Important Trials Recently Reported

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Disclosures

Commercial Interest	**Relationship(s)**
Astra Zeneca	Advisory Board for Adaura Trial dissemination
On Target Laboratories	Steering Committee for ELUCIDATE trial

Last year – 2021 Virtual Meeting

- Nelson Trial
- Violet Trial
- Adaura
- LCMC3
- Nadim
- Lung ART
- 3 yr results of PACIFIC
- RTOG 1010
- Checkmate 577

Overview – 2022

- **Lung Cancer Papers**
  - **(NOT including CM816, IMPOWER 010)**
  - JCOG 0802 segment v lobe
  - Do all segmentectomies yield the same outcome?
  - NADIM update
  - PACIFIC update
  - ASCO Rapid Recommendations – Adjuvant Therapy 2022
  - RVLob (VATS v Robot) trial
  - RCT on level of suction after lobectomy
  - CTC's for Lung Cancer Screening
- **Esophageal Cancer Papers**
  - NeoAEGIS: CROSS v FLOT/MAGIC
  - Checkmate study Advanced SCCA
- **Mesothelioma Papers**
  - SMART trial
- **Recommended Podcasts**

Other Surgical "stuff" – Recommended Reading (will not review today)

COVID-19

- Risk of complications in surgical patients with current or recent COVID
- COVID 19 guidance for Lung Cancer
- Perc Trachs – AnnSurg, ATS
- Skin prep RCT
- Safe and Supported Pregnancy during residency
- Resilience Bank Account

- Awake Robotic Tracheal Surgery
- Management of GGOs Review
- Definitions of Oligometastases
- MARS 2 trial underway
- Neoadjuvant Atezo/Chemo – Shu, Lancet 2020
- Violet Trial
- Adaura
- Lung ART
- Checkmate 577

Last Year's Key Papers, now published

Will send a dropbox link to all papers

Lung Cancer Papers

JCOG 0802
Phase III RCT Lobectomy vs Segmentectomy

https://www.ctsnet.org/article/brompton-grand-rounds-livestreamed-august-13-2021-clinical-implications-jcog-0802

Joel Dunning, Eric Lim Commentary Aug 2021 – Brompton Grand Rounds on CTSnet

Presented at AATS May 2021 – H Asamura, publication pending (still!)

JJCO Japanese Journal of Clinical Oncology

Jpn J Clin Oncol 2010;40(3)271–274
doi:10.1093/jjco/hyp156
Advance Access Publication 22 November 2009

Clinical Trial Note

A Phase III Randomized Trial of Lobectomy Versus Limited Resection for Small-sized Peripheral Non-small Cell Lung Cancer (JCOG0802/WJOG4607L)

Started August 2009

Aimed to recruit 1100 patients from 71 centres. First step registration :

(i) Contrast-enhanced thoracic computed tomography (CT) fulfills all of the following conditions: (a) single tumor, (b) NSCLC suspected, (c) center of tumor located in the outer third of the lung field, (d) tumor not located at middle lobe, and (e) no lymph node metastasis.

(ii) Thin-section CT fulfills both of the following conditions: (a) maximum tumor diameter of <2 cm and (b) not 'radiologically determined non-invasive cancer' (i.e. the proportion of the maximum diameter of the tumor itself to consolidation is 25%).

(iii) Patient age 20 – 79 years old.

(iv) No prior ipsilateral thoracotomy (prior diagnostic thoracoscopy is allowed). (v) No prior chemotherapy or radiation therapy for any malignant diseases. (vi) Expected post-operative FEV1.0 >800 ml and PaO2 ⍰ 65 torr. (vii) Performance status of 0 or 1. (viii)

Study scheme of JCOG0802/WJOG4607L

Key patient inclusion criteria

- Clinical stage IA peripheral NSCLC or suspected nodule
- Maximum tumor diameter ≤2 cm
- C/T ratio (CTR) >0.5

First registration

Intraoperative confirmation of eligibility

Second (final) registration/ Intraoperative randomization

Adjusted for
- Histology
- Gender
- Age
- CTR=1.0 or not
- Institution

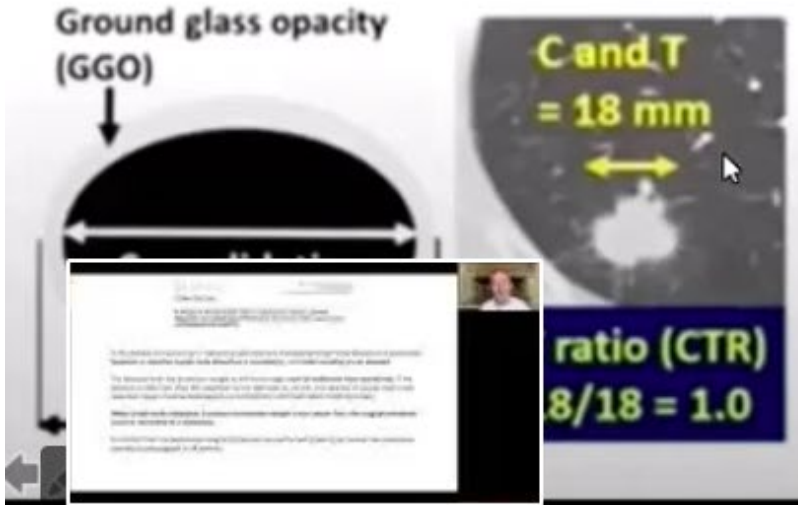
Arm A: Lobectomy N=554

Arm B: Segmentectomy N=552

Primary endpoint
- Overall survival (OS)

Secondary endpoints
- Postoperative respiratory function (6M, 1Y)
- Relapse-free survival (RFS)
- Proportion of local recurrence
- *Adverse events, etc.

