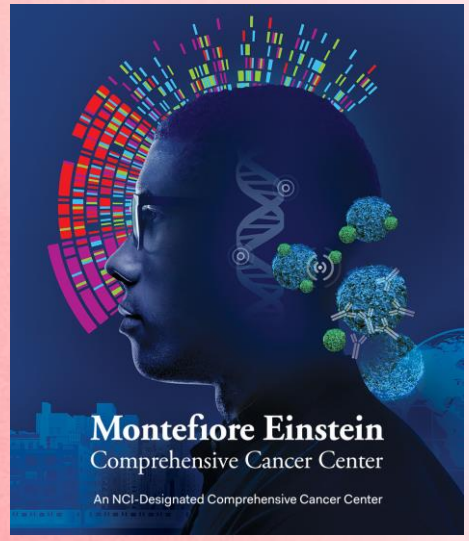


SURGICAL DOGMA, REALITY, AND ASPIRATIONS AFTER NEOADJUVANT THERAPY FOR NSCLC

Speaker: Brendon Stiles, MD
Albert Einstein College of Medicine,
Montefiore Einstein Comprehensive Cancer Center

@BrendonStilesMD

Endorsed by
IASLC International Association for the Study of Lung Cancer
Conquering Thoracic Cancers Worldwide

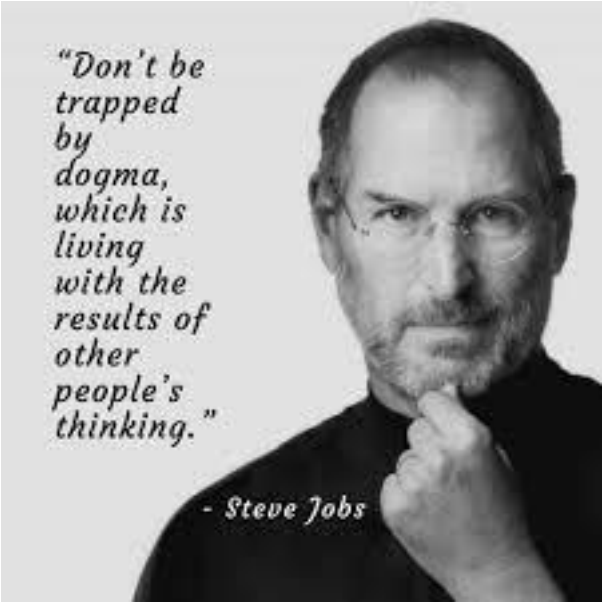
Accredited by
PIM Postgraduate Institute for Medicine
Professional Excellence in Medical Education

Presented by
IDEOlogy Health
Creating Aha! Moments In Healthcare

Surgical Dogma

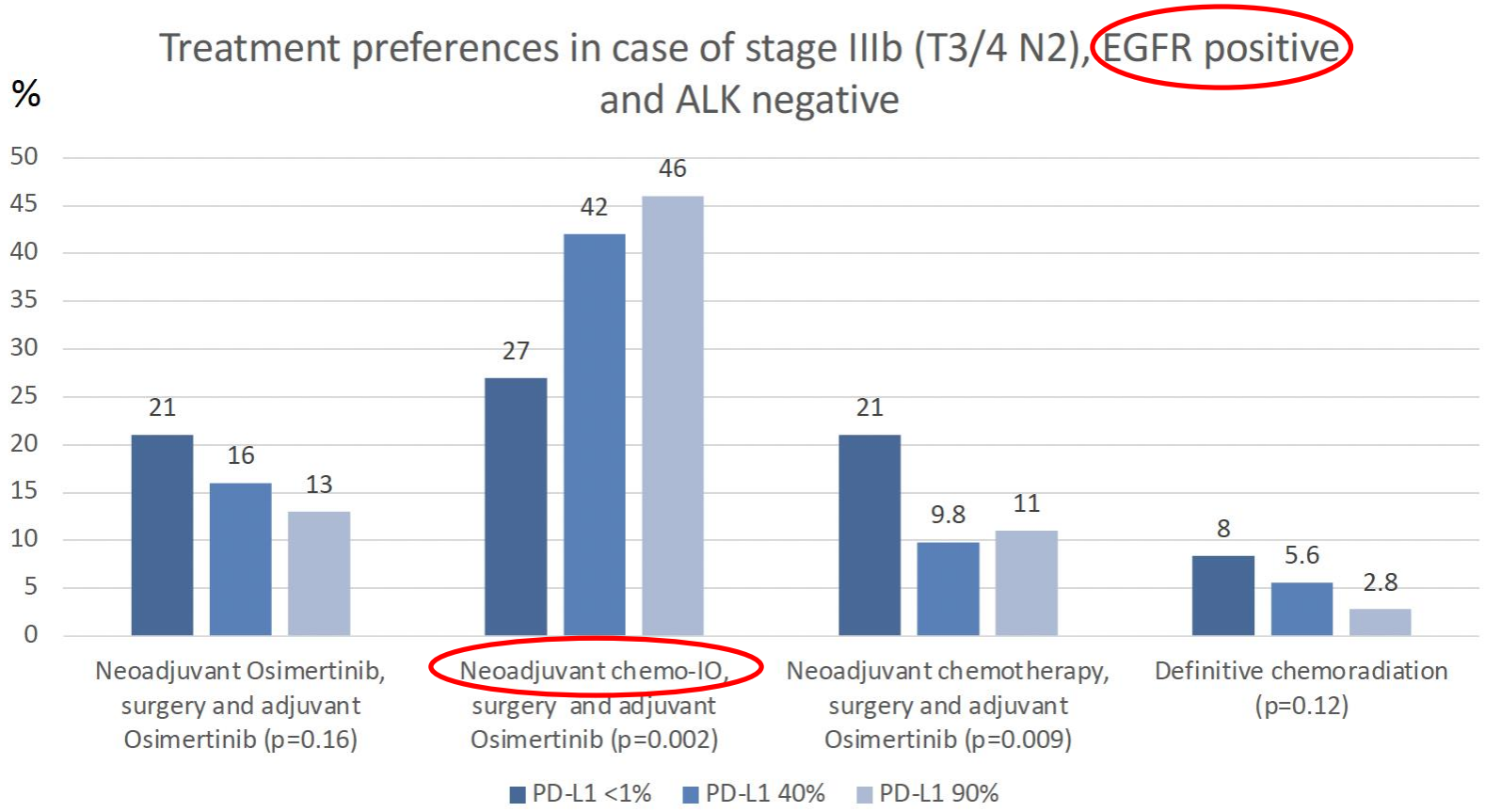
"A principle or set of principles laid down by an authority as incontrovertibly true"

1. The surgeon knows best and only surgeons can define resectability
2. A chance to cut is a chance to cure
3. Stage III NSCLC is a surgical disease
4. Preoperative therapy makes surgery really tough
5. We have to "get it all"



Dogma #1: The surgeon knows best…

Surgeon choices for OWN treatment in locally advanced non-small cell lung cancer: A European Society of Thoracic Surgeons and General Thoracic Surgical Club survey (Alessandro Brunelli et al.)



Only surgeons can define resectability… But…like beauty, it is in the eye of the beholder

"The establishment of criteria for treatment of carcinoma of the lung, especially operability and resectability, is particularly difficult….

…Criteria also vary from group to group, among individual surgeons, and, indeed for the same surgeon from time to time depending on his (her) recent experience."

The Criteria for Operability and Resectability in Lung Cancer

Eugene E. Clifton, MD

Clifton EE, et al. JAMA 1966 Mar 21;195:1031–2

Overcoming bias:
Can AI help us make better decisions?

Figure 2. Optimal and Suboptimal Approaches to Surgical Decision-making

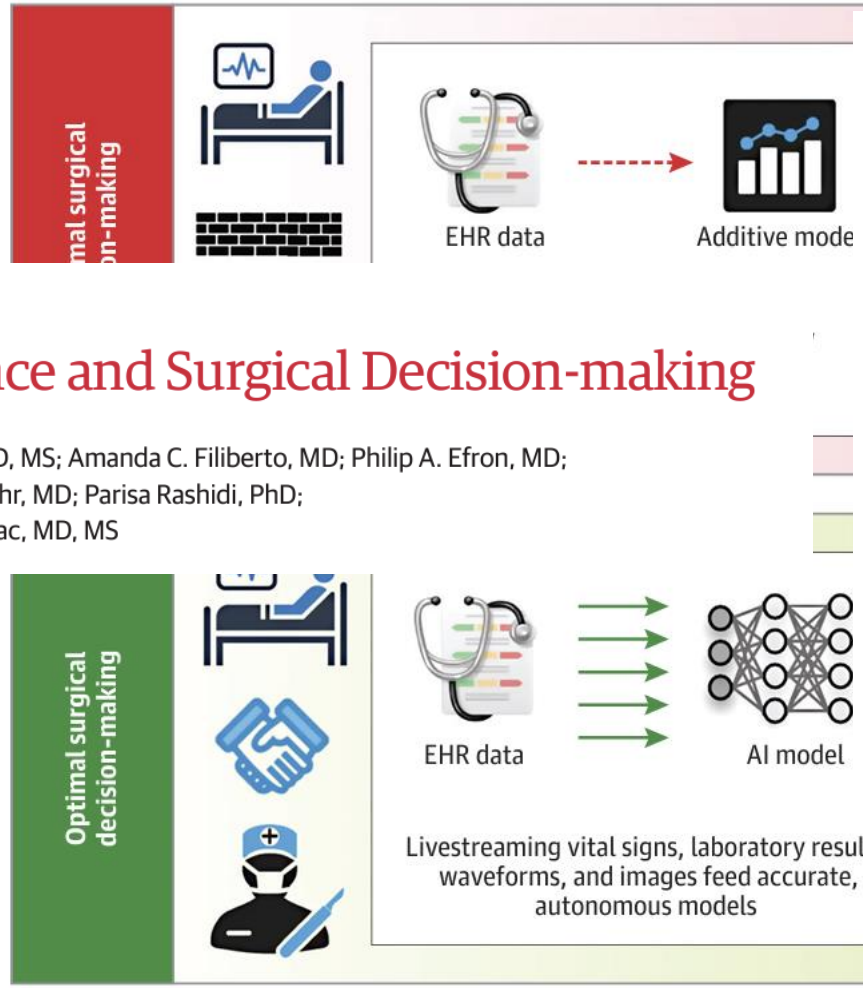


Table 2. Sources of Bias in Surgical Decision-making

Source of Bias	Examples
Framing effect	A clinician presents a clinical scenario to a surgeon in different context than the surgeon would have perceived during an independent assessment
Overconfidence bias	A surgeon falsely perceives that weaknesses and failures disproportionately affect their peers
Commission bias	A surgeon tends toward action when inaction may be preferable, especially in the context of overconfidence bias
Anchoring bias	Patients are informed of expected outcomes using data from aggregate patient populations without adjusting for their personalized risk profile
Recall bias	Recent experiences with a certain patient population or operation disproportionately affect surgical decision-making relative to remote experiences
Confirmation bias	Outcomes are predicted using personal beliefs rather than evidence-based guidelines

JAMA Surgery | Review

Artificial Intelligence and Surgical Decision-making

Tyler J. Loftus, MD; Patrick J. Tighe, MD, MS; Amanda C. Filiberto, MD; Philip A. Efron, MD; Scott C. Brakenridge, MD; Alicia M. Mohr, MD; Parisa Rashidi, PhD; Gilbert R. Upchurch Jr, MD; Azra Bihorac, MD, MS

JAMA Surg. 2020;155(2):148-158. doi:10.1001/jamasurg.2019.4917
Published online December 11, 2019.

Multidisciplinary teams can establish criteria for resectabilty; surgeons should better codify resectability

IASLC 2023 World Conference on Lung Cancer

SEPTEMBER 9-12, 2023 | SINGAPORE

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

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

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

§Some **T4 tumours by infiltration of major structures** are potentially resectable – see Table 1

Biniam Kidane
@biniamkidaneMD

Reposting my thoughts about developing an explicit and objective taxonomy of resectability as I've been getting a lot of questions about it recently. See thread below.
Bottom line: we need to get on the same page & remove linguistic/semantic imprecision about this #tssmn #lcsm

Biniam Kidane @biniamkid... · 8/19/23
1/problem = resectability has always been shrouded in the realm of nebulous subjectivism
Remedy = transparent taxonomy that allows us to clarify our thinking,commun...

