IASLC Staging and Prognostic Factors Committee Total Cases Submitted to the 8th Edition Database By Data Source

Region	Number	%
Europe	46,560	49
Asia	41,705	44
North America	4,660	5
Australia	1,593	1.7
South America	190	0.3
TOTAL	94,708	100





IASLC Staging and Prognostic Factors Committee Number of Cases Analyzed in the 8th Edition Database By Data Source, Diagnosed From 1999 Through 2010

Type of database	Retrospective	Prospective (EDC)	Total
Consortium	41,548	2,089	43,637
Registry	26,122		26,122
Surgical series	5,373	592	5,965
Institutional series		1,185	1,185
Institutional registries	208		208
Unknown		39	39
TOTAL	73,251	3,905	77,156





IASLC Staging and Prognostic Factors Committee Recommendations Regarding 8th Edition T-Descriptors

Descriptor	7th edition	Proposal for 8th edition
= 1 cm</td <td>T1a</td> <td>T1a</td>	T1a	T1a
> 1 - 2 cm	T1a	T1b
> 2 - 3 cm	T1b	T1c
> 3 - 4 cm	T2a	T2a
> 4 - 5 cm	T2a	T2b
> 5 - 7 cm	T2b	Т3
> 7 cm	Т3	T4
Bronchus < 2 cm	Т3	T2
Complete atelectasis/ pneumonitis	Т3	T2
Diaphragm invasion	Т3	T4
Mediastinal pleura	Т3	-





IASLC Staging and Prognostic Factors Committee Recommendations Regarding 8th Edition T-Descriptors Implications for Clinical Practice

Every cm counts; careful follow-up

Accurate tumour size measurement, important

Rules to measure tumour size

Rules to measure part-solid non-mucinous adinocarcinoma

Elastic stains for visceral pleura invasion

Prognosis refinement

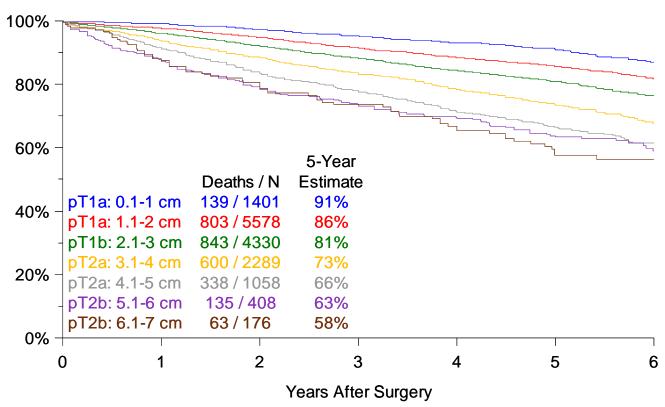
Better stratification for clinical trials





Core IASLC Data in Support of Recommendations for T Survival of pathologically staged T1-T2 N0 R0 tumors according to size only, at 1-cm intervals.

by Size Only pT1-2 N0 M0 R0 NSCLC



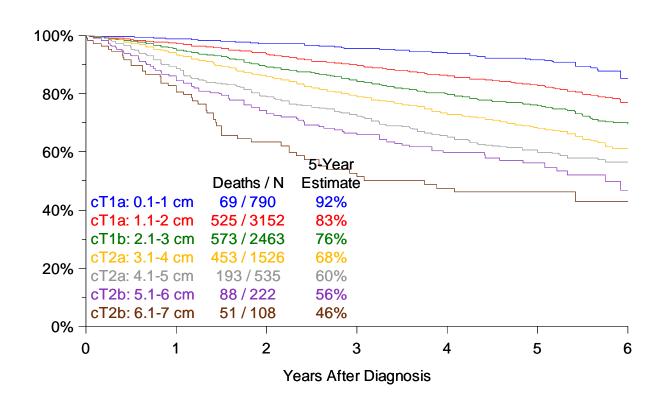


From: Rami-Porta R, Bolejack V, Crowley J, et al. Proposals for the Revisions of the T Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol* 2015;10:990-1003.



Core IASLC Data in Support of Recommendations for T Survival of clinically staged T1-T2 N0 tumors according to size only, at 1-cm intervals.

by Size Only cT1-2 N0 M0 NSCLC





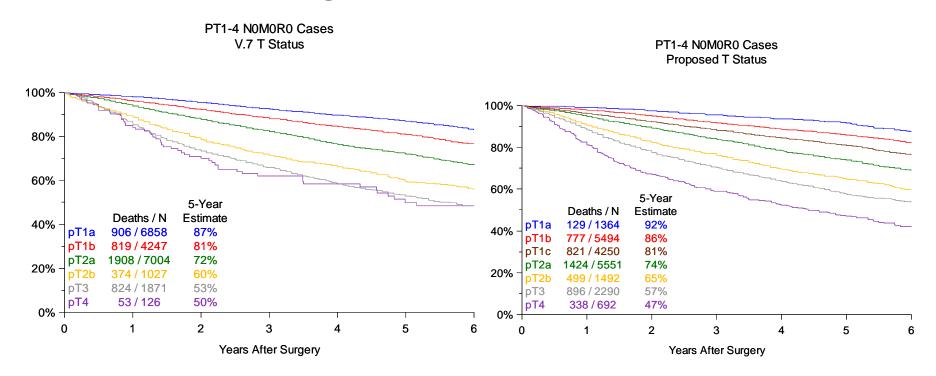
From: Rami-Porta R, Bolejack V, Crowley J, et al. Proposals for the Revisions of the T Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol* 2015;10:990-1003.



