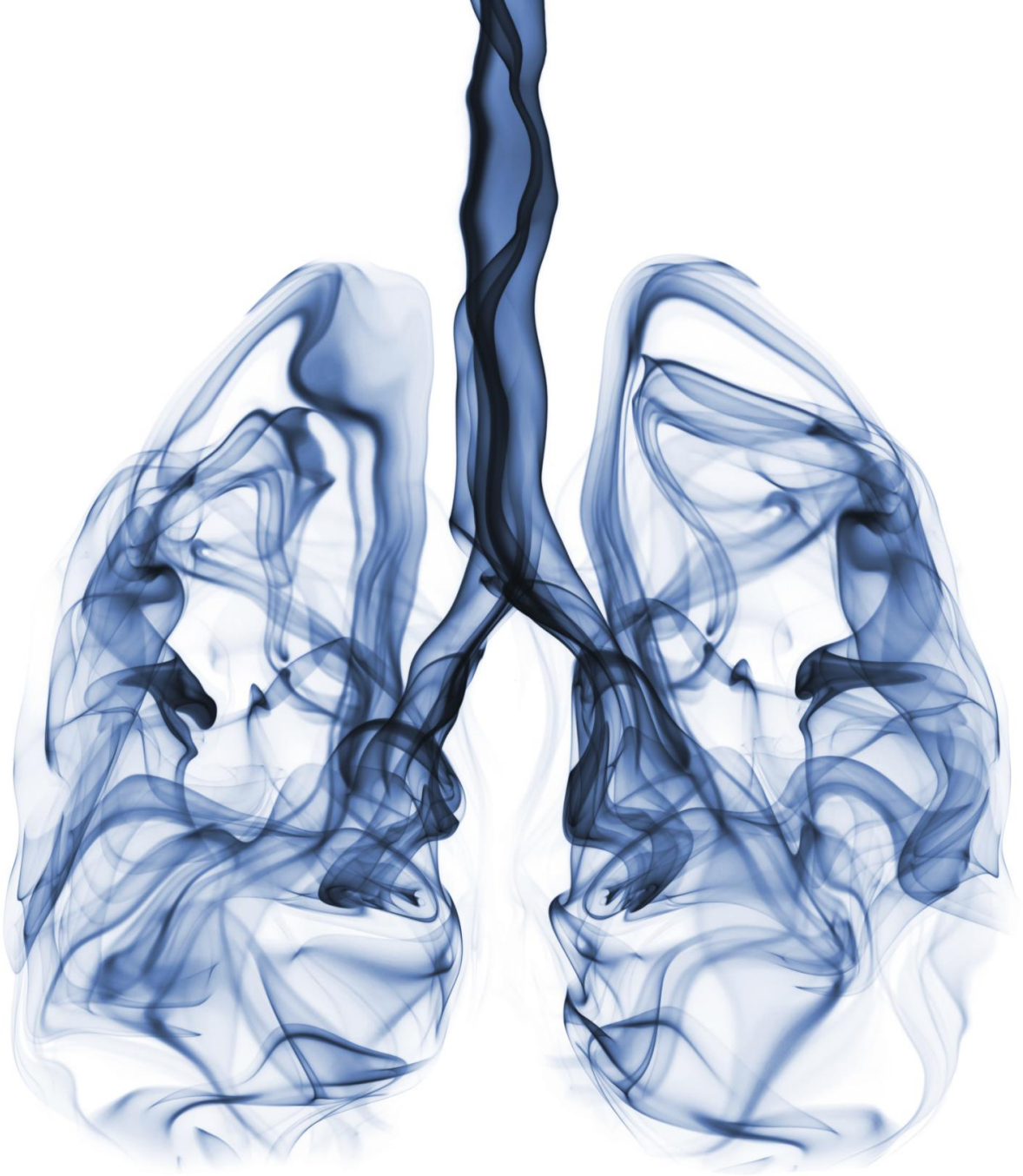
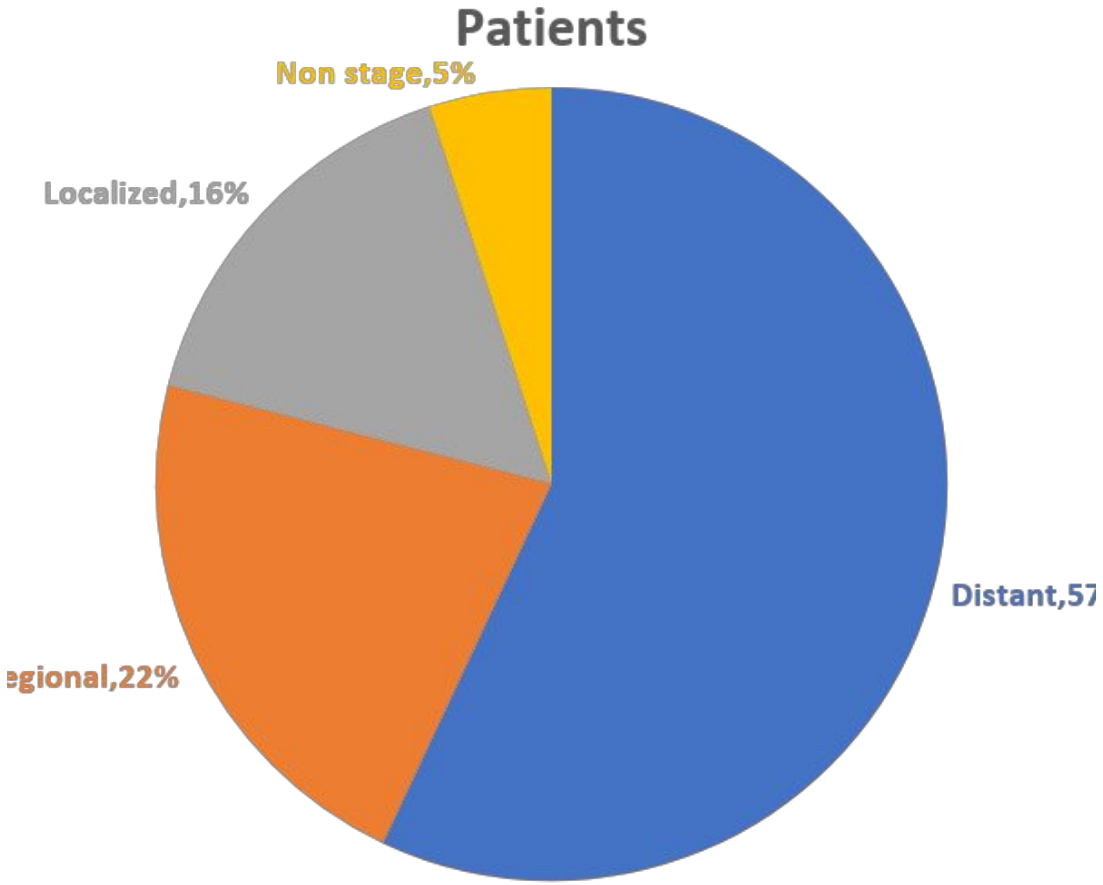


Современные методы лечения НМРЛ или невероятный скачок от анатомии до генетики

Трушин Александр Юрьевич

НМРЛ — одно из наиболее распространённых онкологических заболеваний, для которого характерен высокий уровень смертности



Estimated New Cases

			Males	Females			
Prostate	161,360	19%			Breast	252,710	30%
Lung & bronchus	116,990	14%			Lung & bronchus	105,510	12%
Colon & rectum	71,420	9%			Colon & rectum	64,010	8%
Urinary bladder	60,490	7%			Uterine corpus	61,380	7%
Melanoma of the skin	52,170	6%			Thyroid	42,470	5%
Kidney & renal pelvis	40,610	5%			Melanoma of the skin	34,940	4%
Non-Hodgkin lymphoma	40,080	5%			Non-Hodgkin lymphoma	32,160	4%
Leukemia	36,290	4%			Leukemia	25,840	3%
Oral cavity & pharynx	35,720	4%			Pancreas	25,700	3%
Liver & intrahepatic bile duct	29,200	3%			Kidney & renal pelvis	23,380	3%
All Sites	**836,150**	**100%**			**All Sites**	**852,630**	**100%**

Estimated Deaths

			Males	Females			
Lung & bronchus	84,590	27%			Lung & bronchus	71,280	25%
Colon & rectum	27,150	9%			Breast	40,610	14%
Prostate	26,730	8%			Colon & rectum	23,110	8%
Pancreas	22,300	7%			Pancreas	20,790	7%
Liver & intrahepatic bile duct	19,610	6%			Ovary	14,080	5%
Leukemia	14,300	4%			Uterine corpus	10,920	4%
Esophagus	12,720	4%			Leukemia	10,200	4%
Urinary bladder	12,240	4%			Liver & intrahepatic bile duct	9,310	3%
Non-Hodgkin lymphoma	11,450	4%			Non-Hodgkin lymphoma	8,690	3%
Brain & other nervous system	9,620	3%			Brain & other nervous system	7,080	3%
All Sites	**318,420**	**100%**			**All Sites**	**282,500**	**100%**

FIGURE 1. Ten Leading Cancer Types for the Estimated New Cancer Cases and Deaths by Sex, United States, 2017.
Estimates are rounded to the nearest 10 and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

Cancer Statistics 2017;

Rebecca L. Siegel, MPH; Kimberly D. Miller, MPH; Ahmedin Jemal, DVM, PhD

CA Cancer J Clin 2017;67:7–30. doi: 10.3322/caac.21387

«Клинические исследования в НМРЛ - это олимпийский марафон…»

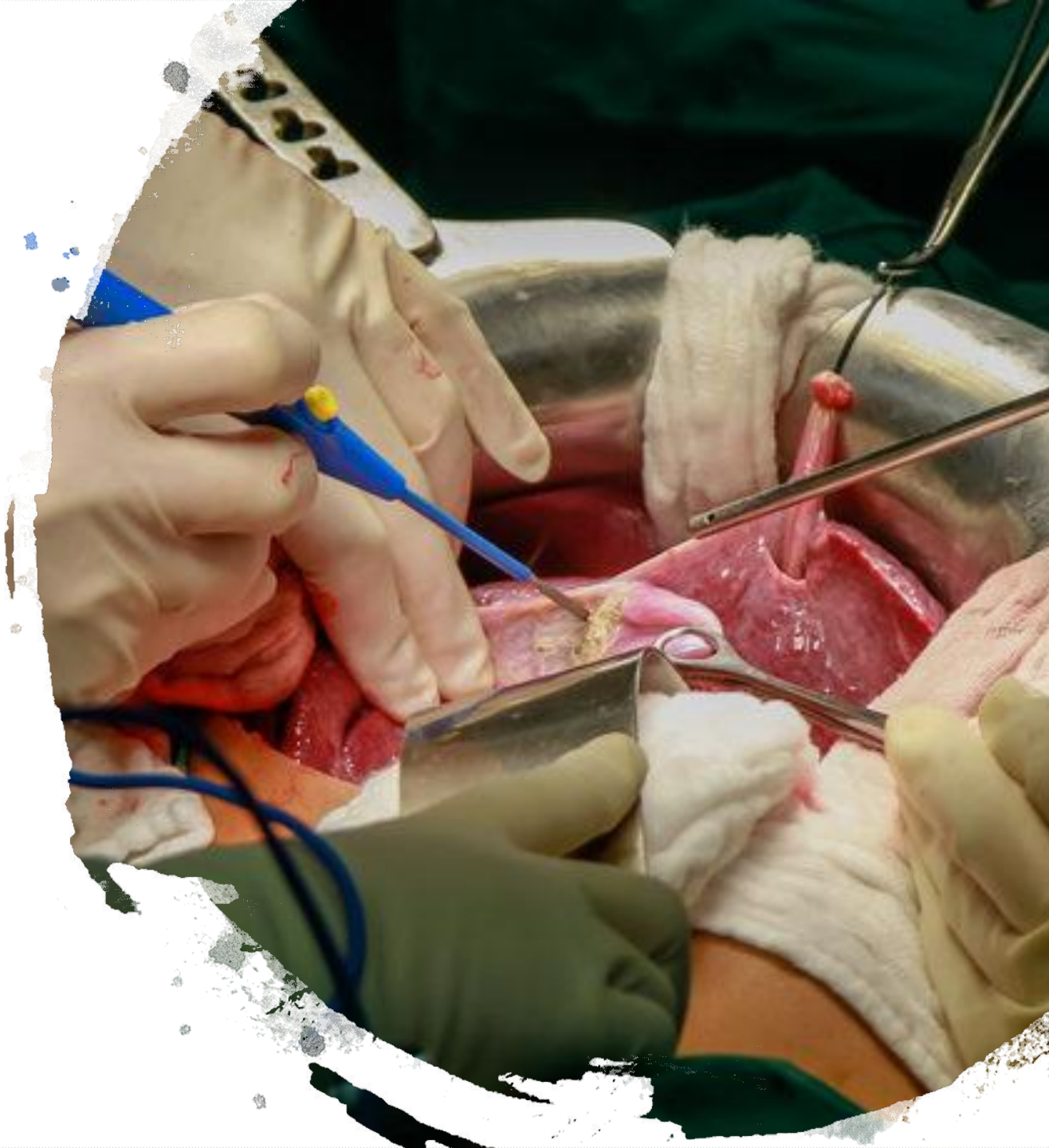
Tom Stinchcombe, MD

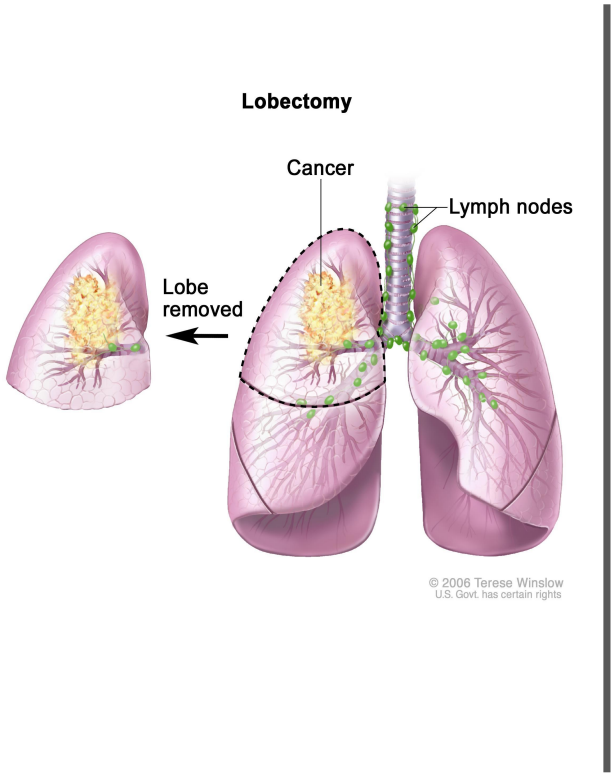
special for

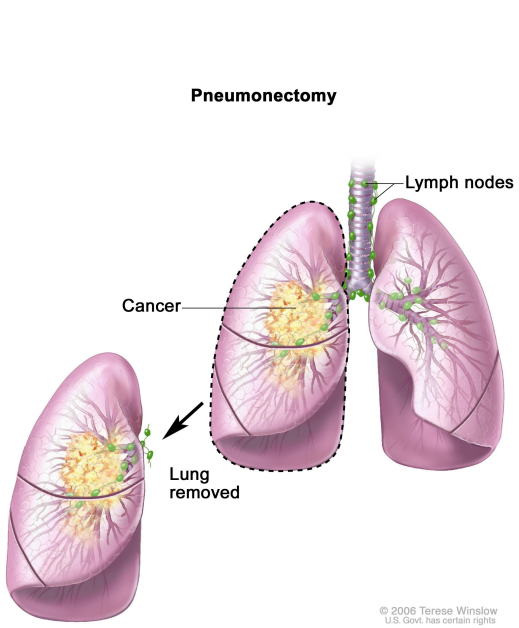
2018 ASCO ANNUAL MEETING

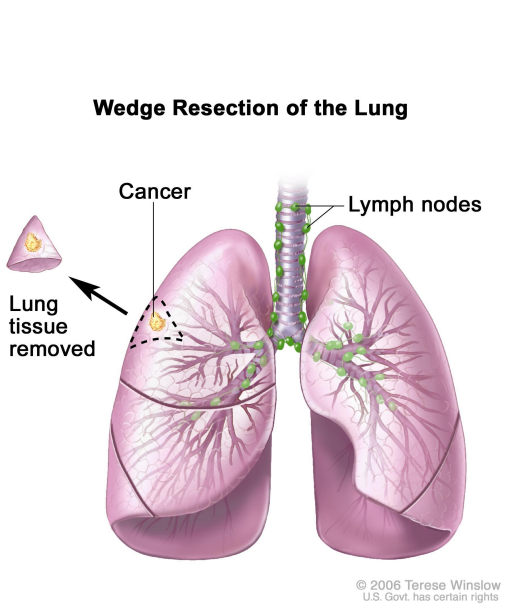
DELIVERING DISCOVERIES: EXPANDING THE REACH OF PRECISION MEDICINE

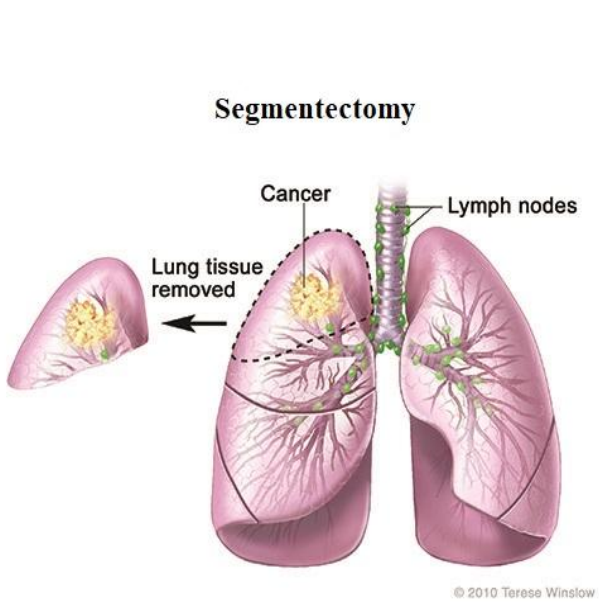
Хирургия











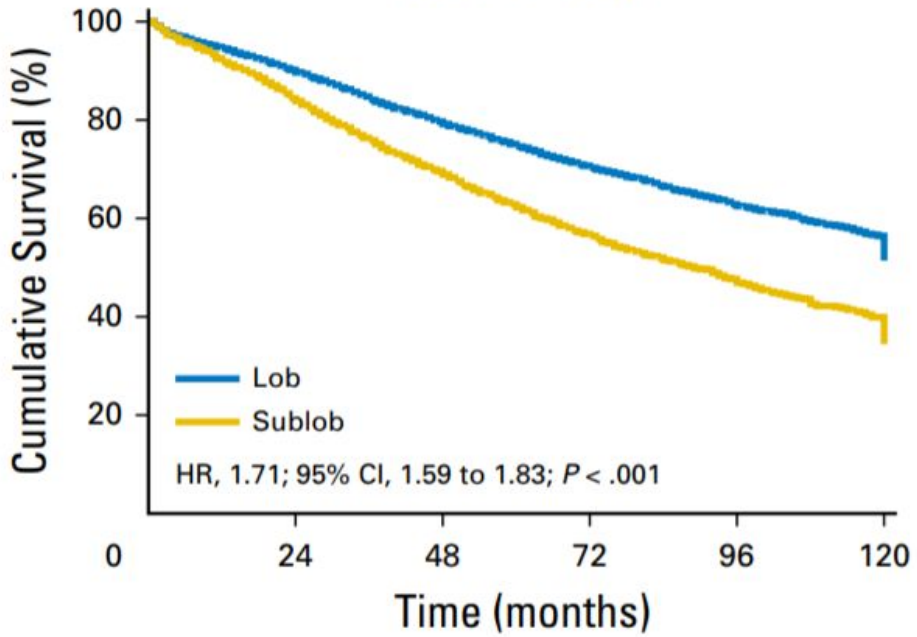
Объем хирургического вмешательства

JOURNAL OF CLINICAL ONCOLOGY

Choice of Surgical Procedure for Patients With NSCLC ≤ 1 cm or > 1 to 2 cm Among Lobectomy, Segmentectomy, and Wedge Resection: A Population-Based Study