European Journal of Cardio-Thoracic Surgery 2024, 65(3), ezae009
https://doi.org/10.1093/ejcts/ezae009 Advance Access publication 23 January 2024

ORIGINAL ARTICLE

Cite this article as: Rodriguez-Quintero JH, Elbahrawy MM, Montal AM, Jindani R, Vimolratana M, Kamel MK *et al.* Minimally invasive surgery for clinical T4 non-small-cell lung cancer: national trends and outcomes. Eur J Cardiothorac Surg 2024; doi:10.1093/ejcts/ezae009.

Minimally invasive surgery for clinical T4 non-small-cell lung cancer: national trends and outcomes

Jorge Humberto Rodriguez-Quintero [a], Mostafa M. Elbahrawy[a], Anne Michelle Montal[a], Rajika Jindani[a], Marc Vimolratana[a], Mohamed K. Kamel [b], Brendon M. Stiles[a] and Neel P. Chudgar [a,*]

[a] Department of Cardiothoracic and Vascular Surgery, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, USA
[b] Division of Thoracic and Foregut Surgery, University of Rochester Medical Center, Rochester, NY, USA

Minimally Invasive Surgery for Clinical T4 Non-Small Cell Lung Cancer National Trends and Outcomes

Key Question

- **P**: Patients with clinical T4 non-small cell lung cancer in the National Cancer Database.
- **I**: Minimally invasive surgery vs. open surgery
- **C**: Pathologic upstaging, trends over time and overall survival.
- **O**:Minimally invasive surgery has increased over time without compromising oncologic outcomes.

Take-home message

- In appropriately selected patients, minimally invasive surgery is safe and feasible.

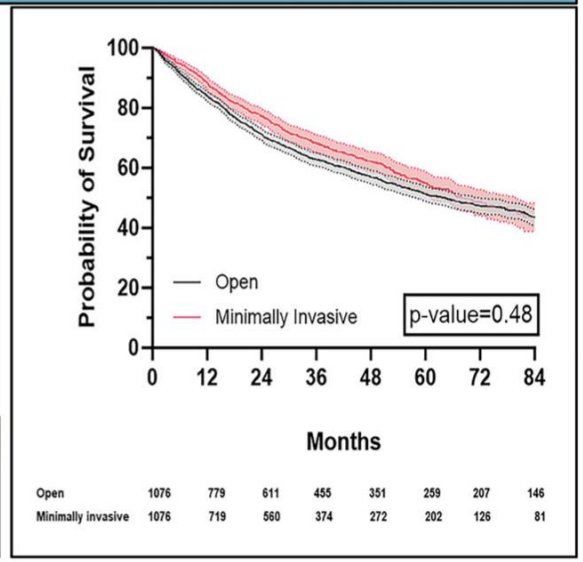


Figure : Survival analysis of minimally invasive vs. open surgery

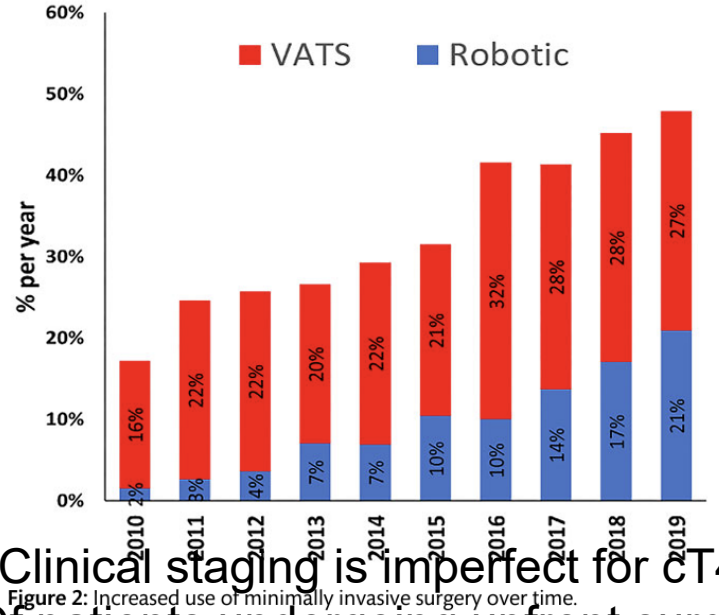
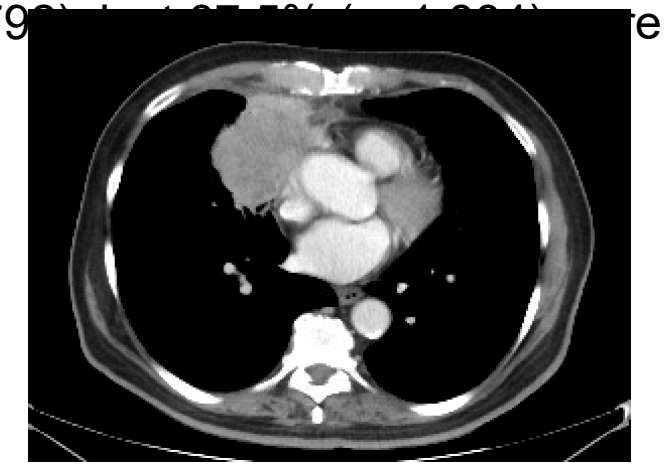


Figure 2: Increased use of minimally invasive surgery over time.

Clinical staging is imperfect for cT4:
Of patients undergoing upfront surgery
(n=2,79 e pT4

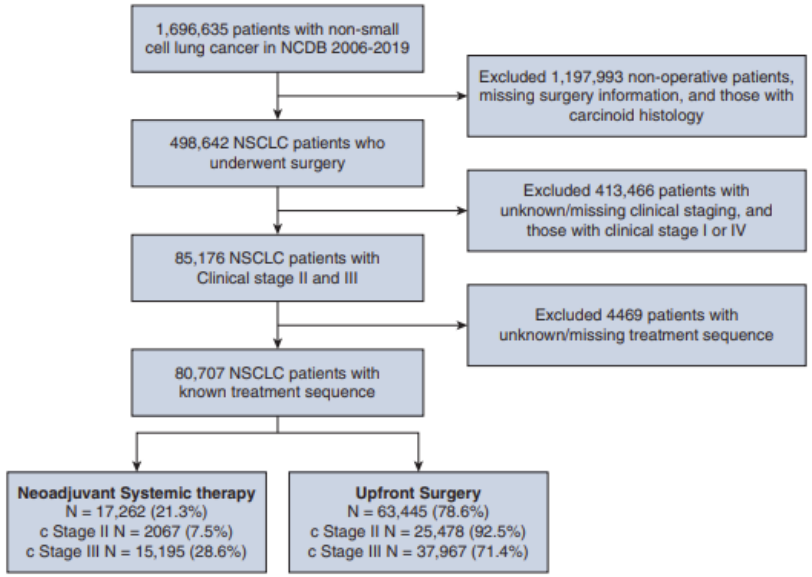


Dogma #2: A chance to cut is a chance to cure…

Association of socioeconomic factors with the receipt of neoadjuvant therapy for patients with non–small cell lung cancer

Mostafa M. Elbahrawy, MD,[a] Mohamed K. Kamel, MD,[b] J. Humberto Rodriguez-Quintero, MD,[a] Marc Vimolratana, MD,[a] Neel P. Chudgar, MD,[a] and Brendon M. Stiles, MD[a]

The Journal of Thoracic and Cardiovascular Surgery • April 2024



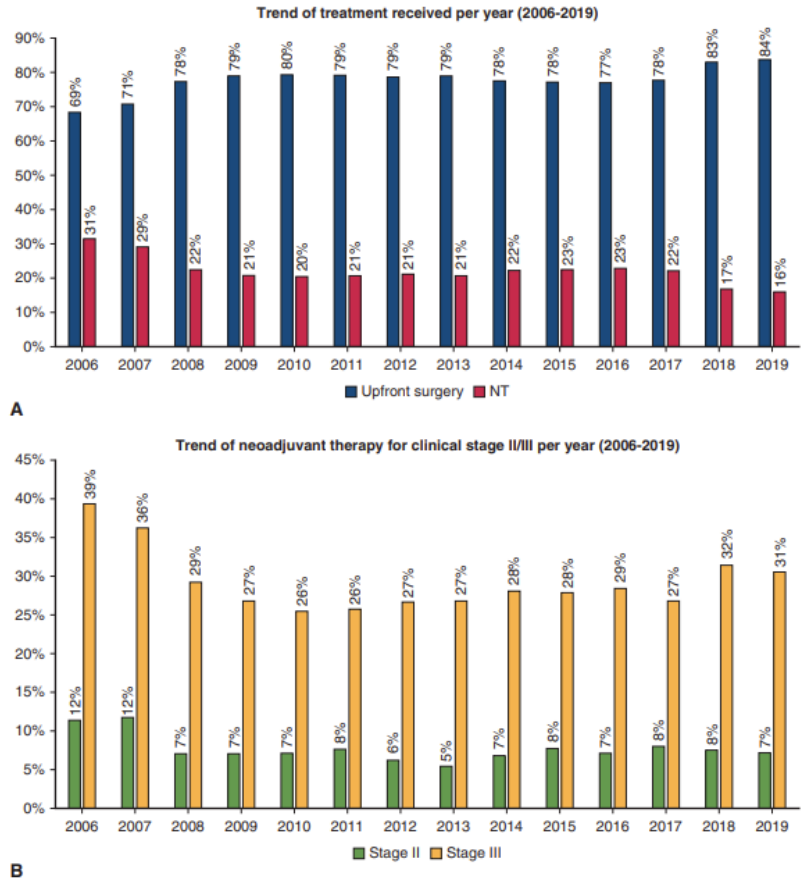


FIGURE 2. Trends in the use of neoadjuvant therapy overtime (2006-2019). A, Proportion of patients receiving upfront surgery of NT stratified by year of diagnosis. B, Proportion of patients who received NT by stage stratified by year of diagnosis. *NT*, Neoadjuvant therapy.

Dogma #2: A chance to cut is a chance to cure…

OXFORD

BJS Open, 2024, zrae008
https://doi.org/10.1093/bjsopen/zrae008
Original Article

Upfront surgery for stage IIIA/B non-small cell lung cancer: retrospective cohort study

Hongsheng Deng[1,†], Jun Liu[1,†], Xiuyu Cai[2,†], Shunjun Jiang[1,3,†], Weixiang Lu[1], Qing Ai[1], Jianfu Li[1], Shan Xiong[1], Xiangyun Qin[4], Wenhua Liang[1,*] and Jianxing He[1,*]

[1]Department of Thoracic Surgery and Oncology, The First Affiliated Hospital of Guangzhou Medical University, State Key Laboratory of Respiratory Disease, National Clinical Research Centre for Respiratory Disease, Guangzhou Institute of Respiratory Health, Guangzhou, China
[2]Department of General Internal Medicine, Sun Yat-sen University Cancer Centre, State Key Laboratory of Oncology in South China, Collaborative Innovation Centre for Cancer Medicine, Guangzhou, China
[3]Department of Pharmacy, The First Affiliated Hospital of Guangzhou Medical University, State Key Laboratory of Respiratory Disease, National Clinical Research Centre for Respiratory Disease, Guangzhou Institute of Respiratory Health, Guangzhou, China
[4]LinkDoc Technology Co. Ltd, Beijing, China