Core IASLC Data in Support of Recommendations for T Survival according to 7th edition and proposed T categories for pathologically staged T1-T4 N0 M0 R0 tumors.

7th Edition T Categories

Proposed T Categories





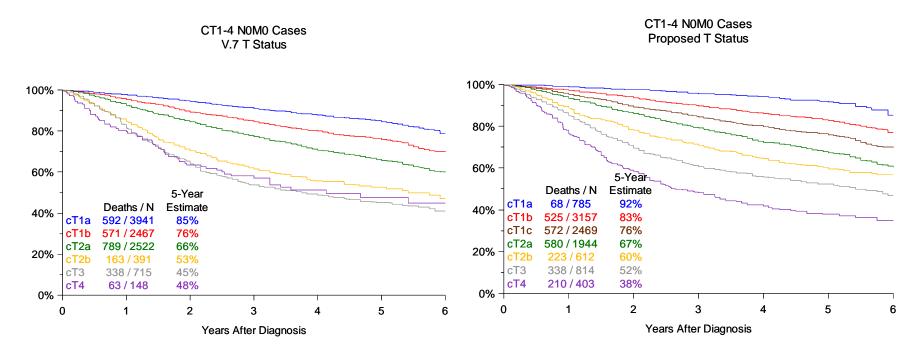
From: Rami-Porta R, Bolejack V, Crowley J, et al. Proposals for the Revisions of the T Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol* 2015;10:990-1003.



Core IASLC Data in Support of Recommendations for T Survival according to 7th edition and proposed T categories for clinically staged T1-T4 N0 M0 tumors.

7th Edition T Categories

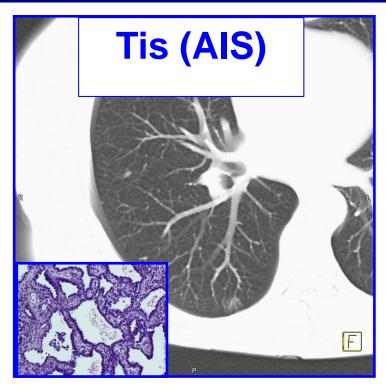
Proposed T Categories



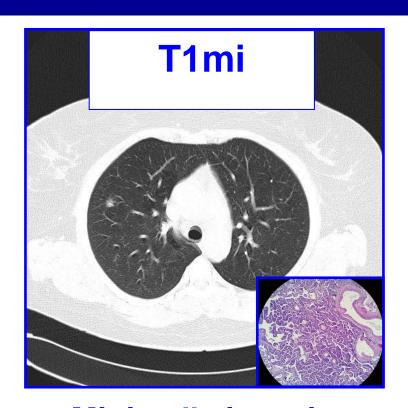




IASLC Staging and Prognostic Factors Committee T categories for the new types of adenocarcinomas



Adenocarcinoma in situ



Minimally invasive adenocarcinoma



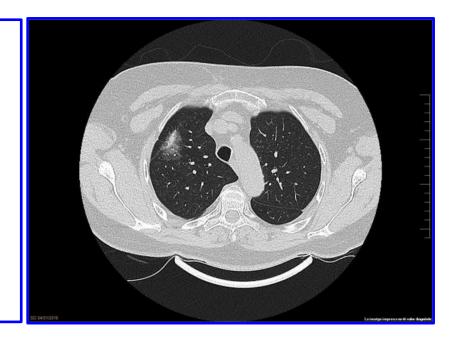
From: Travis WD, Asamura H, Bankier A, et al. The IASLC Lung Cancer Staging Project: Proposals for Coding T Categories for Subsolid Nodules and Assessment of Tumor Size in Part-Solid Tumors in the Forthcoming Eighth Edition of the TNM Classification of Lung Cancer. *J Thorac Oncol* 2016; 11:1204-1223.



IASLC Staging and Prognostic Factors Committee Recommendations Regarding Size Measurement in Part-Solid Non-Mucinous Adenocarcinoma

Clinical size: size of solid component

Pathologic size:
size of
invasive component



From: Travis WD, Asamura H, Bankier A, et al. The IASLC Lung Cancer Staging Project: Proposals for Coding T Categories for Subsolid Nodules and Assessment of Tumor Size in Part-Solid Tumors in the Forthcoming Eighth Edition of the TNM Classification of Lung Cancer. *J Thorac Oncol* 2016; 11:1204-1223.





