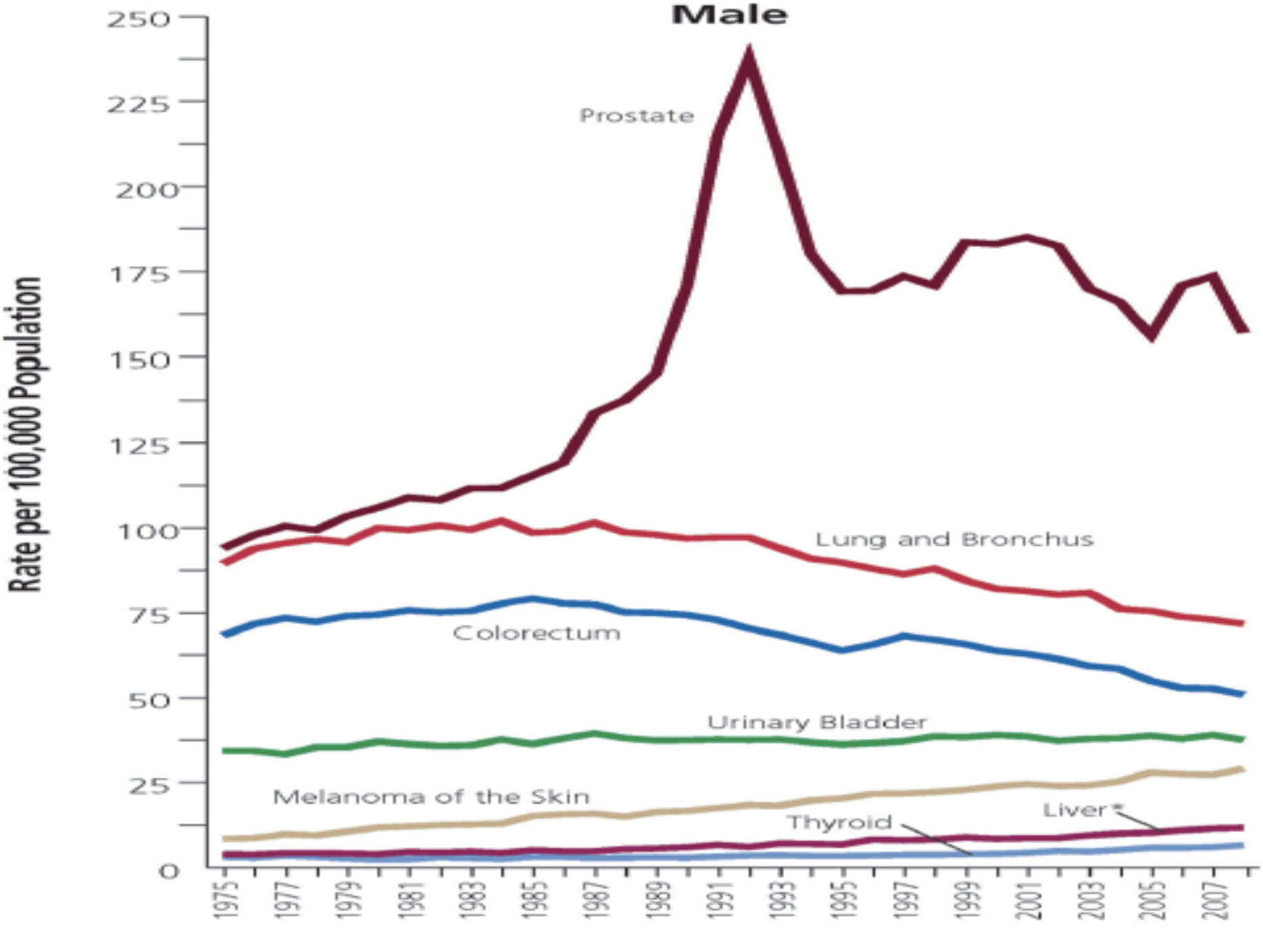
Prostate	241,740	241,740		28,170	28,170	
Testis	8,590	8,590		360	360	
Penis & other genital, male	1,570	1,570		310	310	
Urinary system	**141,140**	**97,610**	**43,530**	**29,330**	**19,670**	**9,660**
Urinary bladder	73,510	55,600	17,910	14,880	10,510	4,370
Kidney & renal pelvis	64,770	40,250	24,520	13,570	8,650	4,920
Ureter & other urinary organs	2,860	1,760	1,100	880	510	370
Eye & orbit	**2,610**	**1,310**	**1,300**	**270**	**120**	**150**
Brain & other nervous system	**22,910**	**12,630**	**10,280**	**13,700**	**7,720**	**5,980**
Endocrine system	**58,980**	**14,600**	**44,380**	**2,700**	**1,240**	**1,460**
Thyroid	56,460	13,250	43,210	1,780	780	1,000
Other endocrine	2,520	1,350	1,170	920	460	460
Lymphoma	**79,190**	**43,120**	**36,070**	**20,130**	**10,990**	**9,140**
Hodgkin lymphoma	9,060	4,960	4,100	1,190	670	520
Non-Hodgkin lymphoma	70,130	38,160	31,970	18,940	10,320	8,620
Myeloma	**21,700**	**12,190**	**9,510**	**10,710**	**6,020**	**4,690**
Leukemia	**47,150**	**26,830**	**20,320**	**23,540**	**13,500**	**10,040**
Acute lymphocytic leukemia	6,050	3,450	2,600	1,440	820	620
Chronic lymphocytic leukemia	16,060	9,490	6,570	4,580	2,730	1,850
Acute myeloid leukemia	13,780	7,350	6,430	10,200	5,790	4,410
Chronic myeloid leukemia	5,430	3,210	2,220	610	370	240
Other leukemia‡	5,830	3,330	2,500	6,710	3,790	2,920
Other & unspecified primary sites‡	31,000	15,620	15,380	45,900	25,150	20,750

Estimated New Cases*

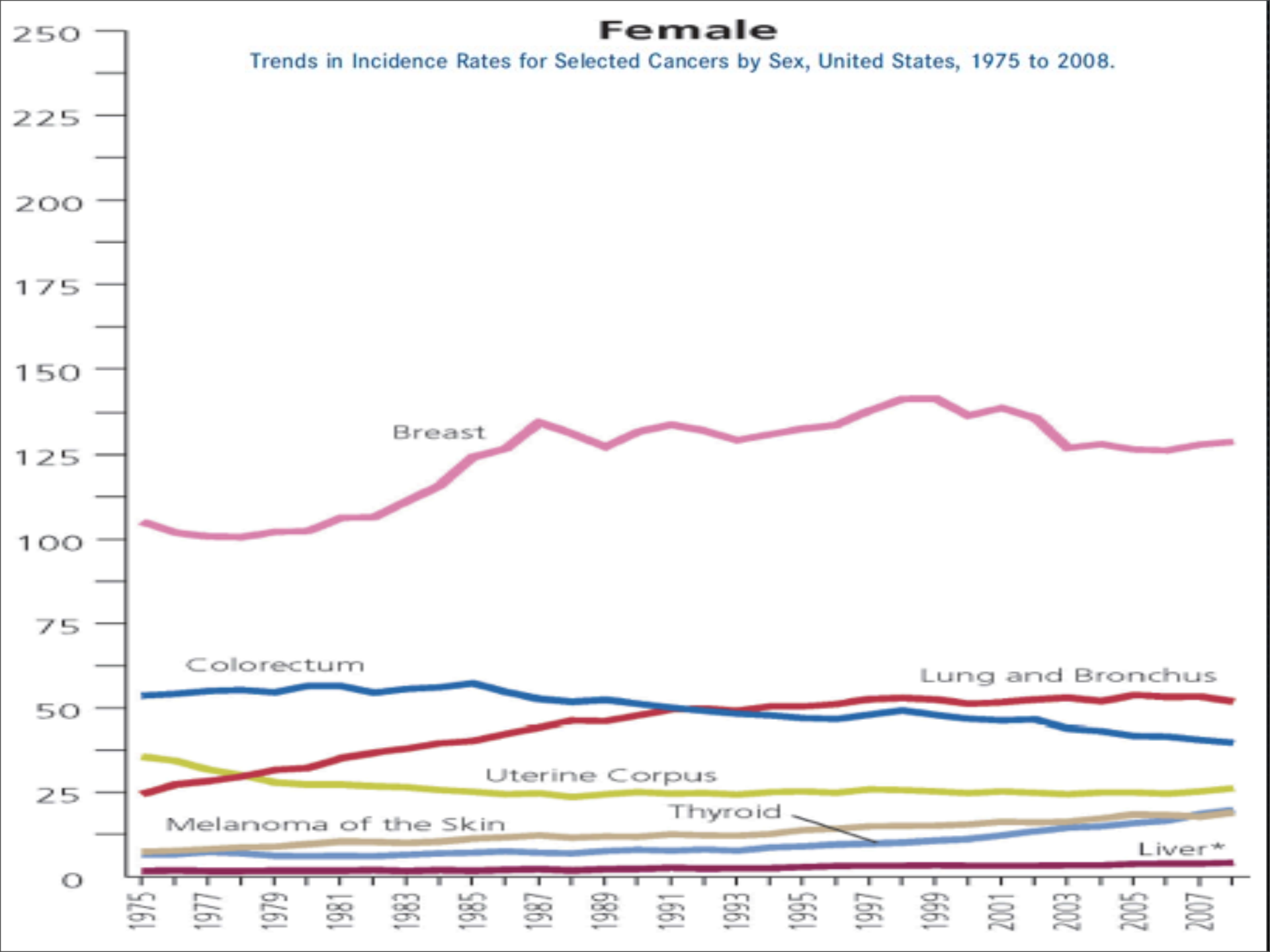
Males			Females		
Prostate	241,740	29%	Breast	226,870	29%
Lung & bronchus	116,470	14%	Lung & bronchus	109,690	14%
Colon & rectum	73,420	9%	Colon & rectum	70,040	9%
Urinary bladder	55,600	7%	Uterine corpus	47,130	6%
Melanoma of the skin	44,250	5%	Thyroid	43,210	5%
Kidney & renal pelvis	40,250	5%	Melanoma of the skin	32,000	4%
Non-Hodgkin lymphoma	38,160	4%	Non-Hodgkin lymphoma	31,970	4%
Oral cavity & pharynx	28,540	3%	Kidney & renal pelvis	24,520	3%
Leukemia	26,830	3%	Ovary	22,280	3%
Pancreas	22,090	3%	Pancreas	21,830	3%
All Sites	**848,170**	**100%**	**All Sites**	**790,740**	**100%**

Estimated Deaths

Males			Females		
Lung & bronchus	87,750	29%	Lung & bronchus	72,590	26%
Prostate	28,170	9%	Breast	39,510	14%
Colon & rectum	26,470	9%	Colon & rectum	25,220	9%
Pancreas	18,850	6%	Pancreas	18,540	7%
Liver & intrahepatic bile duct	13,980	5%	Ovary	15,500	6%
Leukemia	13,500	4%	Leukemia	10,040	4%
Esophagus	12,040	4%	Non-Hodgkin lymphoma	8,620	3%
Urinary bladder	10,510	3%	Uterine Corpus	8,010	3%
Non-Hodgkin lymphoma	10,320	3%	Liver & intrahepatic bile duct	6,570	2%
Kidney & renal pelvis	8,650	3%	Brain & other nervous system	5,980	2%
All Sites	**301,820**	**100%**	**All Sites**	**275,370**	**100%**



Trends in Incidence Rates for Selected Cancers by Sex, United States, 1975 to 2008.


Female
Trends in Incidence Rates for Selected Cancers by Sex, United States, 1975 to 2008.
250
225
200
175
150
125
100
75
50
25
0
Breast
Colorectum
Lung and Bronchus
Uterine Corpus
Thyroid
Melanoma of the Skin
Liver*
1975
1977
1979
1981
1983
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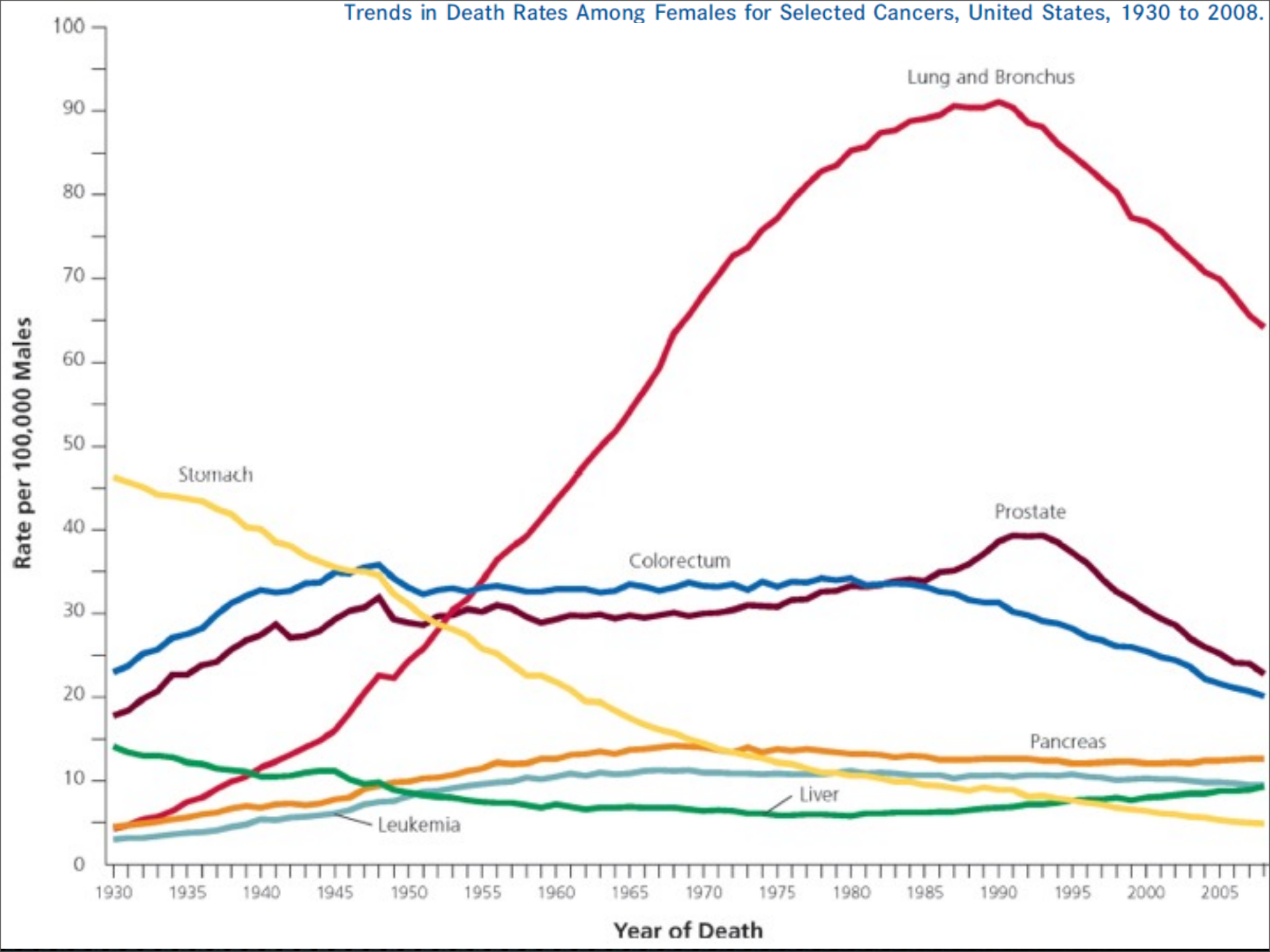
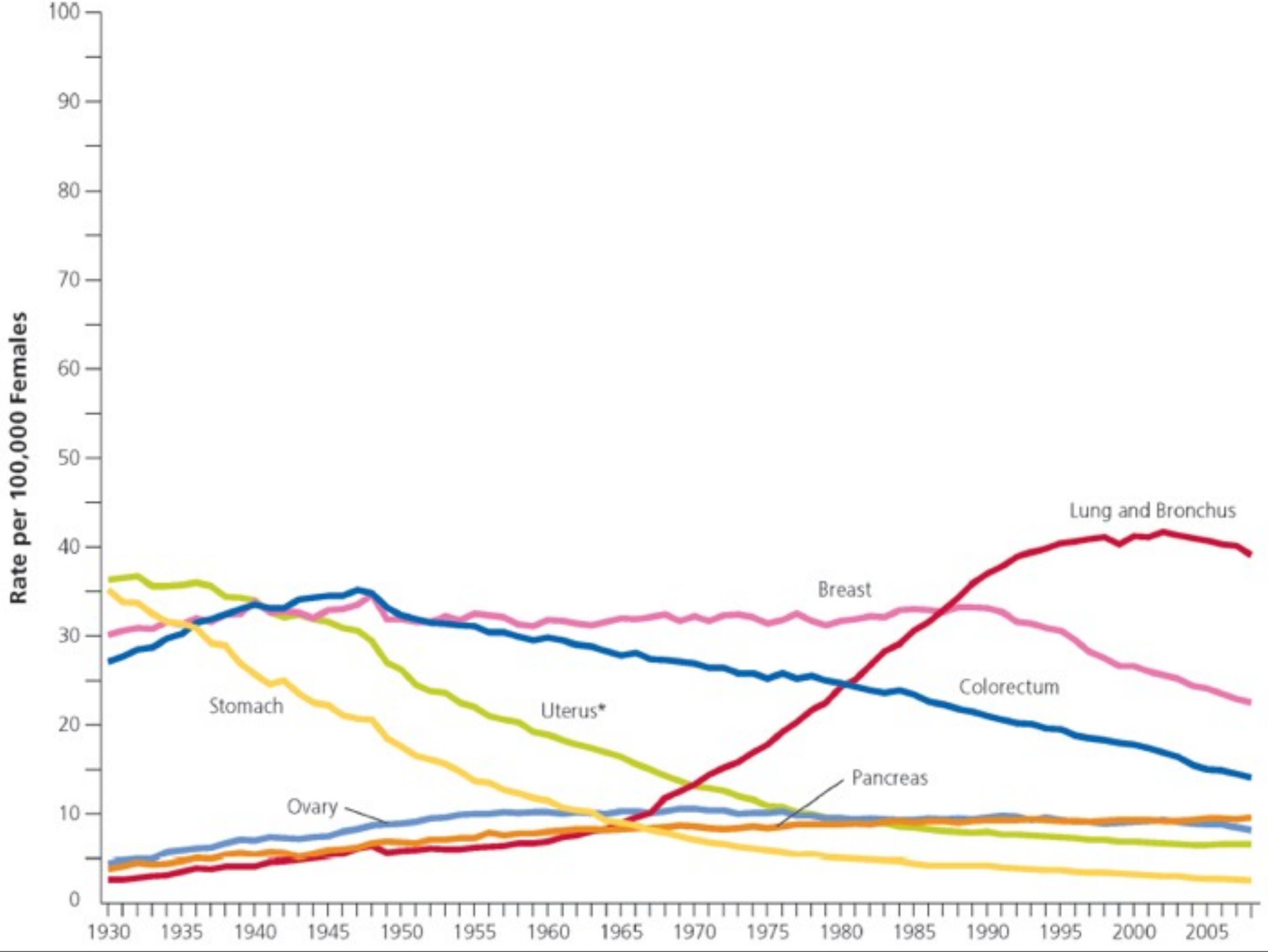
1999
2001
2003
2005
2007

Trends in Death Rates Among Females for Selected Cancers, United States, 1930 to 2008.