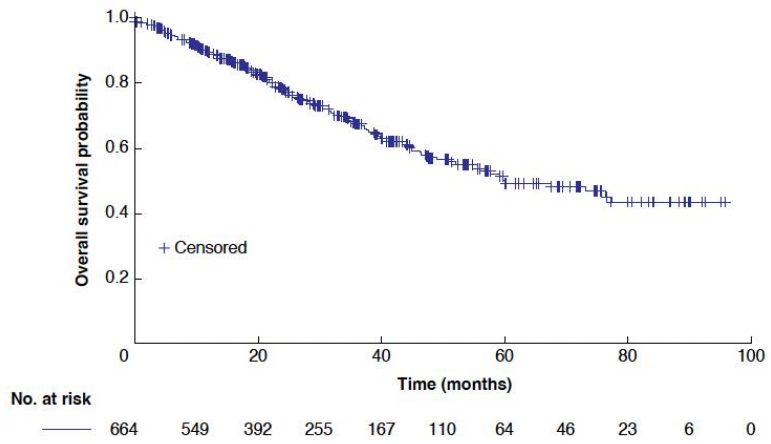


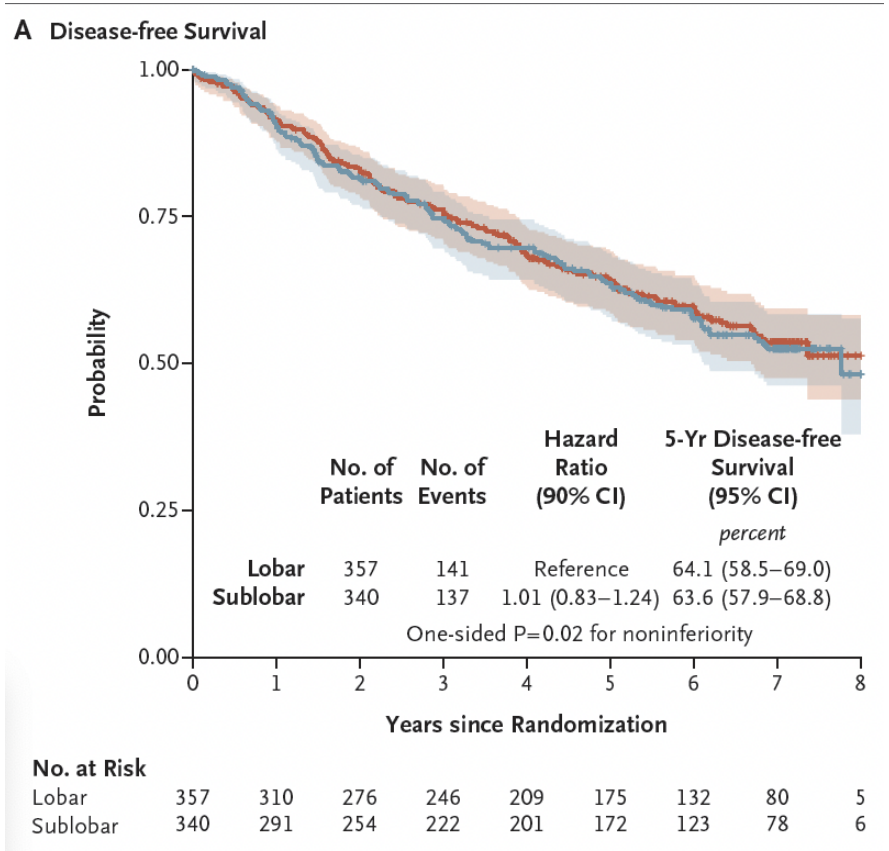
Fig. 1 Kaplan–Meier curve of overall survival for the included patients

Table 3 Postoperative outcomes of all included patients ($n = 664$)

Variable	Value
Adjuvant therapy	473 (71.23)
Chemotherapy	330 (49.70)
Targeted therapy	65 (9.79)
Chemotherapy + anti-angiogenic therapy	24 (3.61)
Chemotherapy + radiotherapy	23 (3.46)
Chemotherapy + targeted therapy	8 (1.20)
Other	23 (3.46)
Recurrence rate at the last follow-up time	247 (37.20)
Recurrence site (for all patients with recurrence)	
Lung	111 (50.45)
Brain	55 (25.00)
Skeleton	43 (19.54)
Liver	19 (8.64)
Lymph node	15 (6.82)
Other	41 (18.64)
Recurrence-free survival probability, %	
1.0 year	74.1
2.0 years	57.4
3.0 years	43.5
5.0 years	26.4
Overall survival (months), median (95% c.i.)	60.0 (51.5,67.6)
Overall survival probability, %	
1.0 year	89.6
2.0 years	77.8
3.0 years	67.2
5.0 years	49.0
Survival status	
Death	202 (30.42)
Live	372 (56.02)
Missing	90 (13.55)

Values are *n* (%) unless otherwise indicated.

Maybe we don't cure as many patients as we like to think…CALGB 140503



The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 FEBRUARY 9, 2023 VOL. 388 NO. 6

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S., Rodney Landrenau, M.D., Dennis Wigle, M.D., Ph.D., Jeffrey Port, M.D., David R. Jones, M.D., Massimo Conti, M.D., Ahmad S. Ashrafi, M.D., Moishe Liberman, M.D., Ph.D., Kazuhiro Yasufuku, M.D., Ph.D., Stephen Yang, M.D., John D. Mitchell, M.D., Harvey Pass, M.D., Robert Keenan, M.D., Thomas Bauer, M.D.,

Table 2. Patterns of Recurrence.

Type of Recurrence	Sublobar Resection (N=336)	Lobar Resection (N=351)	Difference (95% CI)*
	number (percent)		*percentage points*
Overall	102 (30.4)	103 (29.3)	1.0 (–5.8 to 7.9)
Locoregional recurrence	45 (13.4)	35 (10.0)	3.4 (1.0 to 8.3)
Regional recurrence only	6 (1.8)	9 (2.6)	–0.8 (–3.2 to 1.6)
Any distant recurrence	51 (15.2)	59 (16.8)	–1.6 (–7.1 to 3.9)
New primary lung cancer	60 (17.9)	52 (14.8)	3.0 (–2.5 to 8.6)

Dogma #3: Stage III NSCLC is a surgical disease

Management of Stage III Non–Small-Cell Lung Cancer: ASCO Guideline

Megan E. Daly, MD[1]; Navneet Singh, MD, DM[2]; Nofisat Ismaila, MD, MSc[3]; Mara B. Antonoff, MD[4]; Douglas A. Arenberg, MD[5]; Jeffrey Bradley, MD[6]; Elizabeth David, MD[7]; Frank Detterbeck, MD[8]; Martin Früh, MD[9,10]; Matthew A. Gubens, MD, MS[11]; Amy C. Moore, PhD[12]; Sukhmani K. Padda, MD[13]; Jyoti D. Patel, MD[14]; Tanyanika Phillips, MD, MPH[15]; Angel Qin, MD[5]; Clifford Robinson, MD[16]; and Charles B. Simone II, MD[17]

Surgery.

Recommendation 2.1. For patients with stage IIIA (N2) NSCLC, induction therapy followed by surgery (with or without adjuvant therapy) may be offered if all of the following conditions are met: (1) A complete resection (R0) of the primary tumor and involved lymph nodes is deemed possible; (2) N3 lymph nodes are deemed to be not involved by multidisciplinary consensus; (3) Perioperative (90-day) mortality is expected to be low (≤ 5%) (Type: Evidence based; balance of benefit and harm; Evidence quality: moderate; Strength of recommendation: weak).

J Clin Oncol 40:1356-1384. © 2021 by American Society of Clinical Oncology

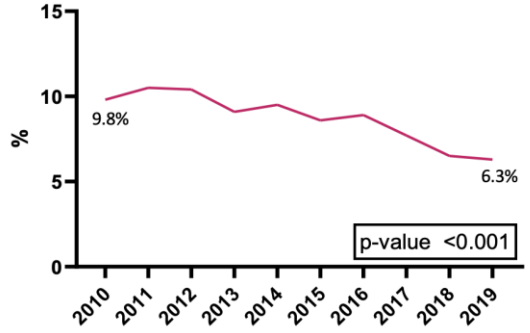
Although avoiding surgery if not proven to be beneficial is a reasonable recommendation, there are factors that justify consideration of surgery in a multimodality approach.

As a first step, evaluate for factors that argue against surgery.

STS 2024

Proportion of patients undergoing surgery by year of diagnosis

cT3/4N2



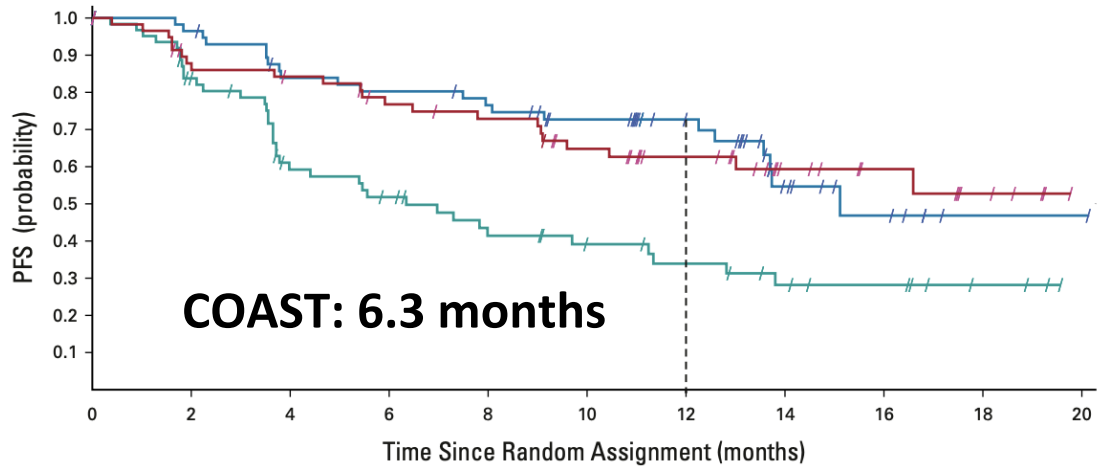
Jorge Humberto Rodríguez Quintero MD @huroqu90

#STS2024

PACIFIC was a groundbreaking trial with incredible results, but…maybe it is time to rethink the paradigm…

Durvalumab Plus Novel Agents for Unresectable, Stage III NSCLC

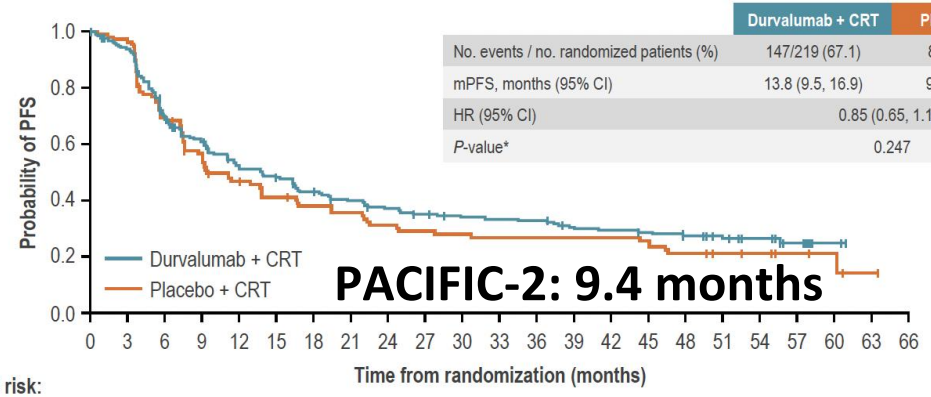
Treatment Arm	No. of Events/ Total No. of Patients (%)	Median PFS, Months (95% CI)[a]	12-Month PFS Rate, % (95% CI)	HR, % (95% CI)[b,c]
Durvalumab + monalizumab	21/62 (33.9)	15.1 (13.6 to NE)	72.7 (58.8 to 82.6)	0.42 (0.24 to 0.72)
Durvalumab + oleclumab	22/60 (36.7)	NR (10.4 to NE)	62.6 (48.1 to 74.2)	0.44 (0.26 to 0.75)
Durvalumab	38/67 (56.7)	6.3 (3.7 to 11.2)	33.9 (21.2 to 47.1)	–



J Clin Oncol 40:3383-3393. © 2022 by American Society of Clinical Oncology

PFS by BICR (ITT population)

	Durvalumab + CRT	Placebo + CRT
No. events / no. randomized patients (%)	147/219 (67.1)	80/109 (73.4)
mPFS, months (95% CI)	13.8 (9.5, 16.9)	9.4 (7.5, 16.6)
HR (95% CI)	0.85 (0.65, 1.12)	
P-value*	0.247	