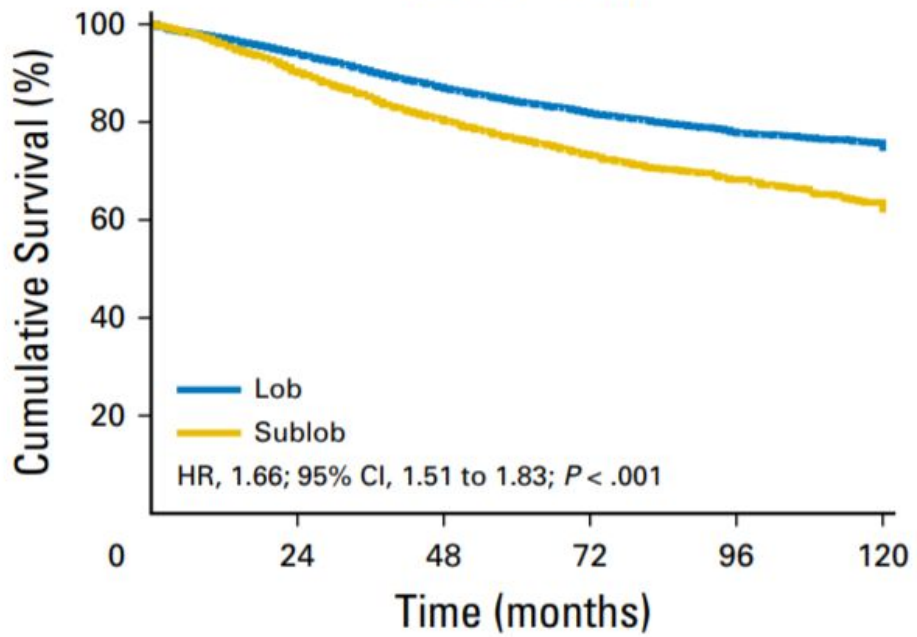
Chenyang Dai, Jianfei Shen, Yijiu Ren, Shengyi Zhong, Hui Zheng, Jiaxi He, Dong Xie, Ke Fei, Wenhua Liang, Gening Jiang, Ping Yang, Rene Horsleben Petersen, Calvin S.H. Ng, Chia-Chuan Liu, Gaetano Rocco, Alessandro Brunelli, Yaxing Shen, Chang Chen, and Jianxing He

A



No. at risk						
Lob	11,520	8,360	5,625	3,546	2,083	1,122
Sublob	4,240	2,752	1,635	895	479	212

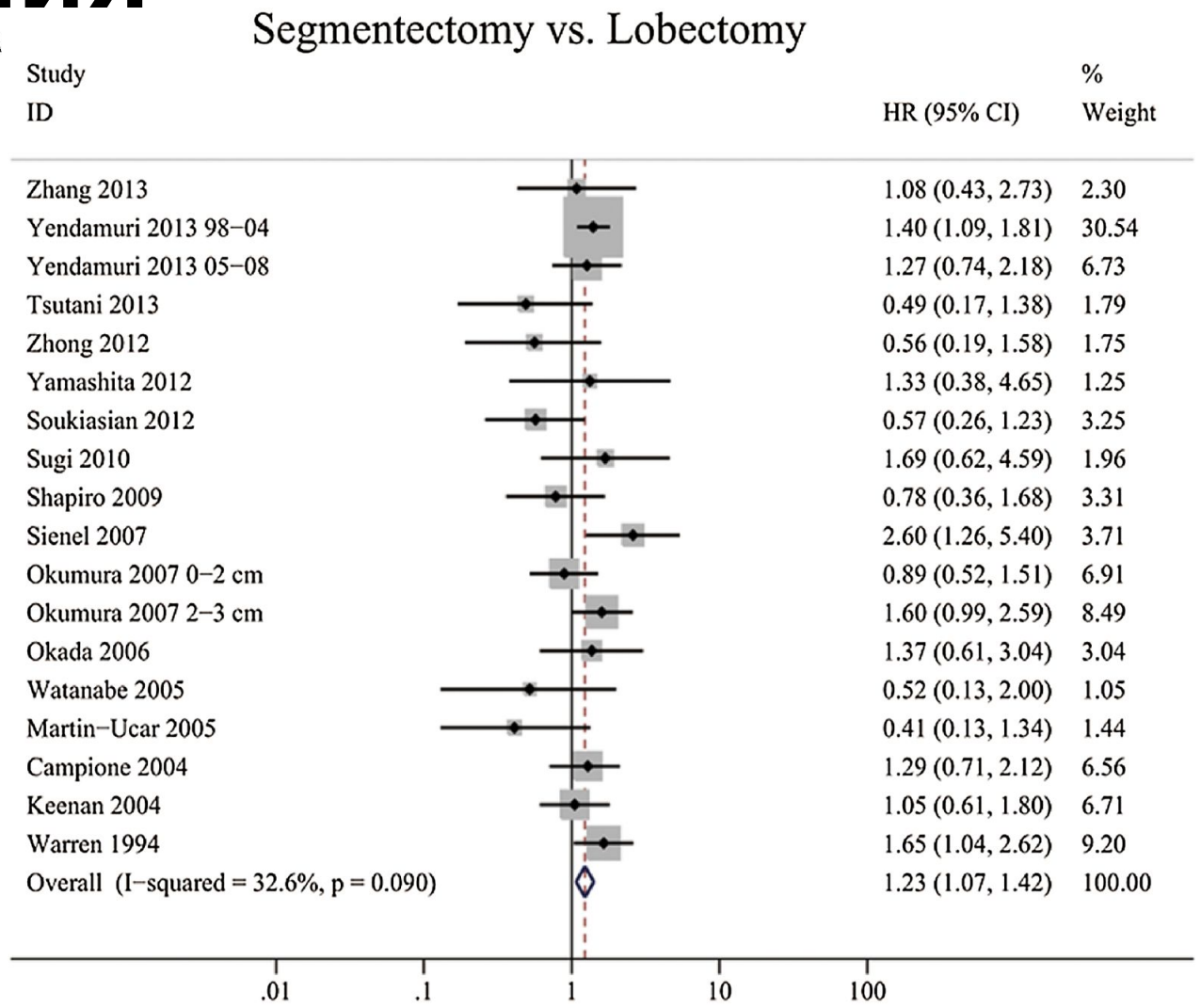
B



No. at risk						
Lob	11,520	8,360	5,625	3,546	2,083	1,122
Sublob	4,240	2,752	1,635	895	479	212

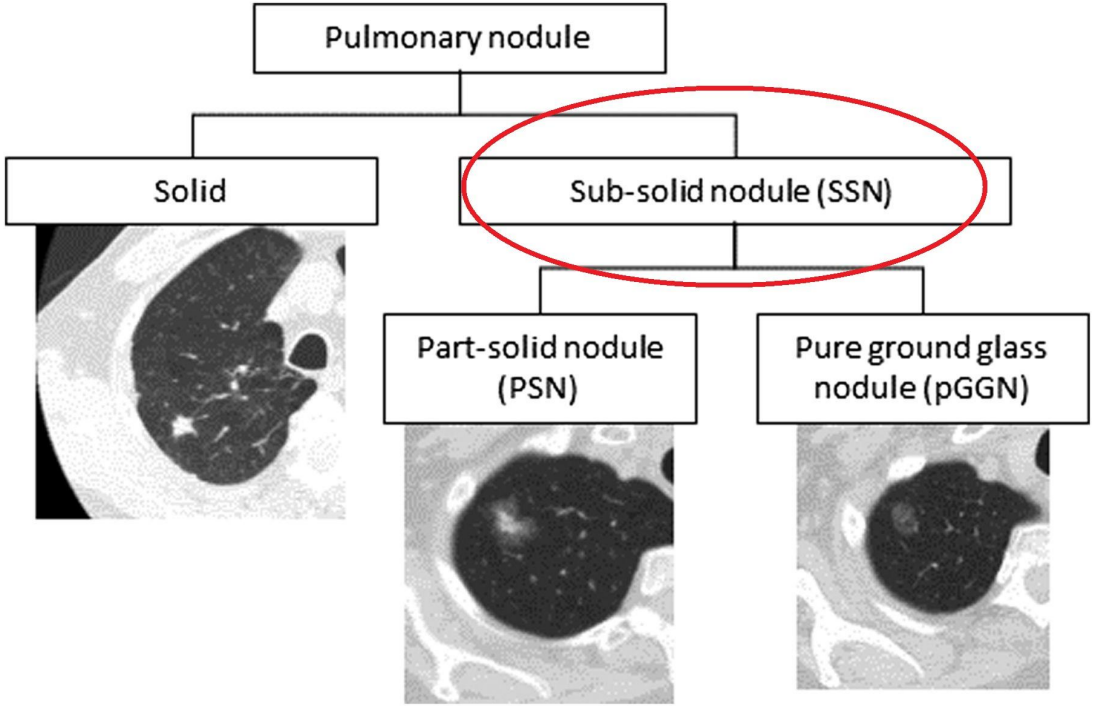
Метаанализ: сегментэктомия vs лобэктомия

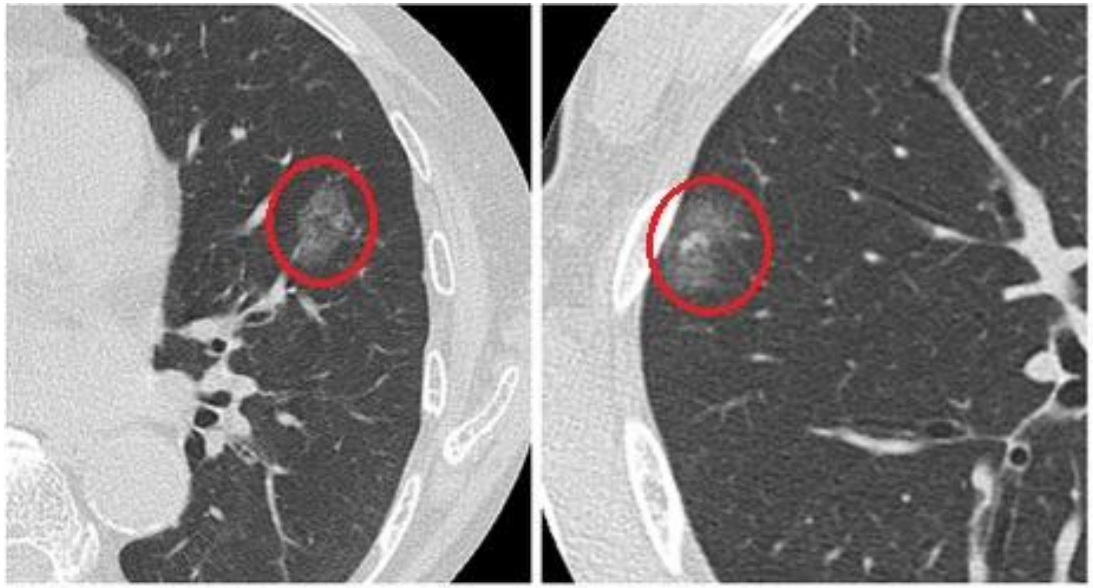
A



Zhang, Y., Sun, Y., Wang, R., Ye, T., Zhang, Y., & Chen, H. (2014). Meta-analysis of lobectomy, segmentectomy, and wedge resection for stage I non-small cell lung cancer. Journal of Surgical Oncology, 111(3), 334–340. doi:10.1002/jso.23800

Субсолидные узелки



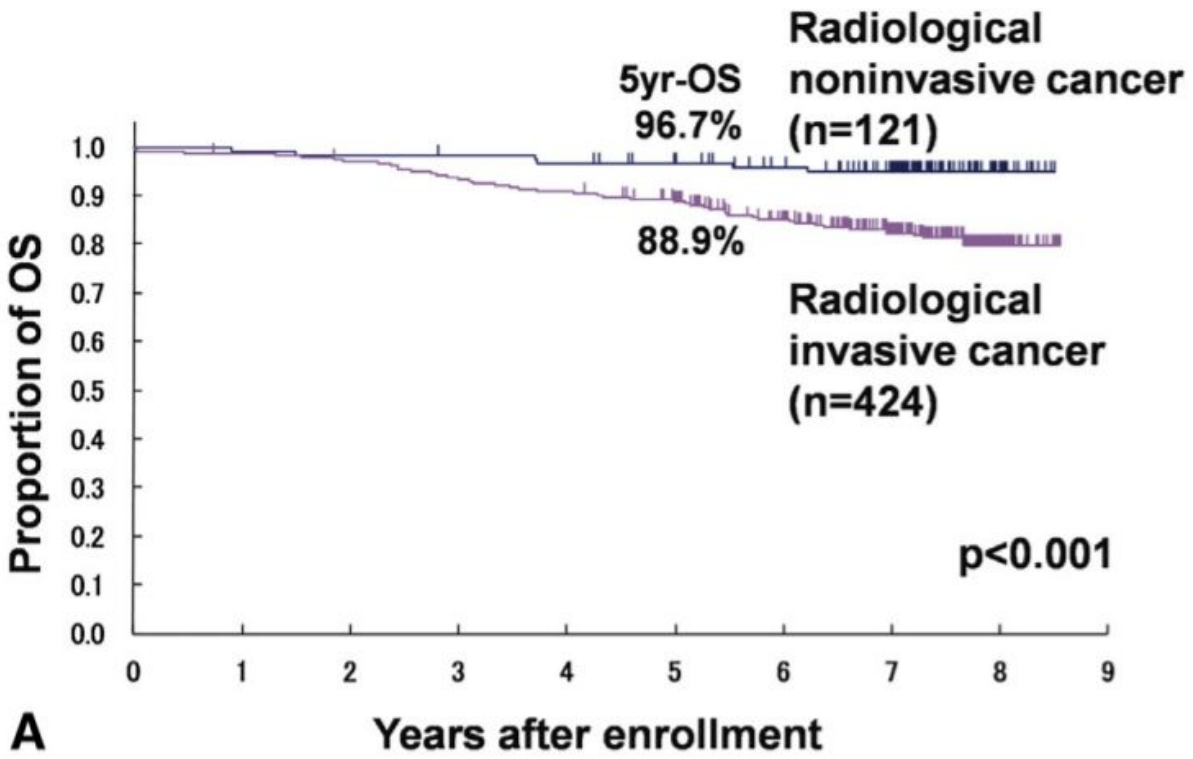


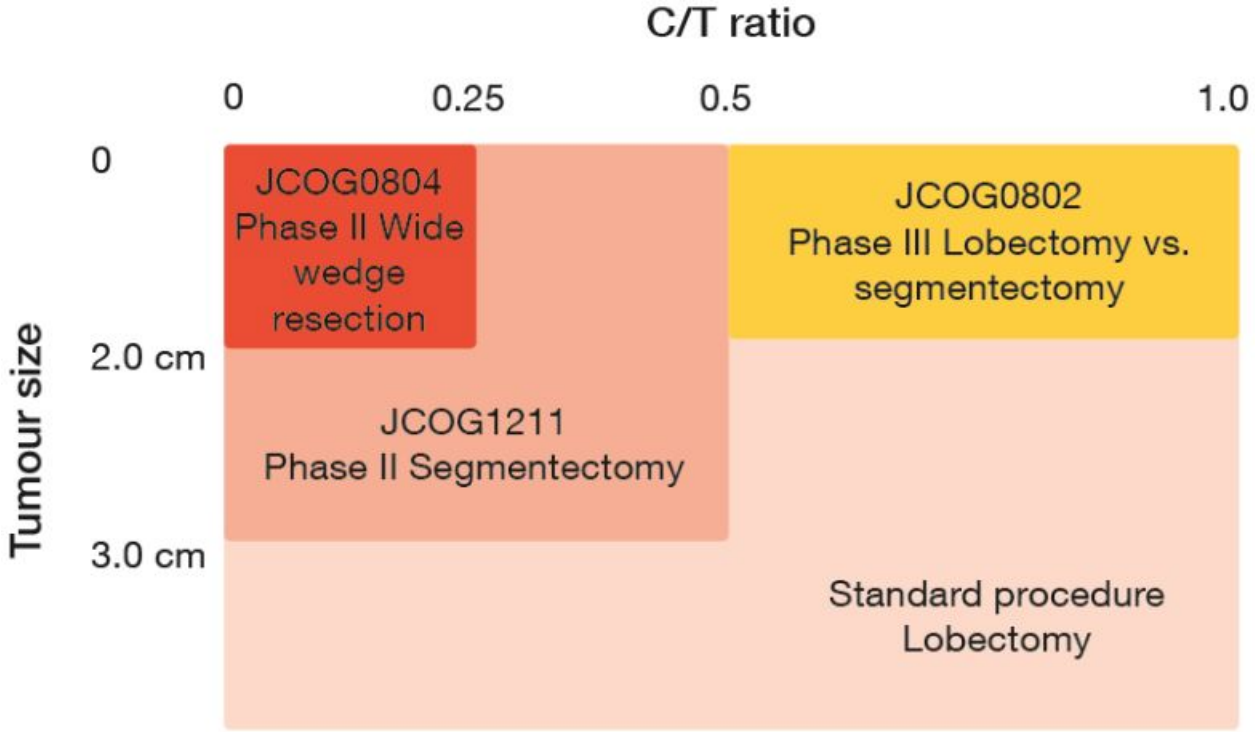
A. GGO-dominant tumor

Sakurai H, Asamura H. Sublobar resection for early-stage lung cancer. Transl Lung Cancer Res 2014;3(3):164-172. doi: 10.3978/j.issn.2218-6751.2014.06.11

Hattori, A., Matsunaga, T., Takamochi, K., Oh, S., & Suzuki, K. (2016). Neither Maximum Tumor Size nor Solid Component Size Is Prognostic in Part-Solid Lung Cancer: Impact of Tumor Size Should Be Applied Exclusively to Solid Lung Cancer. The Annals of Thoracic Surgery, 102(2), 407–415. doi:10.1016/j.athoracsur.2016.02.074

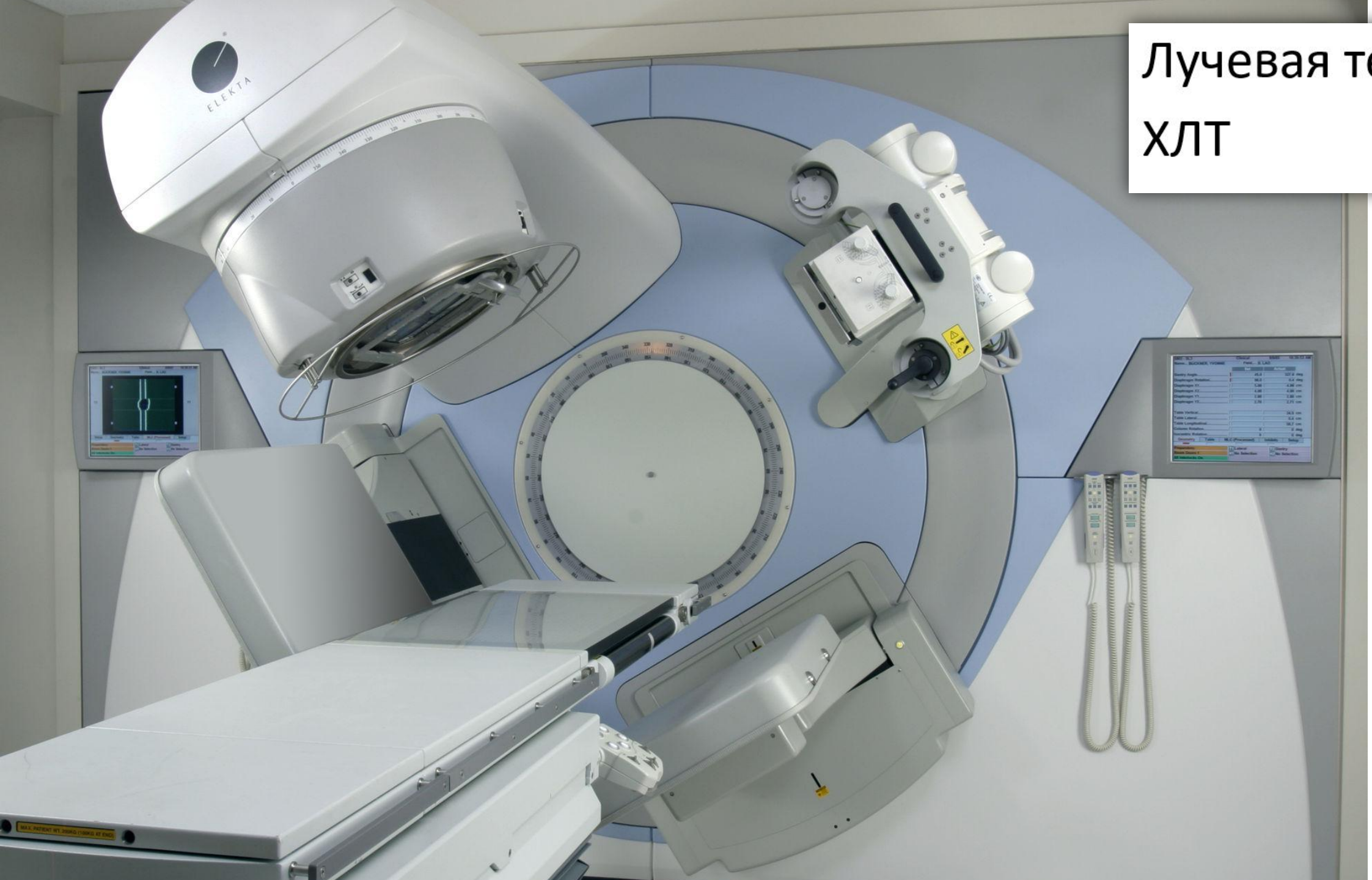
Японский подход





Asamura, H., Hishida, T., Suzuki, K., Koike, T., Nakamura, K., Kusumoto, M., … Fukuda, H. (2013). Radiographically determined noninvasive adenocarcinoma of the lung: Survival outcomes of Japan Clinical Oncology Group 0201. The Journal of Thoracic and Cardiovascular Surgery, 146(1), 24–30. doi:10.1016/j.jtcvs.2012.12.047