Trends in Death Rates Among Females for Selected Cancers, United States, 1930 to 2008.



Manifestaciones clinicas

- **Derivadas de Tumor**
  - Tos
  - Disnea
  - Hemoptisis
  - Pneumonía postobstructiva
  - Dolor torácico
  - Compromiso del ápex
    - Dolor en hombro
    - Plexopatía braquial
    - Sindrome de Horner

Síndromes paraneoplasicos

- Osteoartropatía pulmonar hipertrófica
- Hipercalcemia (Escamocelular)
- Sindrome de secreción inapropiada de hormona antidiurética
- Sindrome de Cushing
- Sistema nervioso
  - Encefalomielitis
  - Neuropatía sensoria subaguda
  - Opsoclonus
  - Mioclonus
  - Neuropatía sensorial
  - Encefalopatía límbica
  - Sindrome de Eaton-Lambert

Estadificacion

"Lung cancer is usually diagnosed at an advanced stage and consequently the overall 5-year survival for patients is approximately 15%. However, patients diagnosed when the primary tumor is resectable experience 5-year survivals ranging from 20 to 80%. Clinical and pathologic staging is critical to selecting patients appropriately for surgery and multimodality therapy."

Resumen de cambios

- Clasificación recomendada para célula pequeña, no pequeña y carcinoides
- Redefinición de clasificación de T
  - T1: T1a < 2 cm, T1b 2 - 3cm
  - T2: T2a: > 3 - 5 cm, T2b: 5 - 7 cm
  - T3: > 7 cm, Múltiples nódulos tumorales en el mismo lóbulo
  - T4: Múltiples nódulos tumorales en el mismo pulmón pero diferente lóbulo

Resumen de cambios

- Redefinición en clasificación de metástasis
  - M1a: Derrame pleural o pericardico maligno

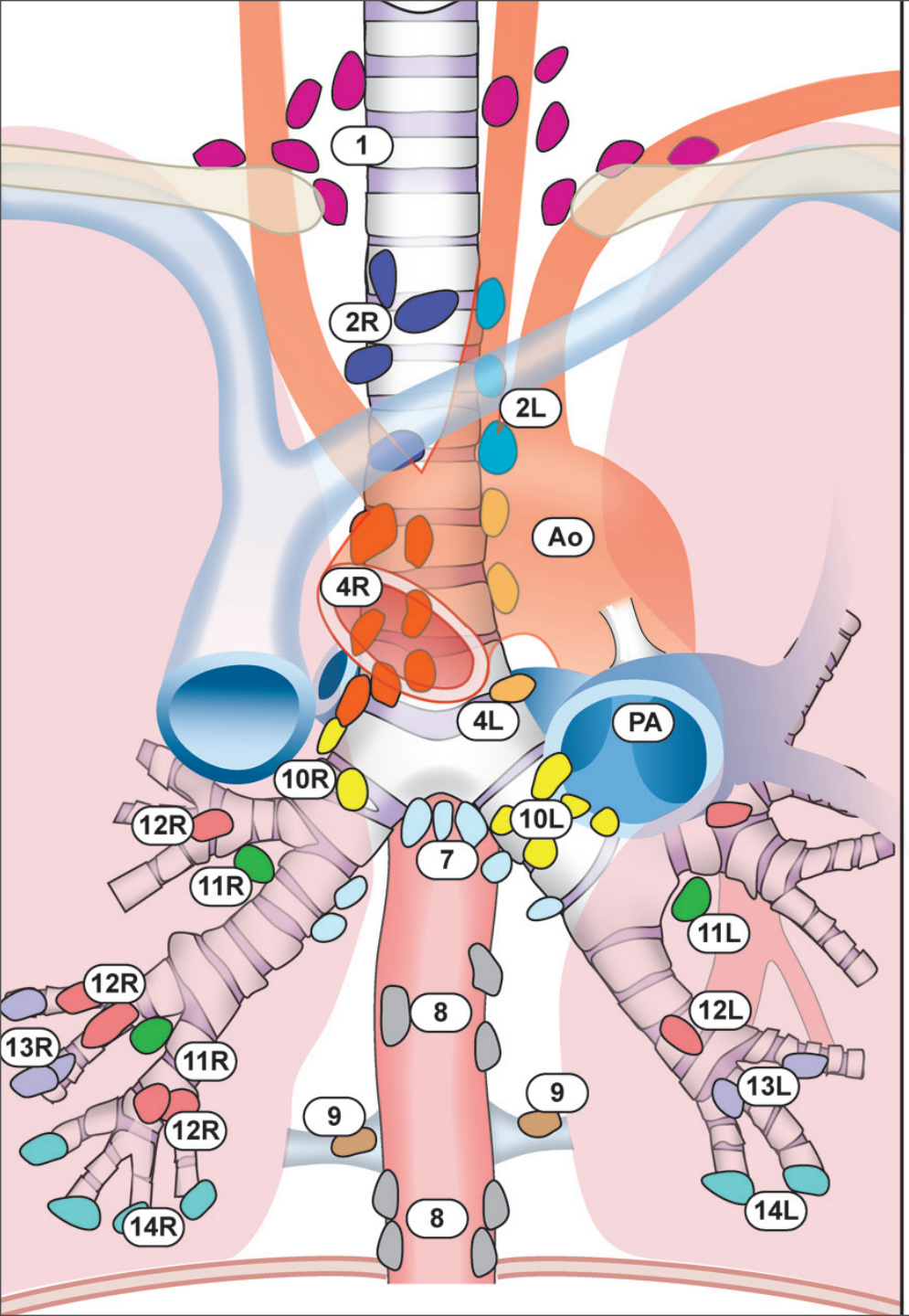
    Nódulos en pulmón contralateral
  - M1b: Metástasis a distancia

Clasificacion de T

- TX Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (for example, not in the main bronchus)
  - T1a Tumor 2 cm or less in greatest dimension
  - T1b Tumor more than 2 cm but 3 cm or less in greatest dimension
- T2 Tumor more than 3 cm but 7 cm or less or tumor with any of the following features (T2 tumors with these features are classified T2a if 5 cm or less): involves main bronchus, 2 cm or more distal to the carina; invades visceral pleura (PL1 or PL2); associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
  - T2a Tumor more than 3 cm but 5 cm or less in greatest dimension
  - T2b Tumor more than 5 cm but 7 cm or less in greatest dimension
- T3 Tumor more than 7 cm or one that directly invades any of the following: parietal pleural (PL3), chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus less than 2 cm distal to the carina[1] but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe
- T4 Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe

Clasificacion de N

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastases
- N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
- N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
- N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node (s)


1
2R
2L
Ao
4R
4L
PA
10R
10L
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11R
7
11L
12R
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12L
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11R
9
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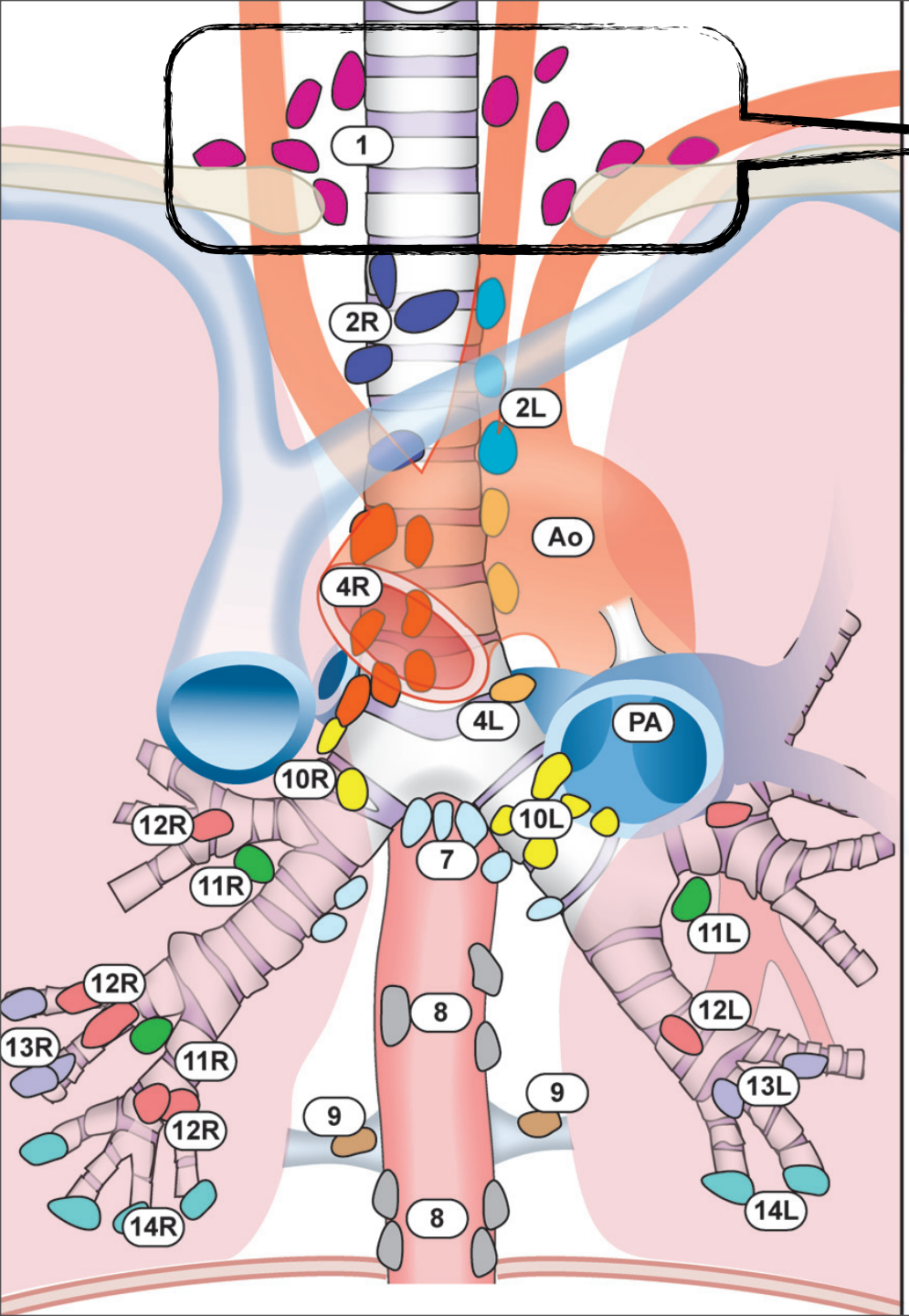
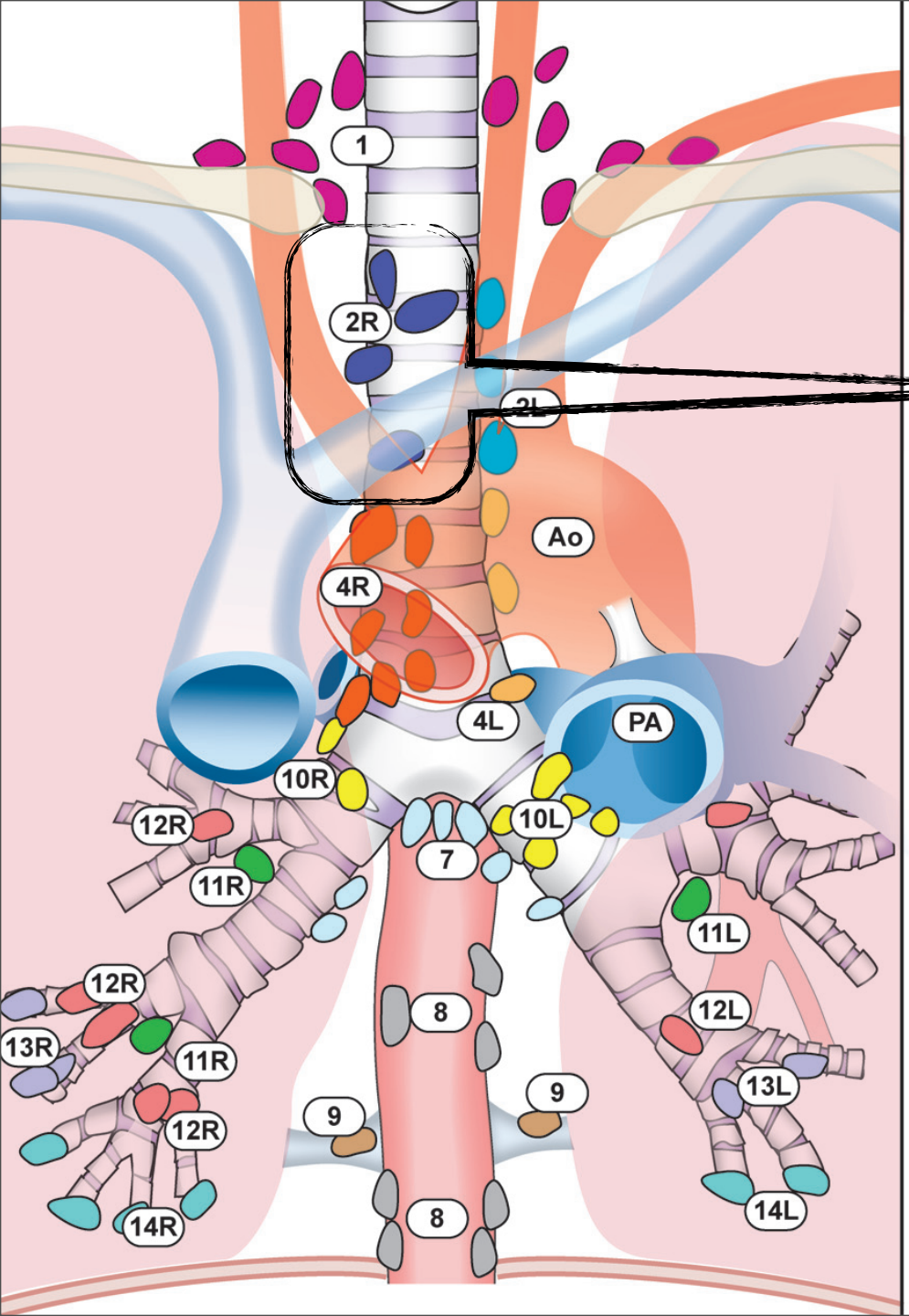
9
12R
8
14R
14L



Supraclavicular zone

1 Low cervical, supraclavicular, and sternal notch nodes



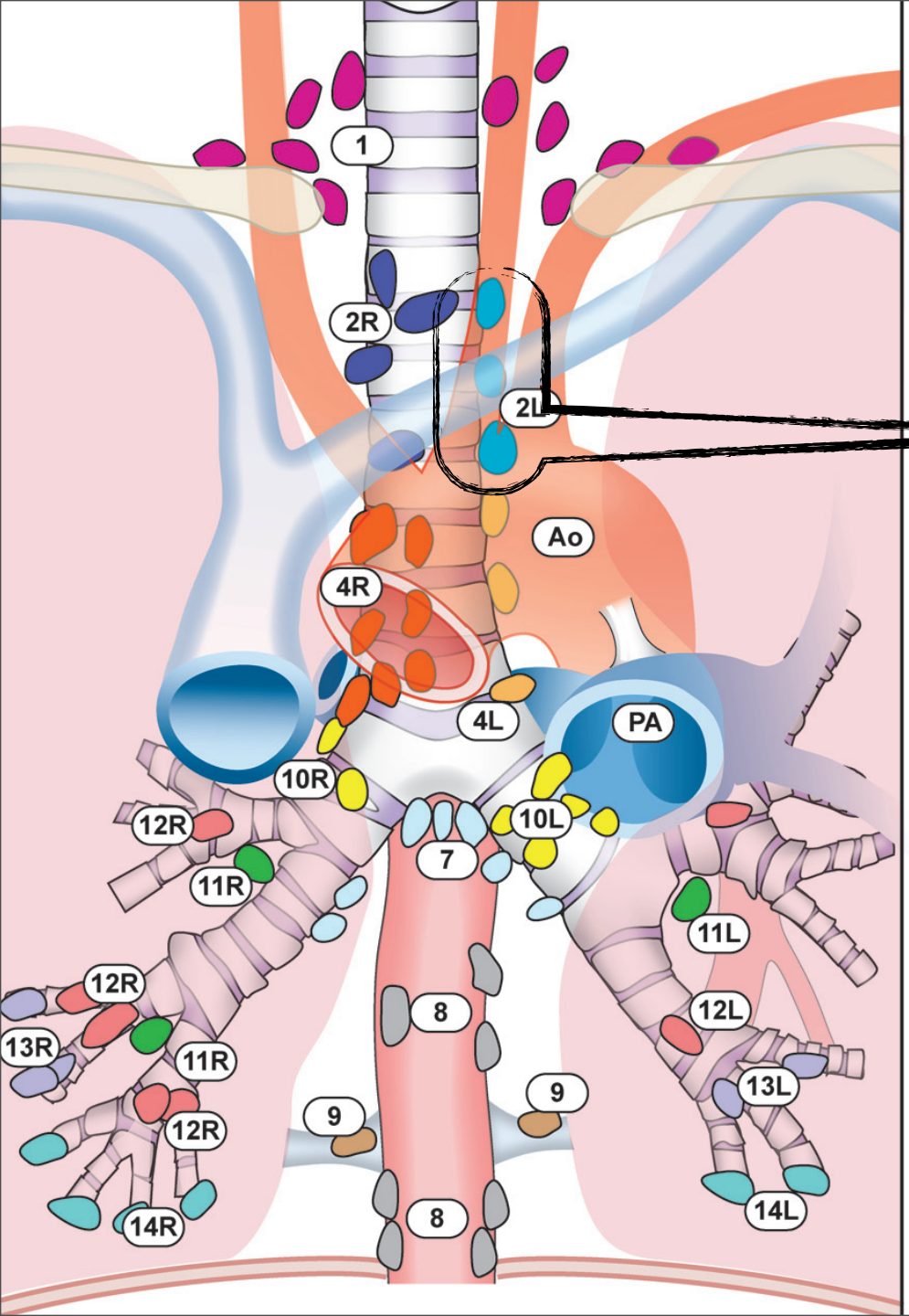
Supraclavicular zone

1 Low cervical, supraclavicular, and sternal notch nodes

Superior Mediastinal Nodes

Upper zone

- **2R** Upper Paratracheal (right)
- **2L** Upper Paratracheal (left)
- **3a** Pre-vascular
- **3p** Retrotracheal
- **4R** Lower Paratracheal (right)
- **4L** Lower Paratracheal (left)