No. at risk:																							
Durvalumab + CRT	219	199	145	124	102	94	83	75	69	64	60	59	58	50	49	47	43	28	24	10	2	0	0
Placebo + CRT	109	104	72	58	44	38	34	32	28	26	25	24	24	24	24	23	19	15	12	7	3	1	0

elcc European Lung Cancer Congress 2024

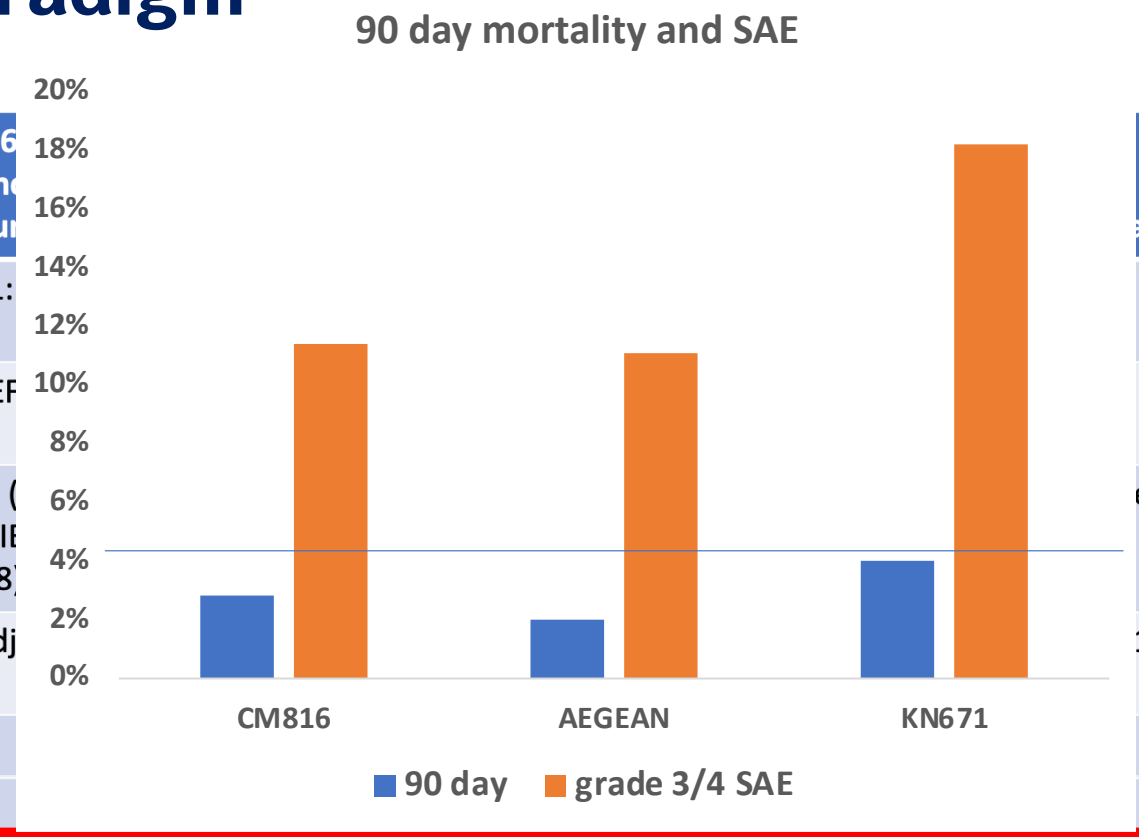
BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mPFS, median PFS; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

Per RECIST v1.1. Tick marks on the curves indicate censored observations. *Based on the Lan and DeMets approach that approximates the O'Brien Fleming spending functions; the 2-sided p-value boundary for declaring statistical significance is 0.0416 for an overall 5% alpha.

LBA1 – Durvalumab in Combination with Chemoradiotherapy for Patients with Unresectable, Stage III NSCLC: Final Results from PACIFIC-2

Jeffrey D. Bradley,[1] Shunichi Sugawara,[2] Ki Hyeong Lee,[3] Gyula Ostoros,[4] Ahmet Demirkazik,[5] Milada Zemanova,[6] Virote Sriuranpong,[7] Ana Caroline Zimmer Gelatti,[8] Juliana Janoski de Menezes,[9] Bogdan Zurawski,[10] Michael Newton,[11] Pratibha Chander,[11] Nan Jia,[12] Zofia F. Bielecka,[13] Mustafa Özgüroğlu[14]

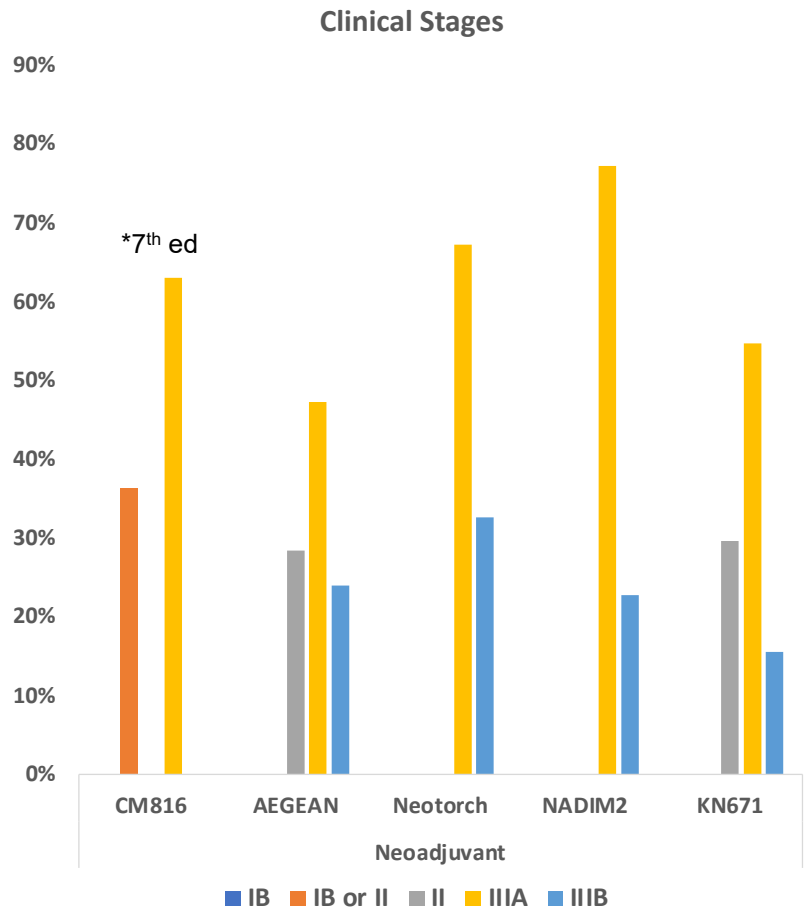
We have a new paradigm

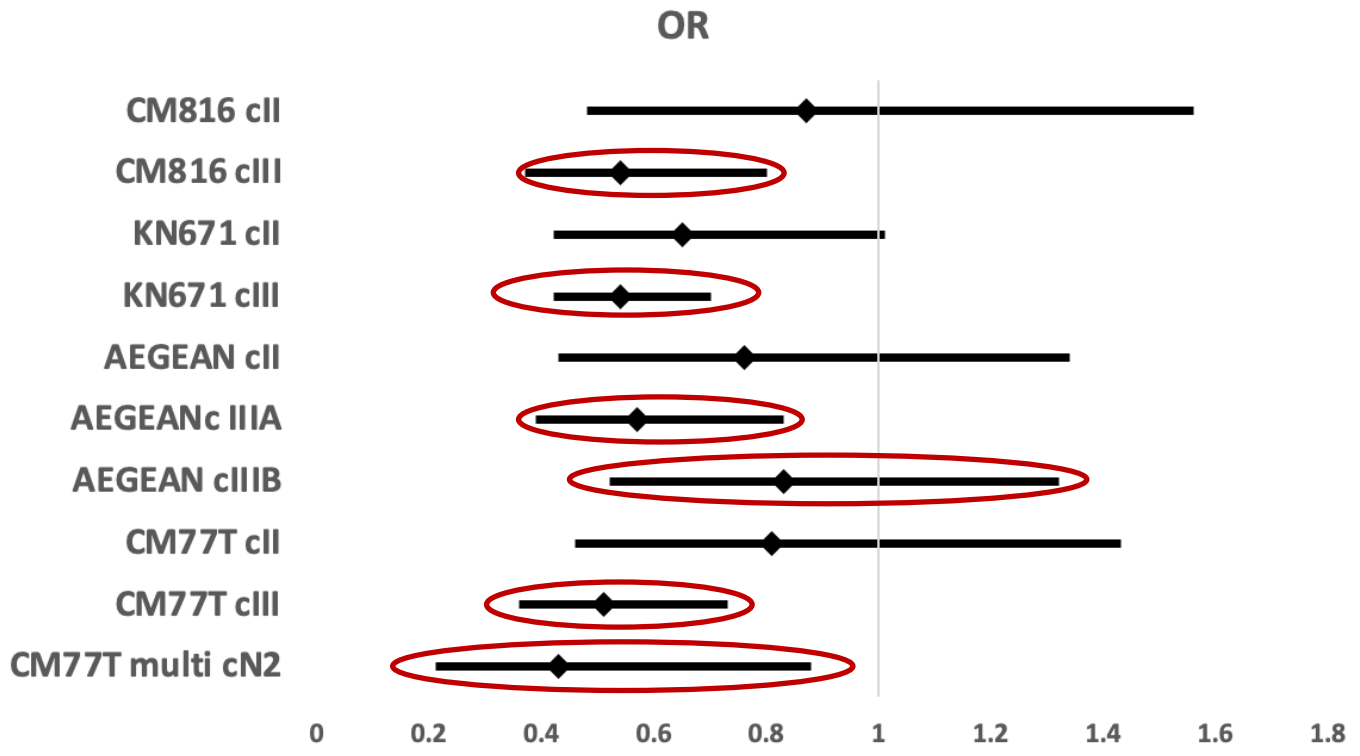


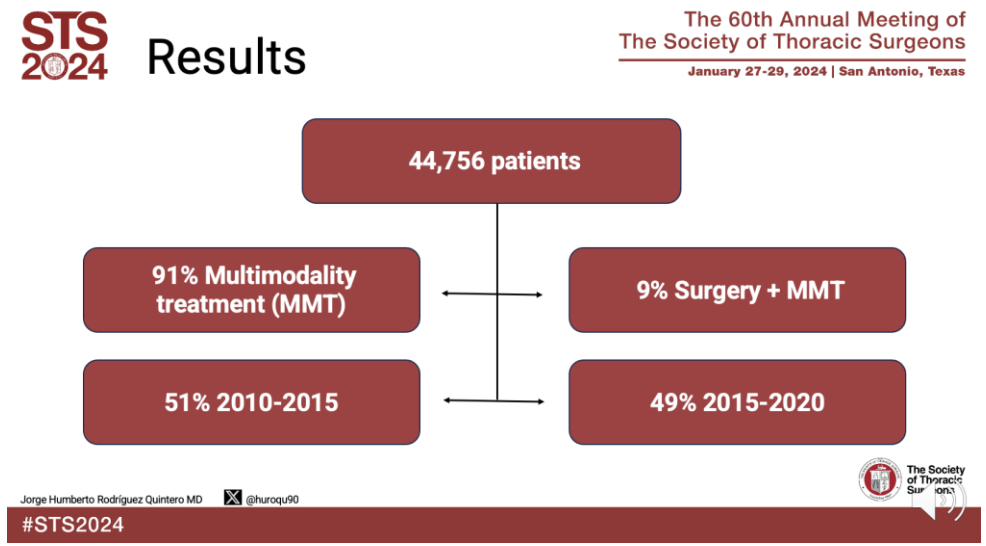
	CM816 (Chemo Nivolu				ab)	CM77T (Chemo-Nivolumab)
Randomized	358 (1:					461 (1:1)
Endpoints	PCR, EF					EFS, OS, PCR
Stages	IB-IIIA (or II-IIIE (AJCC8)				e)	II-IIIB (N2 stage)
Systemic plan	Neoadj				12	Periadj (Adj = 12 mo)
Surgery	83%					78%
R0 rate	83%					89%
EFS @ 2 years	65%	66% (PFS)	63.3%	67%	62.4%	70% (18 mo)
OS @ 2 years	82.7%* (HR 0.57, 95% CI 0.38-0.87)	84.7%* (HR 0.40, 95% CI 0.17-0.34, p=0.034)	NR	81.2%	80.9%	NR