IASLC Staging and Prognostic Factors Committee Recommendations Regarding Size Measurement After Induction Therapy

Pathologic size:

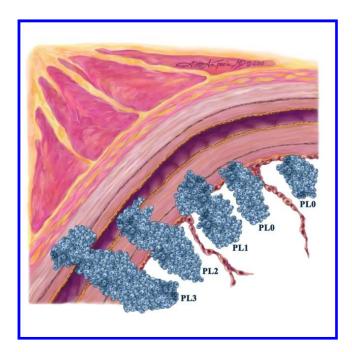
Multiply the percentage of viable cells by the total size of the tumor

From: Travis WD, Asamura H, Bankier A, et al. The IASLC Lung Cancer Staging Project: Proposals for Coding T Categories for Subsolid Nodules and Assessment of Tumor Size in Part-Solid Tumors in the Forthcoming Eighth Edition of the TNM Classification of Lung Cancer. *J Thorac Oncol* 2016; 11:1204-1223





IASLC Staging and Prognostic Factors Committee Recommendations Regarding Subclassification of Visceral Pleural Involvement



PL0: ----

PL1 y PL2: T2

PL3: T3

In case of doubt about the visceral pleura involvement, the use of elastic stains is recommended

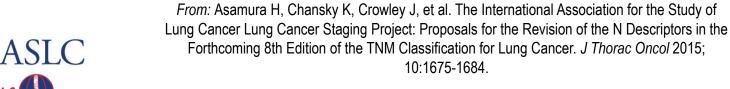
Copyright © 2008 Aletta Ann Frazier, MD





IASLC Staging and Prognostic Factors Committee Recommendations Regarding 8th Edition N-Descriptors

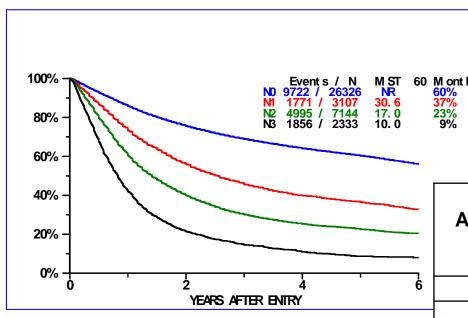
- **Present N descriptors remain the same**
- Quantification of nodal disease is recommended for further study:
 - pN1a: involvement of single pN1 nodal station
 - pN1b: involvement of multiple pN1 nodal stations
 - pN2a1: involvement of single pN2 nodal station without pN1 (skip pN2)
 - pN2a2: involvement of single pN2 nodal station with pN1
 - pN2b: involvement of multiple pN2 nodal stations
 - pN3: as it is







Core IASLC Data in Support of Recommendations for N Survival curves for cN0, cN1, cN2, and cN3, T-any M0 tumors



N3 vs N2 vs N1 vs N0 Comparisons Adjusted for Histology (adeno vs others), Sex, Age 60+, and Region (Cox PH regression)

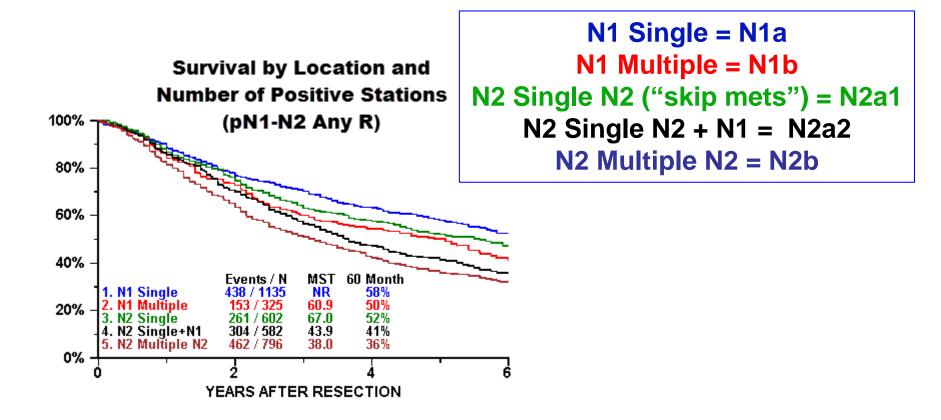
comparison	HR	Р
N1 vs N0	1.68	<0.0001
N2 vs N1	1.42	<0.0001
N3 vs N2	1.38	<0.0001



From: Asamura H, Chansky K, Crowley J, et al. The International Association for the Study of Lung Cancer Lung Cancer Staging Project: Proposals for the Revision of the N Descriptors in the Forthcoming 8th Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol* 2015; 10:1675-1684.