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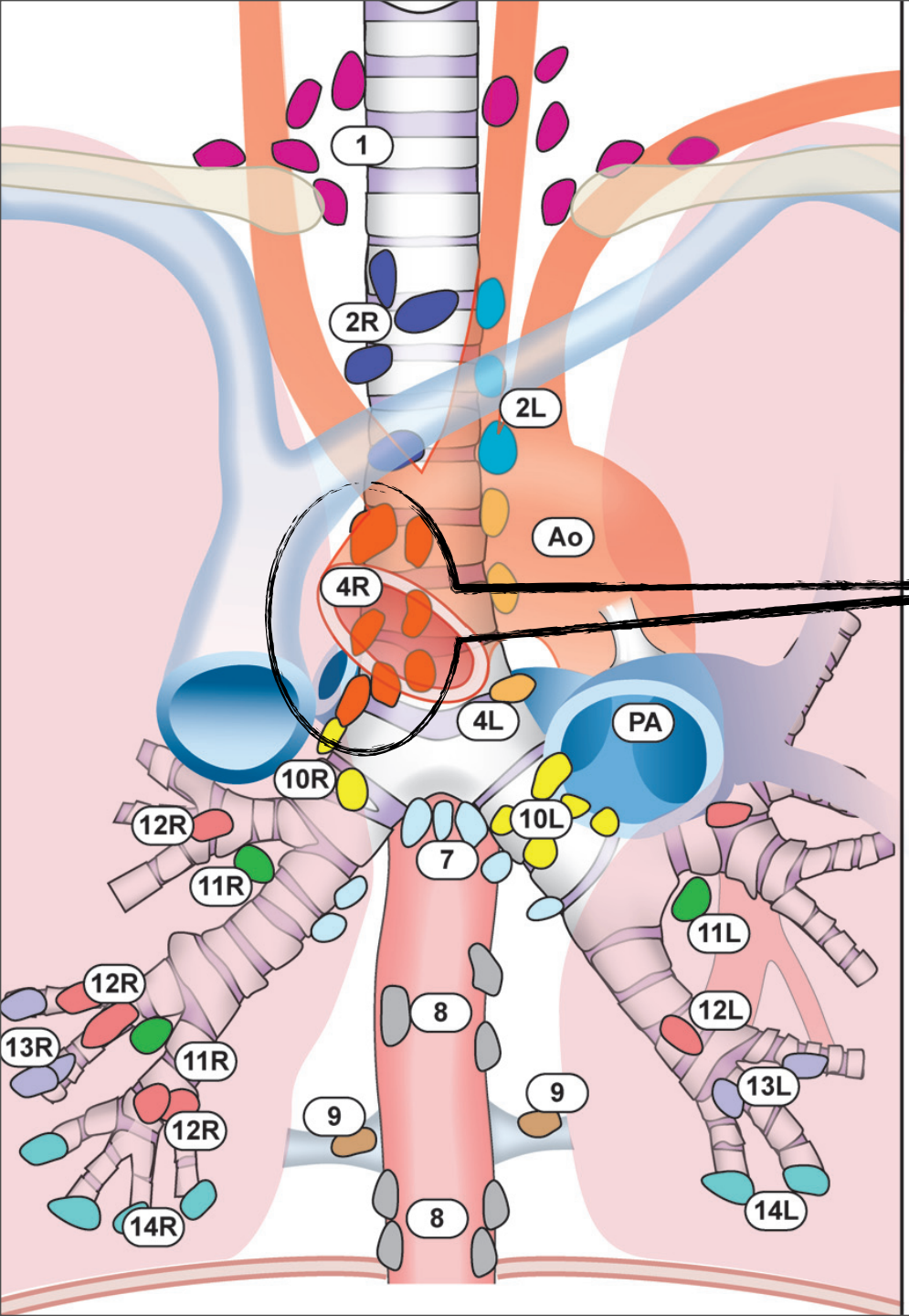

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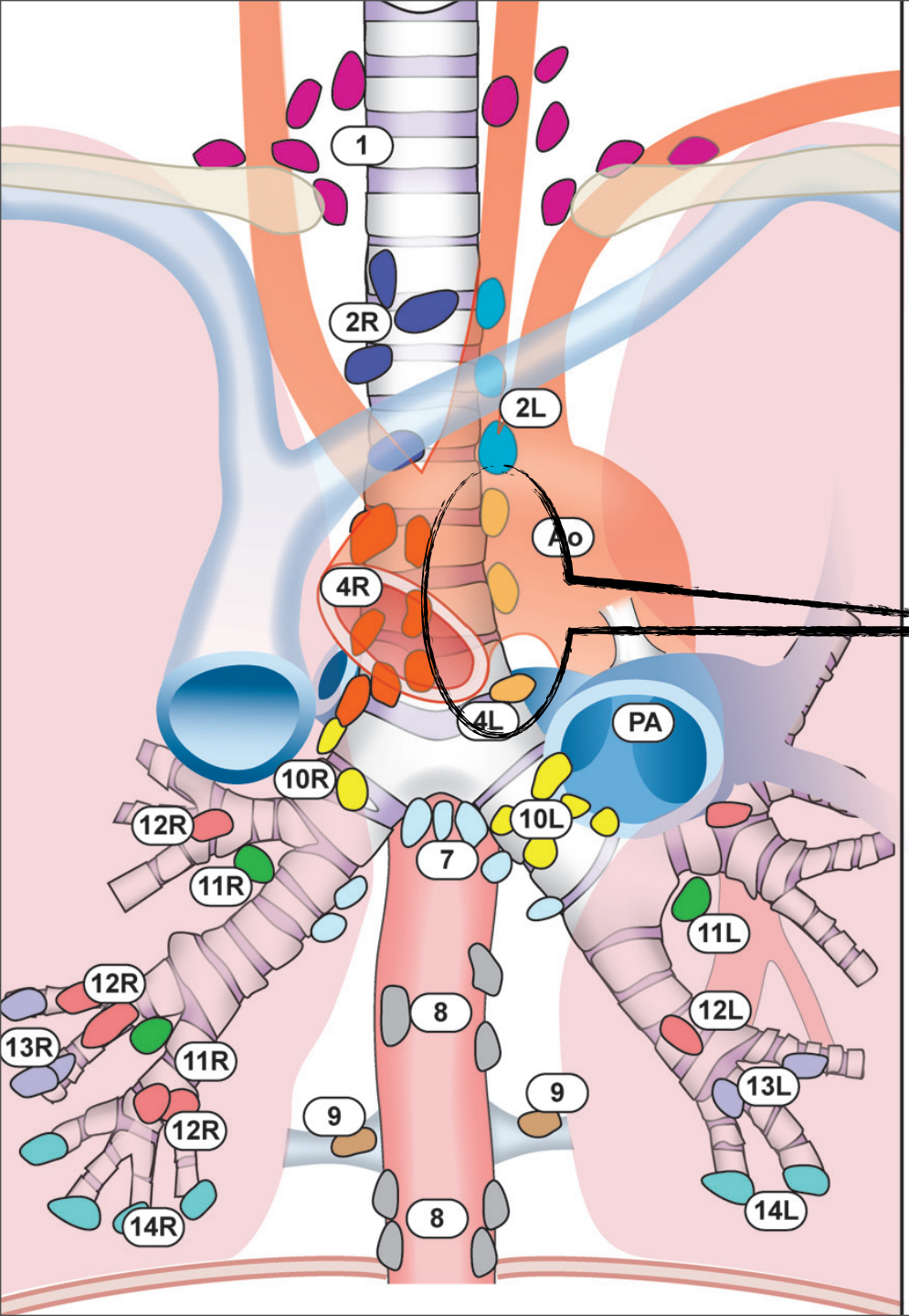

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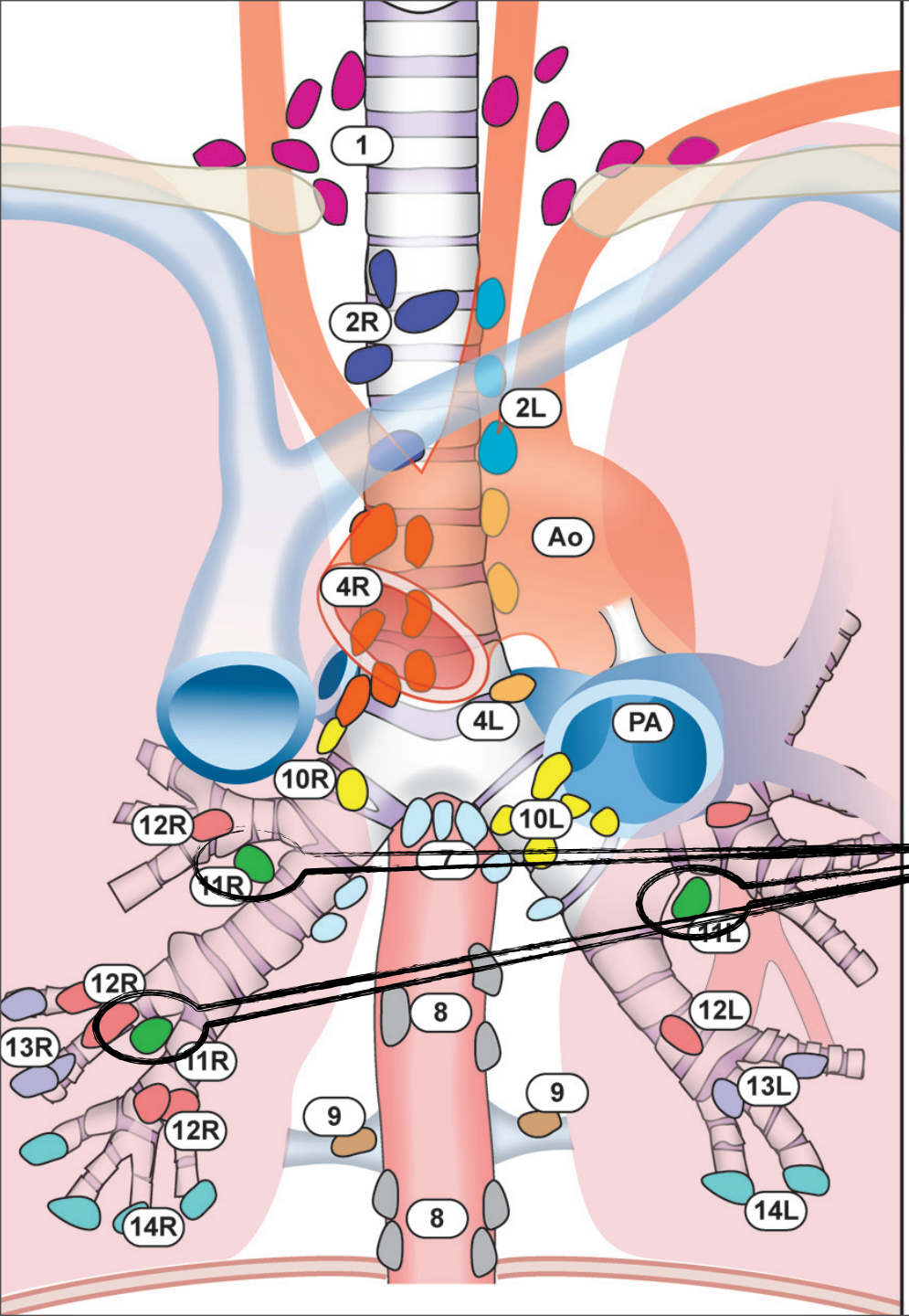


Supraclavicular zone

- **1** Low cervical, supraclavicular, and sternal notch nodes

Superior Mediastinal Nodes

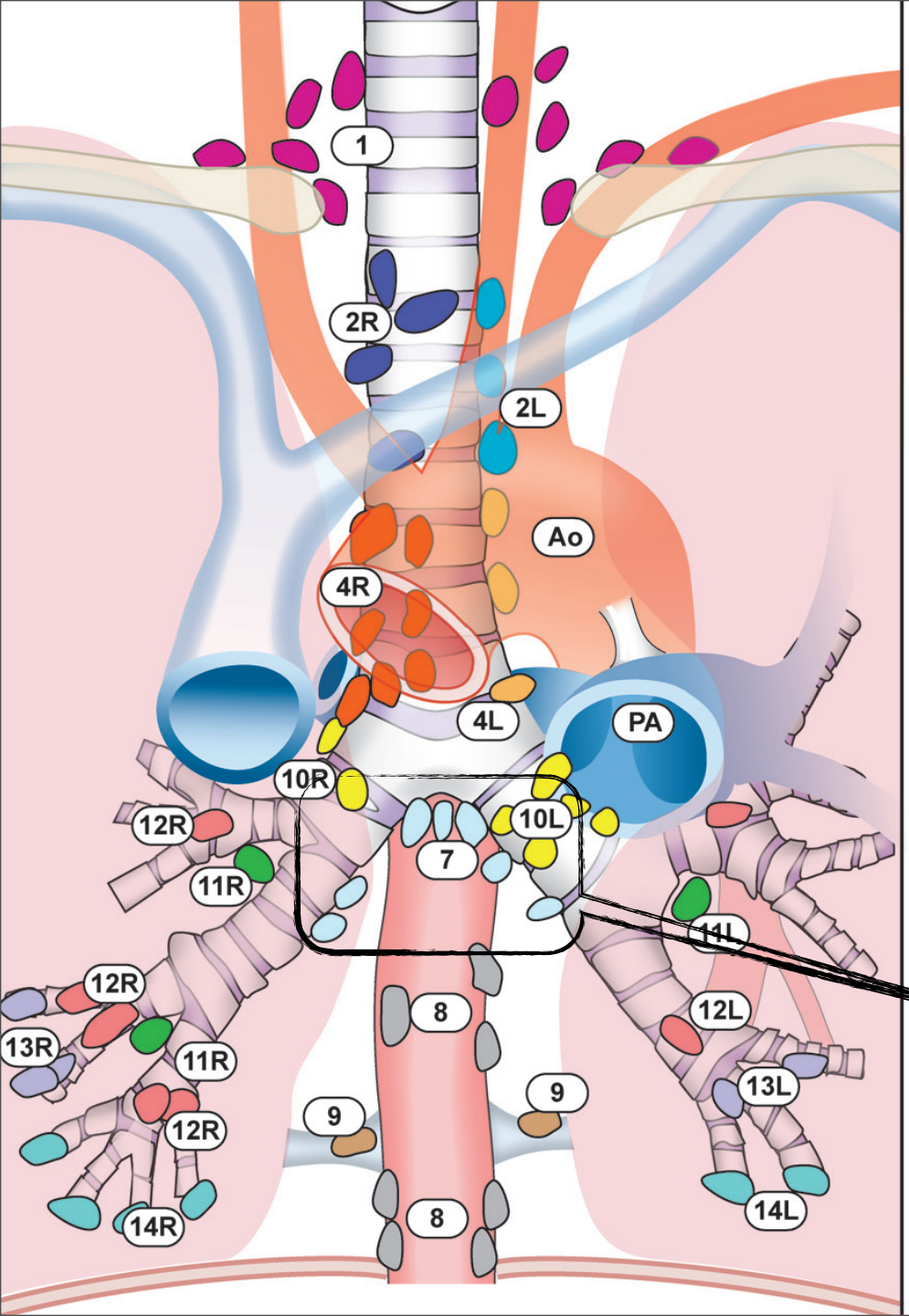
Upper zone

- **2R** Upper Paratracheal (right)
- **2L** Upper Paratracheal (left)
- **3a** Pre-vascular
- **3p** Retrotracheal
- **4R** Lower Paratracheal (right)
- **4L** Lower Paratracheal (left)

Aortic Nodes

AP zone

- **5** Subaortic
- **6** Para-aortic (ascending aorta or phrenic)



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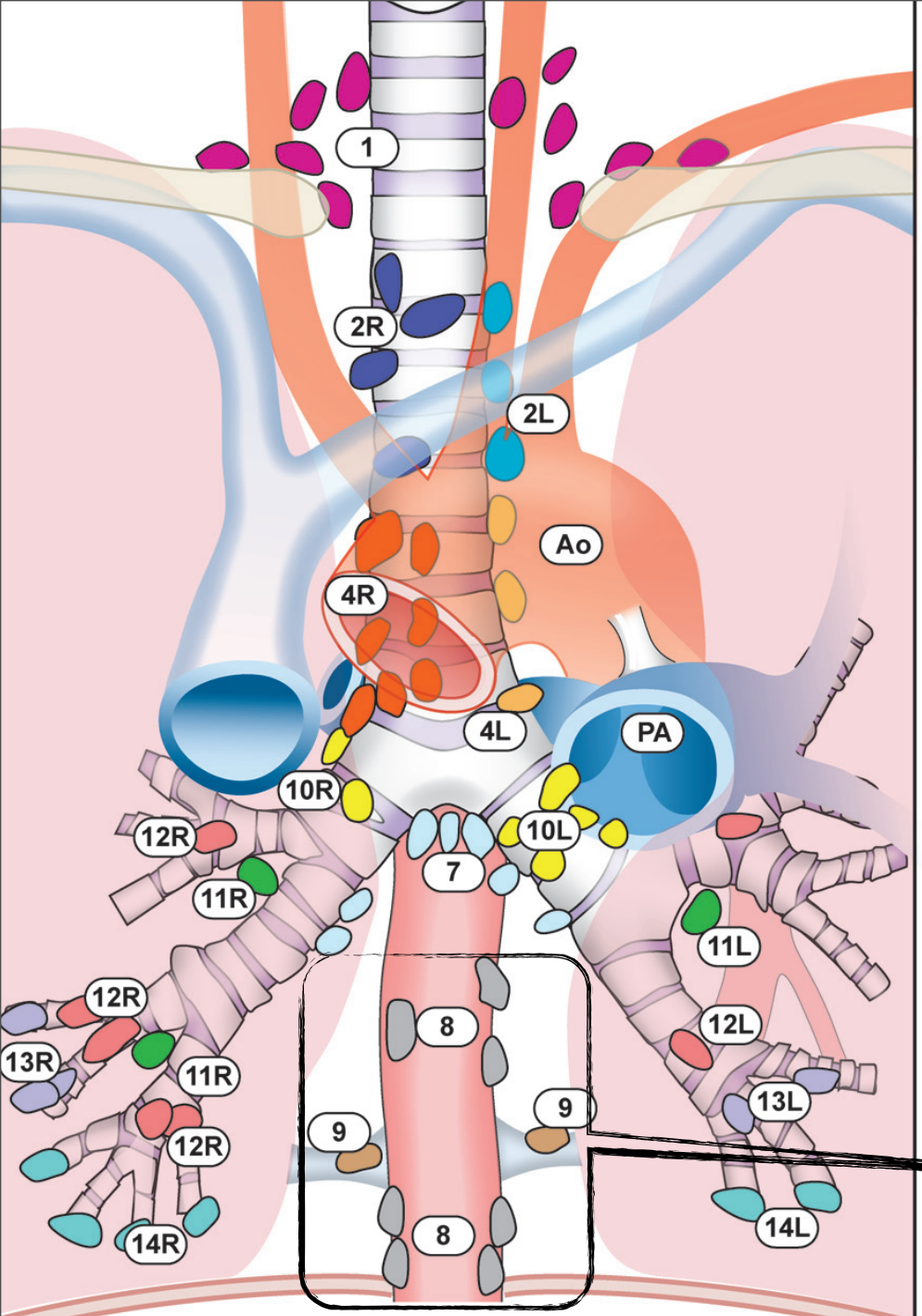
Inferior Mediastinal Nodes