Aokage, K., Yoshida, J., Hishida, T., Tsuboi, M., Saji, H., Okada, M., … Asamura, H. (2016). Limited resection for early-stage non-small cell lung cancer as function-preserving radical surgery: a review. Japanese Journal of Clinical Oncology, 47(1), 7–11. doi:10.1093/jjco/hyw148



Лучевая терапия

ХЛТ

JAMA Oncology

Stereotactic Body Radiation Therapy for Operable Early-Stage Lung Cancer
Findings From the NRG Oncology RTOG 0618 Trial

Robert D. Timmerman, MD; Rebecca Paulus, BS; Harvey I. Pass, MD; Elizabeth M. Gore, MD; Martin J. Edelman, MD; James Galvin, DSc; William L. Straube, MS; Lucien A. Nedzi, MD; Ronald C. McGarry, MD, PhD; Cliff G. Robinson, MD; Peter B. Schiff, MD; Garrick Chang, MD; Billy W. Loo Jr, MD; Jeffrey D. Bradley, MD; Hak Choy, MD

Figure 1. CONSORT Diagram

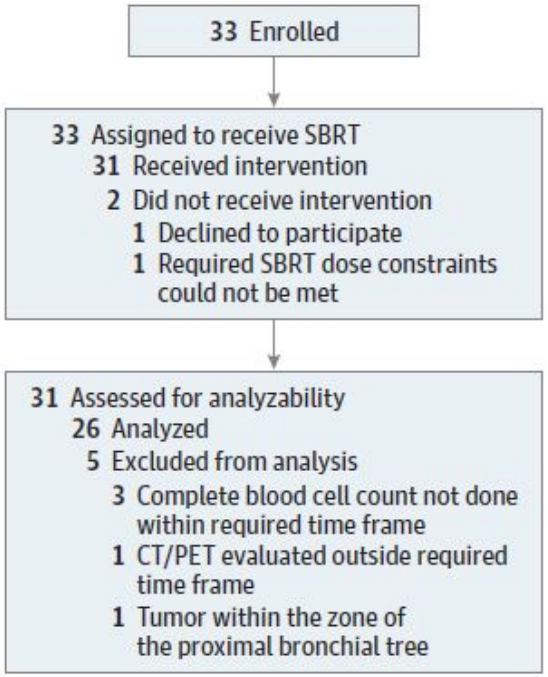
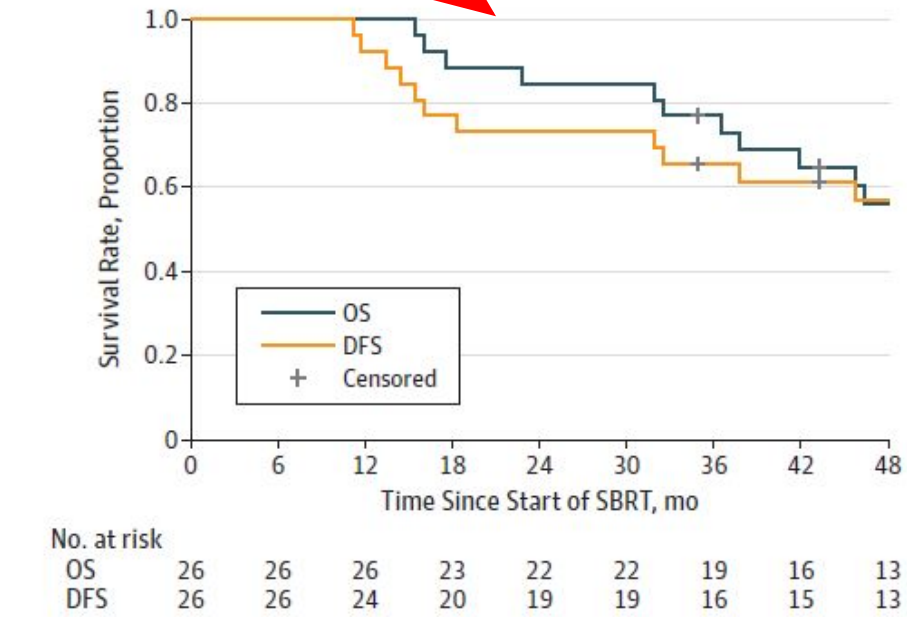
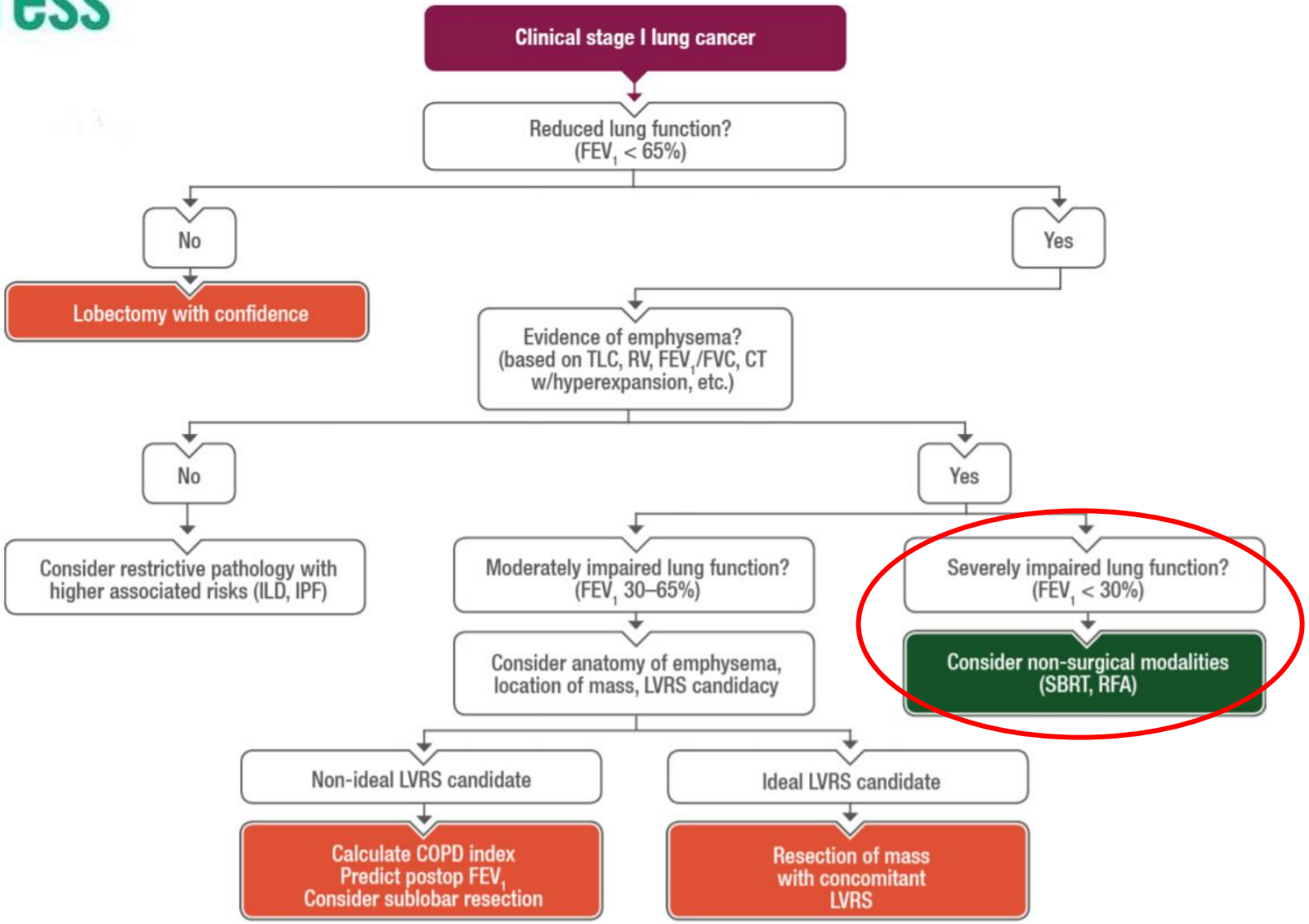


Figure 2. Overall Survival (OS) a -Free Survival (DFS)

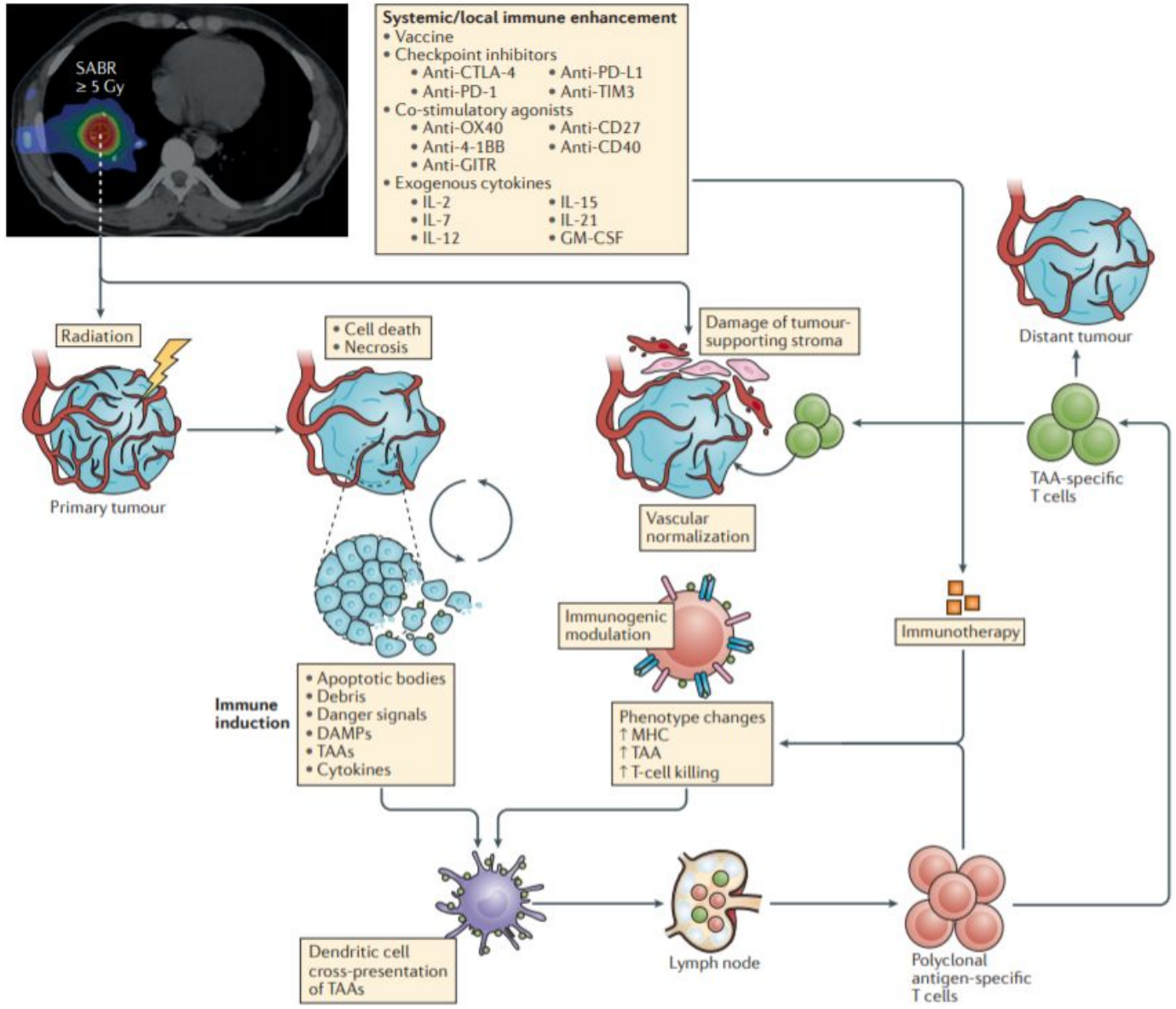


MUNICH 2018 ESMO congress

Пациенты с ограниченной лёгочной функцией вследствие эмфиземы – кандидаты для SBRT

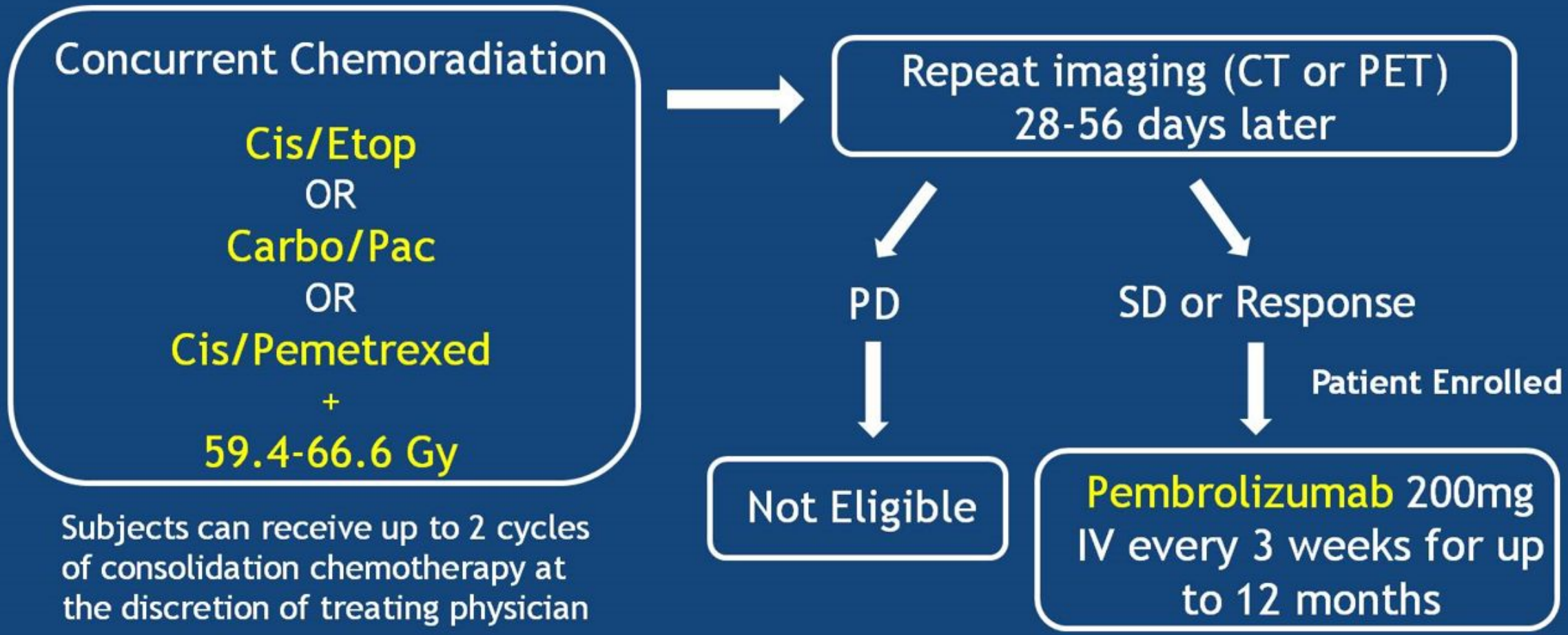


Синергический эффект иммунотерапии и лучевой терапии



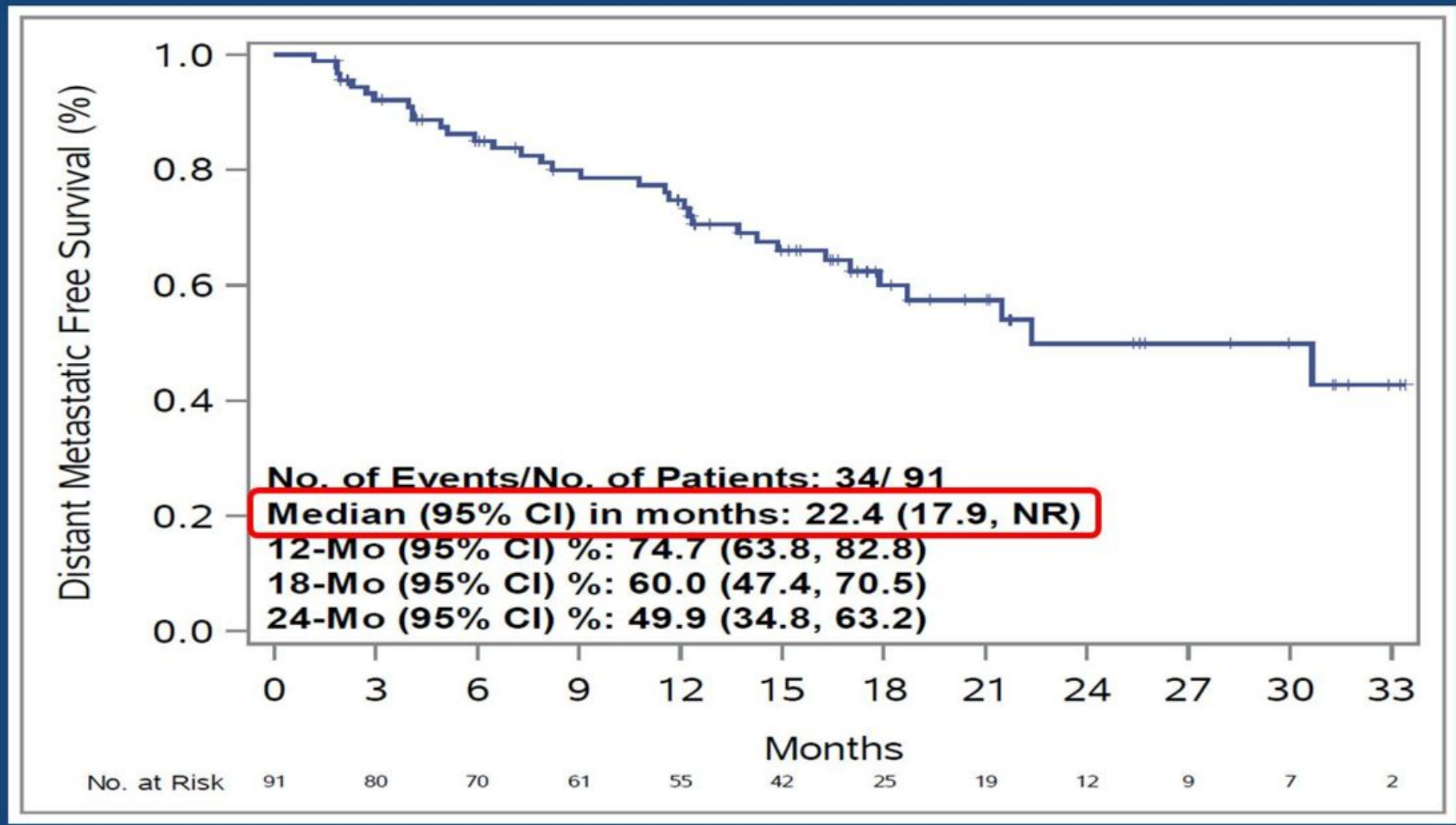
Bernstein, M. B., Krishnan, S., Hodge, J. W., & Chang, J. Y. (2016). Immunotherapy and stereotactic ablative radiotherapy (ISABR): a curative approach? Nature Reviews Clinical Oncology, 13(8), 516–524. doi:10.1038/nrclinonc.2016.30