Core IASLC Data in Support of Recommendations for N Regarding Quantification of Nodal Disease for Further Study







IASLC Staging and Prognostic Factors Committee Recommendations Regarding 8th Edition N-Descriptors Implications for Clinical Practice

- The amount of nodal disease has prognostic impact
- Important to quantify nodal disease both at clinical and pathologic staging
- Upfront resection for single station cN2?
- Prognosis refinement
- Better stratification





IASLC Staging and Prognostic Factors Committee Recommendations Regarding 8th Edition M-Descriptors

Descriptor	7th edition	Proposal for 8th edition
Intrathoraic metastasis (pleural/pericardial effusion, contralateral/bilateral tumor nodules, pleural/pericardial nodules)	M1a	M1a
Single extrathoracic metastatic lesion	M1b	M1b
Multiple extrathoracic lesions	M1b	M1c





IASLC Staging and Prognostic Factors Committee Recommendations Regarding 8th Edition M-Descriptors Implications for Clinical Practice

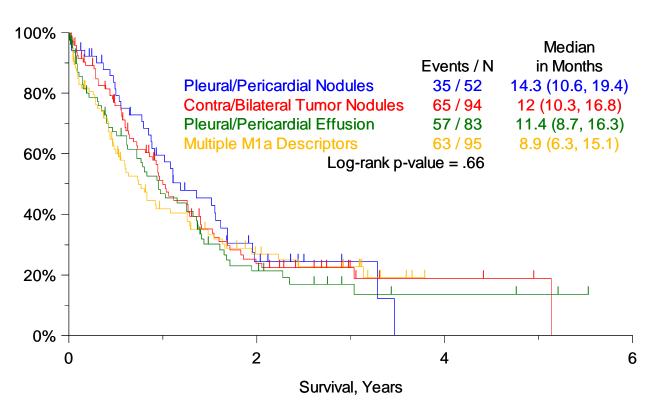
- Number of metastatic lesions appears to be more important than location
- M1b: baseline definition of oligometastases and oligoprogression
- Prognosis refinement
- Better stratification





Core IASLC Data in Support of Recommendations for M Prognostic Impact of M1a Descriptors

Survival By M1a Descriptor M1a Cases from EDC Only

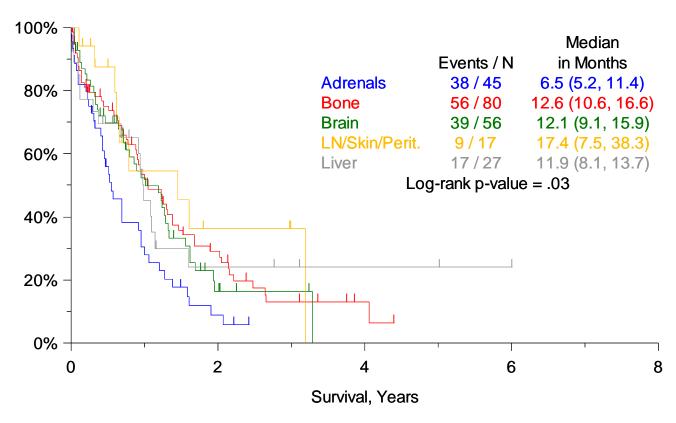






Core IASLC Data in Support of Recommendations for M Single Lesion at Single Site by Organ

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

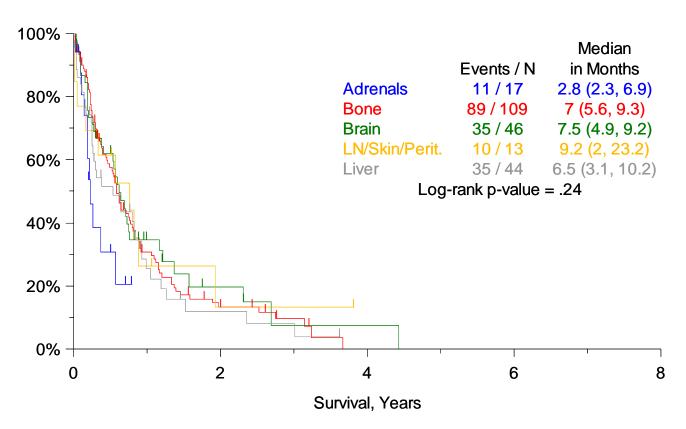






Core IASLC Data in Support of Recommendations for M Multiple Lesions at Single Site by Organ