Subcarinal zone

- **7** Subcarinal

Lower zone

- **8** Paraesophageal (below carina)
- **9** Pulmonary ligament



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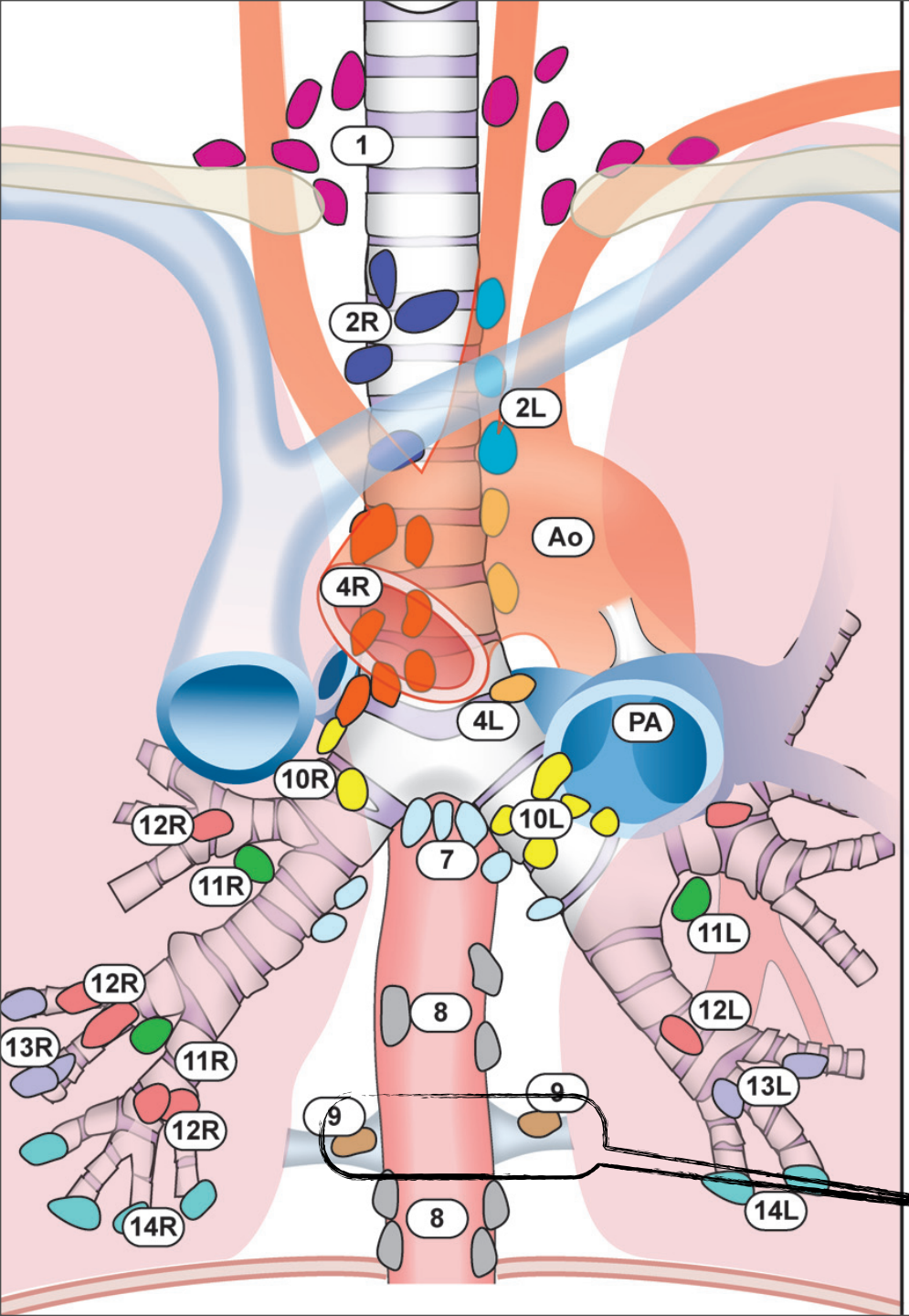

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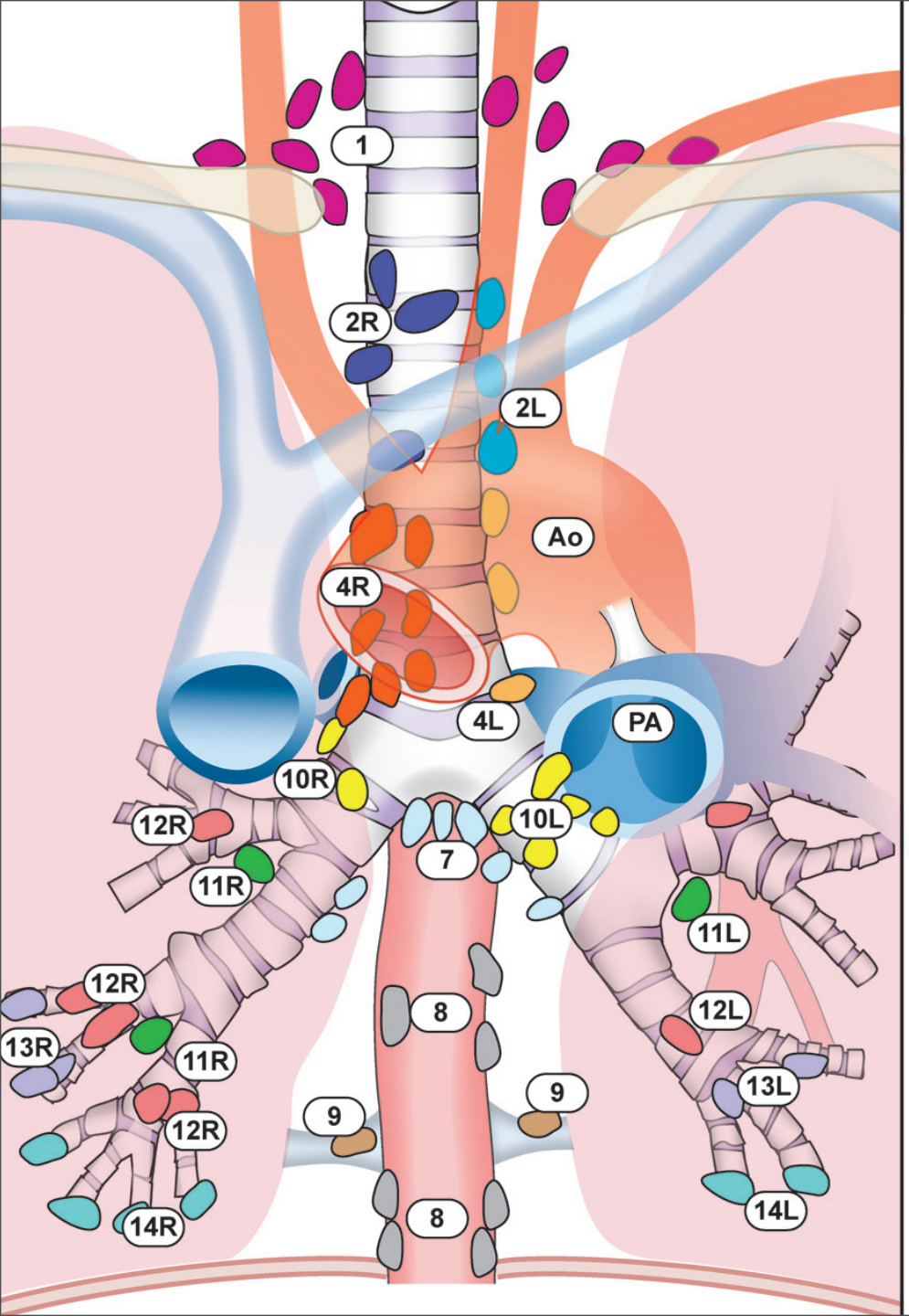

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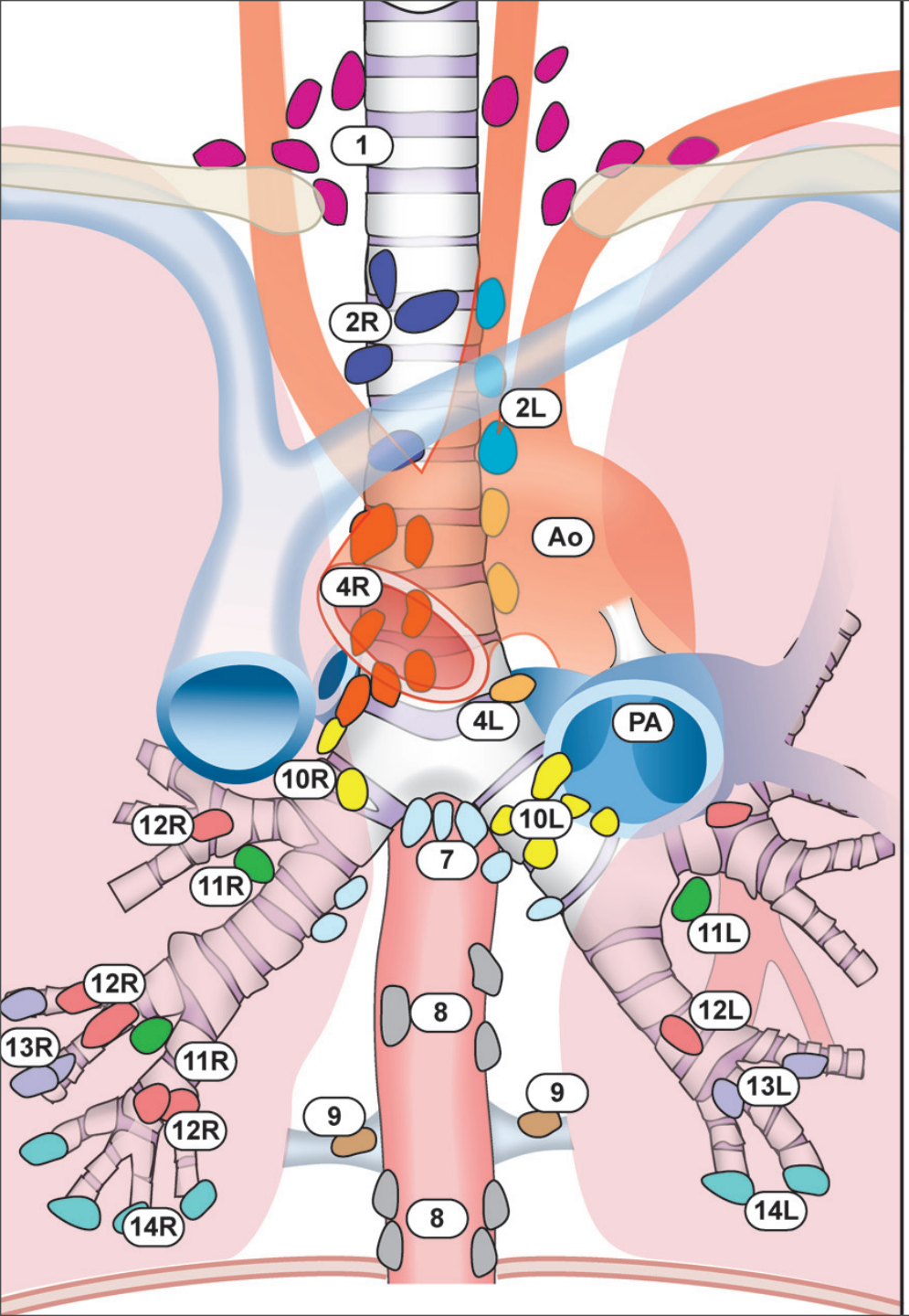
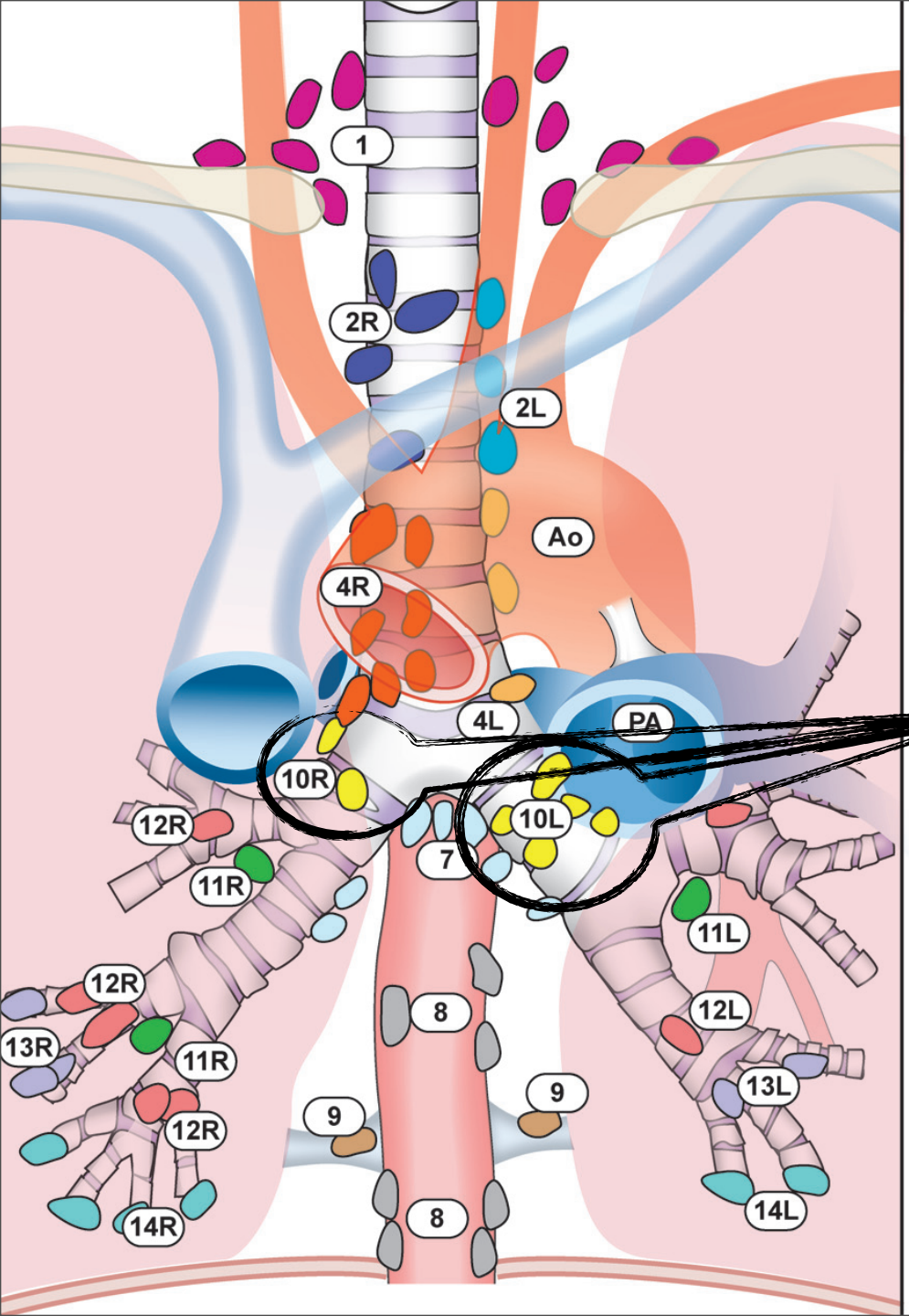