Consolidation Pembrolizumab Following CCRT for Unresectable Stage III NSCLC: LUN 14-179



Subjects can receive up to 2 cycles of consolidation chemotherapy at the discretion of treating physician

Time to Metastatic Disease or Death



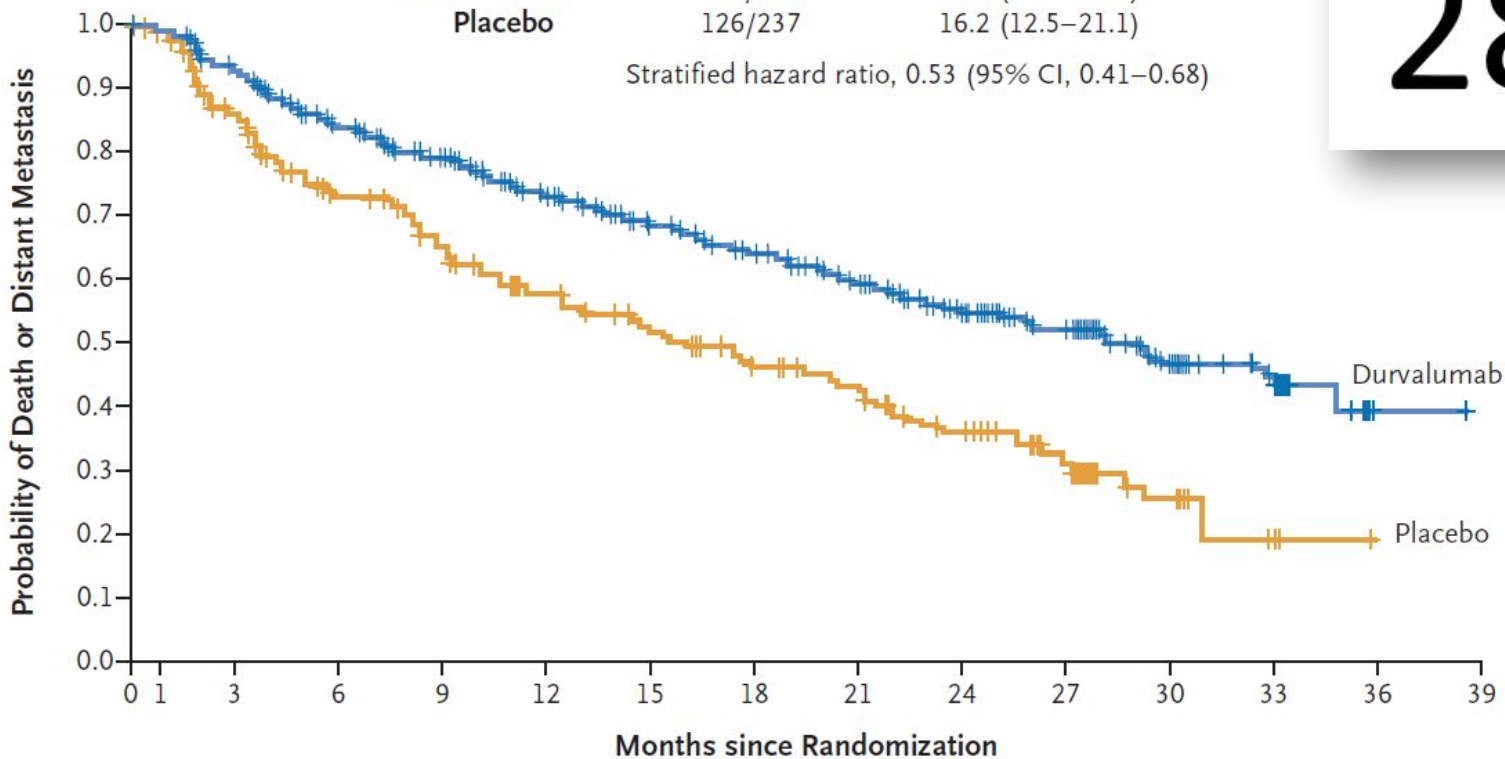
ORIGINAL ARTICLE

Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC

Scott J. Antonia, M.D., Ph.D., Augusto Villegas, M.D., Davey Daniel, M.D., David Vicente, M.D., Shuji Murakami, M.D., Rina Hui, Ph.D., Takayasu Kurata, M.D., Ph.D., Alberto Chiappori, M.D., Ki H. Lee, M.D., Ph.D., Maike de Wit, M.D., Ph.D., Byoung C. Cho, M.D., Ph.D., Maryam Bourhaba, M.D., et al., for the PACIFIC Investigators*

	No. of Events/ Total No. of Patients	Median Time to Death or Distant Metastasis (95% CI)
		mo
Durvalumab	182/476	28.3 (24.0–34.9)
Placebo	126/237	16.2 (12.5–21.1)

Stratified hazard ratio, 0.53 (95% CI, 0.41–0.68)



28.3 m.

Системная терапия

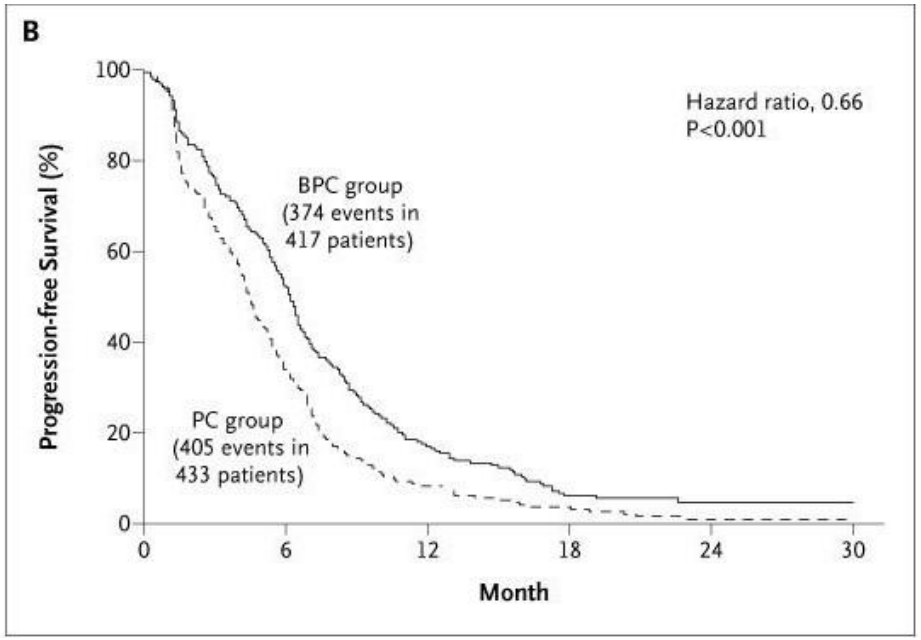
ORIGINAL ARTICLE

Paclitaxel–Carboplatin Alone or with Bevacizumab for Non–Small-Cell Lung Cancer

Alan Sandler, M.D., Robert Gray, Ph.D., Michael C. Perry, M.D., Julie Brahmer, M.D., Joan H. Schiller, M.D., Afshin Dowlati, M.D., Rogerio Lilenbaum, M.D., and David H. Johnson, M.D.

Группа	ЧОО %	Медиана ВБП (мес.)	Медиана ОВ (мес.)
Паклитаксел + Карбоплатин	15	4.5	10.3
Паклитаксел + Карбоплатин + Бевацизумаб	35	6.2	12.3

2006



New Engl J Med 2006; 355:2542-2550
DOI: 10.1056/NEJMoa061884

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2019
Non-Small Cell Lung Cancer

NCCN Guidelines Index
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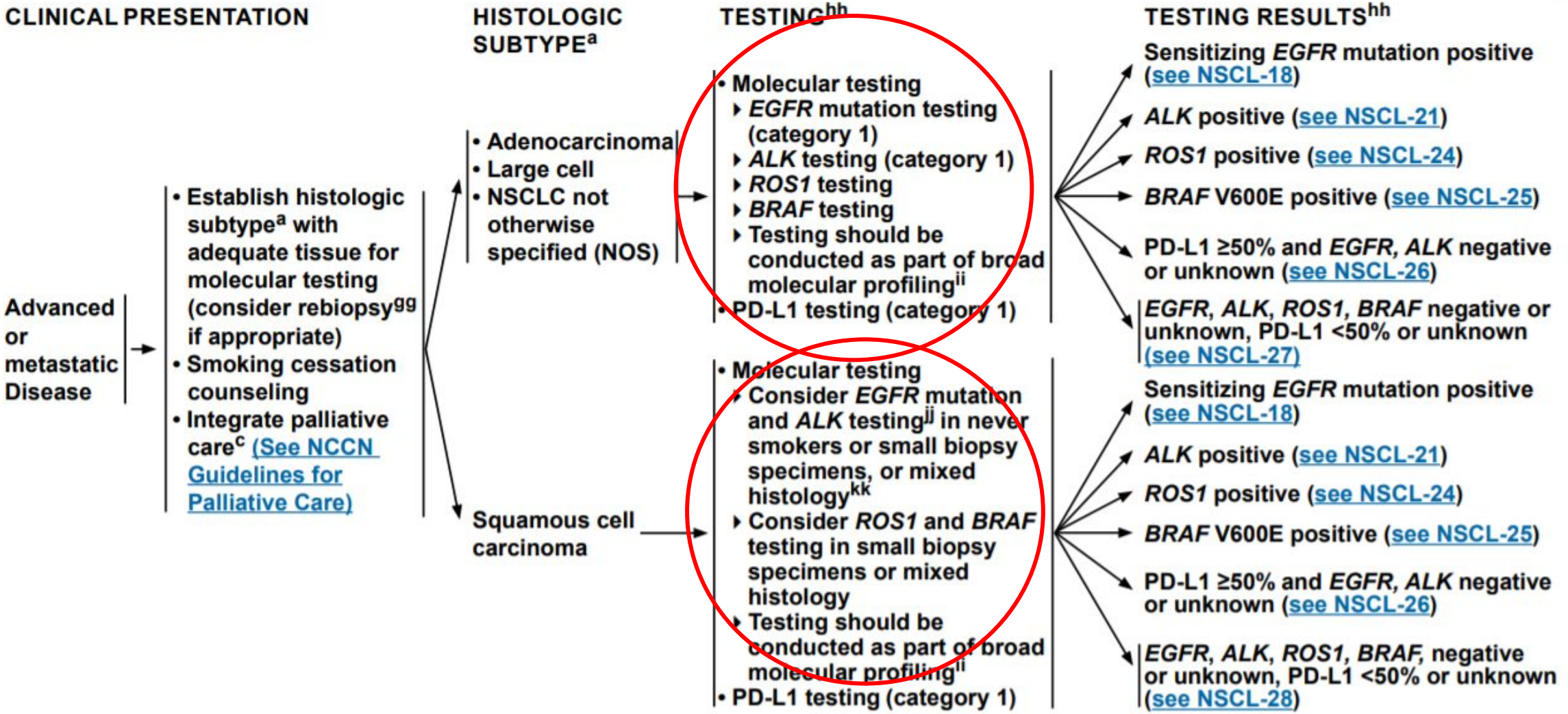
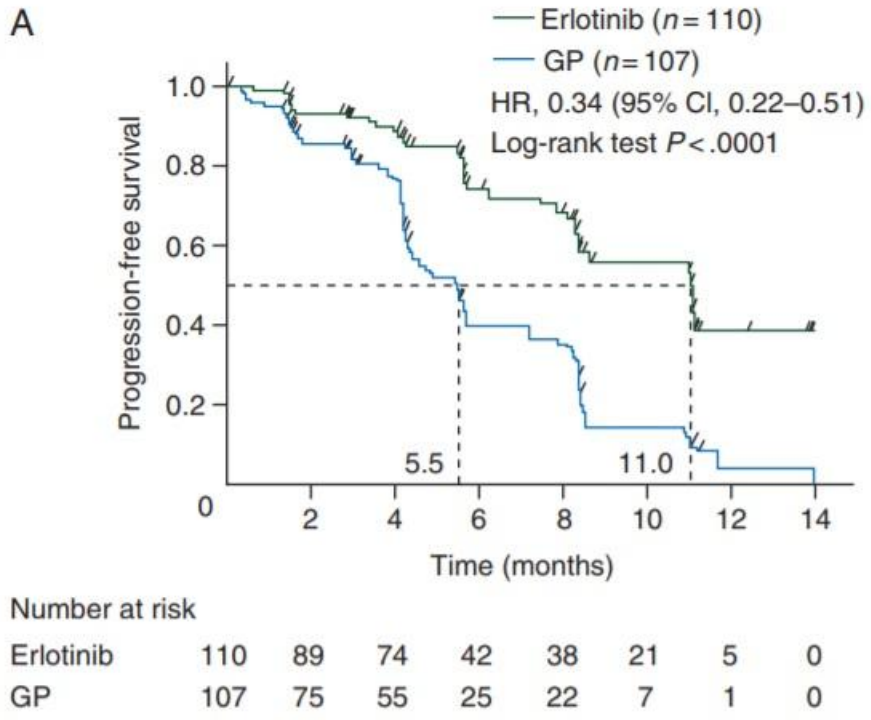
Discussion



First-line erlotinib versus gemcitabine/cisplatin in patients with advanced *EGFR* mutation-positive non-small-cell lung cancer: analyses from the phase III, randomized, open-label, ENSURE study†

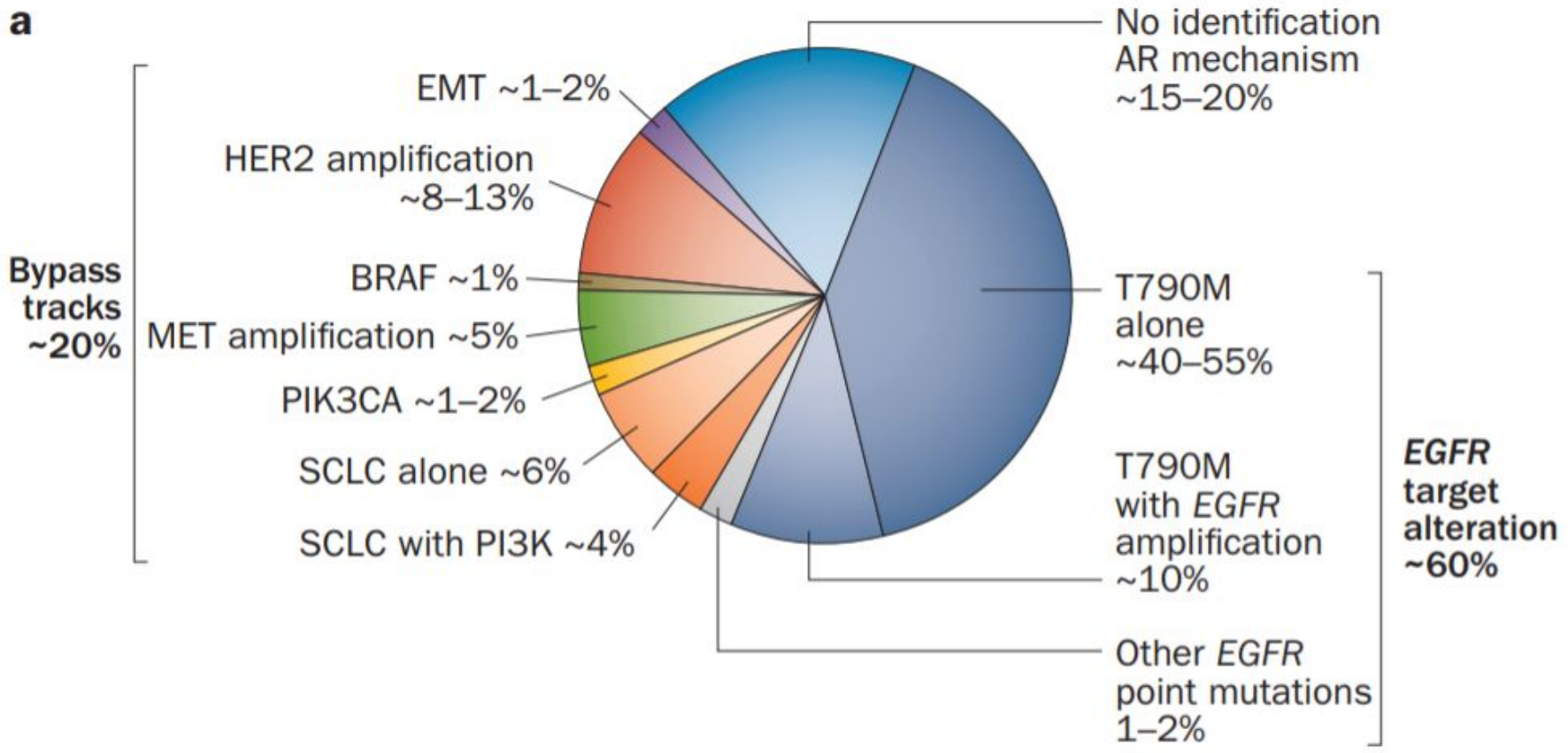
Y.-L. Wu[1*], C. Zhou[2], C.-K. Liam[3], G. Wu[4], X. Liu[5], Z. Zhong[6], S. Lu[7], Y. Cheng[8], B. Han[7], L. Chen[9], C. Huang[10], S. Qin[11], Y. Zhu[12], H. Pan[13], H. Liang[14], E. Li[15], G. Jiang[16], S. H. How[17], M. C. L. Fernando[18], Y. Zhang[19], F. Xia[19] & Y. Zuo[19]

ANNALS OF ONCOLOGY



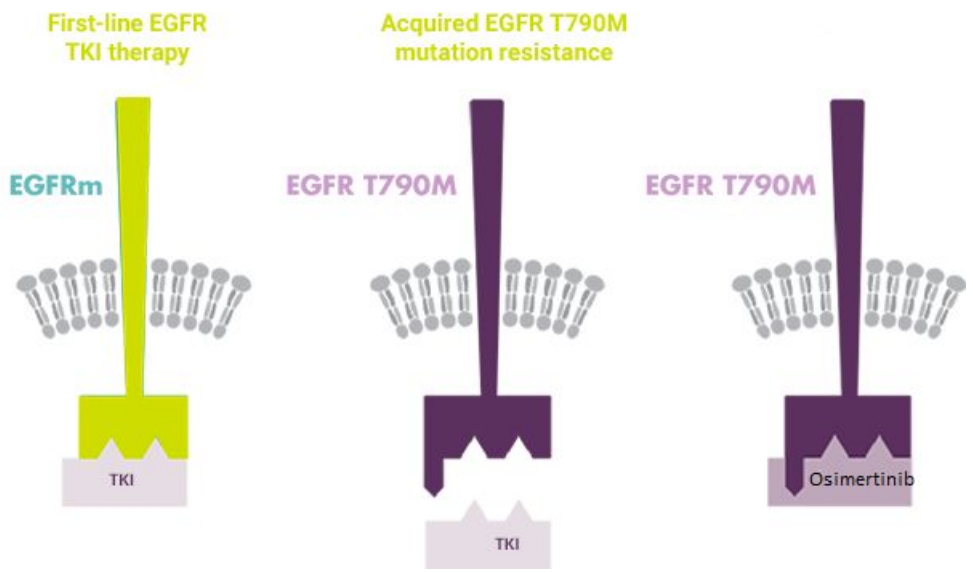
Группы	ЧОО %	Медиана ВБП (мес.)	Медиана ОВ (мес.)	НеЯв. (3-4)
Эрлотиниб	62.7	11.0	26.3	2.7 %
Гемцитабин + цисплатин	33.6	5.5	25.5	10.6%