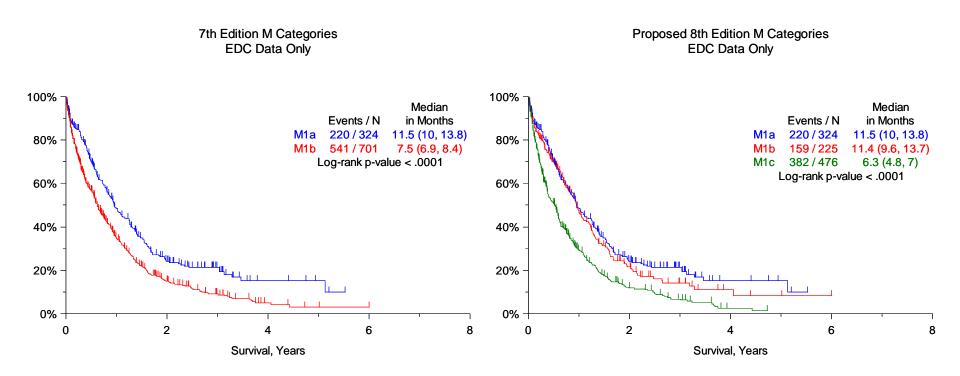
7th Edition M1b - Multiple Lesions at Single Site
By Organ
EDC Data Only







Core IASLC Data in Support of Recommendations for M The 7th Edition and Proposed 8th Edition M Categories







IASLC Staging and Prognostic Factors Committee Recommendations Regarding 8th Edition TNM for Lung Cancers With Multiple Lesions

- Multiple primary tumors:
 One TNM for each tumor
- Separate tumor nodules:
 T3, T4, M1a
- Multiple adenocarcinomas with GGO/lepidic features: Highest T (#/m) N M
- Pneumonic type adenocarcinoma:
 T3, T4, M1a





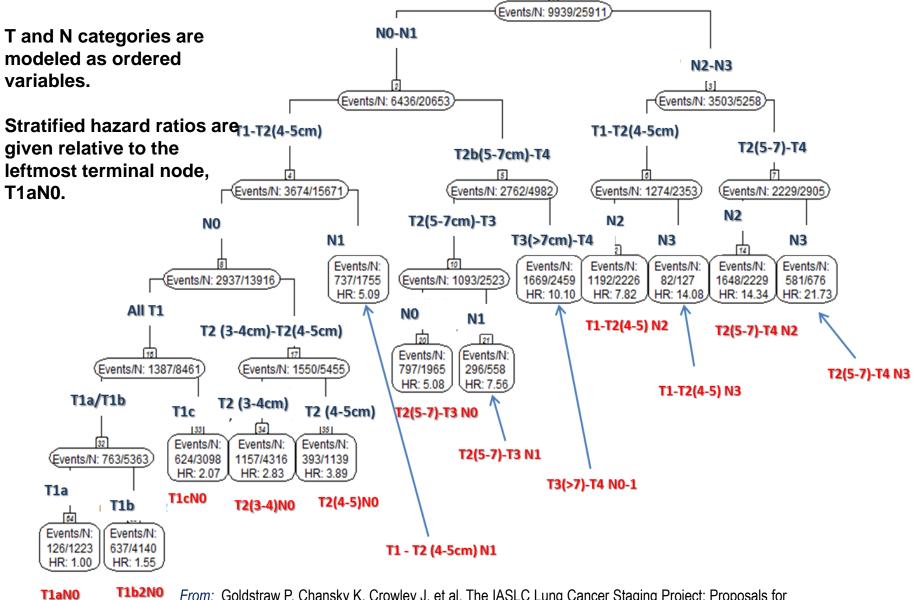
IASLC Staging and Prognostic Factors Committee Recommendations Regarding 8th Edition Stage Groupings

	N0	N1	N2	N3	M1a any N	M1b any N	M1c any N
T1a	IA1	IIB	IIIA	IIIB	IVA	IVA	IVB
T1b	IA2	IIB	IIIA	IIIB	IVA	IVA	IVB
T1c	IA3	IIB	IIIA	IIIB	IVA	IVA	IVB
T2a	IB	IIB	IIIA	IIIB	IVA	IVA	IVB
T2b	IIA	IIB	IIIA	IIIB	IVA	IVA	IVB
T3	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
T4	IIIA	IIIA	IIIB	IIIC	IVA	IVA	IVB





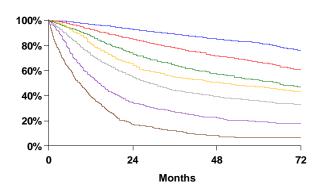
Recursive partitioning and amalgamation-generated survival tree based on best stage for 25,911 M0 training set cases.



From: Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol* 2016;11:39-51.

Core IASLC Data in Support of Recommendations for Stage Groupings Overall Survival by Clinical Stage

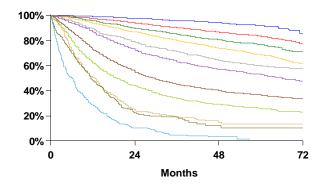
7th Edition Stage Groupings



			24	60
7 th 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%

- MST, median survival time.
- Survival is weighted by type of database submission: registry versus other.