1
2R
2L
Ao
4R
4L
PA
10R
10L
12R
11R
7
11L
12R
8
12L
13R
11R
9
13L
9
12R
8
14R
14L



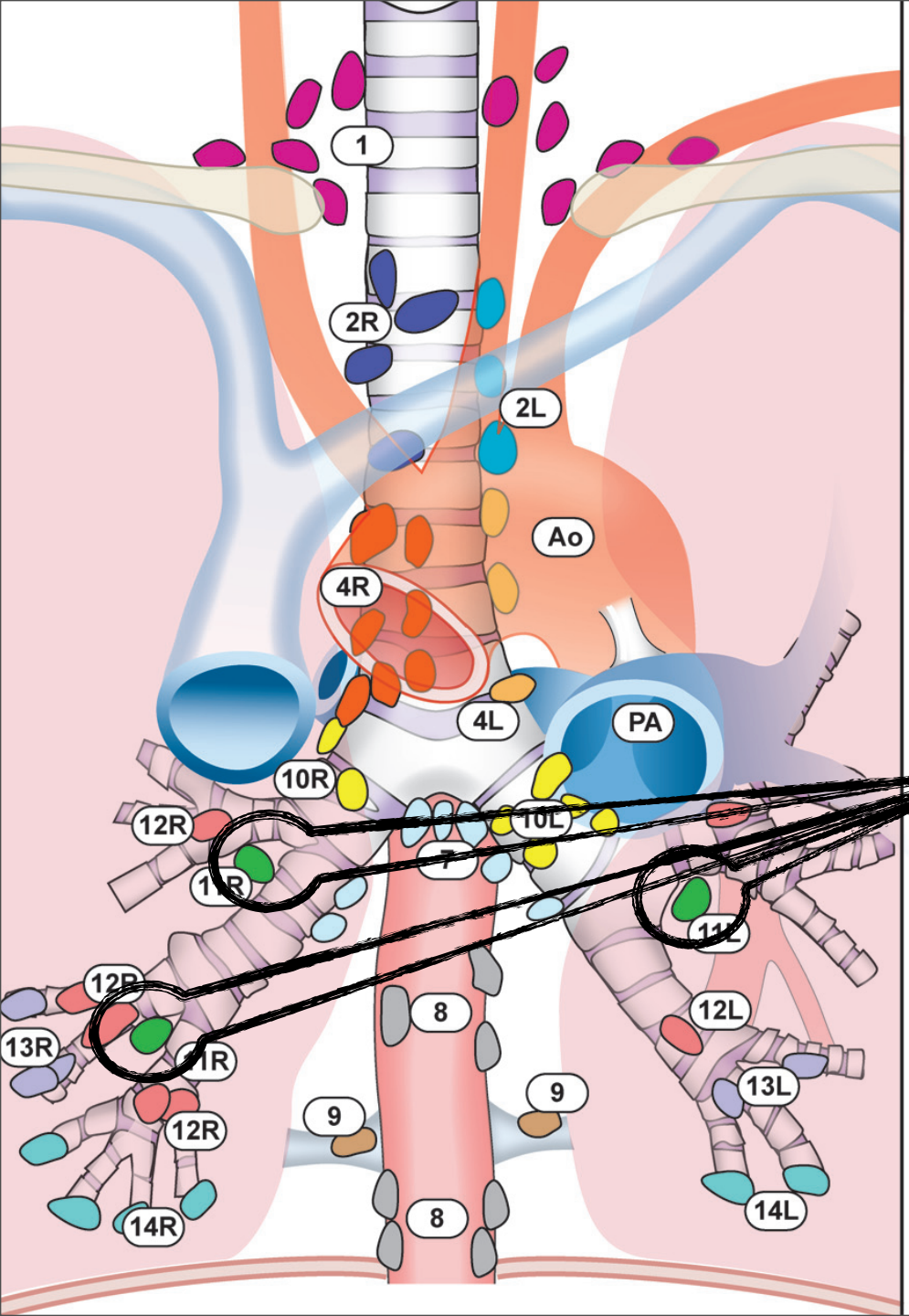
N_1 Nodes

Hilar/Interlobar zone

- **10** Hilar
- **11** Interlobar

Peripheral zone

- **12** Lobar
- **13** Segmental
- **14** Subsegmental



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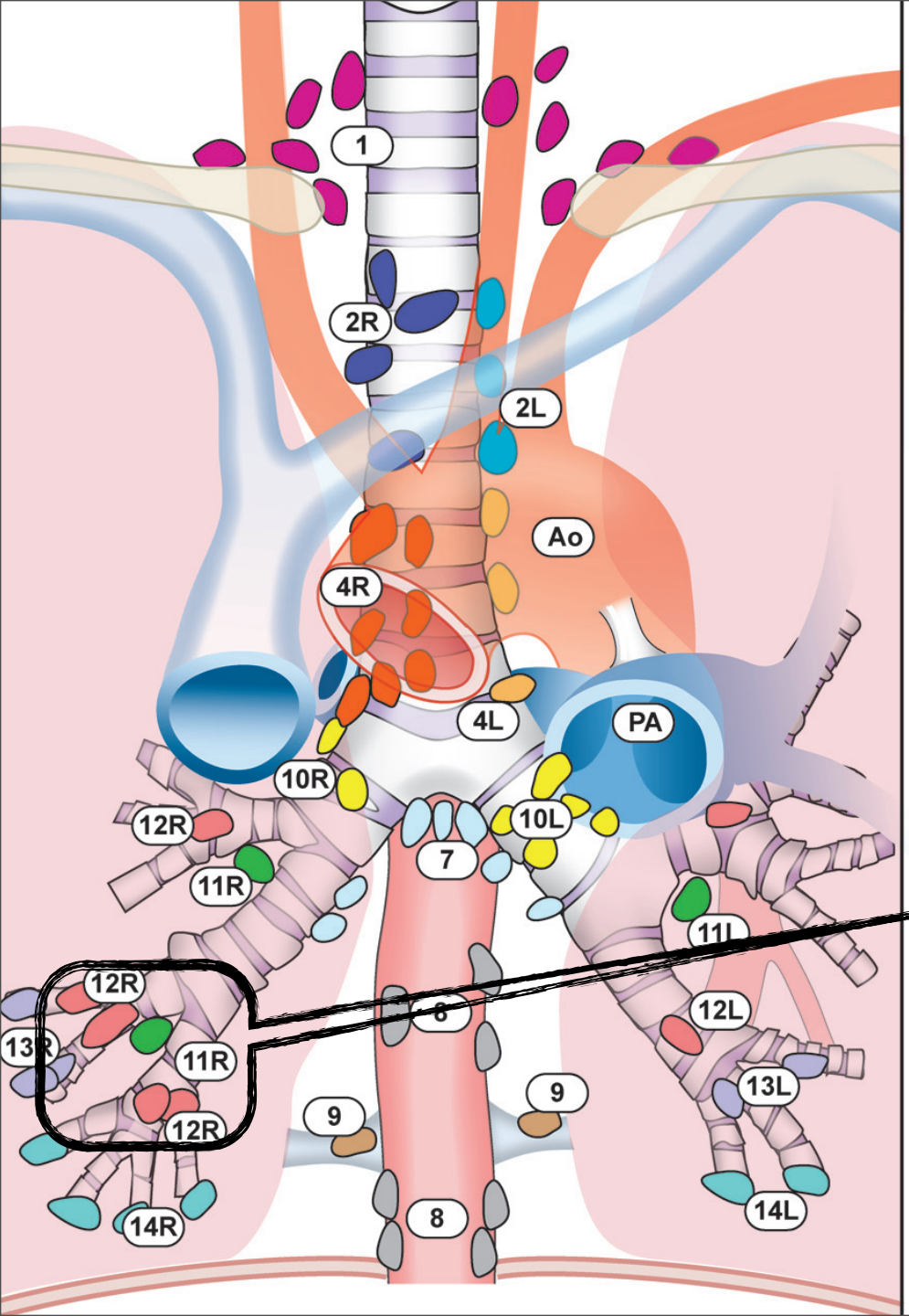

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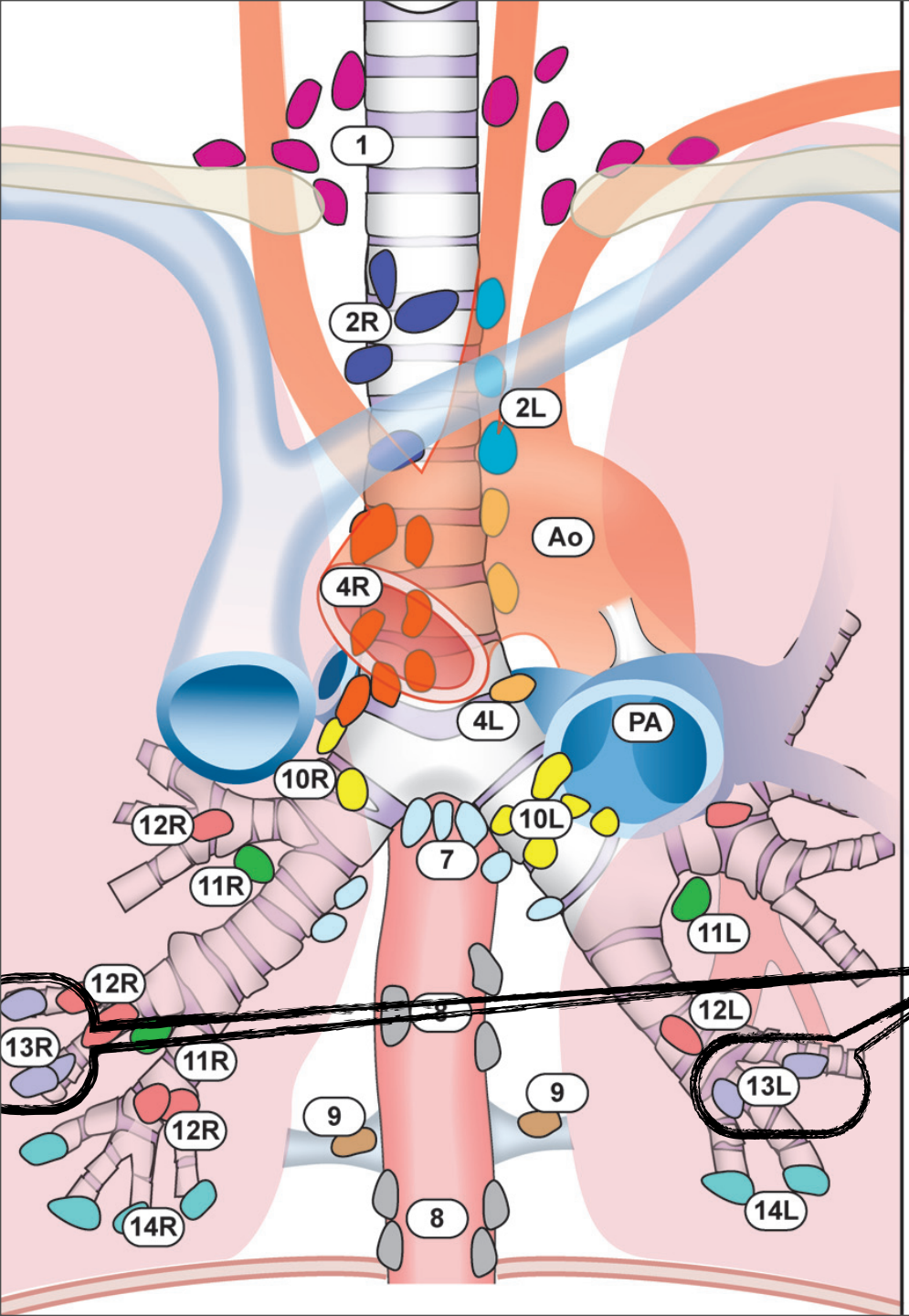

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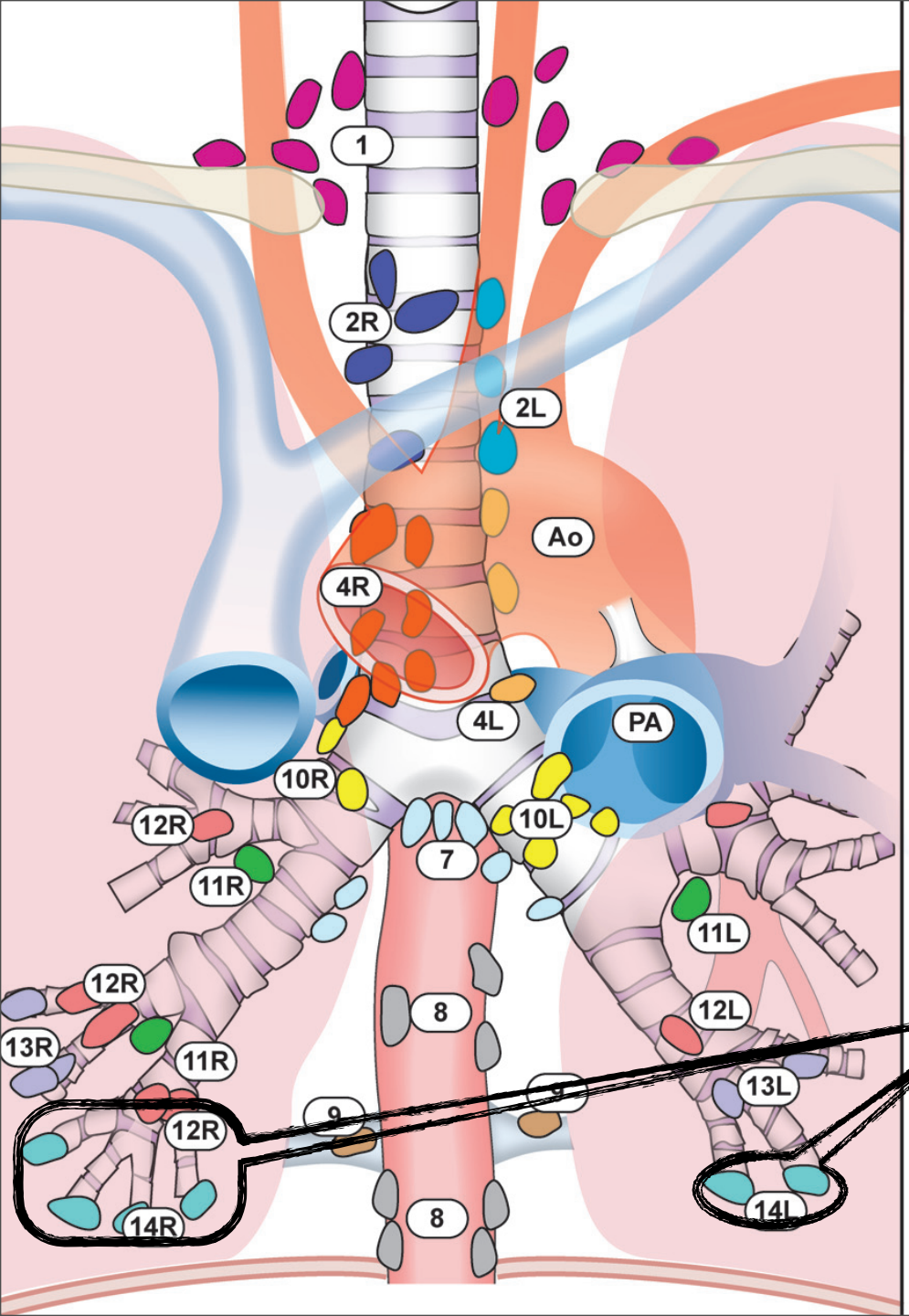

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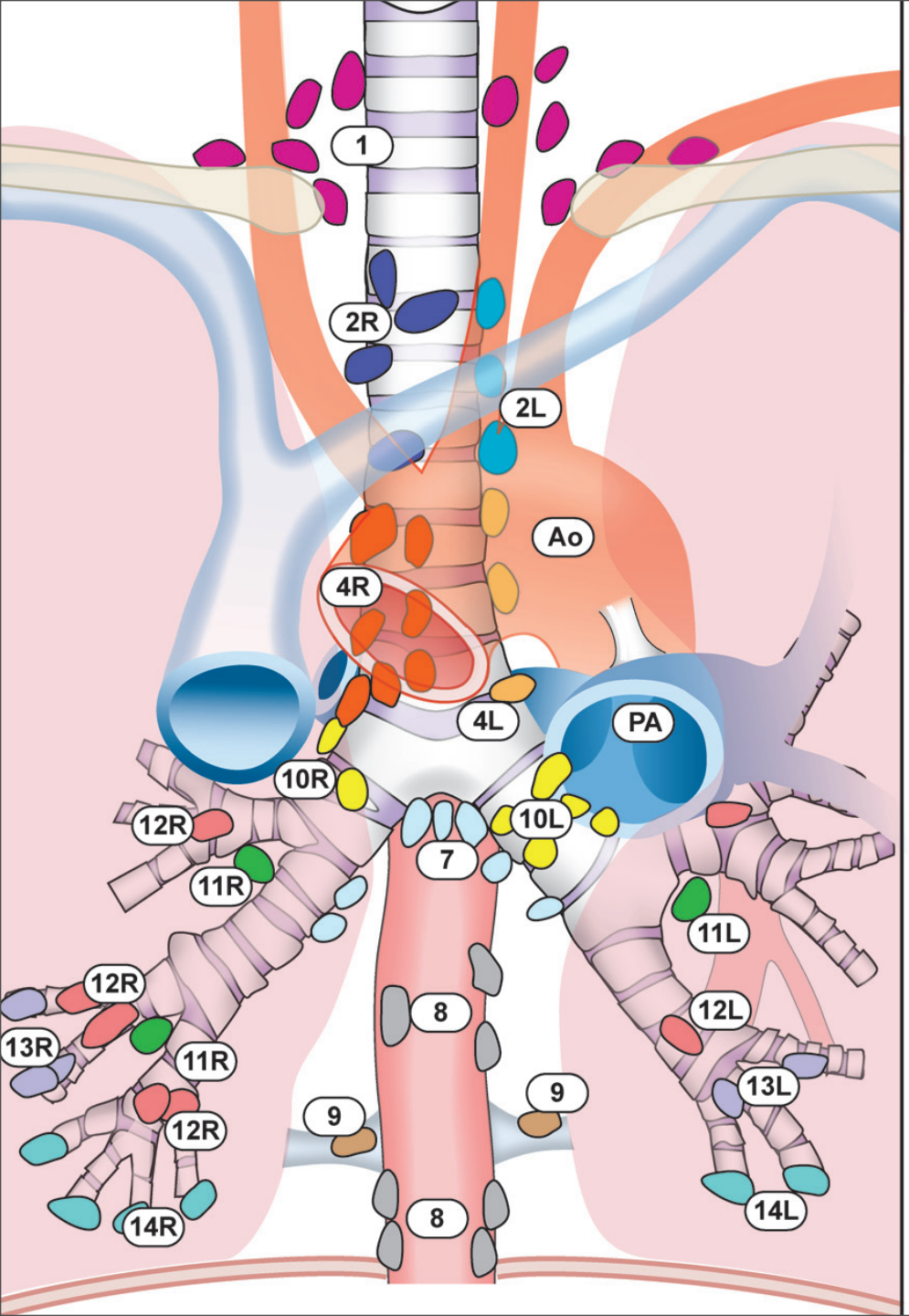

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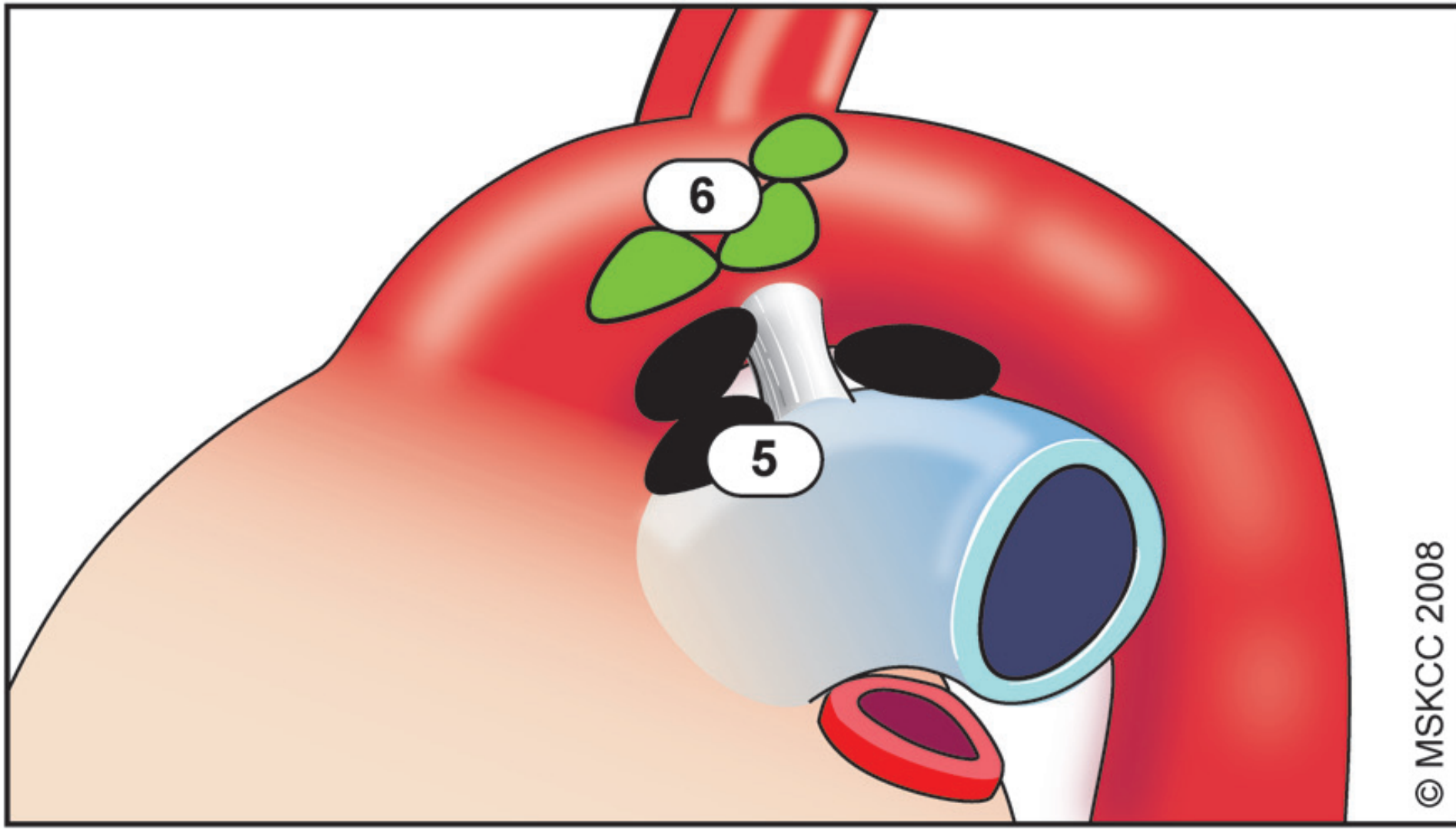