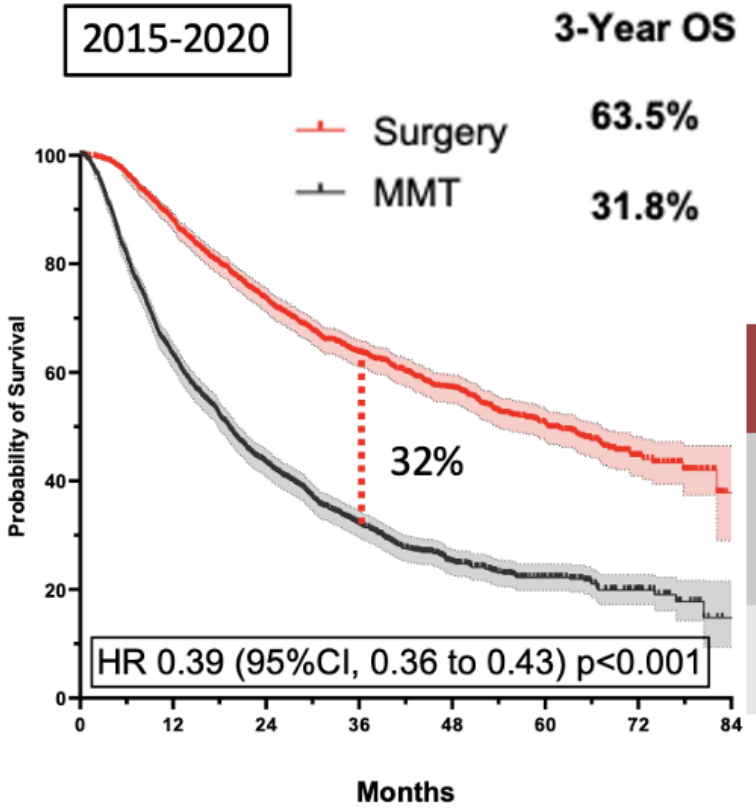
Adapted from Jonathan Spicer

Stage III NSCLC *is* a surgical disease (when neoadjuvant chemo/ICI is utilized)









N=3,342	Median OS
MMT	19 months
S	60 months
Difference	**41 months**

Dogma #4: Preoperative therapy makes surgery really tough .....early series generated bias

Extent of resection (n = 20), n (%)	
Lobectomy	15 (75)
Pneumonectomy	2 (10)
Wedge	1 (5)
Sleeve lobectomy	1 (5)
Bilobectomy	1 (5)
Approach (n = 20), n (%)	
Thoracotomy	14 (70)
Thoracoscopy	3 (14)
Robotic	3 (14)

50% conversion rate

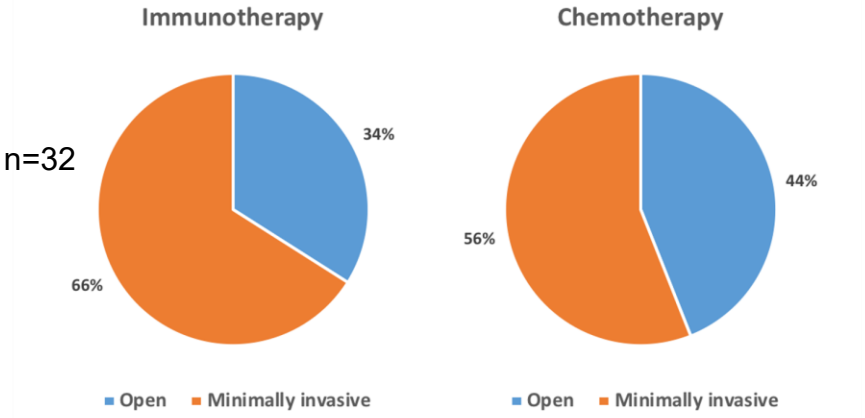
Extent of resection (n = 20)	Value, n (%)
Median surgical time, min (range)	228 (132-312)
Median estimated blood loss, mL (range)	100 (25-1,000)
Median length of stay, d (range)	4 (2-17)
Operative mortality	0[a]
Any morbidity	10 (50)
Atrial arrhythmia	6 (30)
Pneumonia	1 (5)
Pulmonary embolism	1 (5)
Myocardial infarction	1 (5)
Prolonged air leak	1 (5)
Urinary retention	1 (5)
Empyema	1 (5)

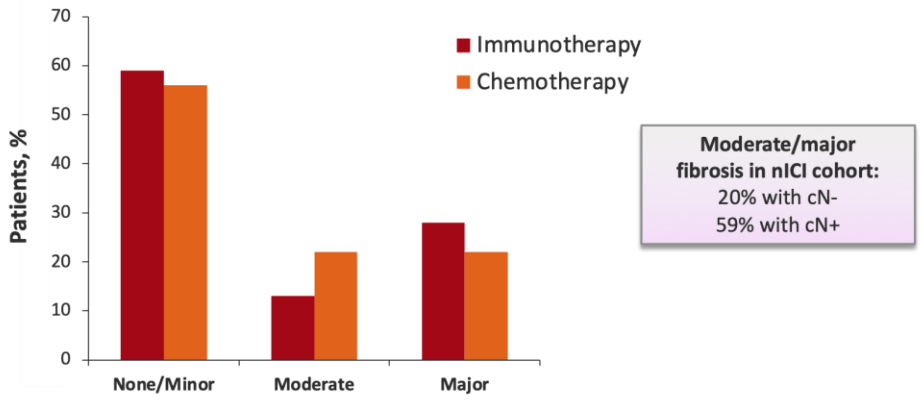
1. Bott MJ et al. *J Thorac Cardiovasc Surg*. 2018. pii: S0022-5223(18)33277-X.

NEJM: Neoadjuvant nivolumab (MSKCC, JHU)

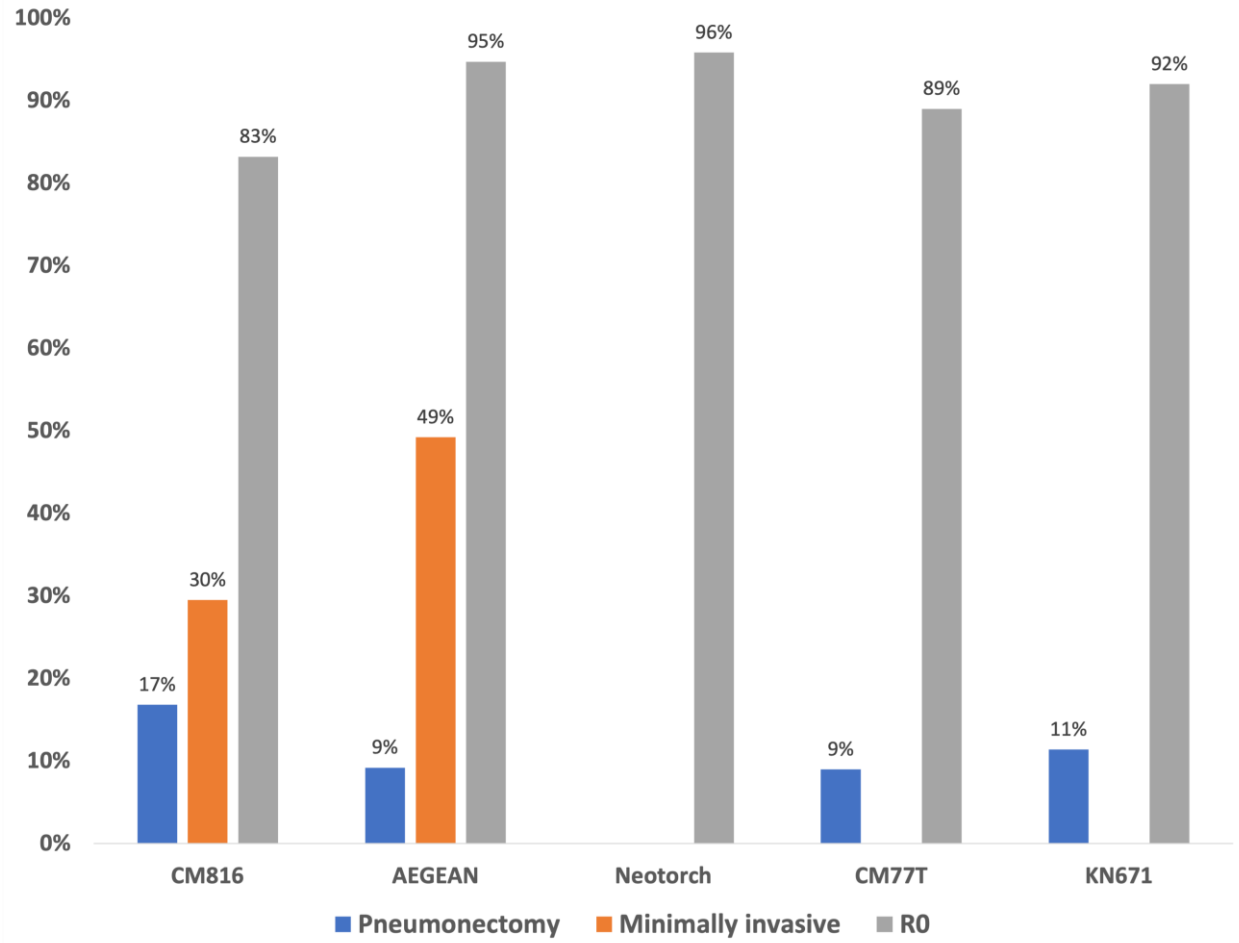
It’s not THAT tough….