Proposed Stage Groupings



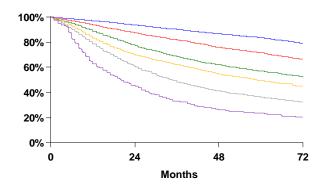
		24	60
Events / N	MST	Month	Month
68 / 781	NR	97%	92%
505 / 3105	NR	94%	83%
546 / 2417	NR	90%	77%
560 / 1928	NR	87%	68%
215 / 585	NR	79%	60%
605 / 1453	66.0	72%	53%
2052 / 3200	29.3	55%	36%
1551 / 2140	19.0	44%	26%
831 / 986	12.6	24%	13%
336 / 484	11.5	23%	10%
328 / 398	6.0	10%	0%
	68 / 781 505 / 3105 546 / 2417 560 / 1928 215 / 585 605 / 1453 2052 / 3200 1551 / 2140 831 / 986 336 / 484	68 / 781 NR 505 / 3105 NR 546 / 2417 NR 560 / 1928 NR 215 / 585 NR 605 / 1453 66.0 2052 / 3200 29.3 1551 / 2140 19.0 831 / 986 12.6 336 / 484 11.5	Events / N MST Month 68 / 781 NR 97% 505 / 3105 NR 94% 546 / 2417 NR 90% 560 / 1928 NR 87% 215 / 585 NR 79% 605 / 1453 66.0 72% 2052 / 3200 29.3 55% 1551 / 2140 19.0 44% 831 / 986 12.6 24% 336 / 484 11.5 23%





Core IASLC Data in Support of Recommendations for Stage Groupings Overall Survival by Pathologic Stage

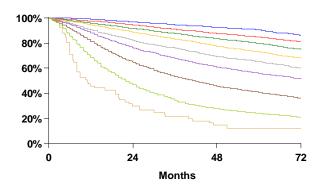
7th Edition Stage Groupings



			24	60
7 th Ed.	Events / N	MST	Month	Month
IA	1837 / 11423	NR	94%	83%
IB	2168 / 7711	NR	87%	71%
IIA	1514 / 3702	NR	77%	57%
IIB	1325 / 2776	58.9	70%	49%
IIIA	3467 / 5818	35.0	61%	36%
IIIB	364 / 506	20.0	45%	23%

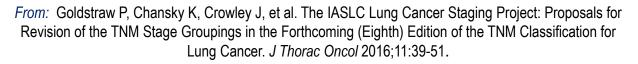
- MST, median survival time.
- Survival is weighted by type of database submission: registry versus other.

Proposed Stage Groupings



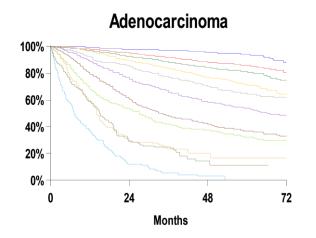
			24	60
Proposed	Events / N	MST	Month	Month
IA1	139 / 1389	NR	97%	90%
IA2	823 / 5633	NR	94%	85%
IA3	875 / 4401	NR	92%	80%
IB	1618 / 6095	NR	89%	73%
IIA	556 / 1638	NR	82%	65%
IIB	2175 / 5226	NR	76%	56%
IIIA	3219 / 5756	41.9	65%	41%
IIIB	1215 / 1729	22.0	47%	24%
IIIC	55 / 69	11.0	30%	12%

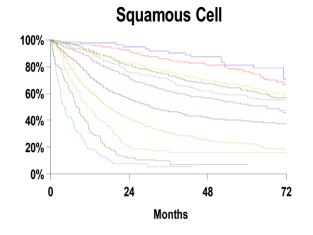






Core IASLC Data in Support of Recommendations for Stage Groupings Internal Validation: Clinical TNM Stage Within Histologic Types





		Other Hi	stologies	
100% ¬	A Commence			
80% -	A STANCE OF THE		The same of the sa	
60% -	J. Contraction of the state of	The same of the sa		
40% -	Jana Jana	Art or		
20% -				
0%				
0		24	48	72
		Мо	nths	

			24	60
cgrp6	Events / N	MST	Month	Month
IA1	47 / 678	NR	98%	94%
IA2	355 / 2521	NR	95%	86%
IA3	343 / 1818	NR	92%	81%
IB	331 / 1239	NR	89%	71%
IIA	98 / 299	NR	85%	64%
IIB	273 / 670	67.0	76%	53%
IIIA	731 / 1203	34.0	61%	37%
IIIB	422 / 655	27.0	53%	32%
IIIC	233 / 292	14.0	30%	17%
IVA	158 / 254	15.1	29%	11%
IVB	178 / 220	7.1	12%	0%

			24	60
cgrp6	Events / N	MST	Month	Month
IA1	14 / 78	NR	95%	82%
IA2	90 / 397	NR	92%	76%
IA3	145 / 422	NR	81%	62%
IB	166 / 533	NR	84%	65%
IIA	81 / 212	NR	76%	58%
IIB	251 / 592	66.0	72%	52%
IIIA	717 / 1173	30.8	55%	40%
IIIB	650 / 868	17.4	41%	22%
IIIC	291 / 340	11.0	20%	16%
IVA	127 / 153	8.3	12%	7%
IVB	80 / 96	4.0	8%	