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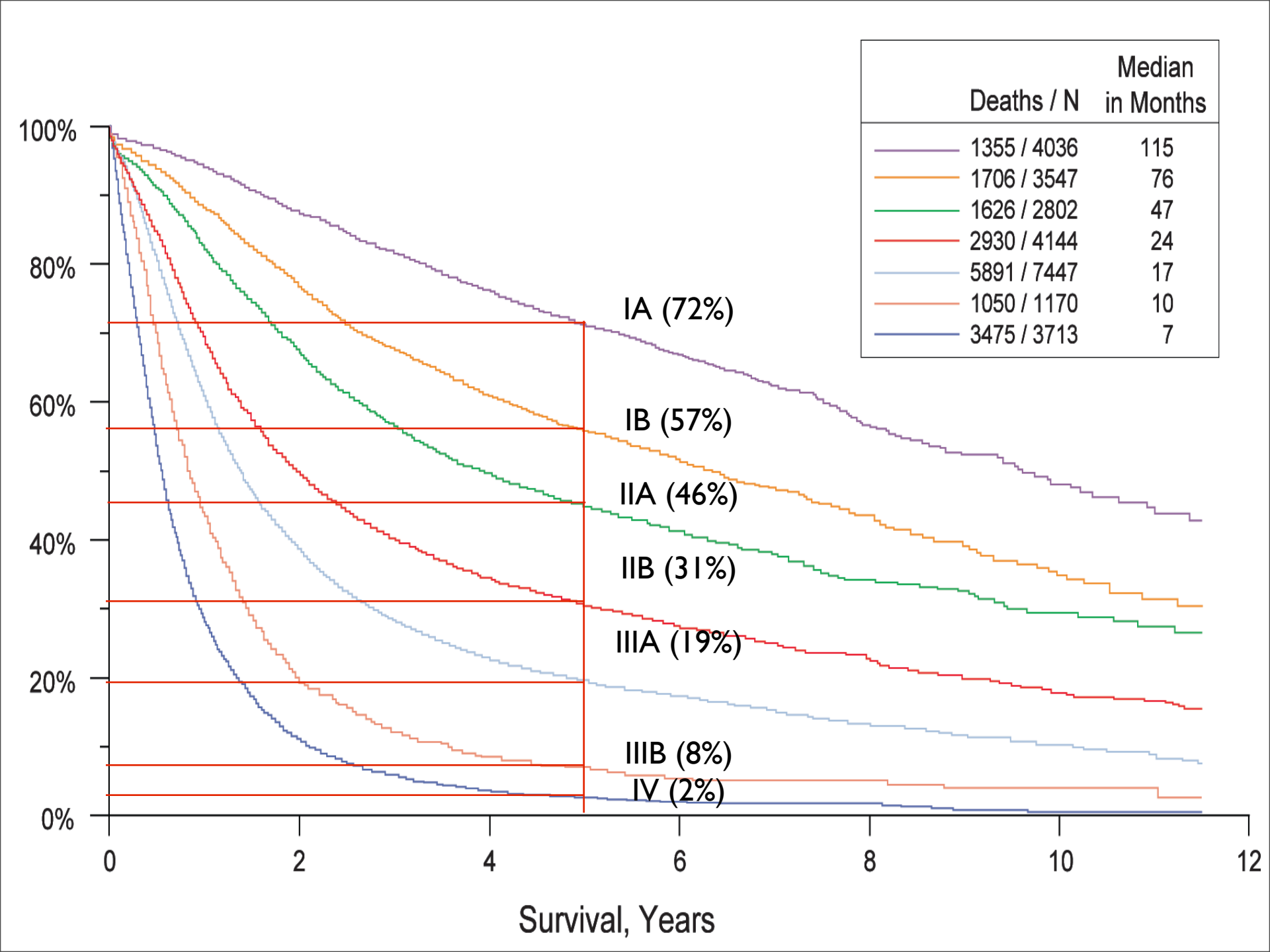
ANATOMIC STAGE/PROGNOSTIC GROUPS

Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
Stage IV	Any T	Any N	M1a
	Any T	Any N	M1b


Deaths / N
Median in Months
1355 / 4036 115
1706 / 3547 76
1626 / 2802 47
2930 / 4144 24
5891 / 7447 17
1050 / 1170 10
3475 / 3713 7
100%
80%
60%
40%
20%
0%
IA (72%)
IB (57%)
IIA (46%)
IIB (31%)
IIIA (19%)
IIIB (8%)
IV (2%)
0
2
4
6
8
10
12
Survival, Years

SCLC

- 1950 - Clasificación de *Veterans Administration Lung Study Group*
- Depende extensión y posibilidad de campo de RT
  - Enfermedad limitada: Compromiso de un hemitorax, aun en compromiso local o supraclavicular ipsilateral
  - IASLC - 1989: Tumores limitados a un hemitorax, con compromiso nodal regional, incluidos los ganglios hiliares, mediastinales ipsi y contralaterales y supraclaviculares bilaterales
    - Incluye derrame pleural ipsilateral independiente de citología

Clasificación Histologica

Especímenes de Resección

TABLE 1. IASLC/ATS/ERS Classification of Lung Adenocarcinoma in Resection Specimens

- Preinvasive lesions
  - Atypical adenomatous hyperplasia
  - Adenocarcinoma in situ (≤3 cm formerly BAC)
    - Nonmucinous
    - Mucinous
    - Mixed mucinous/nonmucinous
  - Minimally invasive adenocarcinoma (≤3 cm lepidic predominant tumor with ≤5 mm invasion)
    - Nonmucinous
    - Mucinous
    - Mixed mucinous/nonmucinous
- Invasive adenocarcinoma
  - Lepidic predominant (formerly nonmucinous BAC pattern, with >5 mm invasion)
  - Acinar predominant
  - Papillary predominant
  - Micropapillary predominant
  - Solid predominant with mucin production
- Variants of invasive adenocarcinoma
  - Invasive mucinous adenocarcinoma (formerly mucinous BAC)
  - Colloid
  - Fetal (low and high grade)
  - Enteric

Requiere diferenciación de Metástasis colorectal

J Thorac Oncol. 2011;6: 244–285

Lesiones preinvasivas

- Presente 5 – 23% tejido adyacente a adenocarcinoma
- Comparte:
  - Clonalidad
  - Mutación y polimorfismo de KRAS
  - Mutaciones EGFR
  - Expresión de p53
  - Perdida de heterocigozidad y metilacion
  - Alteraciones epigeneticas en *Wnt1*
  - Expresión de FHIT

J Thorac Oncol. 2011;6: 244–285

Consideraciones

- Hiperplasia alveolar atípica
  - Continuum hacia Adenocarcinoma in situ
  - Difícil de distinguir de progresión

- Adenocarcinoma in situ
  - Limitada a estructuras alveolares preexistentes
  - 100% sobrevida libre de enfermedad a 3 años

J Thorac Oncol. 2011;6: 244–285

Adenocarcinoma microinvasivo

- Subtipo histologico diferente a Lepidico
- Células tumorales con infiltración al estroma miofibroblastico
- No considerable si:
  - Invade linfáticos, vasos o pleura
  - Contiene necrosis tumoral
    - Tamaño??
    - < 5 mm
- Sobrevida 100% con resección

J Thorac Oncol. 2011;6: 244–285

Acerca del TTF-1..

- División anatómica de acuerdo a origen embriologico
  - Sistema de conducción aerea
    - Expresión ubicua de TTF-1 en células epiteliales
    - Regulación en desarrollo de vías aéreas pequeñas y alveolos
    - Expresión por células Claras y neumocitos de tipo II
  - Parenquima Pulmonar periférico.
    - Expresión negativa para TTF-1
    - Tumores no relacionados a unidades de transporte aéreo
    - Expresión de MUC 2-5-6 originado en células ***Globet***

J Thorac Oncol. 2011;6: 244–285

SCLC

- Disminución constante de la incidencia a partir de 1986 (25 → 12.5%)
- Cambios en la clasificación histologica en 4 ocasiones en las ultimas tres décadas
- Introducción del carcinoma neuroendocrino de célula grande en NSCLC en 1999
- Dificultades en la distinción de este ultimo con SCLC

Table 1. WHO Classifications of SCLC

WHO (1967)	WHO (1981)	WHO/IASLC (1991)	WHO (2004)
Lymphocyte-like	Oat cell	Small cell	Small cell
Polygonal	Intermediate		
Fusiform			
Other	Combined oat cell carcinoma	Combined small cell carcinoma	Combined small cell carcinoma

Table 1. Summary of Diagnostic Criteria and Grading of Lung Neuroendocrine Tumors Based on the 2004 World Health Organization Classification

	Typical Carcinoid	Atypical Carcinoid	Large Cell Neuroendocrine Carcinoma	Small Cell Lung Carcinoma
Grade	Low	Intermediate	High	High
Morphology	Well-differentiated NET	Well-differentiated NET	Poorly differentiated NET	Poorly differentiated NET
Mitoses per 10 HPFs[a]	<2	2–10	>10 (median, 70)	>10 (median, 80)
Necrosis	None	Present (focal punctate)	Present (extensive)	Present (extensive)

Para destacar ...

- Pulmón:
  - Origen de 95% de Carcinoma de célula pequeña
  - Origen de 30% de Tumores neuroendocrinos bien diferenciados
  - Ligado casi exclusivamente al habito de fumar (SCLC)
  - Carcinoides pulmonares: 5% MEN1

Indicaciones quirurgicas

- Ausencia de compromiso mediastinal
- Ausencia de compromiso metastasico
- Diseccion de ganglios linfaticos mediastinales
  - Evaluacion de al menos 6 ganglios
    - 3 mediastinales
    - 3 N1 de existir
    - Incluir ganglios de estacion 9 para tumores de LI
    - Mejores desenlaces con la diseccion medistinal completa que con el muestreo ganglionar

Cochrane Database Syst Rev. 2005 Jan 25;(1):CD004699.

Limitaciones para intervencion

- Sindrome de vena cava superior
- Paralisis de cuerda vocal o N. Frenico
- Derrame pleural maligno
- Tumor a < 2 cm de la carina
- Metastasis en ganglios contralaterales
- Compromiso de la A. Pulmonar principal
- HTP moderada - FEV1 < 1l - CVF < 40%

Opciones de tratamiento

Estadio 0	Cirugia Terapia endobronquial	
Estadio IA y IB	Cirugia Radioterapia**	** Pacientes Inoperables 60 Gy, T< 4 cm Resultados similares a reseccion
Estadio IIA y IIB	Cirugia QT neoadyuvante ** Qumioterapia adyuvante Radioterapia ***	** Sin beneficio claro en supervivencia global *** Pacientes inoperables 60 Gy, 10% OS a 5 años

Noordijk EM, Radiother Oncol 13 (2): 83-9, 1988

Gilligan D, Lancet 369 (9577): 1929-37, 2007

Dosoretz DE, Int J Radiat Oncol Biol Phys 24 (1): 3-9, 1992

Opciones de tratamiento

IIIA	Resecada	Cirugia Neoadyuvancia ** Adyuvancia	** HR, 0.88; 95% CI, 0.76–1.01; *P* = .07 Beneficio Absoluto 5%
	Irresecable	Radioterapia Quimioradioterapia	* Reduccion 10% en mortalidad con CRT * Combinacion de CDDP/VP16
	Tumores de sulcus superior	Radioterapia Quimioradioterapia Radioterapia y Cx	** Solo hay 64% de posibilidad de reseccion de T3 y 39% de T4
	Tumores que invaden la pared toracica	Cirugia Cirugia y RT ** RT sola CRT seguida de CX	** Indicada si hay margenes poco claros

Gilligan D, Lancet 369 (9577): 1929-37, 2007

Rowell NP, Cochrane Database Syst Rev (4): CD002140, 2004

Rusch VW, J Thorac Cardiovasc Surg 119 (6): 1147-53, 2000

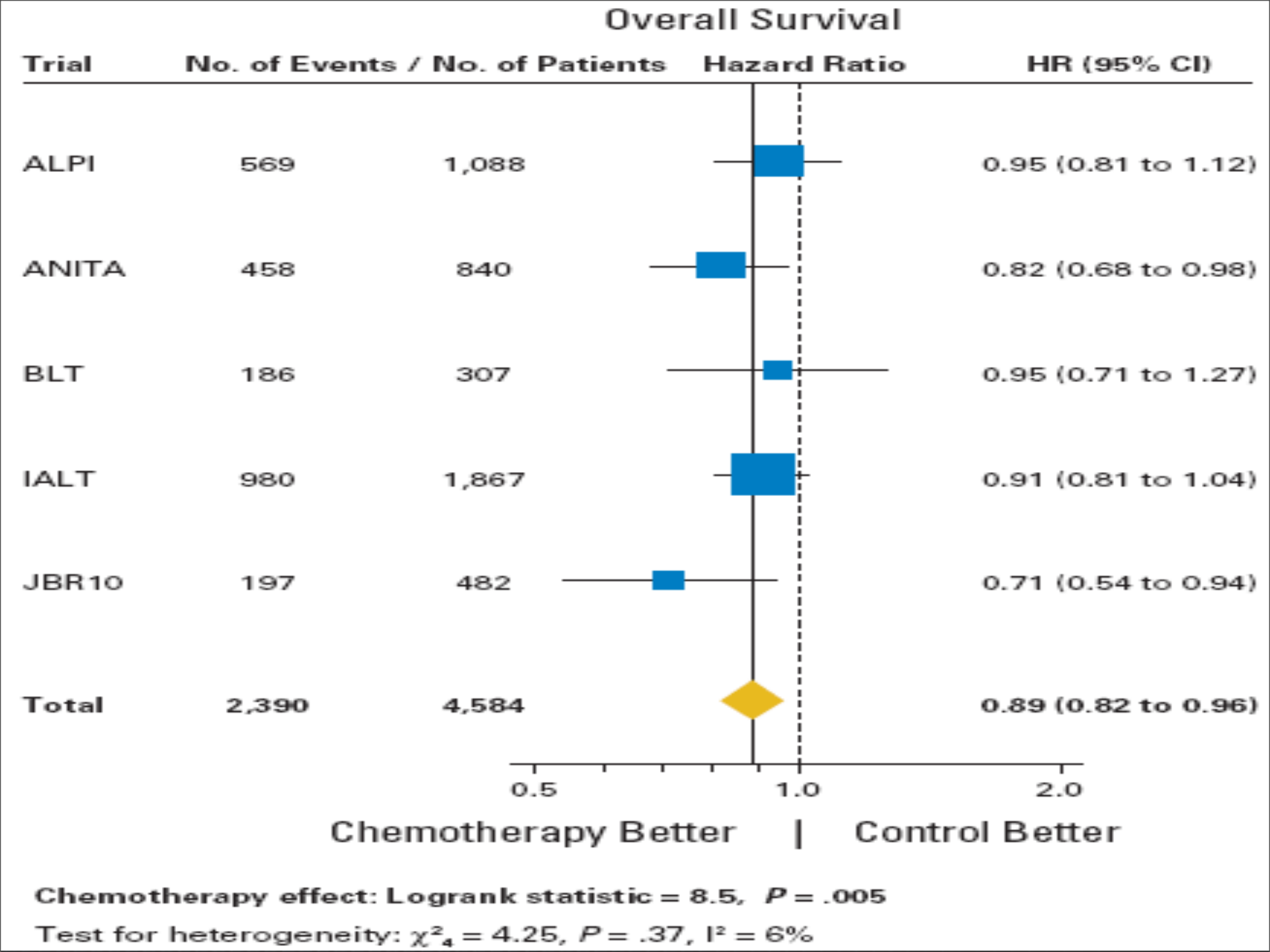
VOLUME 26 · NUMBER 21 · JULY 20 2008

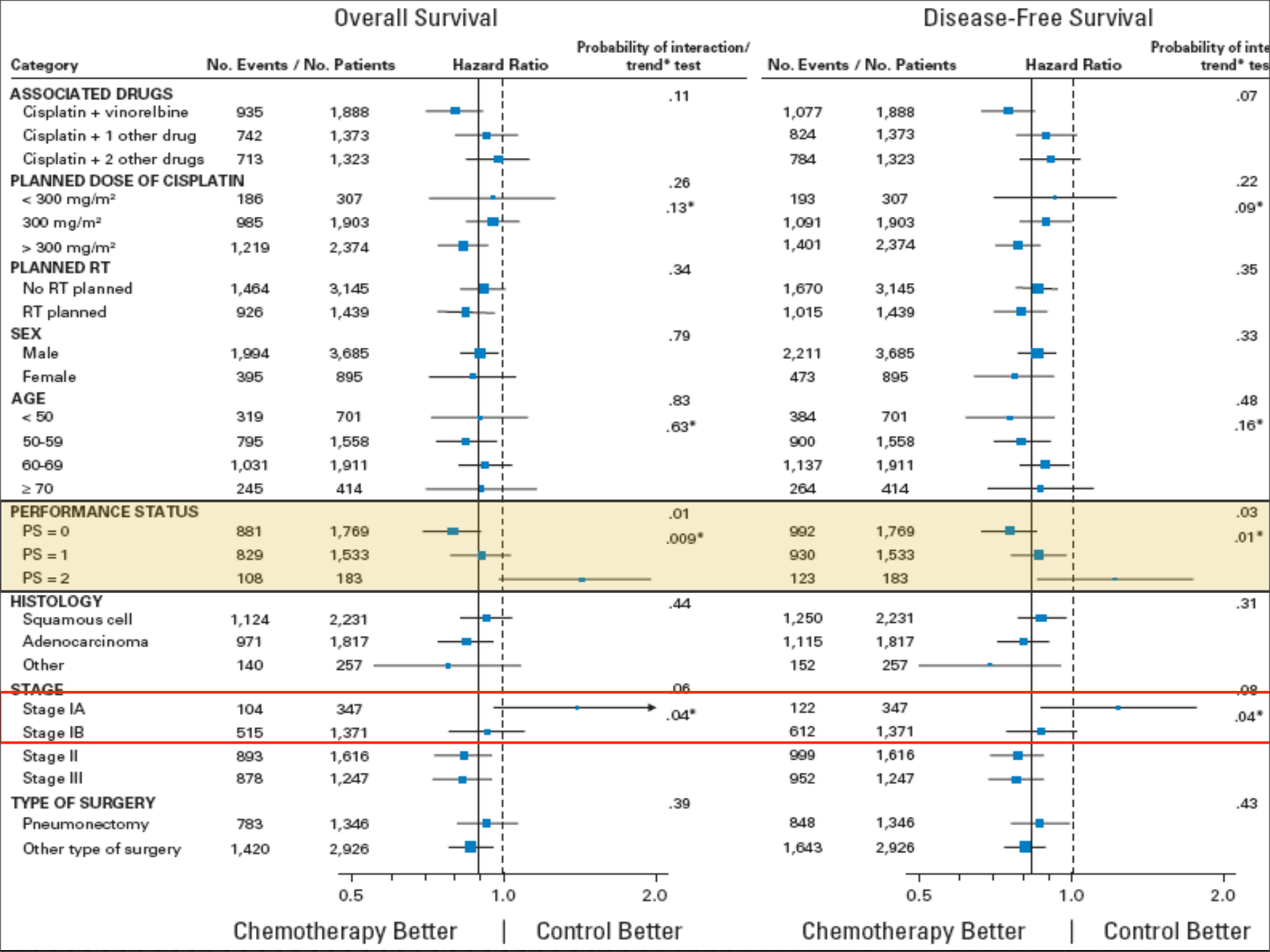
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Lung Adjuvant Cisplatin Evaluation: A Pooled Analysis by the LACE Collaborative Group