n=32



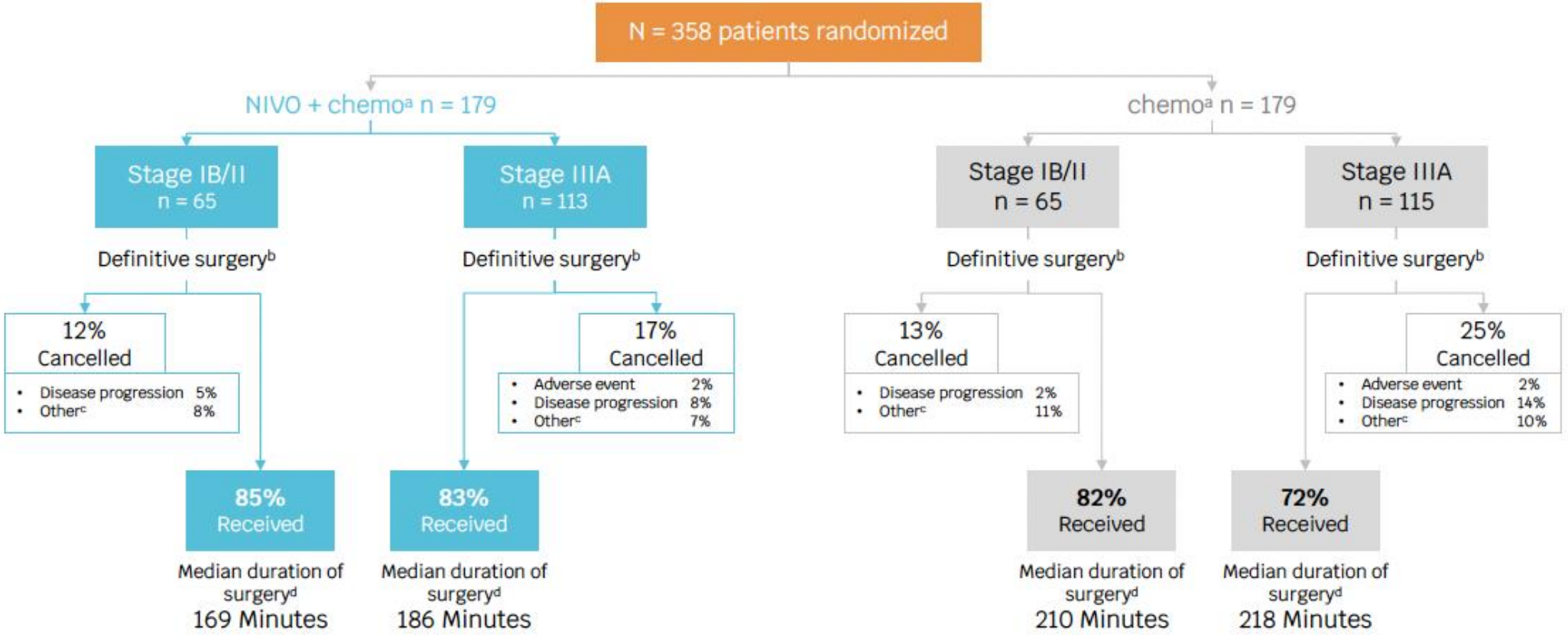


Moderate/major fibrosis in nICI cohort:
20% with cN-
59% with cN+



1. Stiles BM et al. AATS 2019. Abstract 22.

The surgical tipping point: CheckMate 816

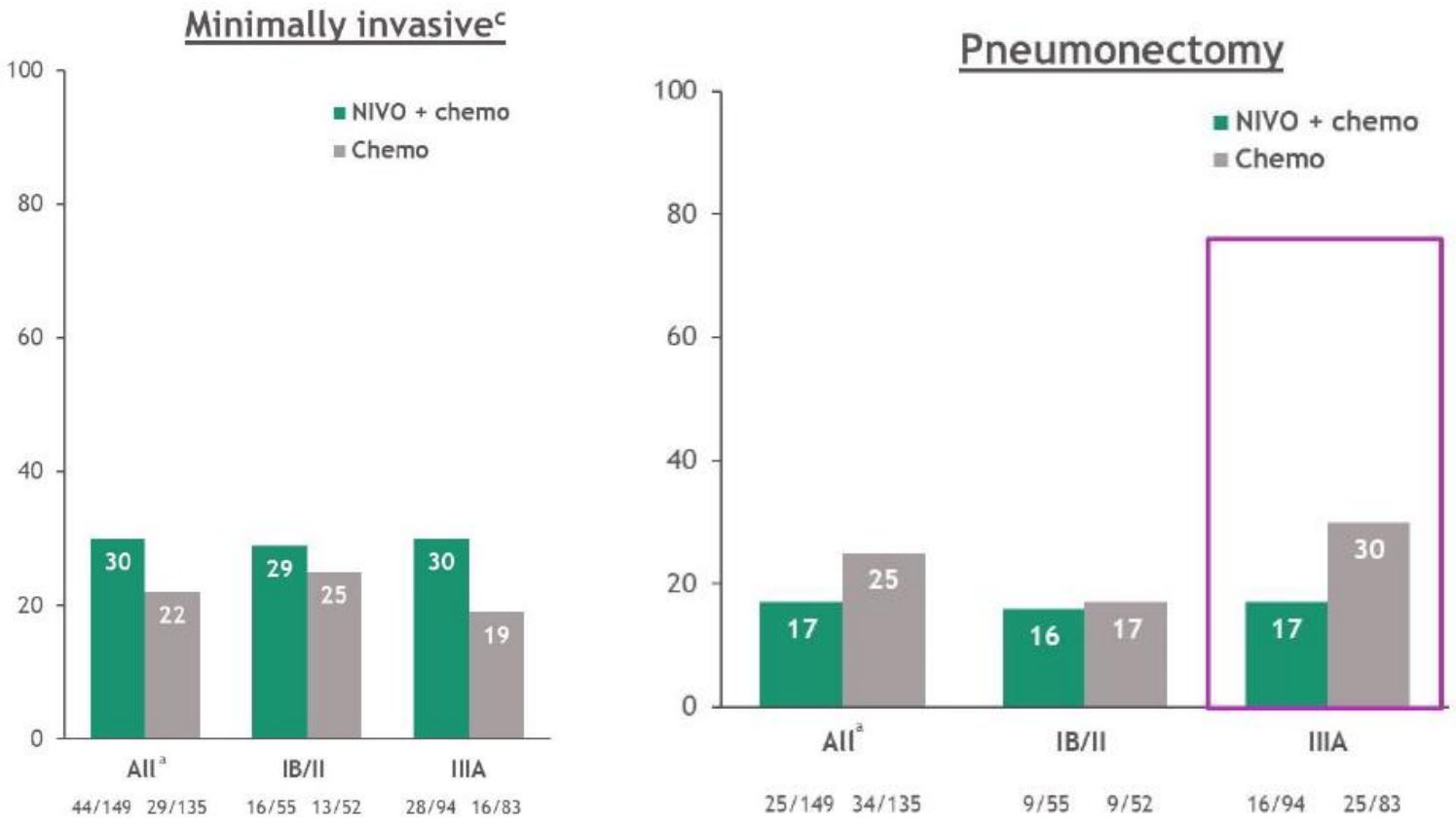


[a]1 patients with stage IV in each arm; [b]patients with definitive surgery not reported : NIVO + chemo, 3% (stage IB/II), 0 (stage IIIA); chemo, 5% (stage IB/II), 3% (stage IIIA); [c]Other reasons included patient refusal, unresectability, and poor lung function; [d]Patients (n) with reported duration of surgery : NIVO + chemo, 46 (stage IB/II), 76 (stage IIIA); chemo, 47 (stage IB/II), 74 (stage IIIA); IQR for median duration of surgery : NIVO + Chemo, 126.0-275.0 (stage IB/II) and 134.5-245.5 (stage IIIA); chemo, 150.0-267.0 (stage IB/II) and 147.0-290.0 (stage IIIA)

Jonathan Spicer, MD
Division of General Surgery,
McGill University Health Center,
Montreal, Quebec
Canada

2021 ASCO ANNUAL MEETING

Could nICI/chemo make surgery easier for patients with stage III NSCLC???



Chemo, chemotherapy; NIVO, nivolumab
Spicer J, et al. N Engl J Med 2022;386:1973–85
Figures courtesy of Spicer J, et al. ASCO 2021 (Abstract 8503)

- **More patients made it to surgery**

  (83% vs. 72%, Stage IIIA)
- **Duration of surgery shorter**

  (32 minutes, Stage IIIA)
- **More minimally invasive**

  (30% vs. 19%, Stage IIIA)
- **Less pneumonectomies**

  (17% vs. 30%, Stage IIIA)

Surgical Outcomes with Neoadjuvant Durvalumab + Chemotherapy Followed by Adjuvant Durvalumab in Resectable NSCLC (AEGEAN)

Tetsuya Mitsudomi[1], John V. Heymach[2], Martin Reck[3], Janis M. Taube[4], Shugeng Gao[5], Yoshitsugu Horio[6], Jian You[7], Gaofeng Li[8], Dinh Van Luong[9], Somcharoen Saeteng[10], Fumihiro Tanaka[11], Grzegorz Kulesza[12], Stefan B. Watzka[13], Laszlo Urban[14], Zsuzsanna Szalai[15], Hiroaki Akamatsu[16], Jin Hyoung Kang[17], Francisco J. Orlandi[18], Guzel Z. Mukhametshina[19], Andreas Pircher[20], Carlos Henrique Andrade Teixeira[21], Mike Aperghis[22], Gary J. Doherty[22], Ruth Doake[22], Tamer M. Fouad[23], David Harpole[24]

AEs possibly related to surgery and surgical complications summary (underwent surgery; modified safety analysis set)

Post-surgery period*	D arm (N=296)	PBO arm (N=301)
Any-grade AEs possibly related to surgery, n (%)†	**119 (40.2)**	**118 (39.2)**
Max. grade 3 or 4	25 (8.4)	28 (9.3)
SAE	33 (11.1)	33 (11.0)
Outcome of death‡¶	6 (2.0)	4 (1.3)

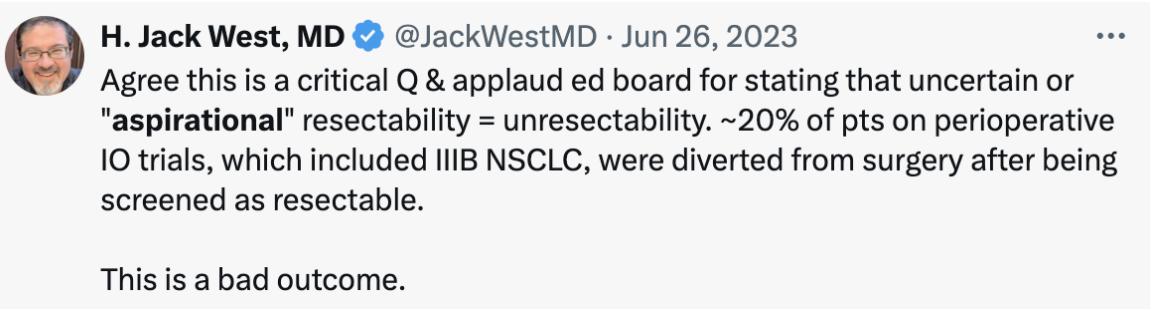
	D arm (N=296)	PBO arm (N=301)
Patients with any surgical complication, n (%)	**175 (59.1)**	**181 (60.1)**
Max. reported by Clavien-Dindo classification grade[1]		
1	125 (42.2)	131 (43.5)
2	32 (10.8)	25 (8.3)
≥3	18 (6.1)	25 (8.3)

DCO = Nov 10, 2022. *This includes AEs between the date of surgery (including day of surgery) and the earliest of the date of surgery + 90 days or first dose of subsequent anti-cancer therapy; this also includes AEs with an onset date during this period and AEs with an onset date prior to dosing which worsen during this period. The summary of AEs possibly related to surgery and surgical complications summary reflect data collected for all patients in the modified safety analysis set who underwent surgery (including one patient assigned to the PBO arm who erroneously received a single cycle of D and was therefore included in the D arm for safety assessment), with AEs graded using the National Cancer Institute Common Toxicity Criteria for AEs, version 5.0.‡Included infectious pleural effusion (PBO arm, n=1), pneumonia (D arm, n=2; PBO arm, n=1), septic shock (D arm, n=1), acute respiratory failure (PBO arm, n=1), bronchopleural fistula (D arm, n=1), interstitial lung disease (D arm, n=1; also possibly related to D), pneumonitis (D arm, n=1; also possibly related to D), pulmonary hemorrhage (PBO arm, n=1), and post-procedural pulmonary embolism (D arm, n=1). ¶There were no AEs with outcome of death, possibly related to surgery, within 1 day of surgery in either arm. Note: All deaths regardless of any causality within 30 days of surgery = 12 (D arm, n=4; PBO arm, n=8). SAE, serious AE.

[1]Dindo D, et al. *Ann Surg* 2004;240:205-13.