Механизмы резистентности



Camidge, D. R., Pao, W., & Sequist, L. V. (2014). Acquired resistance to TKIs in solid tumours: learning from lung cancer. Nature Reviews Clinical Oncology, 11(8), 473–481. doi:10.1038/nrclinonc.2014.104

Мутация T 790 m – около 60 % случаев



- Происходит изменение конфигурации рецептора EGFR
- Ингибиторы тирозинкиназы 1 и 2 поколения не могут взаимодействовать
- Разработан новый препарат – Osimertinib

When patients with EGFRm NSCLC have progressed due to the T790M mutation, TAGRISSO offers powerful efficacy and consistent tolerability

- Рандомизированное двойное слепое исследование 3 фазы **FLAURA** (Osimertinib в 1-й линии)
- 556 пациентов
- EGFR + (делеция в 19 экзоне или L858R)
- Местнораспространённый и метастатический НМРЛ
- Рандомизация 1:1
- Первичная конечная точка - PFS

ORIGINAL ARTICLE

Osimertinib in Untreated *EGFR*-Mutated Advanced Non–Small-Cell Lung Cancer

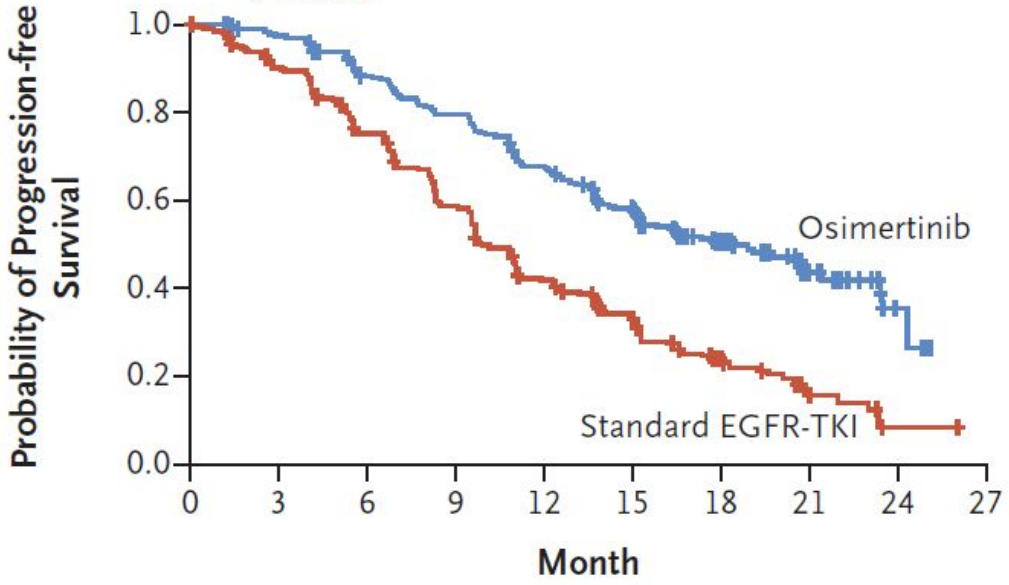
J.-C. Soria, Y. Ohe, J. Vansteenkiste, T. Reungwetwattana, B. Chewaskulyong, K.H. Lee, A. Dechaphunkul, F. Imamura, N. Nogami, T. Kurata, I. Okamoto, C. Zhou, B.C. Cho, Y. Cheng, E.K. Cho, P.J. Voon, D. Planchard, W.-C. Su, J.E. Gray, S.-M. Lee, R. Hodge, M. Marotti, Y. Rukazenkov, and S.S. Ramalingam, for the FLAURA Investigators*

Потрясающие результаты!

A Progression-free Survival in Full Analysis Set

	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Osimertinib	279	18.9 (15.2–21.4)
Standard EGFR-TKI	277	10.2 (9.6–11.1)

Hazard ratio for disease progression or death, 0.46 (95% CI, 0.37–0.57)
P<0.001

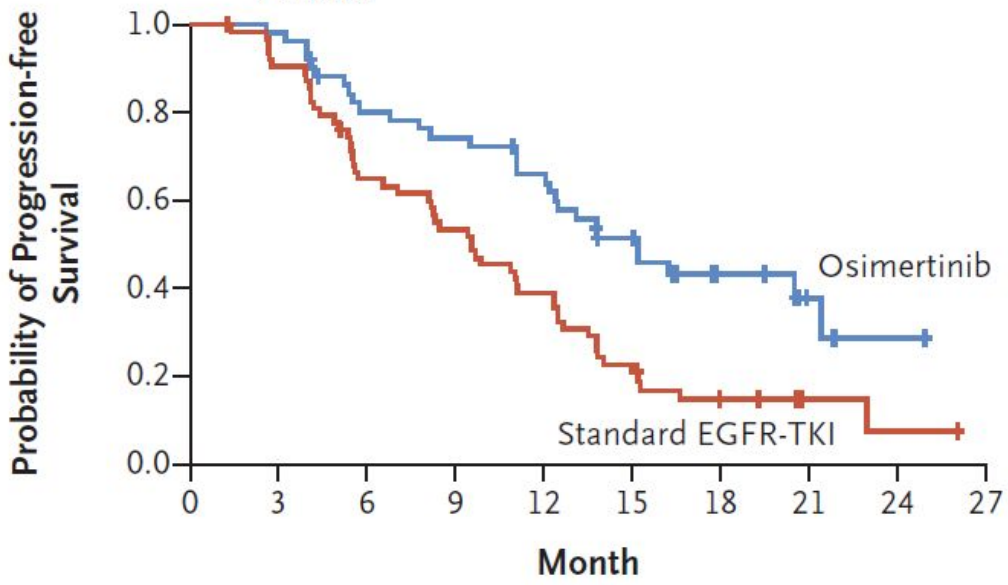


No. at Risk										
Osimertinib	279	262	233	210	178	139	71	26	4	0
Standard EGFR-TKI	277	239	197	152	107	78	37	10	2	0

B Progression-free Survival in Patients with CNS Metastases

	No. of Patients	Median Progression-free Survival (95% CI)
		mo
Osimertinib	53	15.2 (12.1–21.4)
Standard EGFR-TKI	63	9.6 (7.0–12.4)

Hazard ratio for disease progression or death, 0.47 (95% CI, 0.30–0.74)
P<0.001



No. at Risk										
Osimertinib	53	51	40	37	32	22	9	4	1	0
Standard EGFR-TKI	63	57	40	33	24	13	6	2	1	0

Сложный выбор

- Erlotinib
- Gefitinib
- Afatinib
- Osimertinib

Park, K., Tan, E.-H., O'Byrne, K., Zhang, L., Boyer, M., Mok, T., … Paz-Ares, L. (2016). Afatinib versus gefitinib as first-line treatment of patients with EGFR mutation-positive non-small-cell lung cancer (LUX-Lung 7): a phase 2B, open-label, randomised controlled trial. The Lancet Oncology, 17(5), 577–589. doi:10.1016/s1470-2045(16)30033-x

Soria, J.-C., Ohe, Y., Vansteenkiste, J., Reungwetwattana, T., Chewaskulyong, B., Lee, K. H., … Ramalingam, S. S. (2018). Osimertinib in Untreated EGFR-Mutated Advanced Non–Small-Cell Lung Cancer. New England Journal of Medicine, 378(2), 113–125. doi:10.1056/nejmoa1713137

ARCHER 1050: Study Design

- Phase 3 randomized open-label study to evaluate dacomitinib as an alternative first-line treatment for patients with advanced NSCLC with an *EGFR*-activating mutation

- Advanced NSCLC with *EGFR*-activating mutation(s)
- No prior systemic treatment of advanced NSCLC
- No CNS metastases
- No prior EGFR TKI or other TKI
- ECOG PS of 0 or 1

N = 452

R
1:1

Dacomitinib 45 mg
PO QD
(n = 227)

Gefitinib 250 mg
PO QD
(n = 225)

Primary endpoint

PFS by blinded independent review (IR)

- Target HR ≤0.667 (50%↑)
- 90% power
- 1-sided α = 0.025
- Assumed median PFS: 14.3 vs 9.5 months

Stratification factors

Race (including Asian vs non-Asian)

EGFR mutation type (exon 19 vs 21)

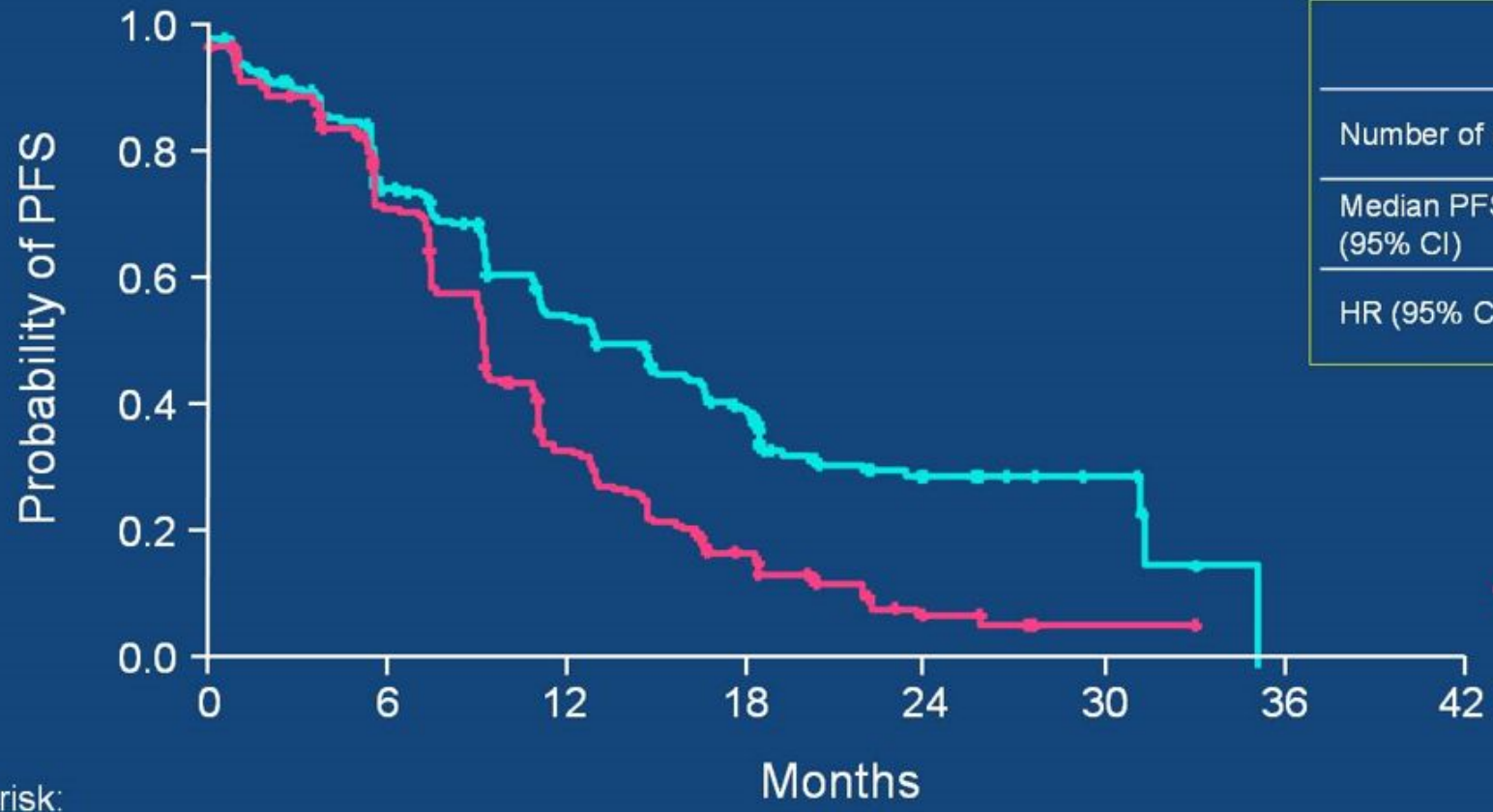
Secondary endpoints

OS

PFS (investigator assessed), ORR, DOR, TTF, Safety, PROs

ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT01774721.
CNS, central nervous system; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; ORR, objective response rate; PO, orally; PROs, patient-reported outcomes; PS, performance status; QD, once daily; R, randomized; TTF, time to treatment failure.

PFS: Blinded Independent Review
(Intention-to-Treat Population)



	Dacomitinib (n = 227)	Gefitinib (n = 225)
Number of events, n (%)	136 (59.9)	179 (79.6)
Median PFS, months (95% CI)	14.7 (11.1, 16.6)	9.2 (9.1, 11.0)
HR (95% CI)	0.59 (0.47, 0.74) *P* < 0.0001	

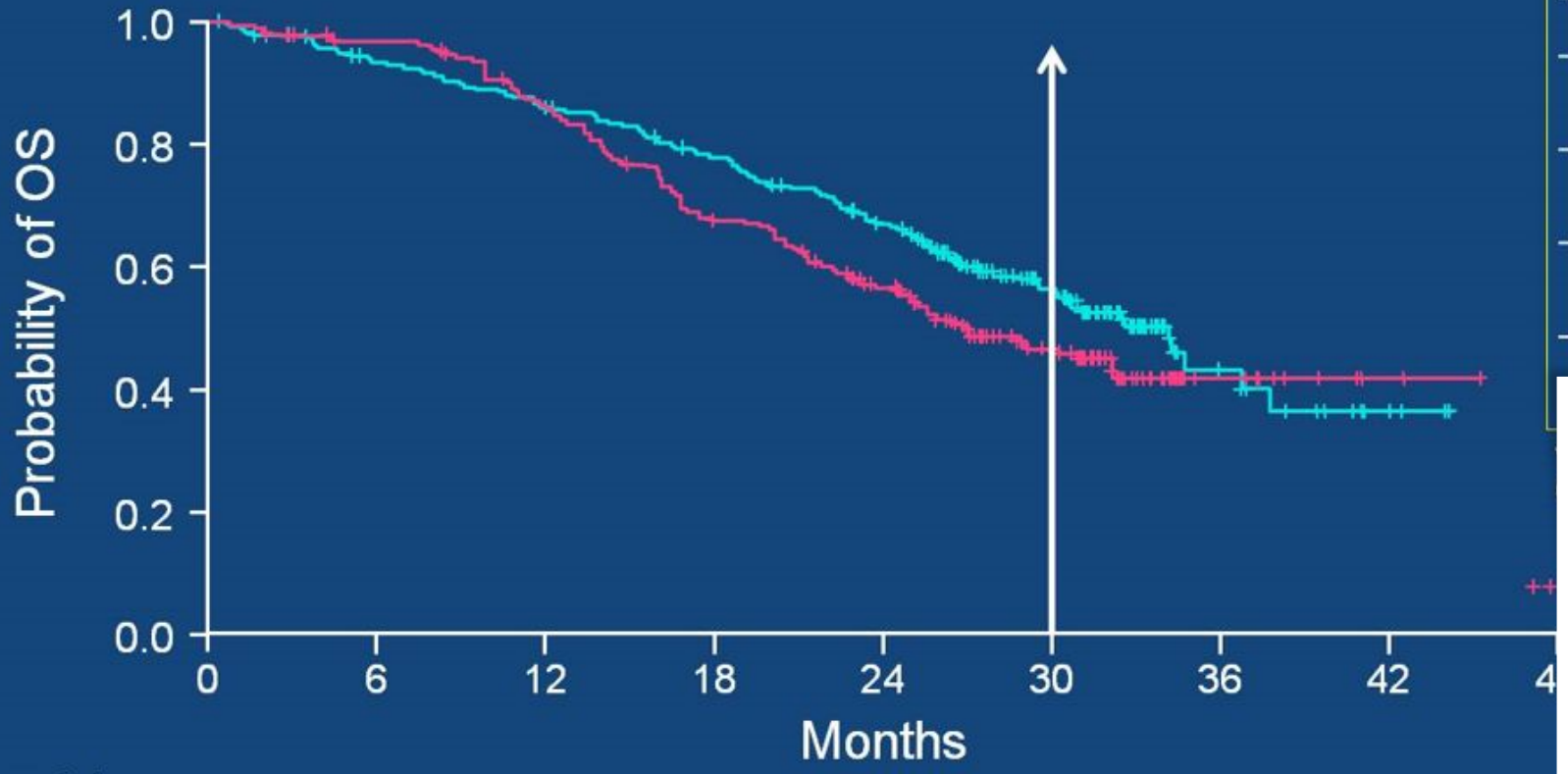
Data cutoff date: July 29, 2016

No. at risk:

Dacomitinib	227	154	106	73	20	6	0	0
Gefitinib	225	155	69	34	7	1	0	0

Wu YL, et al. *Lancet Oncol* 2017;18(11):1454–1466

Final OS (Primary Analysis)



	Dacomitinib (n = 227)	Gefitinib (n = 225)
Number of deaths, n (%)	103 (45.4)	117 (52.0)
Median OS, months (95% CI)	34.1 (29.5, 37.7)	26.8 (23.7, 32.1)
HR* (95% CI)	0.760 (0.582, 0.993) 2-sided *P** = 0.0438	
OS probability at 30 months, %	56.2	46.3
CNS metastases at		

No. at risk:

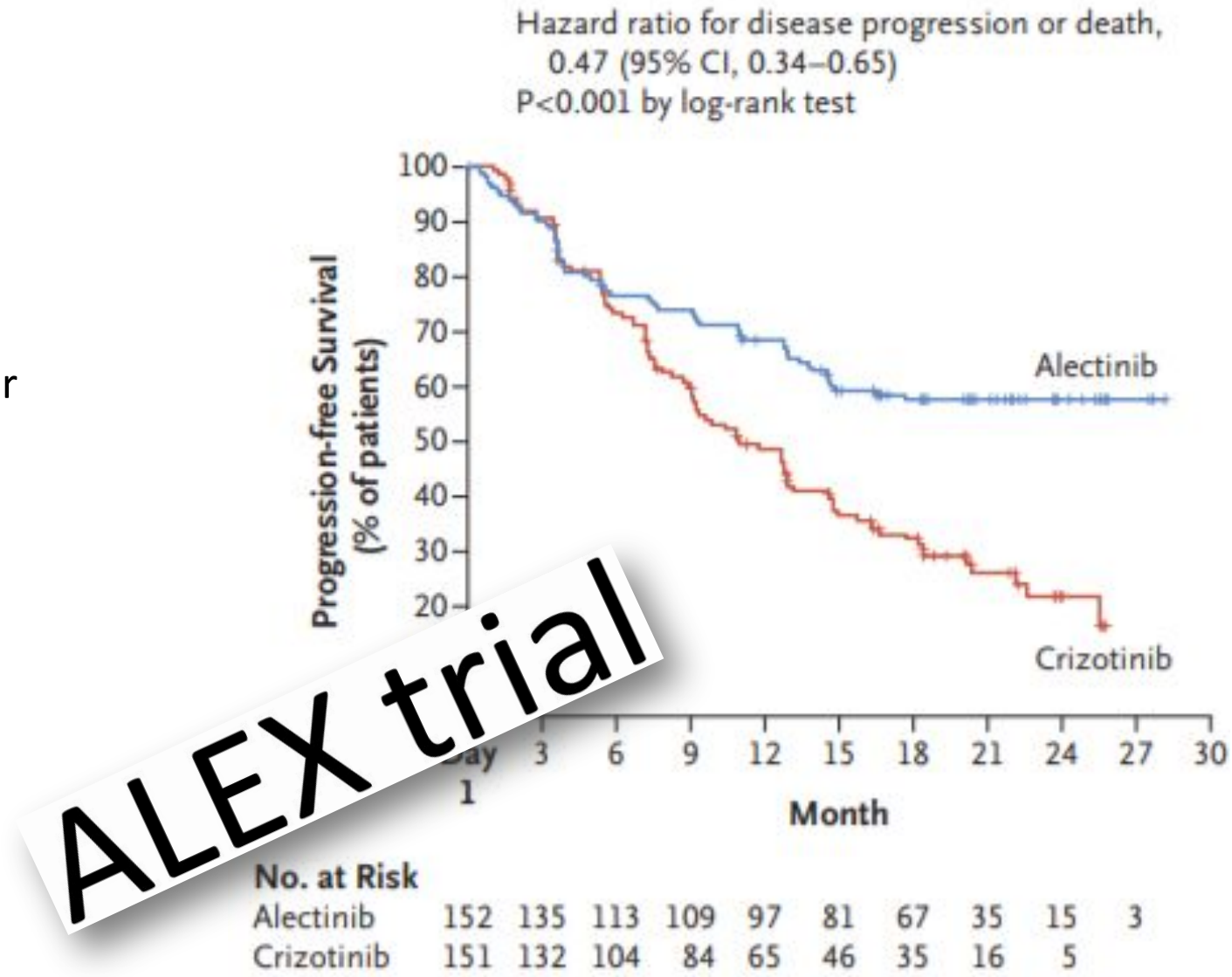
Dacomitinib	227	206	188	167	138	77	14	3	0
Gefitinib	225	213	186	144	113	63	12	3	0