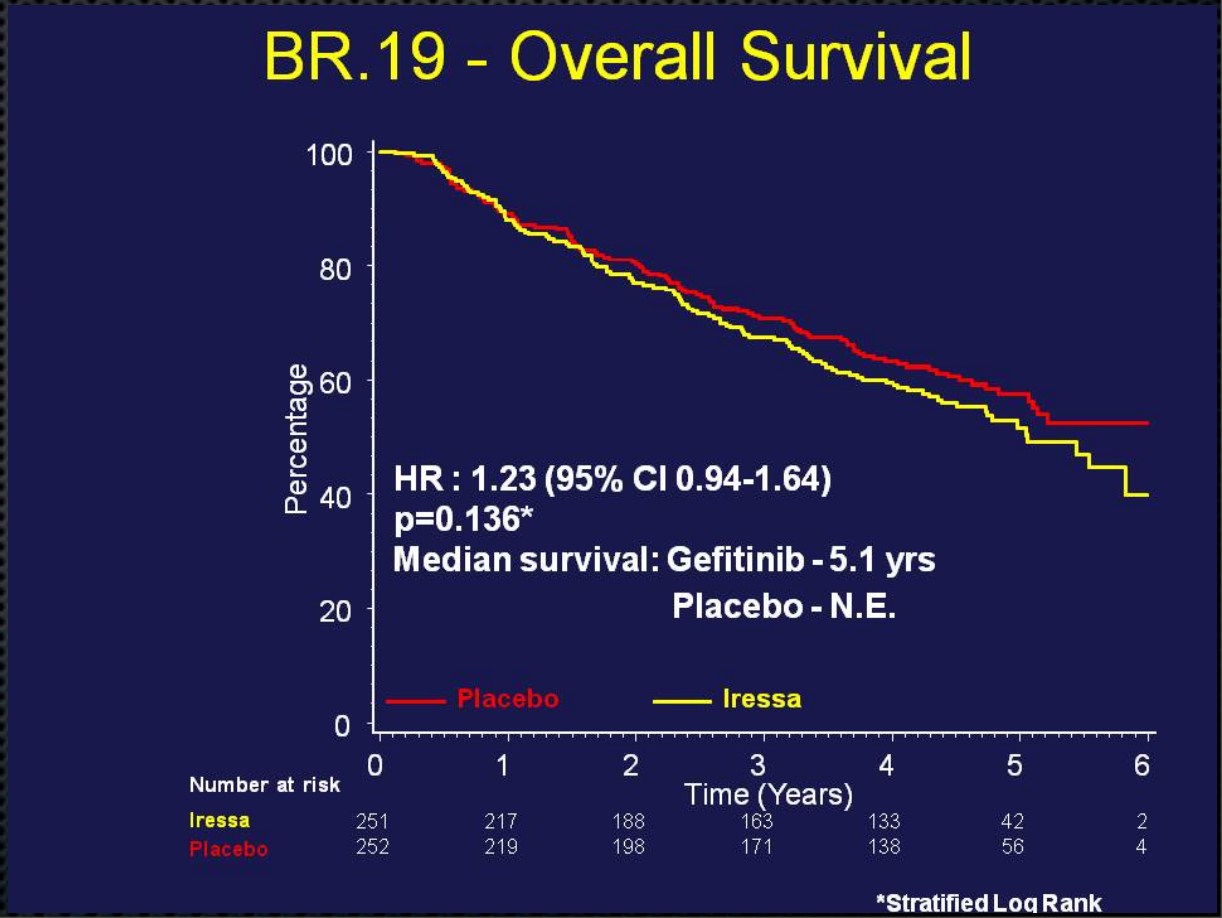
- Identificar opciones de tratamiento efectivas para pacientes en postoperatorio
- 5 estudios incluidos
  - 4584 pacientes
  - Quimioterapia basada en CDDP
  - Tumores completamente resecados
  - Seguimiento promedio 5.2 años


Overall Survival
Trial
No. of Events / No. of Patients
Hazard Ratio
HR (95% CI)
ALPI 569 1,088 0.95 (0.81 to 1.12)
ANITA 458 840 0.82 (0.68 to 0.98)
BLT 186 307 0.95 (0.71 to 1.27)
IALT 980 1,867 0.91 (0.81 to 1.04)
JBR10 197 482 0.71 (0.54 to 0.94)
Total 2,390 4,584 0.89 (0.82 to 0.96)
0.5
1.0
2.0
Chemotherapy Better | Control Better
Chemotherapy effect: Logrank statistic = 8.5, P = .005
Test for heterogeneity: $\chi^2_4 = 4.25$, $P = .37$, $I^2 = 6\%$


Overall Survival
Disease-Free Survival
Category
No. Events / No. Patients
Hazard Ratio
Probability of interaction/ trend* test
No. Events / No. Patients
Hazard Ratio
Probability of inte trend* tes
ASSOCIATED DRUGS .11 .07
Cisplatin + vinorelbine 935 1,888 1,077 1,888
Cisplatin + 1 other drug 742 1,373 824 1,373
Cisplatin + 2 other drugs 713 1,323 784 1,323
PLANNED DOSE OF CISPLATIN .26 .22
< 300 mg/m² 186 307 .13* 193 307 .09*
300 mg/m² 985 1,903 1,091 1,903
> 300 mg/m² 1,219 2,374 1,401 2,374
PLANNED RT .34 .35
No RT planned 1,464 3,145 1,670 3,145
RT planned 926 1,439 1,015 1,439
SEX .79 .33
Male 1,994 3,685 2,211 3,685
Female 395 895 473 895
AGE .83 .48
< 50 319 701 .63* 384 701 .16*
50-59 795 1,558 900 1,558
60-69 1,031 1,911 1,137 1,911
≥ 70 245 414 264 414
PERFORMANCE STATUS .01 .03
PS = 0 881 1,769 .009* 992 1,769 .01*
PS = 1 829 1,533 930 1,533
PS = 2 108 183 123 183
HISTOLOGY .44 .31
Squamous cell 1,124 2,231 1,250 2,231
Adenocarcinoma 971 1,817 1,115 1,817
Other 140 257 152 257
STAGE .06 .08
Stage IA 104 347 .04* 122 347 .04*
Stage IB 515 1,371 612 1,371
Stage II 893 1,616 999 1,616
Stage III 878 1,247 952 1,247
TYPE OF SURGERY .39 .43
Pneumonectomy 783 1,346 848 1,346
Other type of surgery 1,420 2,926 1,643 2,926
0.5
1.0
2.0
Chemotherapy Better
Control Better
0.5
1.0
2.0
Chemotherapy Better
Control Better

Terapia dirigida

- No hay datos que apoyen el uso de ITK en el escenario adyuvante
  - Estudio BR-19



Opciones de tratamiento

Estadio IIIB	Quimioradioterapia Radioterapia sola Quimioterapia paliativa	
Estadio IV	QT combinada Adicion de Bev o Cet Inhibidores de ITK ** Inhibidores de EML4/ALK QT de mantenimiento ** Paliacion	** ITK solo para pacientes con mutacion de EGFR ** En pacientes con respuesta global a regimen inicial
Enfermedad recurrente	Radioterapia QT o ITK ** Inhibidores de EML4/ALK Paliacion	** Uso de ITK independiente de mutacion - Si se conoce Mut -, preferir QT

Tratamiento enfermedad metastasica

- La intervencion es superior a la observacion
- Terapia con monoagente
  - Pacientes ancianos o debilitados
- Beneficio en supervivencia con regimenes combinados
  - Considerar la adicion de Bevacizumab o Cetuximab
  - Sin deterioro importante en la calidad de vida
  - Estudios iniciales para pacientes jovenes con buen estado funcional

VOLUME 26 · NUMBER 28 · OCTOBER 1 2008

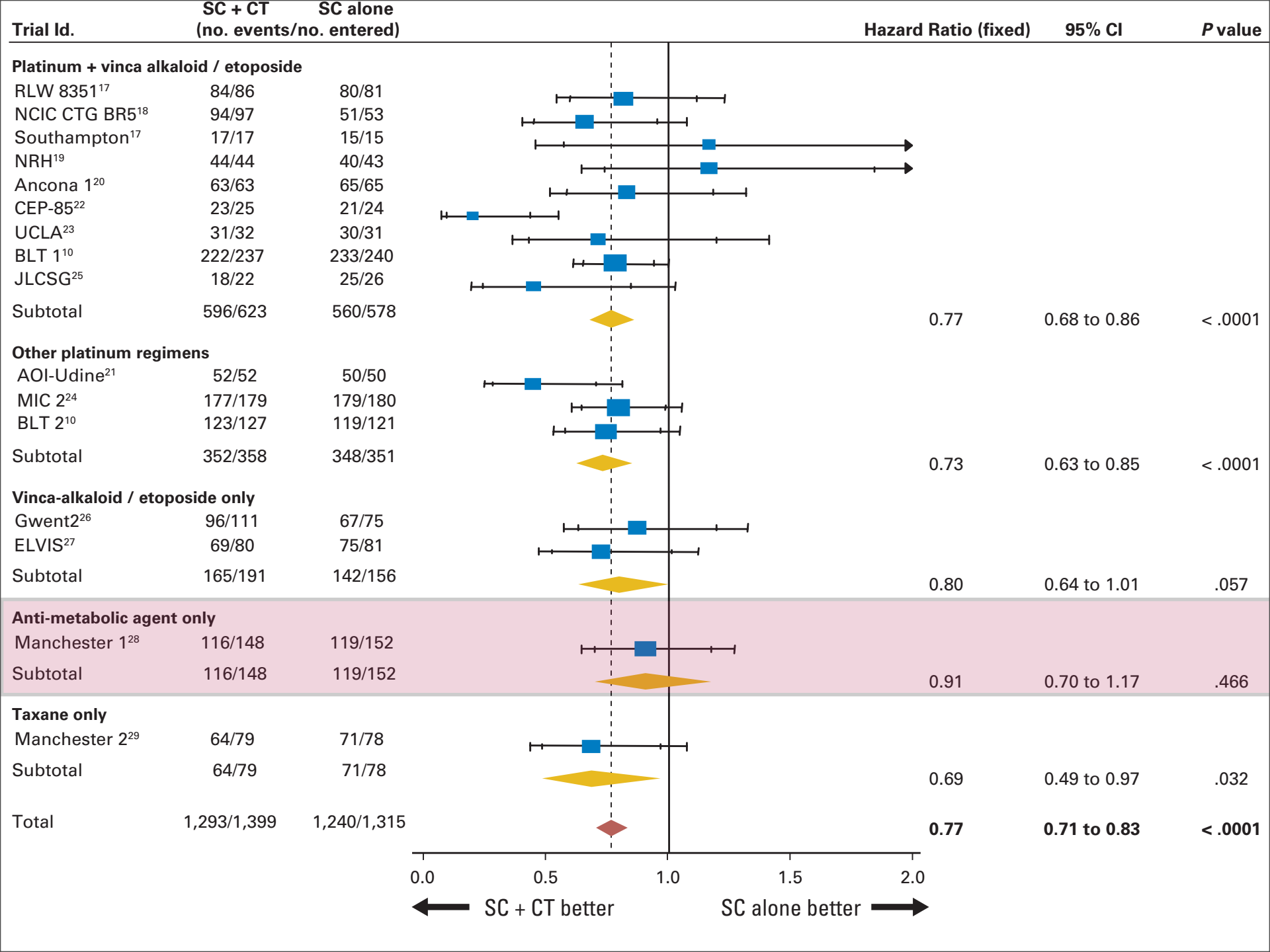
JOURNAL OF CLINICAL ONCOLOGY

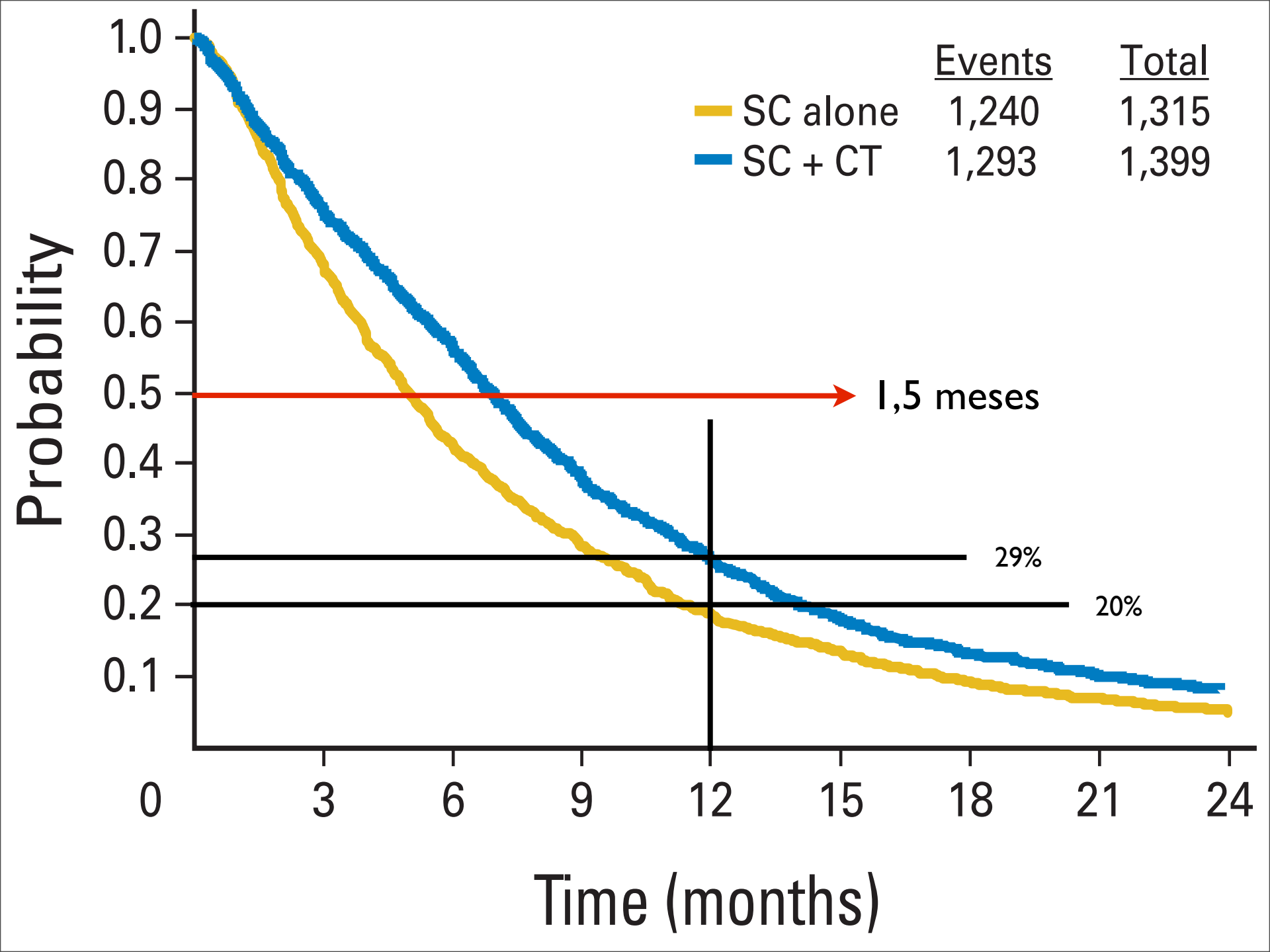
ORIGINAL REPORT

Chemotherapy in Addition to Supportive Care Improves Survival in Advanced Non–Small-Cell Lung Cancer: A Systematic Review and Meta-Analysis of Individual Patient Data From 16 Randomized Controlled Trials

NSCLC Meta-Analyses Collaborative Group

- 16 estudios clinicos
- 90% de pacientes en EC IIIB y IV
  - 2714 pacientes
    - 1399 pacientes en BSC
    - 1315 asignados a QT
- Sin efecto en resultados por tipo de medicamento utilizado