Tetsuya Mitsudomi, Division of Thoracic Surgery, Department of Surgery, Kindai University Faculty of Medicine, Osaka-Sayama, Japan

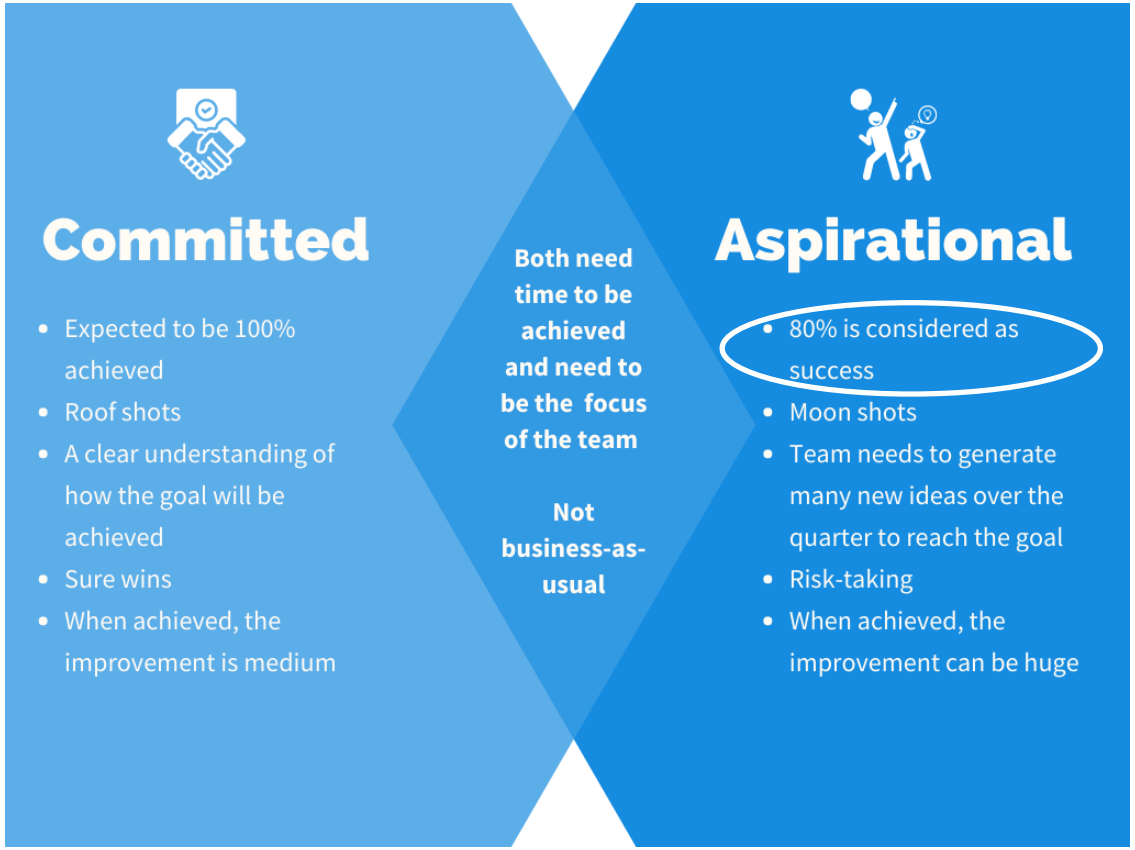
A word regarding “aspirational” surgery



Miriam-Webster:

“having or showing a desire to achieve a high level of success or social status”

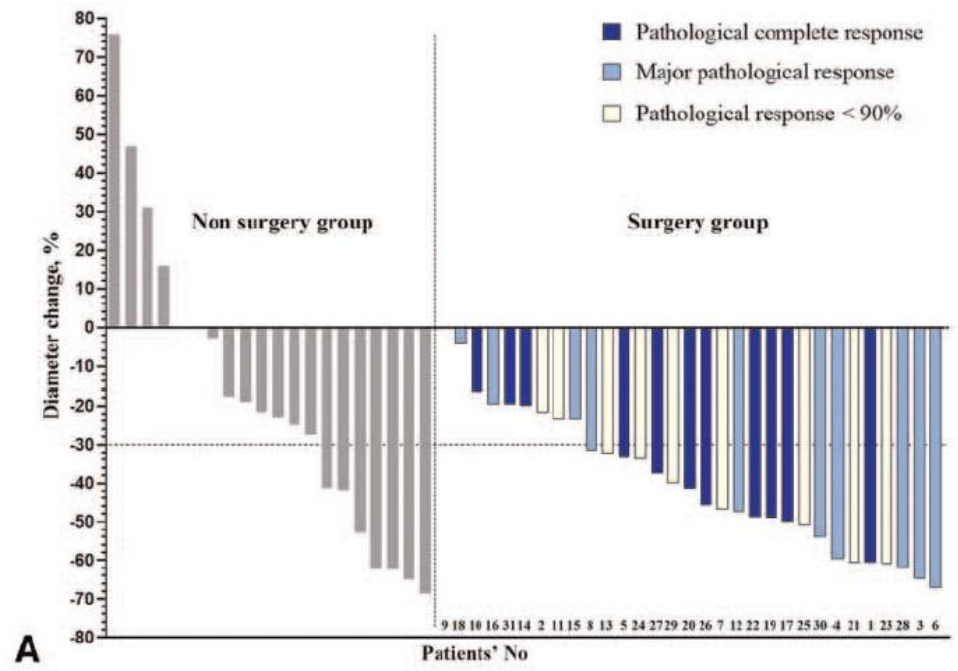
Is this “bad”?

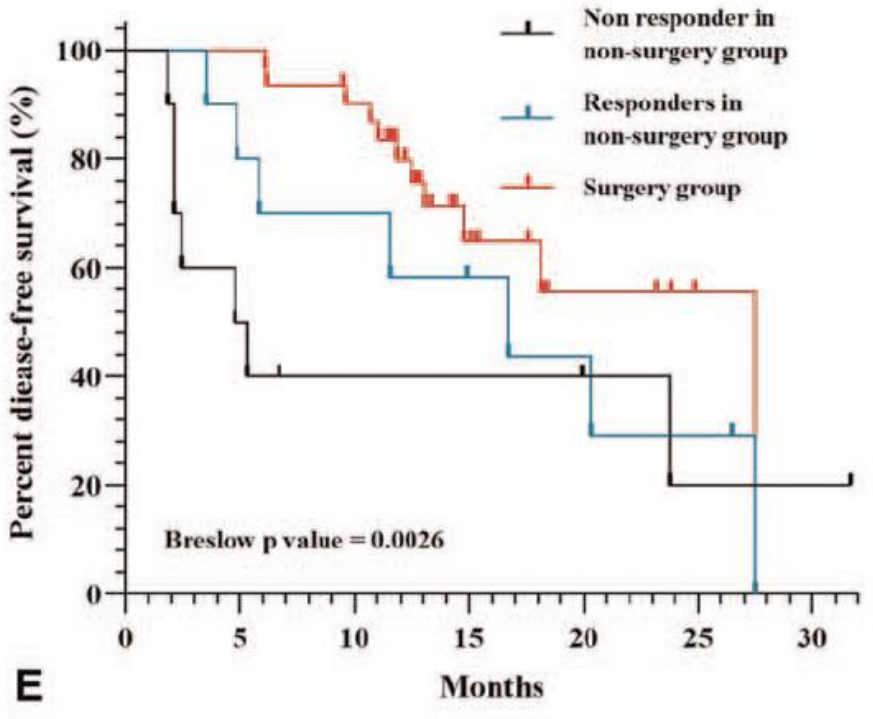


https://blog.weekdone.com/the-difference-between-committed-and-aspirational-okrs/

Radical Minimally Invasive Surgery After Immuno-chemotherapy in Initially-unresectable Stage IIIB Non-small cell Lung Cancer

Hongsheng Deng, MD, Jun Liu, MD,* Xiuyu Cai, MD,† Jiawei Chen, MD,* Gaetano Rocco, MD, FRCSEd,‡ René Horsleben Petersen, MD,§ Alessandro Brunelli, MD,¶ Calvin S. H. Ng, MD,|| Thomas A. D'Amico, MD,** Wenhua Liang, MD,*✉ and Jianxing He, MD, PhD, FACS*✉*

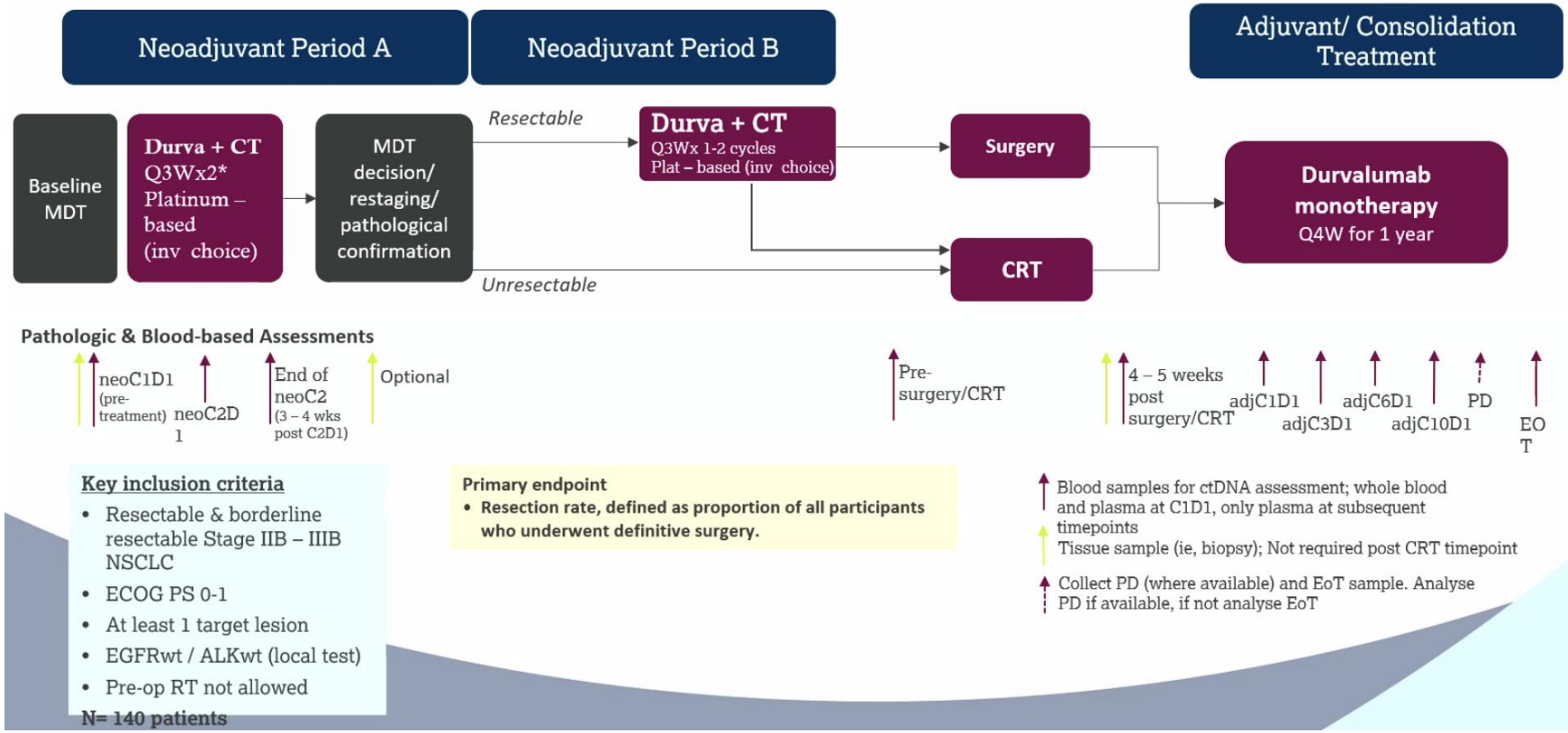




Ann Surg 2022;275:e600-e602

Phase 2 Study to Assess Neoadjuvant Durvalumab (D) and Platinum-Based Chemotherapy (CT), Followed by Either Surgery and Adjuvant D or CRT and Consolidation D, in Resectable or Borderline Resectable Stage IIB-IIIB NSCLC (MDT-BRIDGE)

AZ IO TRIALS MDT BRIDGE



Dogma #5: We have to "get it all" Well…what happens if we don't?

Improved Outcomes with Systemic Therapy Following R+ Resection for Non-Small Cell Lung Cancer in a Contemporary Multicentric Cohort

Jorge Humberto Rodriguez-Quintero MD[1], Roger Zhu MD[1], Mohamed K Kamel MD[2], Rajika Jindani MD[1], Marc Vimolratana MD[1], Neel P Chudgar MD[1], Brendon Stiles MD[1].
[1]Department of Cardiovascular and Thoracic Surgery Montefiore Medical Center/Albert Einstein College of Medicine. [2]Department of Thoracic Surgery. University of Rochester Medical Center.

Methods

	OS (Months)	95%CI	5-Yr (%)
2009-2015	26.1	25.2 27.1	32
2015-2020	38.5	36.5 40.5	40

- 1,340 propensity-matched (1:1) Systemic Therapy vs. Surgery only)

	OS (Months)	95%CI	5-Yr (%)
Systemic therapy	45.2	36.4 54.0	44
Surgery only	26.1	20.5 31.7	34

OS defined from surgery to last follow-up or death.