NSCLC ALK +

Alectinib versus Crizotinib in Untreated ALK-Positive Non–Small-Cell Lung Cancer

Peters, M.D., et al. August 31, 2017

N Engl J Med 2017; 377:829-838 DOI: 10.1056/NEJMoa1704795

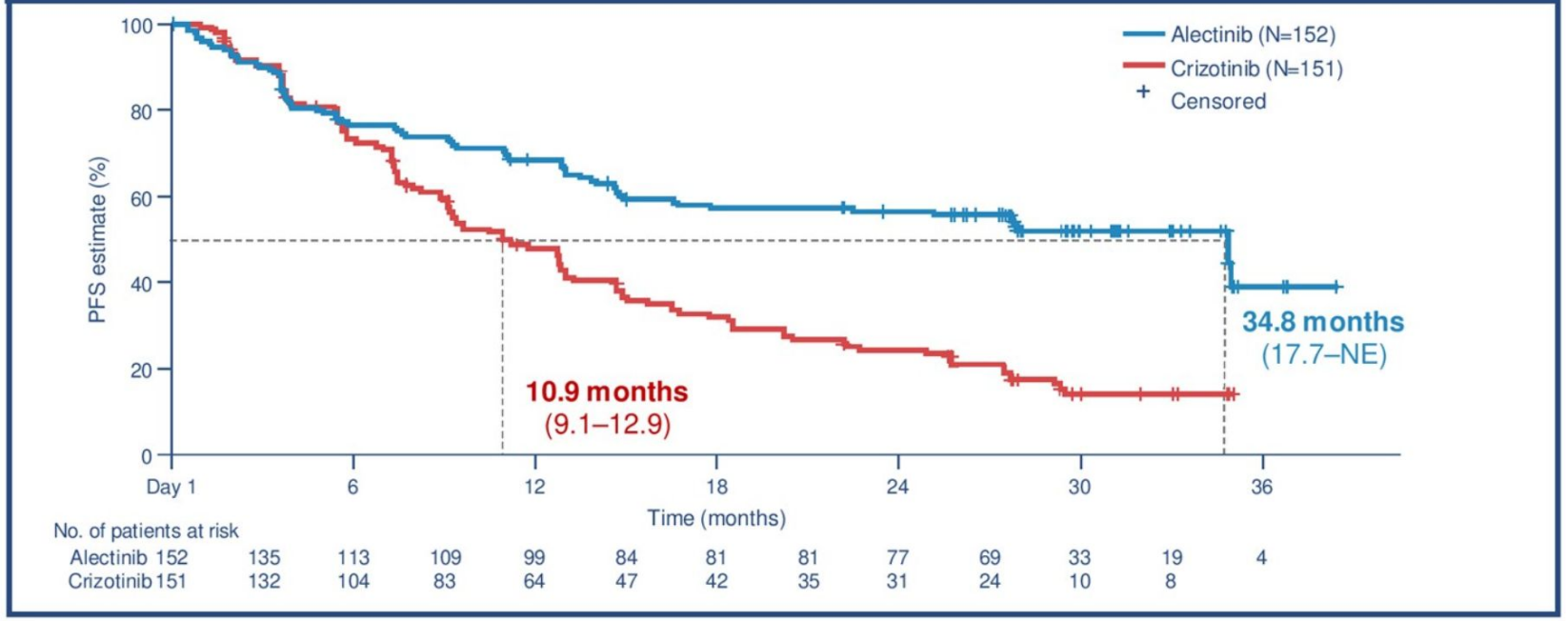


ALEX trial

Alectinib - обновлённые даннь

2018 ASCO ANNUAL MEETING
DELIVERING DISCOVERIES: EXPANDING THE REACH OF PRECISION MEDICINE

Figure 1. Investigator-assessed PFS.

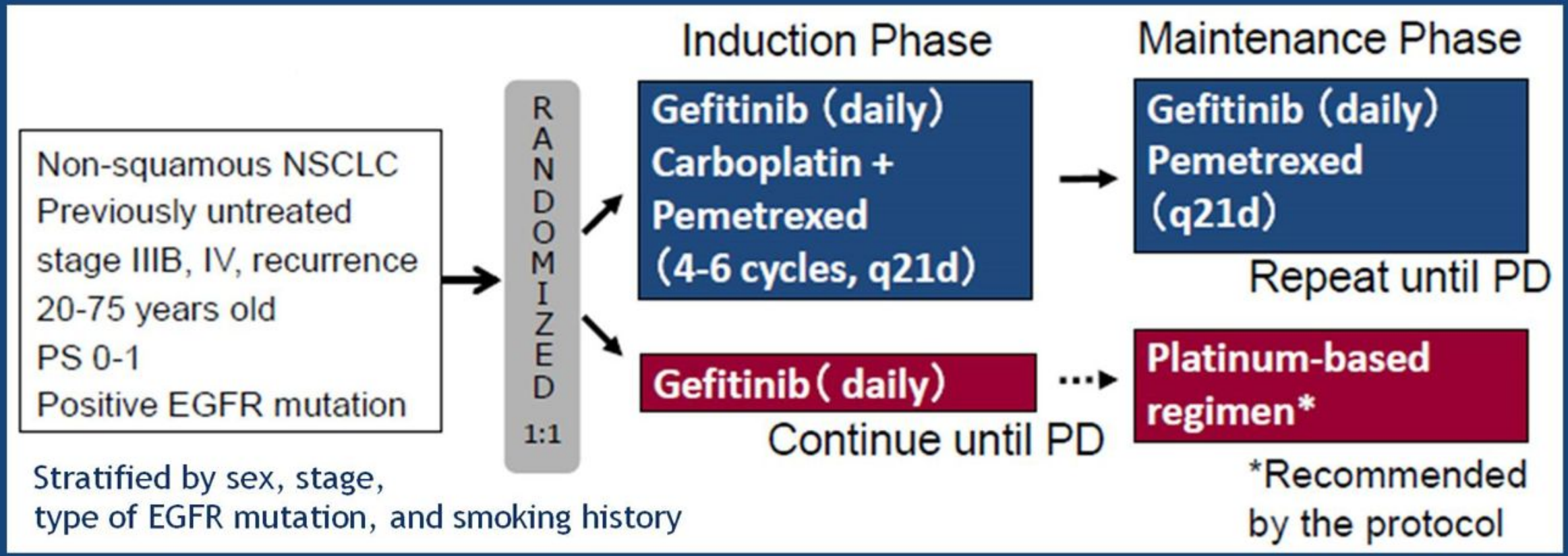


Updated efficacy and safety data from the global phase III ALEX study of alectinib (ALC) vs crizotinib (CZ) in untreated advanced ALK+ NSCLC.

D. Ross Camidge, Solange Peters, Tony Mok, Shirish M. Gadgeel and al.

2018 ASCO Meeting Abstract #9043

Study Design of NEJ009

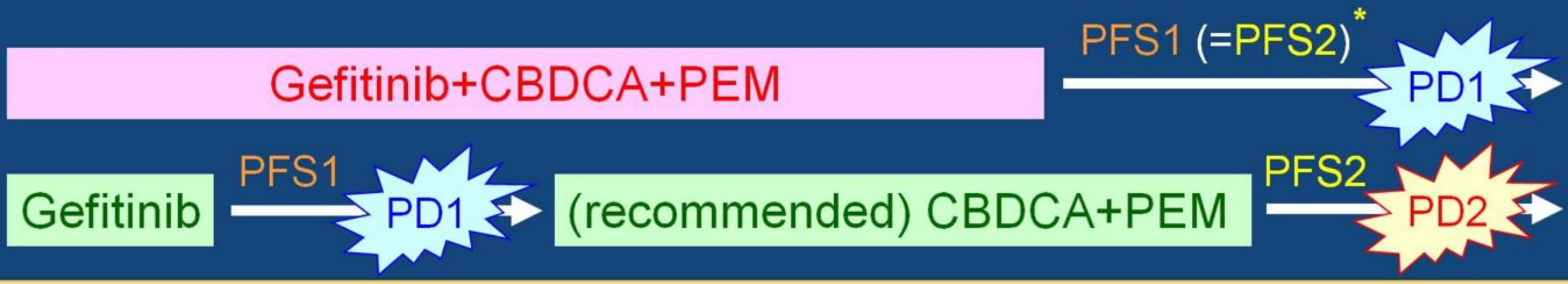


- From Oct. 2011 to Sep. 2014, 345 patients were enrolled from 47 institutions across Japan. In Oct.2017, a number of pre-planned events for primary endpoint analysis were observed.

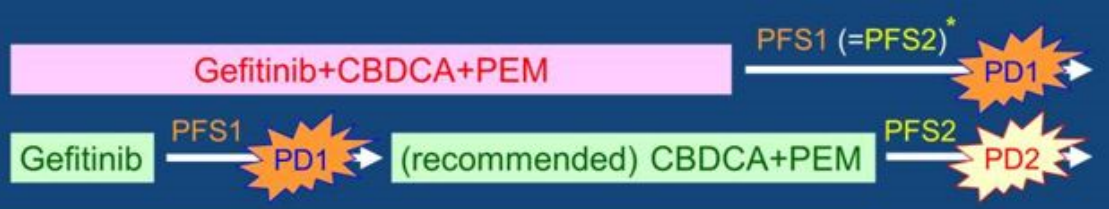
Endpoints

- Initial protocol setting in Oct. 2011
  Primary endpoint: OS
  Secondary endpoints: PFS, PFS2*, ORR, Safety, QOL
- Protocol amendment in Feb. 2016 before the interim analysis
  Multiple primary endpoints: PFS, PFS2*, and OS
  Secondary endpoints: ORR, Safety, QOL

*PFS2 in this study indicates a comparison of PD2 in the reference arm and PD1 in the experimental arm.

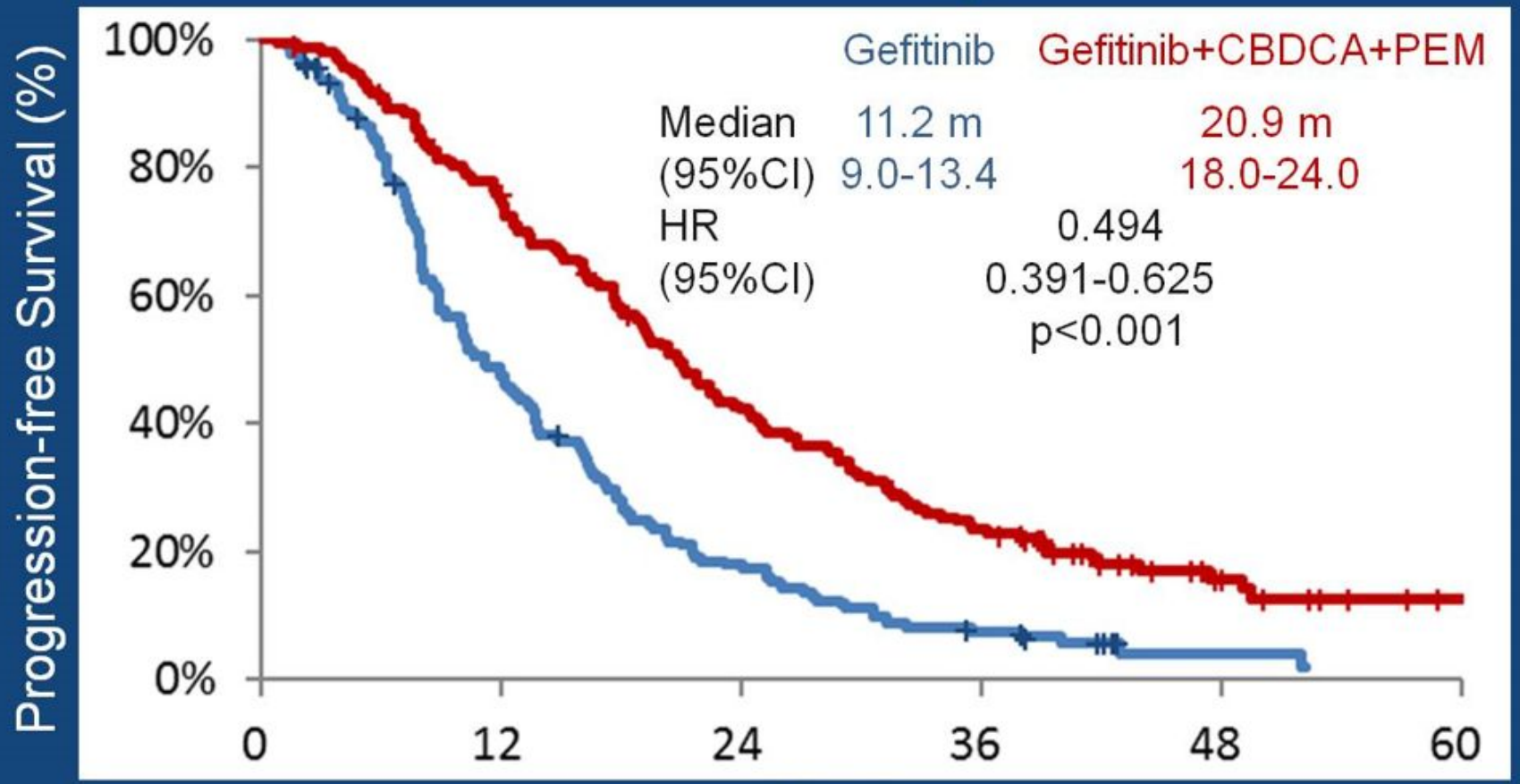


Progression-Free Survival 1



Response Rate (%)

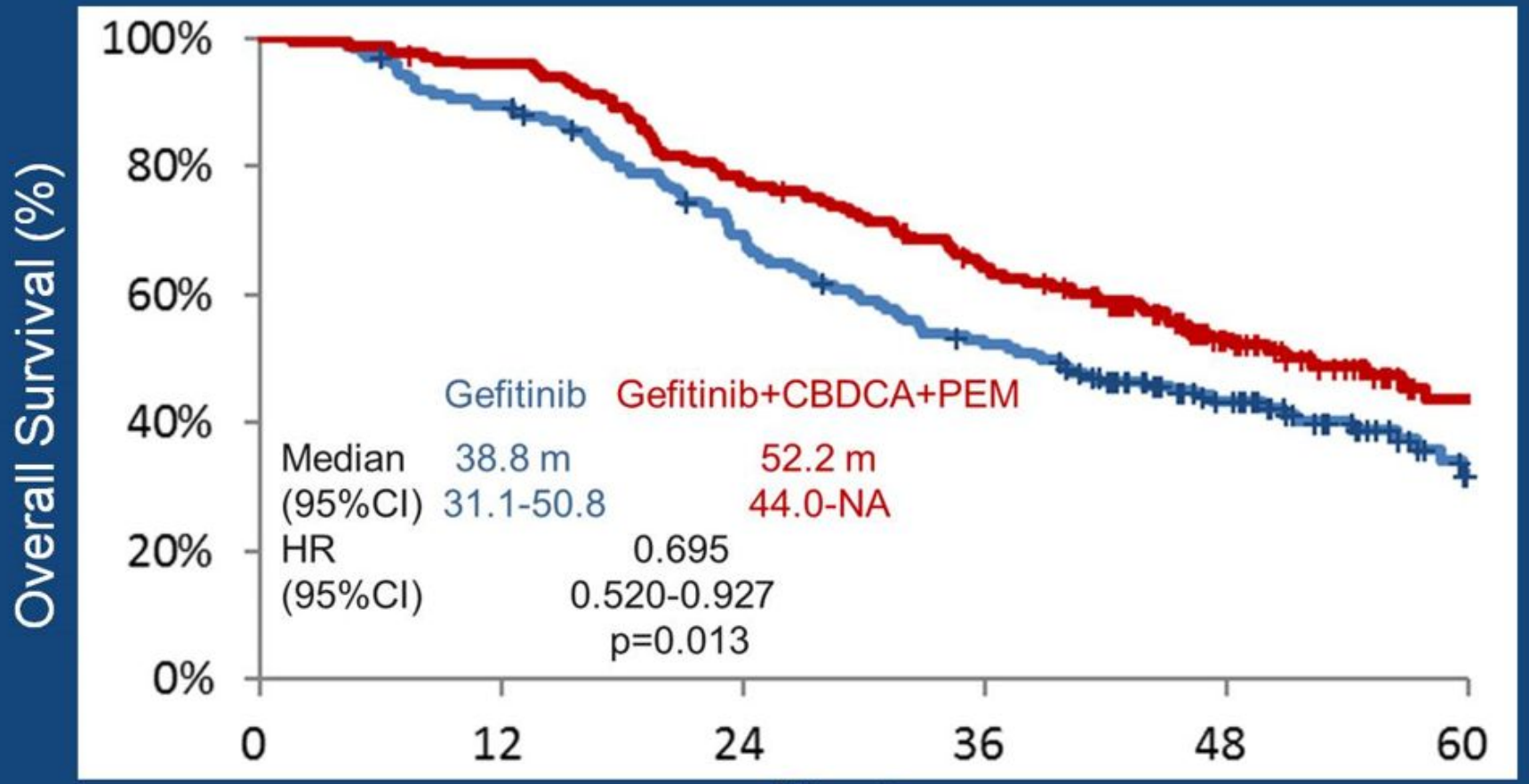
	Gefitinib	combo
CR	3.5	4.7
PR	64.0	79.3
SD	25.0	13.6
PD	4.7	1.2
ORR	67.4	84.0