Trial Id.
SC + CT (no. events/no. entered)
SC alone (no. entered)
Hazard Ratio (fixed)
95% CI
P value
Platinum + vinca alkaloid / etoposide
RLW 8351[17] 84/86 80/81
NCIC CTG BR5[18] 94/97 51/53
Southampton[17] 17/17 15/15
NRH[19] 44/44 40/43
Ancona 1[20] 63/63 65/65
CEP-85[22] 23/25 21/24
UCLA[23] 31/32 30/31
BLT 1[10] 222/237 233/240
JLCSG[25] 18/22 25/26
Subtotal 596/623 560/578 0.77 0.68 to 0.86 < .0001
Other platinum regimens
AOI-Udine[21] 52/52 50/50
MIC 2[24] 177/179 179/180
BLT 2[10] 123/127 119/121
Subtotal 352/358 348/351 0.73 0.63 to 0.85 < .0001
Vinca-alkaloid / etoposide only
Gwent2[26] 96/111 67/75
ELVIS[27] 69/80 75/81
Subtotal 165/191 142/156 0.80 0.64 to 1.01 .057
Anti-metabolic agent only
Manchester 1[28] 116/148 119/152
Subtotal 116/148 119/152 0.91 0.70 to 1.17 .466
Taxane only
Manchester 2[29] 64/79 71/78
Subtotal 64/79 71/78 0.69 0.49 to 0.97 .032
Total 1,293/1,399 1,240/1,315 0.77 0.71 to 0.83 < .0001
0.0
0.5
1.0
1.5
2.0
SC + CT better
SC alone better


Events
Total
SC alone
1,240
1,315
SC + CT
1,293
1,399
1,5 meses
29%
20%
Probability
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
3
6
9
12
15
18
21
24
Time (months)

Combinaciones

- Cisplatino/Paclitaxel
- Cisplatino/Gemcitabina
- Cisplatino/Docetaxel
- Cisplatino/Pemetrexed
- Carboplatino/Paclitaxel
- Carboplatino/Pemetrexed

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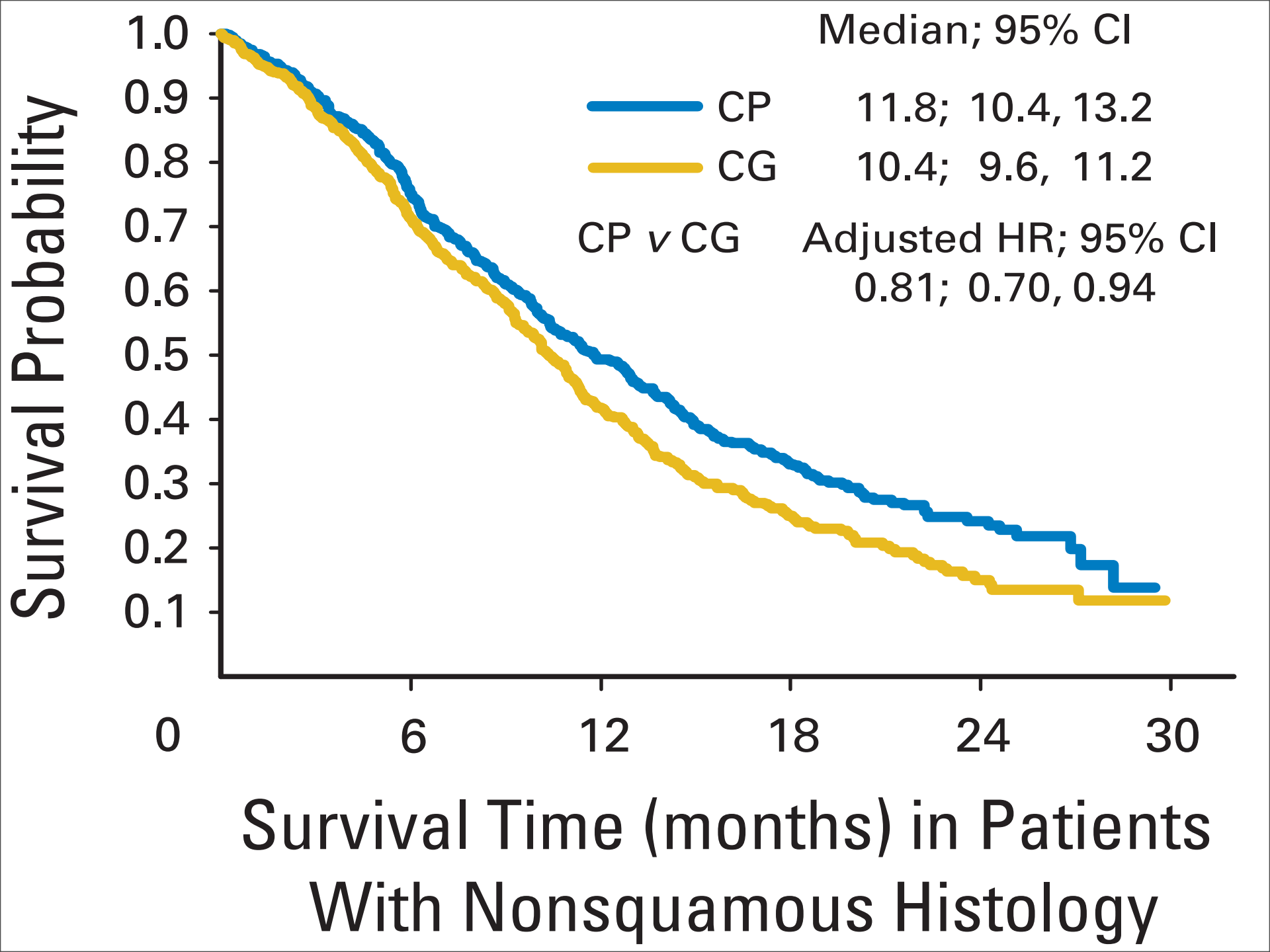
ORIGINAL REPORT

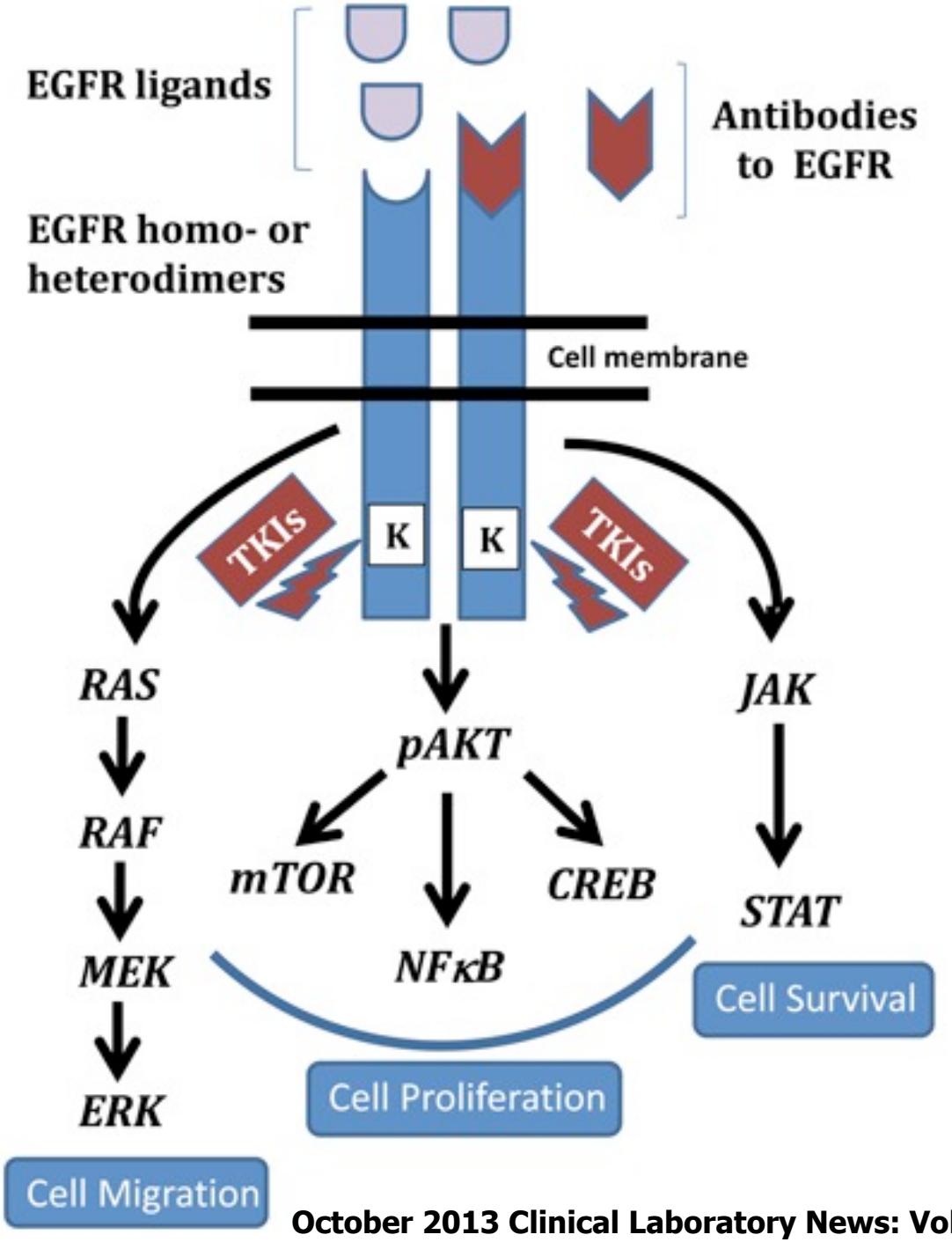
Phase III Study Comparing Cisplatin Plus Gemcitabine With Cisplatin Plus Pemetrexed in Chemotherapy-Naive Patients With Advanced-Stage Non–Small-Cell Lung Cancer

- Estudio de no inferioridad
- Impacto en supervivencia global
- 1725 pacientes - Estadio IIIb ó IV
- Cisplatino (75) + Gemcitabina (1,5) n=863
- Cisplatino (75) + Pemetrexed (500) n= 862
  - Perfil de toxicidad


Survival Probability
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
6
12
18
24
30
Median; 95% CI
CP
11.8; 10.4, 13.2
CG
10.4; 9.6, 11.2
CP v CG
Adjusted HR; 95% CI
0.81; 0.70, 0.94
Survival Time (months) in Patients With Nonsquamous Histology

Terapia dirigida

- Mutaciones de EGFR (10% USA - 35% Asia)
  - Delecion exon 19
    - 48% NSCLC Mut +
  - Mutacion exon 21: L858R
    - 43% NSCLC Mut + - L861Q (2%)
  - Insercion Exon 20 (t790M)
    - 4-9.2% de EGFR +
    - 50% formas resistentes



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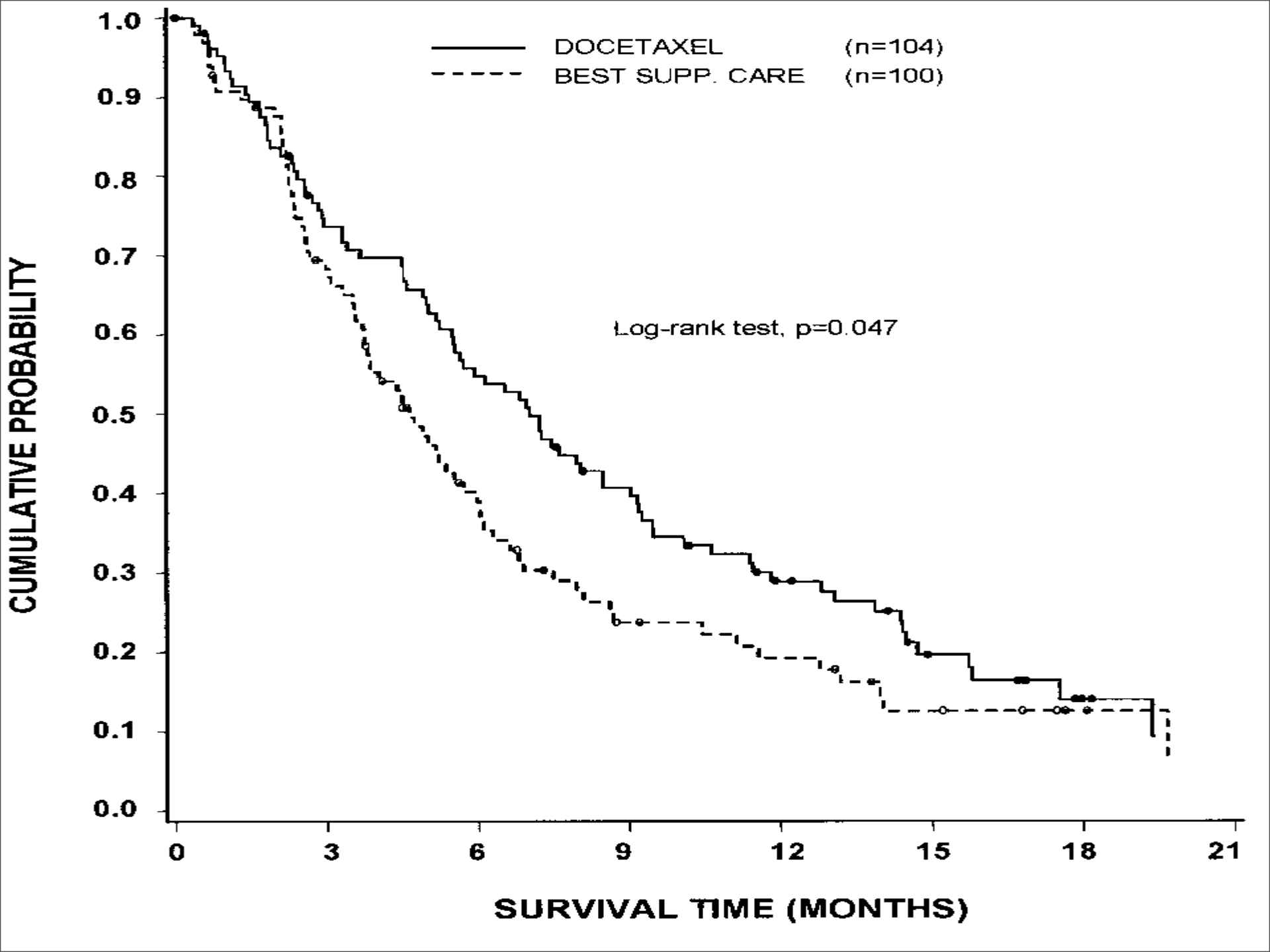
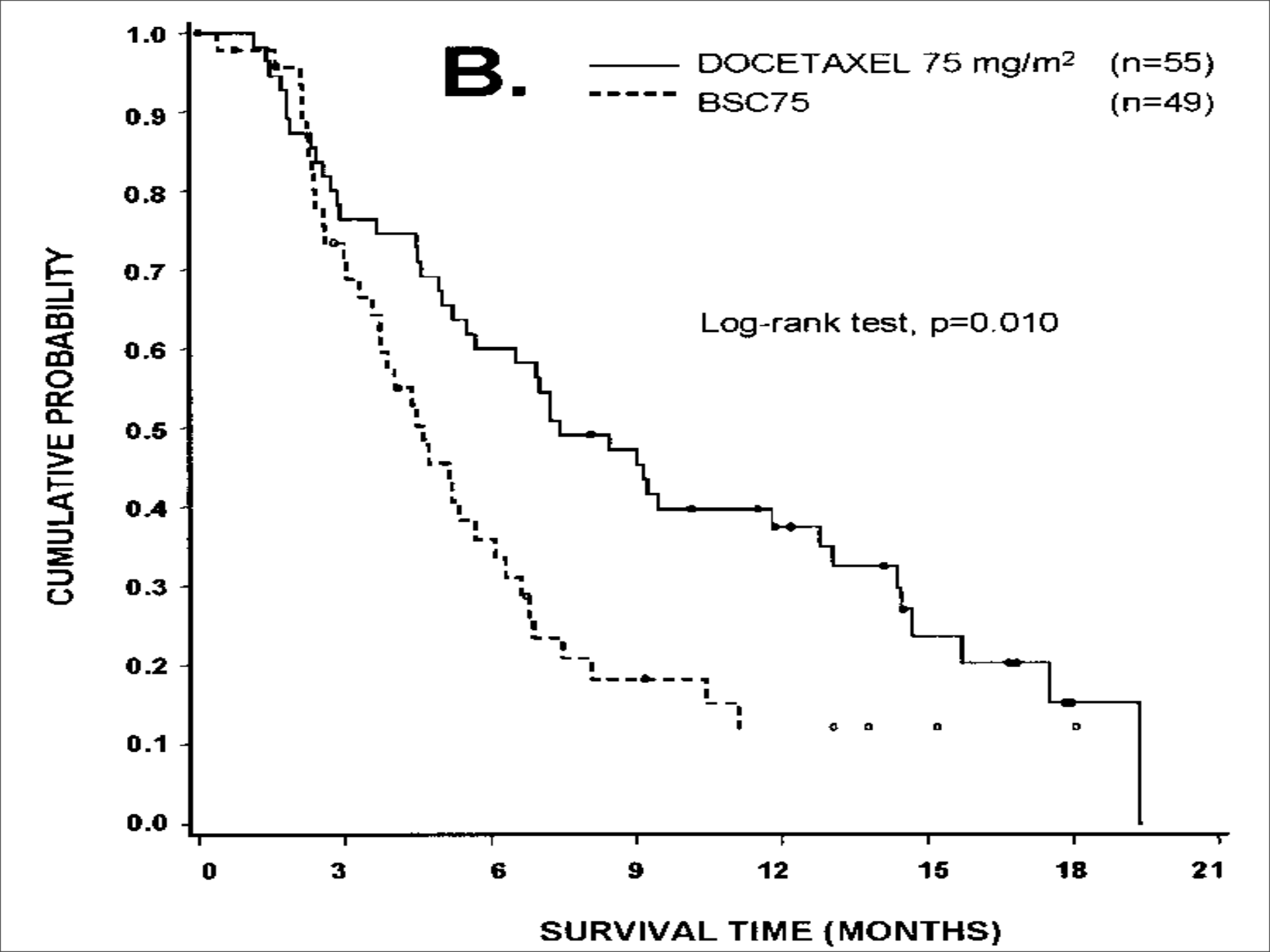
Evidencia

- Erlotinib
  - EURTAC (9,7 vs 5,2 meses)
  - OPTIMAL (13,7 vs 4,6 meses)
- Gefitinib
  - IPASS (9,5 vs 6,3 meses)
  - WJTOG 3405 (9,6 vs 6,6 meses)
  - NEJ002 (10,8 vs 5,4 meses)

Terapia de segunda linea

- Consideracion de tratamientos previos
- Estado organico y funcional
- Extension de la enfermedad
- Consideracion de terapia sistemica VS Radiacion
  - Manejo sistemico Vs Paliacion local


DOCETAXEL (n=104)
BEST SUPP. CARE (n=100)
Log-rank test, p=0.047
CUMULATIVE PROBABILITY
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
3
6
9
12
15
18
21
SURVIVAL TIME (MONTHS)


B.
DOCETAXEL 75 mg/m2 (n=55)
BSC75 (n=49)
Log-rank test, p=0.010
CUMULATIVE PROBABILITY
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
3
6
9
12
15
18
21
SURVIVAL TIME (MONTHS)

Otras opciones

- Pemetrexed
- Erlotinib
- Gefitinib
- Afatinib
- Inhibidores de MetMAB