24,234 patients

ITSOS/AATS 2023

Fig 1) Survival comparison between A) 2009-2015 vs. 2015-2020 and B) Systemic therapy (ST) vs. Surgery only (S)

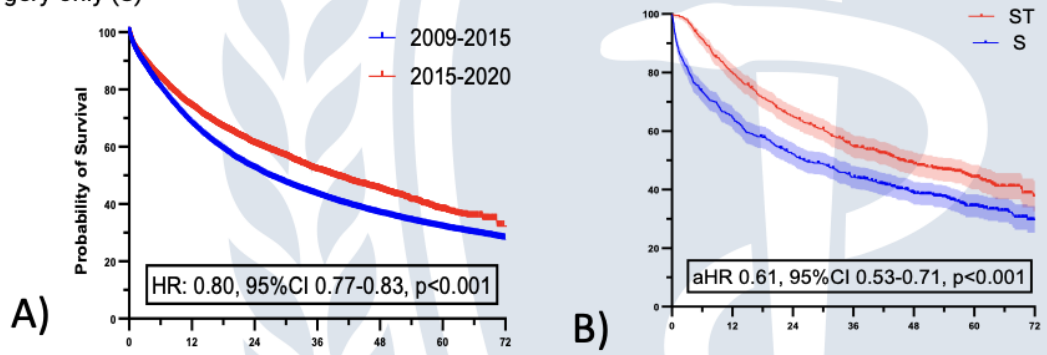
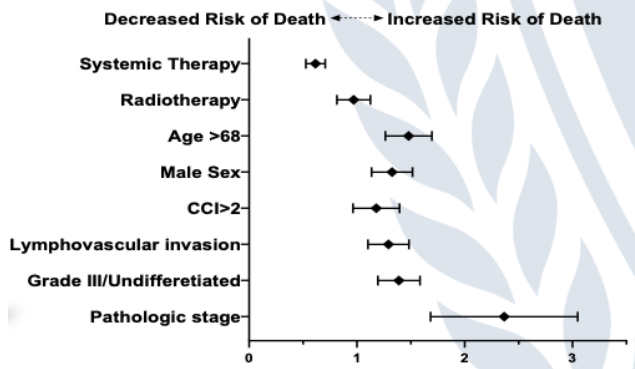


Fig 2) Multivariable Cox regression for factors associated with survival in the 2015-2020 cohort



	OR	95%CI	
Systemic Therapy	0.61	0.53	0.71
Radiotherapy	0.96	0.82	1.13
Age (>68)	1.47	1.27	1.70
Male Sex	1.32	1.14	1.52
CCI≥2	1.17	0.97	1.40
Grade III/U	1.38	1.20	1.59
LVI	1.28	1.11	1.49
Pathologic stage	2.30	1.72	3.08

Montefiore

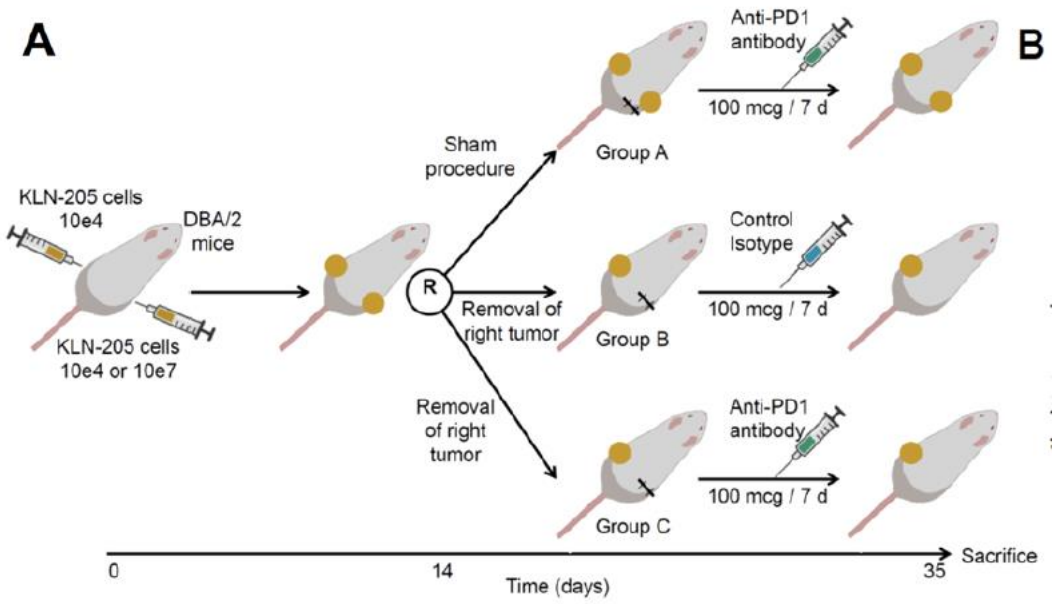
EINSTEIN
Albert Einstein College of Medicine

Surgical debulking as an immune primer?

SCIENTIFIC REPORTS
nature research

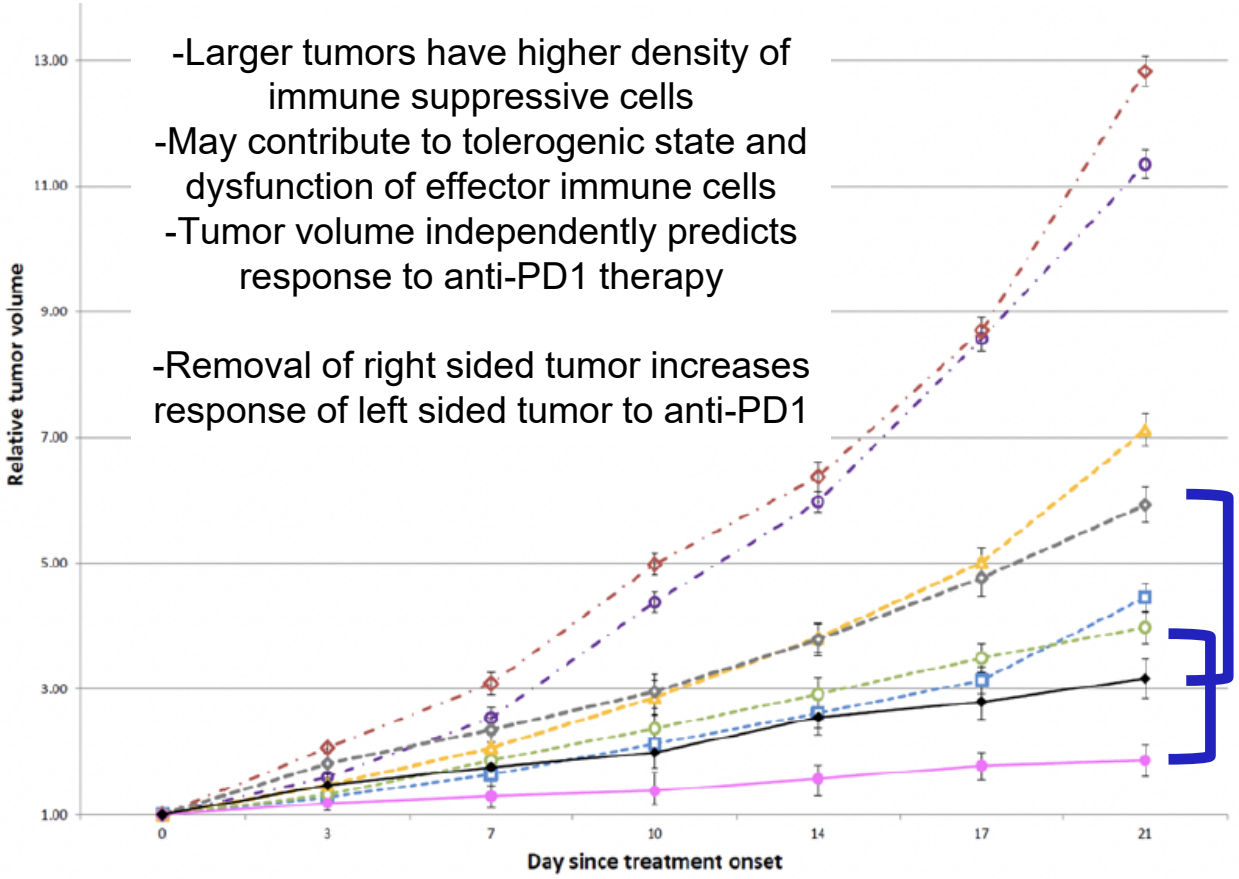
A rationale for surgical debulking to improve anti-PD1 therapy outcome in non small cell lung cancer

Florian Guisier[1,2,3*], Stephanie Cousse[1,2], Mathilde Jeanvoine[1,2], Luc Thiberville[1,2,3] & Mathieu Salaun[1,2,3]



-Larger tumors have higher density of immune suppressive cells
-May contribute to tolerogenic state and dysfunction of effector immune cells
-Tumor volume independently predicts response to anti-PD1 therapy

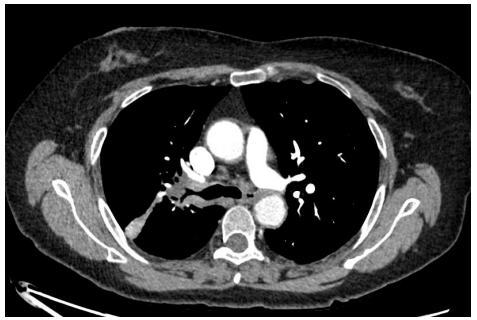
-Removal of right sided tumor increases response of left sided tumor to anti-PD1

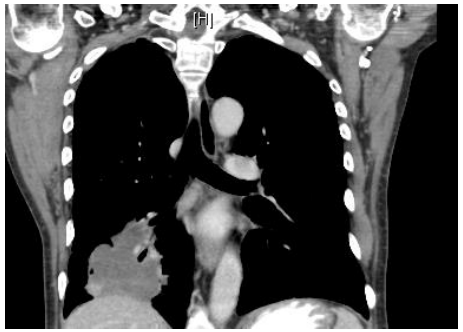


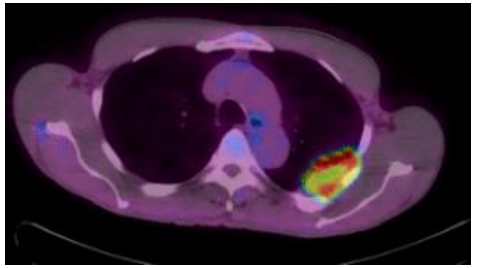
Scientific Reports (2019)9:16902

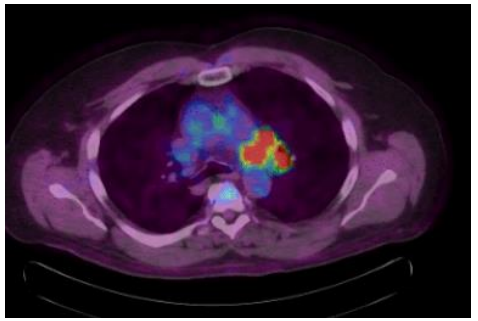
Conclusions

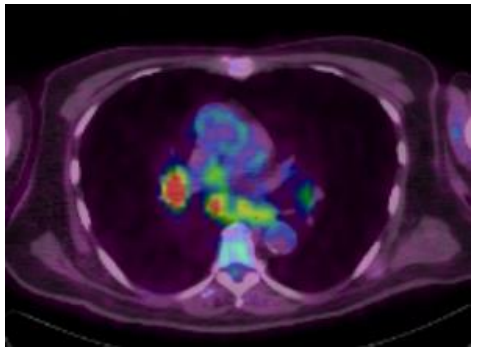
- Surgical dogma provides good discussion points, but few absolute guidelines
- We must challenge dogma and be aspirational for our patients with locally advanced lung cancer
- Multidisciplinary teams can work together to develop criteria for resectability, which can potentially be determined *after* nICI/chemo
- Surgery after neoadjuvant chemotherapy and immunotherapy is safe and provides the best opportunity to cure patients with stage IIIA and IIIB lung cancer











Montefiore

EINSTEIN

Albert Einstein College of Medicine