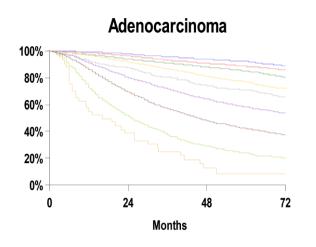
			24	60
cgrp6	Events / N	MST	Month	Month
IA1	7 / 25	NR	91%	62%
IA2	60 / 187	NR	86%	66%
IA3	58 / 177	NR	81%	66%
IB	63 / 156	68.0	75%	56%
IIA	36 / 74	47.0	61%	48%
IIB	81 / 191	67.0	62%	53%
IIIA	604 / 824	17.5	43%	29%
IIIB	479 / 617	13.8	35%	23%
IIIC	307 / 354	8.9	25%	6%
IVA	51 / 77	12.6	24%	20%
IVB	70 / 82	3.7	8%	

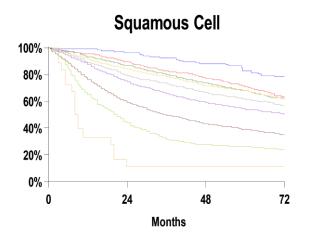


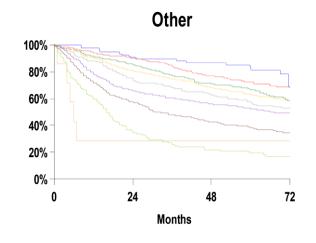
From: Detterbeck F, Chansky K, Groome P, et al. The IASLC Lung Cancer Staging Project: Methodology and Validation Used in the Development of Proposals for Revision of the Stage Classification of Non-Small Cell Lung Cancer in the Forthcoming (Eighth) Edition of the TNM Classification of Lung Cancer. J Thorac Oncol 2016; 11: 1433-1446.



Core IASLC Data in Support of Recommendations for Stage Groupings Internal Validation: Pathologic TNM Stage Within Histologic Types







			24	60
pgrp6	Events / N	MST	Month	Month
IA1	89 / 1098	NR	97%	92%
IA2	490 / 4358	NR	96%	88%
IA3	474 / 3119	NR	94%	85%
IB	911 / 3942	NR	92%	77%
IIA	218 / 745	NR	87%	71%
IIB	985 / 2497	NR	80%	58%
IIIA	1719 / 3173	45.0	69%	42%
IIIB	649 / 924	25.0	51%	24%
IIIC	34 / 44	16.0	39%	8%

			24	60
pgrp6	Events / N	MST	Month	Month
IA1	34 / 192	NR	96%	83%
IA2	241 / 887	NR	89%	71%
IA3	287 / 933	NR	86%	68%
IB	537 / 1659	NR	84%	68%
IIA	256 / 697	NR	79%	61%
IIB	929 / 2155	71.9	75%	54%
IIIA	1113 / 1918	35.0	59%	39%
IIIB	424 / 612	21.0	44%	26%
IIIC	16 / 18	9.0	11%	11%

			24	60
pgrp6	Events / N	MST	Month	Month
IA1	16 / 99	NR	90%	81%
IA2	92 / 388	NR	91%	72%
IA3	114 / 349	NR	85%	67%
IB	170 / 494	NR	80%	63%
IIA	82 / 196	NR	75%	57%
IIB	261 / 574	67.0	66%	52%
IIIA	387 / 665	32.0	57%	38%
IIIB	142 / 193	16.0	34%	19%
IIIC	5/7	6.0	29%	29%

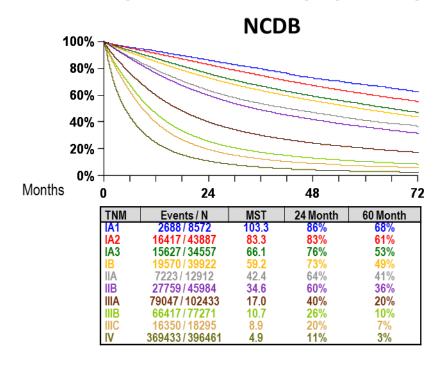


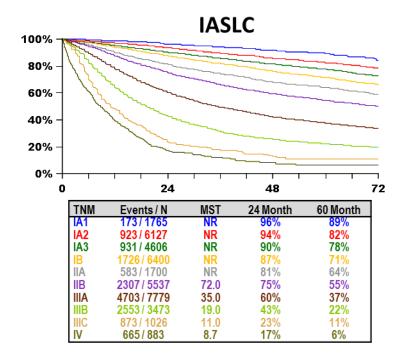
From: Detterbeck F, Chansky K, Groome P, et al. The IASLC Lung Cancer Staging Project: Methodology and Validation Used in the Development of Proposals for Revision of the Stage Classification of Non-Small Cell Lung Cancer in the Forthcoming (Eighth) Edition of the TNM Classification of Lung Cancer. J Thorac Oncol 2016; 11: 1433-1446.