No. at Risk

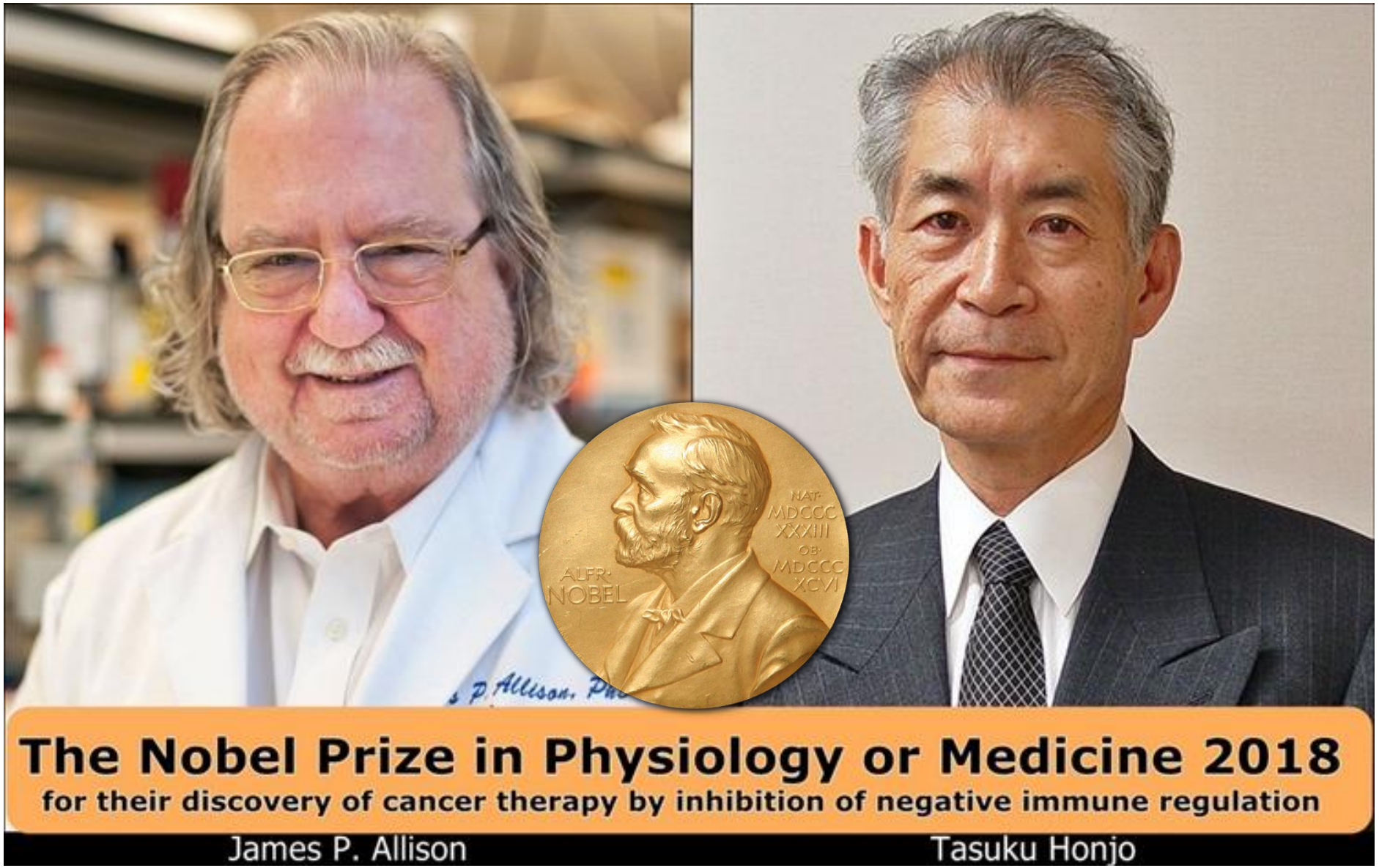
Gefitinib	172	78	29	11	2	0
Gefitinib+CBDCA+PEM	169	123	68	37	10	2

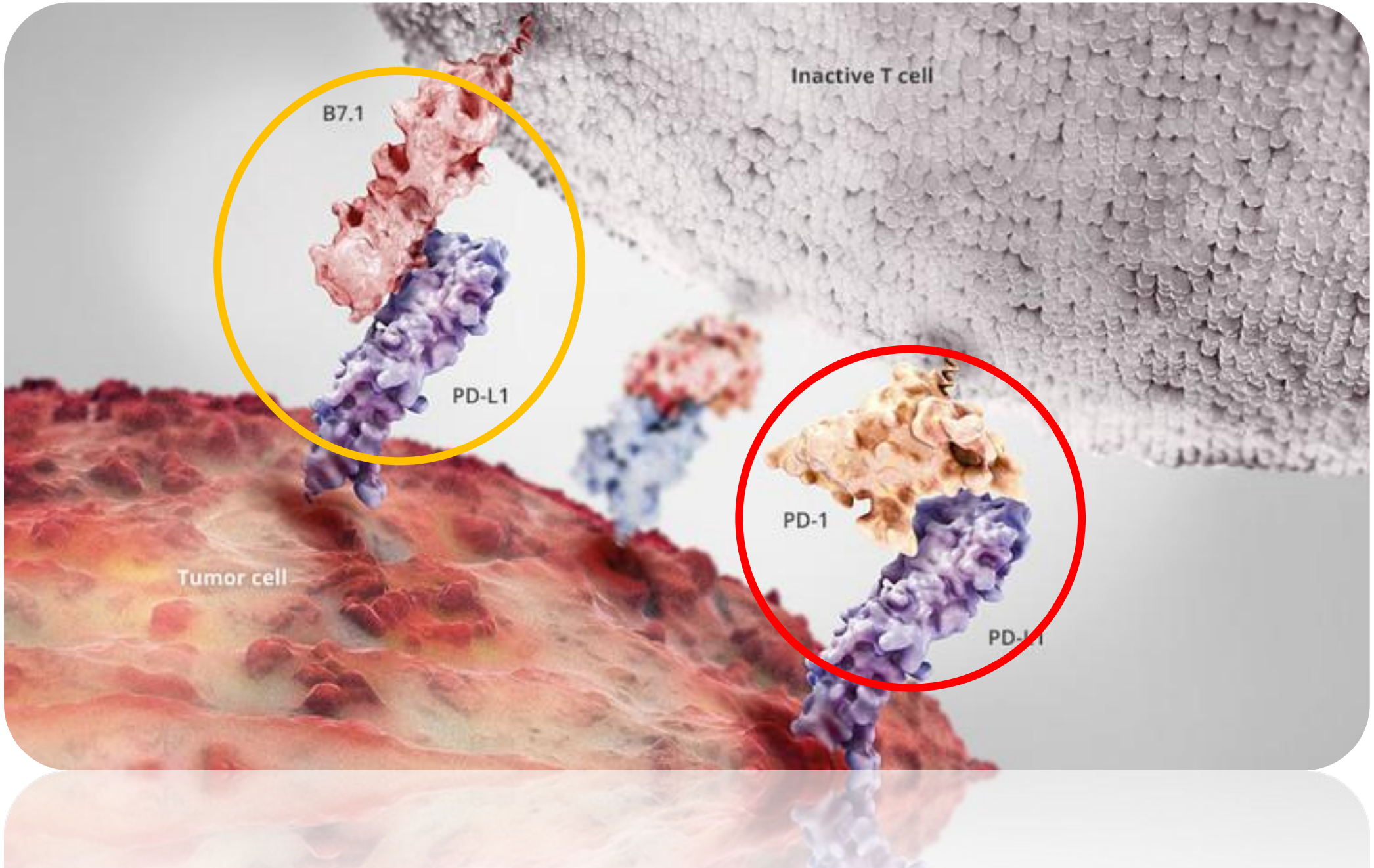
Overall Survival



No. at Risk						
Gefitinib	172	153	115	86	50	14
Gefitinib+CBDCA+PEM	170	162	131	105	57	20

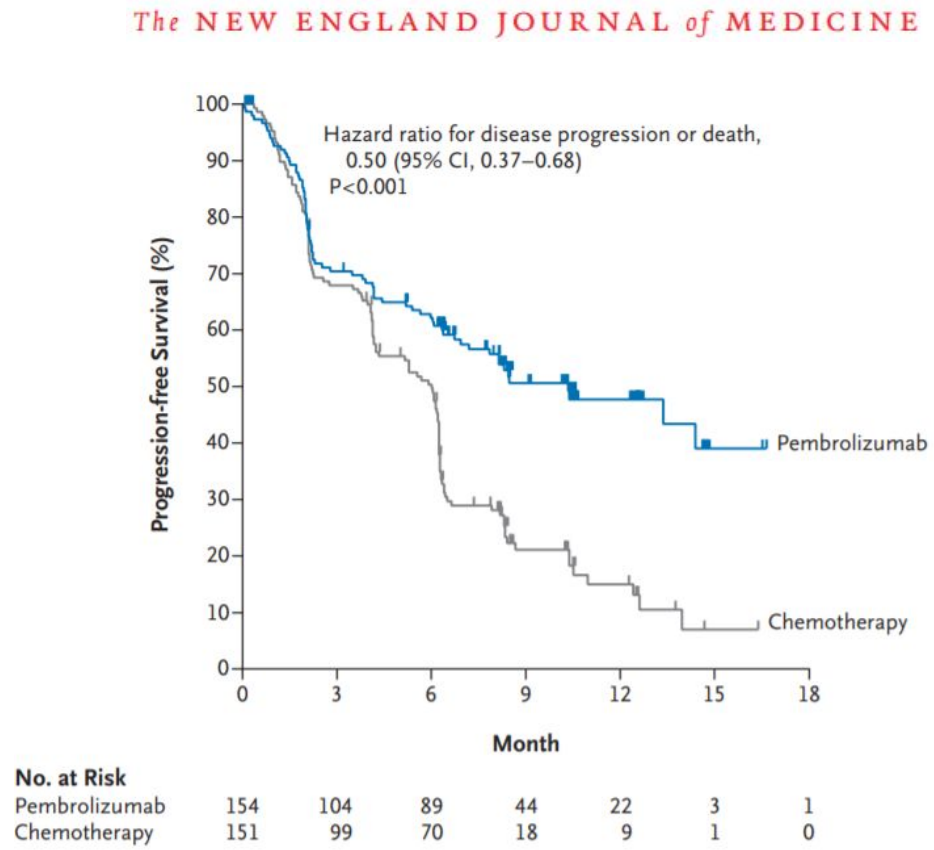
Иммунотерапия уже стандарт




Inactive T cell
B7.1
PD-L1
PD-1
Tumor cell

≥ 50%

- Около 30 % пациентов с распространённым НМРЛ имеют высокий уровень PD-L1, которая определена как мембранная экспрессия PD-L1 не менее 50%, независимо от интенсивности окрашивания.
- Данные KEYNOTE-001 и KEYNOTE-010 указали, что пациенты с продвинутым НМРЛ и показателем PD-L1 50% или больше имеют больше шансов получить ответ на Pembrolizumab



Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced nonsmall-cell lung cancer (KEYNOTE-010): a randomised controlled trial. Lancet 2016;387:1540-50.

Garon EB, Rizvi NA, Hui R, et al. Pembrolizumab for the treatment of non–small-cell lung N Engl J Med 2015;372:2018-28

Pembrolizumab versus Chemotherapy for PD-L1–Positive Non–Small-Cell Lung Cancer Martin Reck, M.D., Ph.D., et al., KEYNOTE-024 N Engl J Med 2016;375:1823-33.

DOI: 10.1056/NEJMoa1606774

NCCN National Comprehensive Cancer Network®

Смена парадигмы

- Неплоскоклеточный НМРЛ

Initial Systemic Therapy Options
Adenocarcinoma, Large Cell, NSCLC NOS (PS 0-1)
No contraindications to the addition of pembrolizumab or atezolizumab[c]
- **Pembrolizumab/carboplatin/pemetrexed (category 1)[1,2,d] (preferred)**
- **Pembrolizumab/cisplatin/pemetrexed (category 1)[2,d] (preferred)**
- **Atezolizumab/carboplatin/paclitaxel/bevacizumab (category 1)[3,d,e,f,g]**

Contraindications to the addition of pembrolizumab or atezolizumab[c]
- **Bevacizumab/carboplatin/paclitaxel (category 1)[4,e,f,g]**
- **Bevacizumab/carboplatin/pemetrexed[4,e,f,g]**
- **Bevacizumab/cisplatin/pemetrexed[6,e,f,g]**
- **Carboplatin/albumin-bound paclitaxel (category 1)[7]**
- **Carboplatin/docetaxel (category 1)[8]**
- **Carboplatin/etoposide (category 1)[9,10]**
- **Carboplatin/gemcitabine (category 1)[11]**
- **Carboplatin/paclitaxel (category 1)[12]**
- **Carboplatin/pemetrexed (category 1)[13]**
- **Cisplatin/docetaxel (category 1)[8]**
- **Cisplatin/etoposide (category 1)[14]**
- **Cisplatin/gemcitabine (category 1)[12,15]**
- **Cisplatin/paclitaxel (category 1)[16]**
- **Cisplatin/pemetrexed (category 1)[15]**
- **Gemcitabine/docetaxel (category 1)[17]**
- **Gemcitabine/vinorelbine (category 1)[18]**

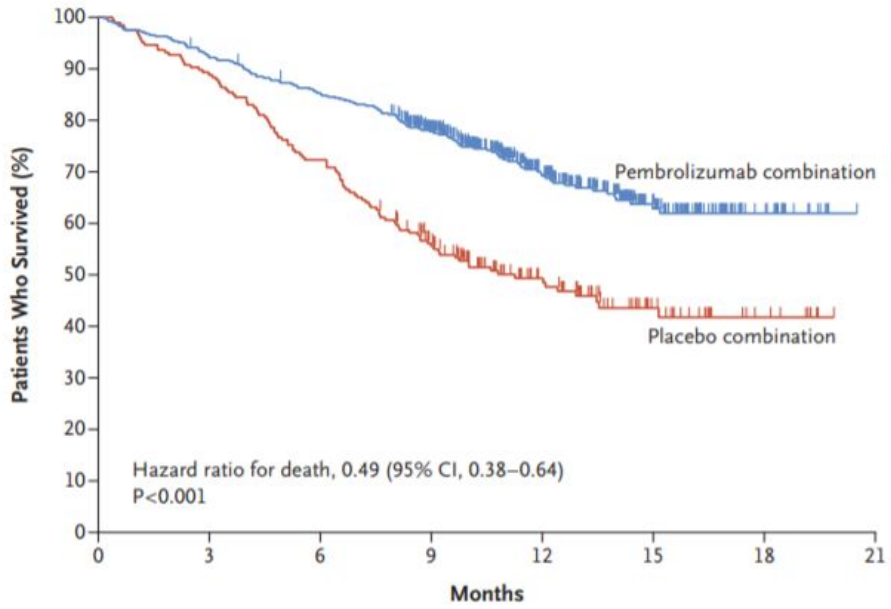
- Плоскоклеточный НМРЛ

Initial Systemic Therapy Options
Squamous Cell Carcinoma (PS 0-1)
No contraindications to the addition of pembrolizumab[c]
- **Pembrolizumab/carboplatin/paclitaxel[31,d] (category 1) (preferred)**
- **Pembrolizumab/carboplatin/albumin-bound paclitaxel[31,d] (category 1) (preferred)**
- **Pembrolizumab/cisplatin/paclitaxel[d]**
- **Pembrolizumab/cisplatin/albumin-bound paclitaxel[d]**

Contraindications to the addition of pembrolizumab[c]
- **Carboplatin/albumin-bound paclitaxel (category 1)[7]**
- **Carboplatin/docetaxel (category 1)[8]**
- **Carboplatin/gemcitabine (category 1)[11]**
- **Carboplatin/paclitaxel (category 1)[12]**
- **Cisplatin/docetaxel (category 1)[8]**
- **Cisplatin/etoposide (category 1)[14]**
- **Cisplatin/gemcitabine (category 1)[12,15]**
- **Cisplatin/paclitaxel (category 1)[16]**
- **Gemcitabine/docetaxel (category 1)[17]**
- **Gemcitabine/vinorelbine (category 1)[18]**

KEYNOTE 189: Pembrolizumab plus Chemo

A Overall Survival

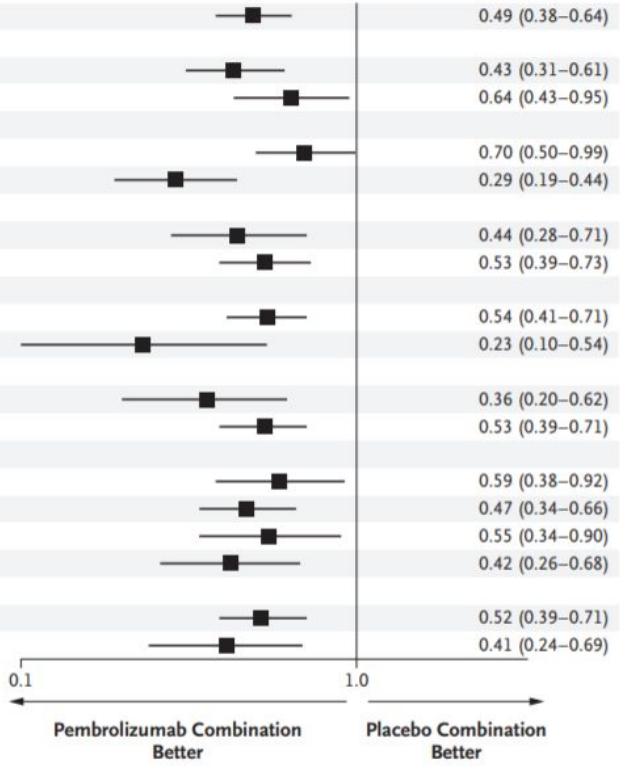


No. at Risk

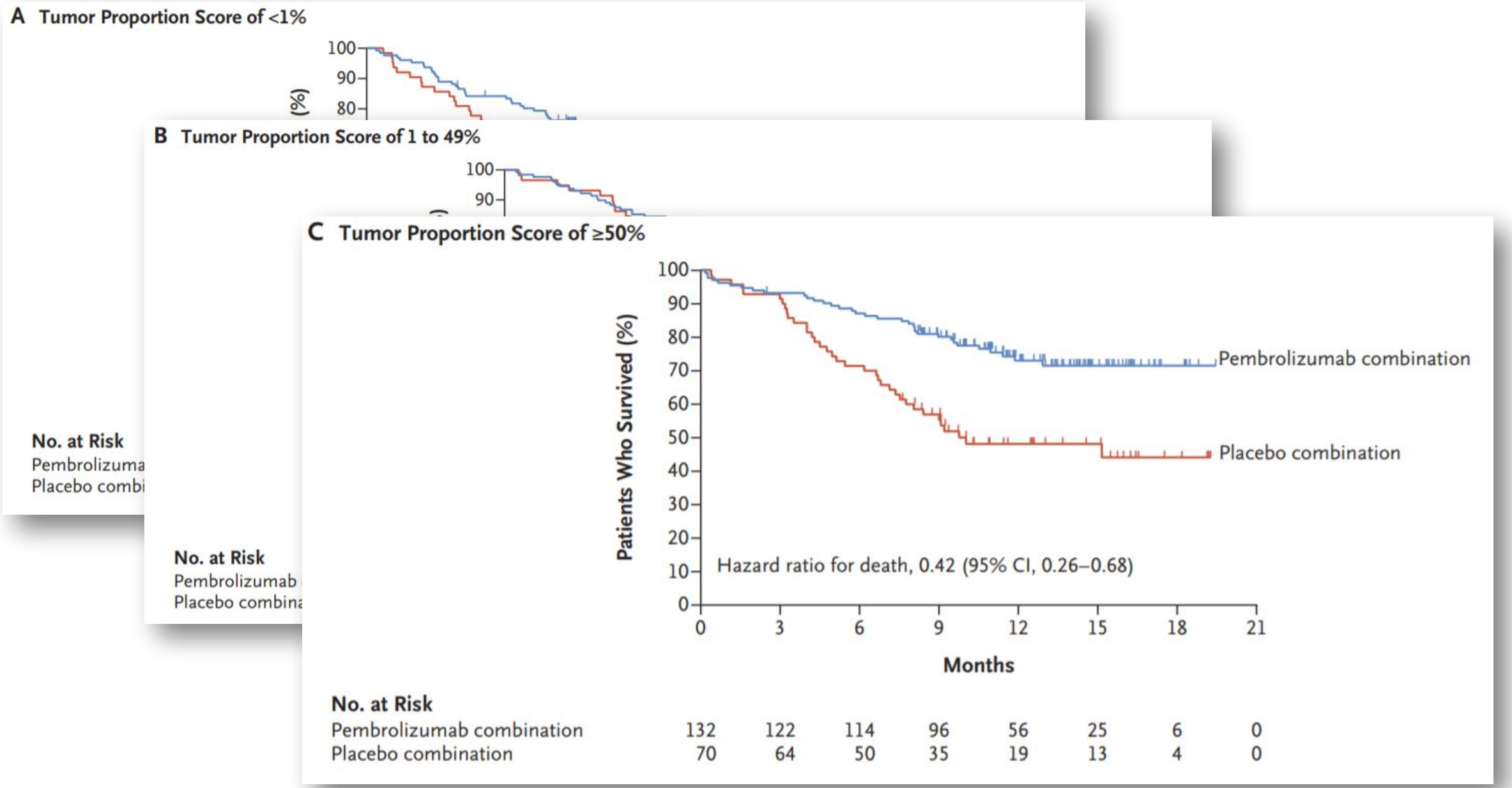
Pembrolizumab combination	410	377	347	278	163	71	18	0
Placebo combination	206	183	149	104	59	25	8	0

B Subgroup Analysis of Overall Survival

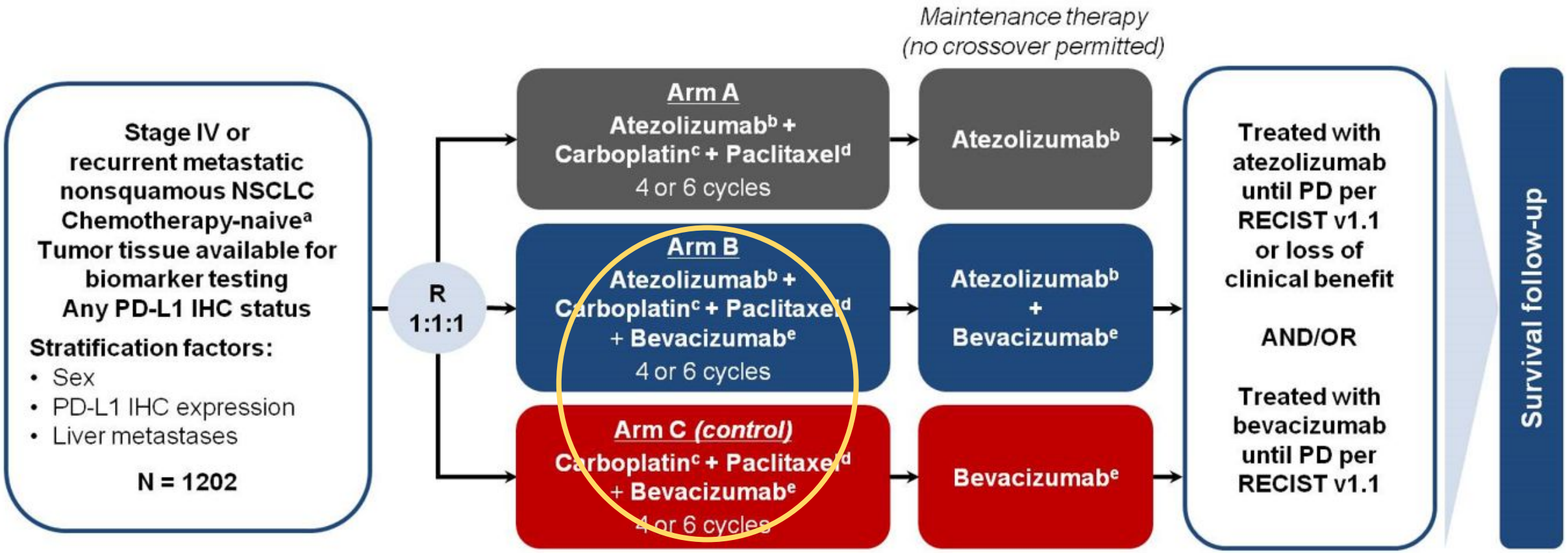
Subgroup	No. of Events/ No. of Patients	Hazard Ratio for Death (95% CI)
Overall	235/616	0.49 (0.38–0.64)
Age		
<65 yr	133/312	0.43 (0.31–0.61)
≥65 yr	102/304	0.64 (0.43–0.95)
Sex		
Male	143/363	0.70 (0.50–0.99)
Female	92/253	0.29 (0.19–0.44)
ECOG performance-status score		
0	74/266	0.44 (0.28–0.71)
1	159/346	0.53 (0.39–0.73)
Smoking status		
Current or former	211/543	0.54 (0.41–0.71)
Never	24/73	0.23 (0.10–0.54)
Brain metastases at baseline		
Yes	51/108	0.36 (0.20–0.62)
No	184/508	0.53 (0.39–0.71)
PD-L1 tumor proportion score		
<1%	84/190	0.59 (0.38–0.92)
≥1%	135/388	0.47 (0.34–0.66)
1–49%	65/186	0.55 (0.34–0.90)
≥50%	70/202	0.42 (0.26–0.68)
Platinum-based drug		
Carboplatin	176/445	0.52 (0.39–0.71)
Cisplatin	59/171	0.41 (0.24–0.69)



Gandhi, L., Rodríguez-Abreu, D., Gadgeel, S., Esteban, E., Felip, E., De Angelis, F., … Garassino, M. C. (2018). Pembrolizumab plus Chemotherapy in Metastatic Non–Small-Cell Lung Cancer. New England Journal of Medicine, 378(22), 2078–2092. doi:10.1056/nejmoa1801005


A Tumor Proportion Score of <1%
100
90
80
(%)
No. at Risk
Pembrolizuma
Placebo combi
B Tumor Proportion Score of 1 to 49%
100
90
No. at Risk
Pembrolizumab
Placebo combina
C Tumor Proportion Score of ≥50%
Patients Who Survived (%)
100
90
80
70
60
50
40
30
20
10
0
Pembrolizumab combination
Placebo combination
Hazard ratio for death, 0.42 (95% CI, 0.26–0.68)
0
3
6
9
12
15
18
21
Months
No. at Risk
Pembrolizumab combination 132 122 114 96 56 25 6 0
Placebo combination 70 64 50 35 19 13 4 0

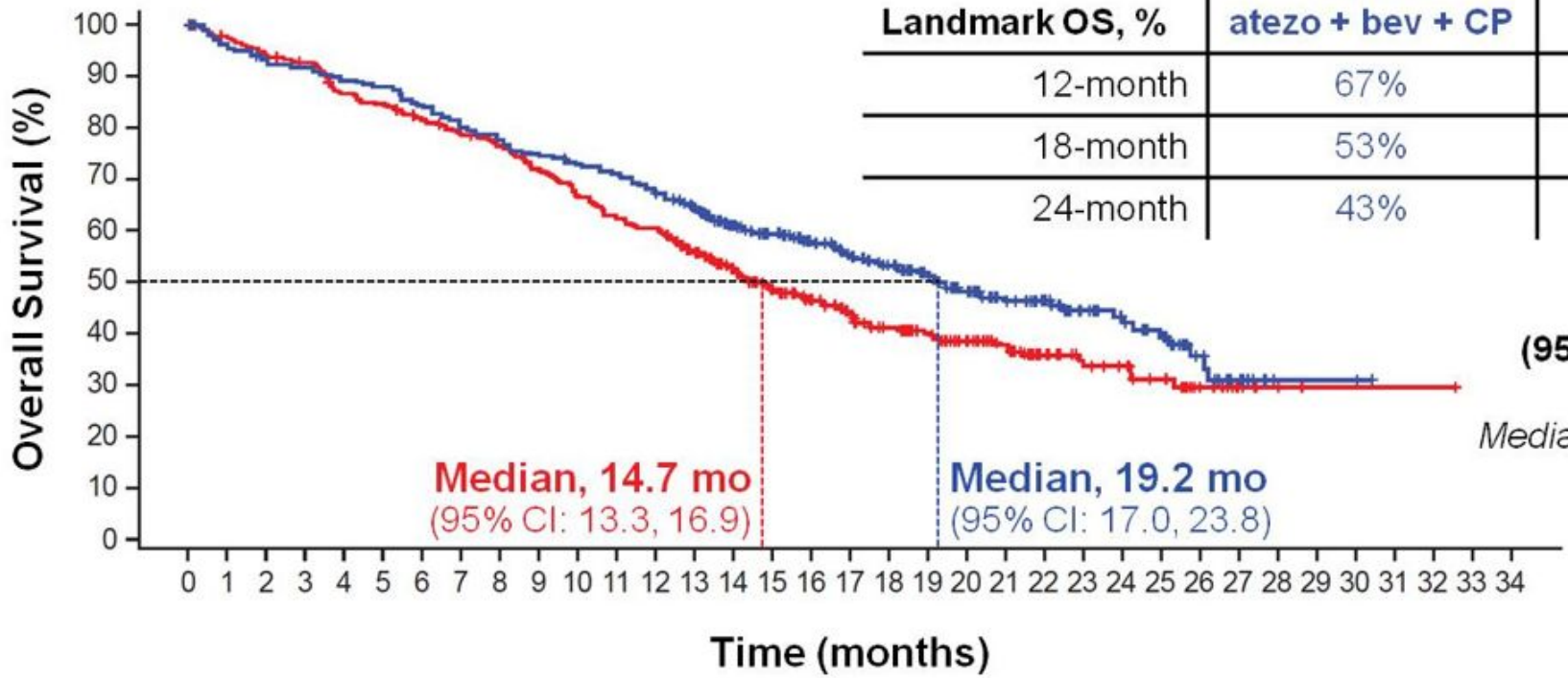
IMpower150 Study Design



[a] Patients with a sensitizing *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies.
[b] Atezolizumab: 1200 mg IV q3w. [c] Carboplatin: AUC 6 IV q3w. [d] Paclitaxel: 200 mg/m^2 IV q3w. [e] Bevacizumab: 15 mg/kg IV q3w.

OS in the ITT-WT (Arm B vs Arm C)

Landmark OS, %	Arm B: atezo + bev + CP	Arm C: bev + CP
12-month	67%	61%
18-month	53%	41%
24-month	43%	34%



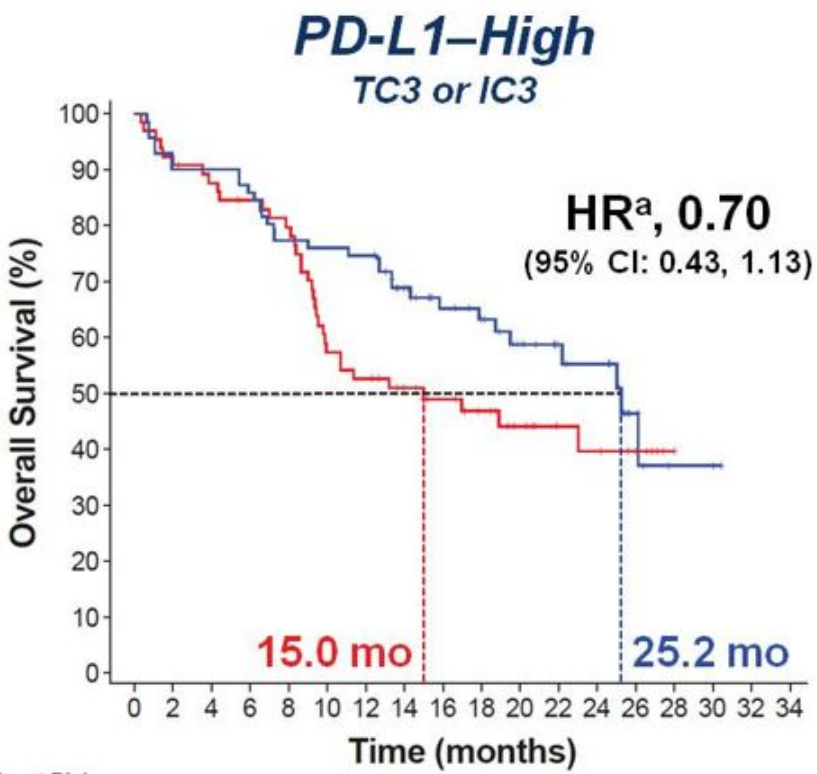
HR[a], 0.78
(95% CI: 0.64, 0.96)
***P* = 0.0164**
Median follow-up: ~20 mo

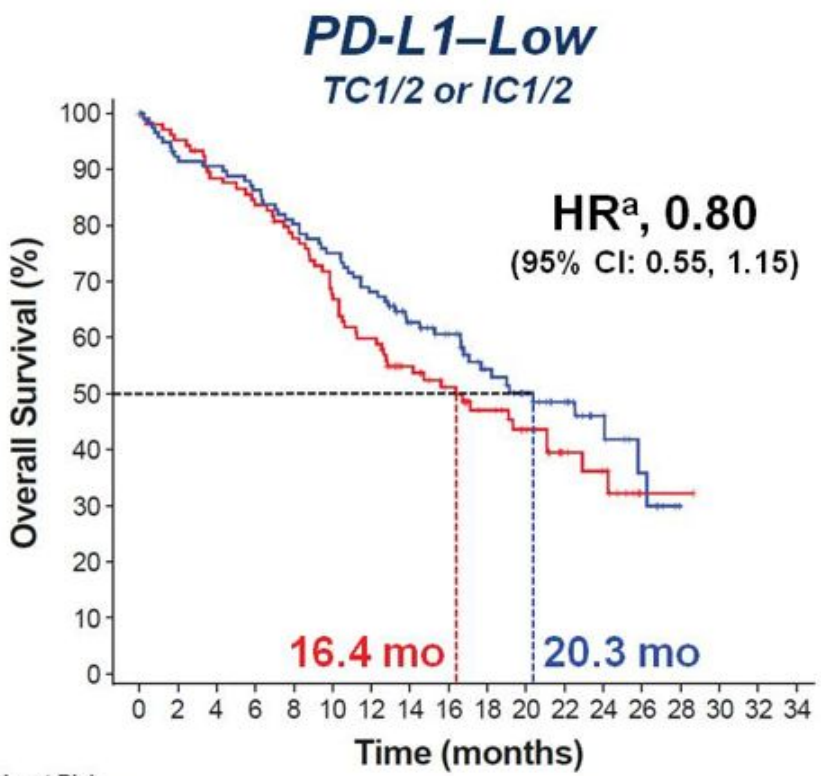
No. at Risk																																
Atezo+Bev+CP	359	339	328	323	314	310	296	284	273	264	256	250	235	218	188	167	147	133	119	103	84	66	57	41	34	28	16	9	2	2	2	
Bev+CP	337	326	315	308	287	280	268	255	247	233	216	203	196	174	152	129	115	101	87	77	66	56	40	32	29	22	13	6	3	1	1	1	1

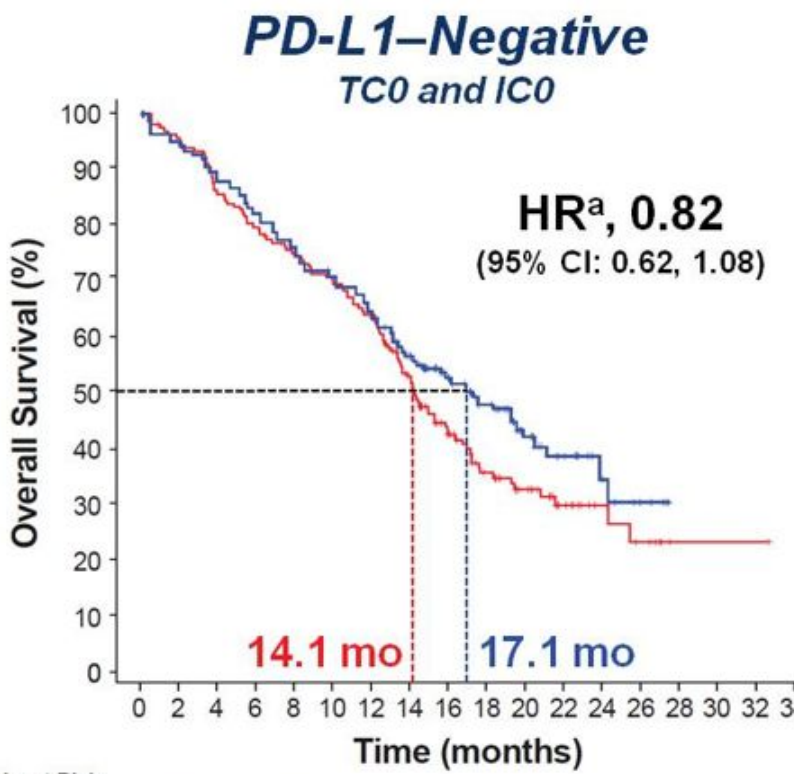
- Statistically significant and clinically meaningful OS benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy was observed

[a] Stratified HR.
Data cutoff: January 22, 2018

Survival Benefit Was Observed Across All PD-L1 Subgroups in the ITT-WT (Arm B vs Arm C)







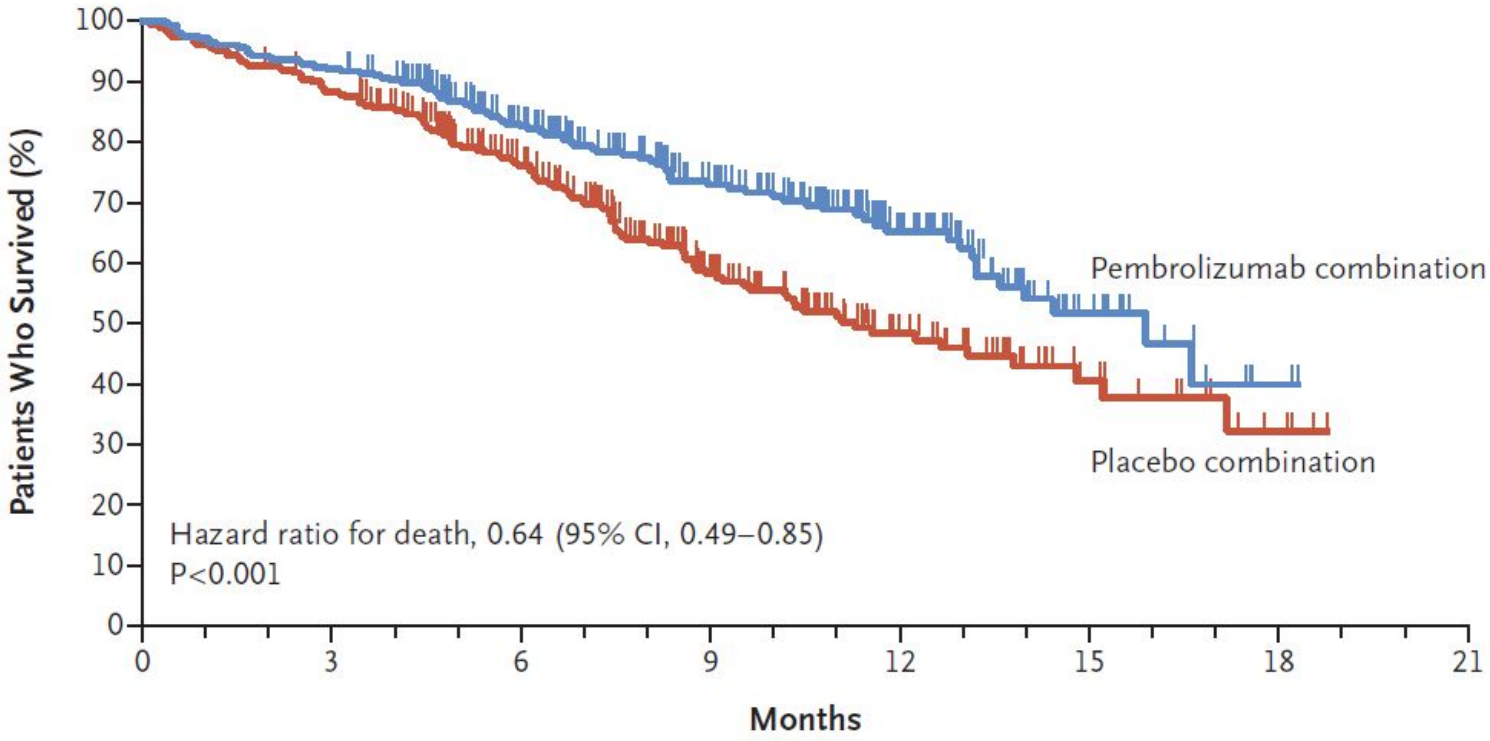
Atezo+Bev+CP Bev+CP

[a] Unstratified HR.
Data cutoff: January 22, 2018

KEYNOTE 407 (плоскоклеточный НМРЛ)

Медиана ОВ

- Pemrolizumab combi **15.9 м**
- Placebo combi 11.3 м
- 95% ДИ, 0.49-0.85; P <0.001
- Независимо от PD-L1



Paz-Ares, L., Luft, A., Vicente, D., Tafreshi, A., Gümüş, M., Mazières, J., … Kowalski, D. M. (2018). Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer. New England Journal of Medicine. doi:10.1056/nejmoa1810865

Выводы

- Лечение НМРЛ – сложная проблема современной онкологии
- Лечение: сочетание локальных и системных методов
- Разделение пациентов на группы, в основе которого лежат молекулярно-генетические тесты, позволяет добиваться гораздо лучших результатов в лечении

Благодарю за внимание!

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