Core IASLC Data in Support of Recommendations for Stage Groupings External Validation

The objective of external validation was to apply the proposed revised staging criteria to an external database. The external database chosen was the National Cancer Database (NCDB) of the American College of Surgeons Committee on Cancer. Survival by best stage is shown for the NCDB and IASLC databases, according to proposed stage groupings.



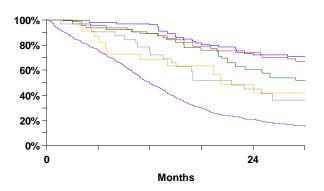






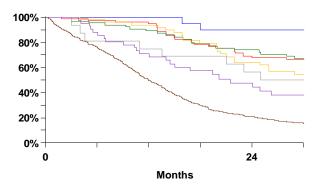
Core IASLC Data in Support of Recommendations for Small Cell Lung Cancer Overall Survival by Clinical T Category

7th Edition T Categories



	Events /		12	24
cT 7 th Ed.	N	MST	Month	Month
T1a	39 / 104	NR	96%	72 %
T1b	25 / 68	NR	89%	74%
T2a	34 / 68	33.0	89%	61%
T2b	12 / 24	20.2	68%	49%
T3	21 / 35	21.5	75%	45%
T4	800 / 966	12.0	49%	21%

Proposed T Categories



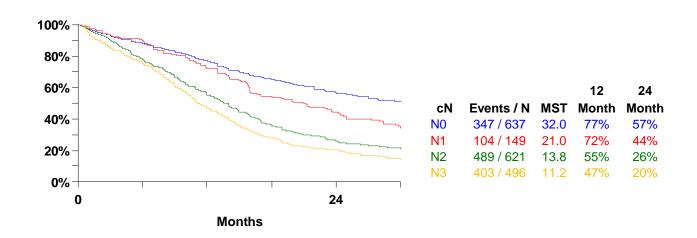
			12	24
cT Proposed	Events / N	MST	Month	Month
T1a	5 / 20	NR	100%	90%
T1b	34 / 84	NR	95%	68%
T1c	25 / 68	NR	89%	74%
T2a	26 / 53	33.0	94%	64%
T2b	8 / 17	NR	75%	56%
T3	26 / 44	21.5	71%	48%
T4	807 / 979	12.0	50%	21%





Core IASLC Data in Support of Recommendations for Small Cell Lung Cancer Overall Survival by Clinical N Category

8th Edition N Categories

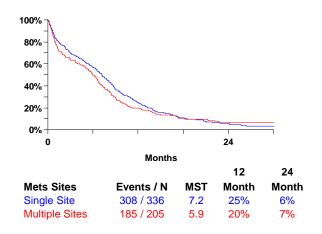




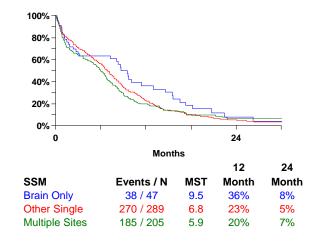


Core IASLC Data in Support of Recommendations for Small Cell Lung Cancer Overall Survival by Single Versus Multiple Metastatic Sites

Single vs Multiple Metastatic Sites



Brain Only vs Single vs Multiple Metastatic Sites



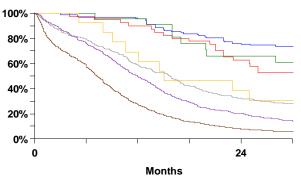




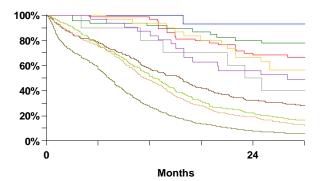
Core IASLC Data in Support of Recommendations for Small Cell Lung Cancer Overall Survival by Clinical Stage

7th Edition Stage Groupings





cTNM			12	24
7 th Ed.	Events / N	MST	Month	Month
IA	45 / 129	NR	95%	75 %
IB	22 / 42	32.4	90%	63%
IIA	10 / 28	41.0	96%	66%
IIB	10 / 14	15.0	69%	38%
IIIA	203 / 270	15.7	59%	32%
IIIB	641 / 782	12.0	49%	20%
IV	2620 / 2926	7.3	27%	8%



CINIVI			12	24
Proposed	Events / N	MST	Month	Month
IA1	3 / 14	NR	100%	93%
IA2	27 / 67	NR	97%	68%
IA3	15 / 48	NR	91%	80%
IB	16 / 32	33.0	93%	67%
IIA	6 / 10	24.1	80%	50%
IIB	17 / 38	28.0	87%	56%
IIIA	191 / 254	15.6	58%	32%
IIIB	326 / 402	12.6	52%	22%
IIIC	330 / 400	11.4	48%	19%
IV	2620 / 2926	7.3	27%	8%

MIATA