Sample size: N=1100
- 5-yr OS of Lob & Seg: 90%
- Non-inferiority margin of HR: 1.54 (5-yr OS of 5%)
- Power: 80%
- One-sided type I error: 0.05
- Accrual period: 3 years
- Follow-up period: 5 years

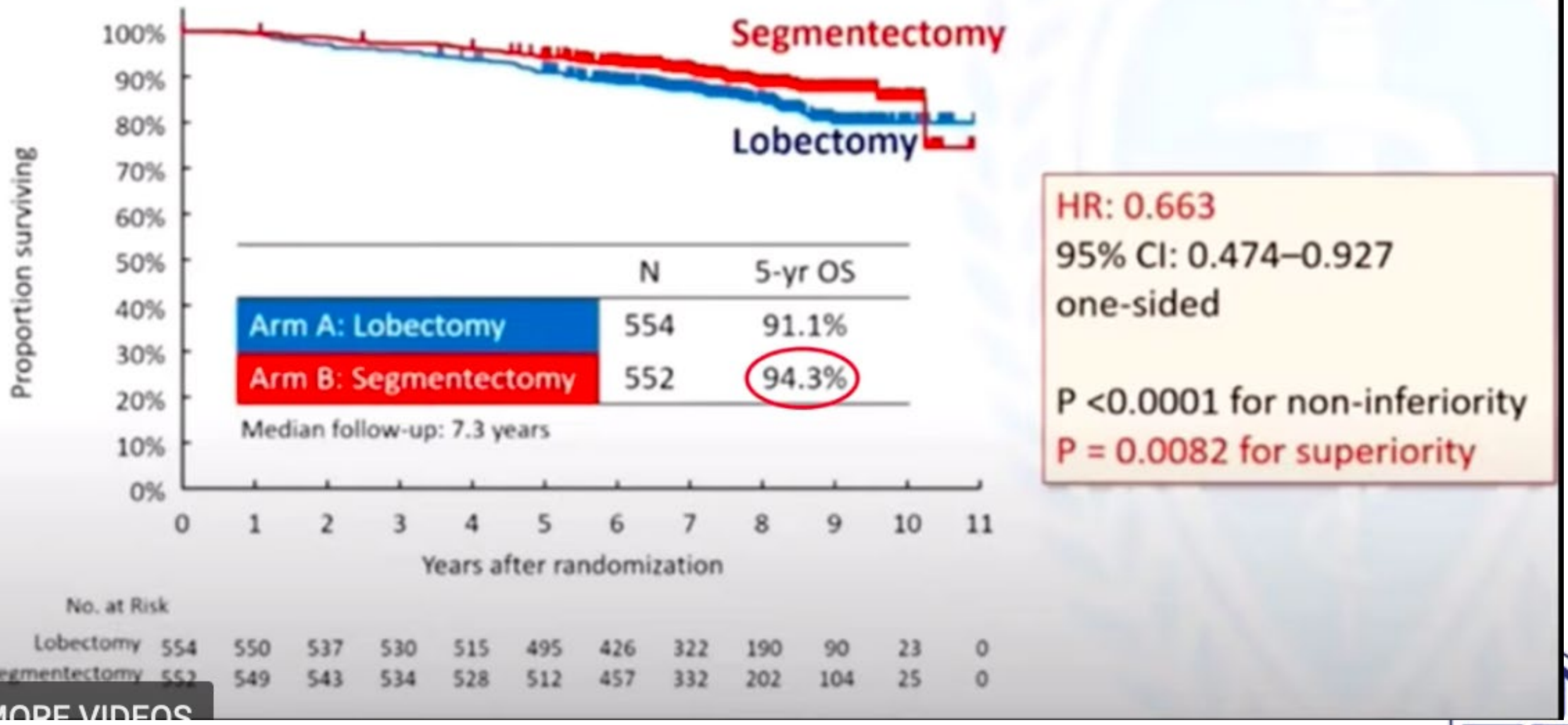


*Details of adverse events previously reported in J Thorac Cardiovasc Surg 2020

Patient characteristics at final registration

Characteristics	Arm A: Lobectomy (N=554)	Arm B: Segmentectomy (N=552)
Median age, years (range)	67 (35-85)	67 (32-83)
Male / Female (%)	293 (52.9%) / 261 (47.1%)	290 (52.5%) / 262 (47.5%)
ECOG performance status: 0 / 1 (%)	541 (97.7%) / 13 (2.3%)	542 (98.2%) / 10 (1.8%)
Smoking history: Yes / No (%)	246 (44.4%) / 308 (55.6%)	244 (44.2%) / 308 (55.8%)
Median max. tumor diameter, cm (range)	1.60 (0.6-2.0)	1.59 (0.6-2.0)
Consolidation / tumor ratio (CTR) (%)		
0≤ CTR ≤0.25	1 (0·2%)	0 (0%)
0.25< CTR ≤0.5	62 (11·2%)	73 (13.2%)
0.5< CTR <1.0	208 (37·6%)	194 (35.1%)
CTR = 1.0	283 (51.1%)	285 (51.6%)
Median FEV1.0, mL (range)	2260 (1110-4760)	2280 (1010-4900)
Median FVC, mL (range)	3050 (1370-5990)	3095 (1590-5940)
Histological type		
Adenocarcinoma	501 (90.4%)	502 (90.9%)
Squamous cell carcinoma	38 (6.9%)	37 (6.7%)
Others	15 (2.7%)	13 (2.4%)
Pathological stage (7th TNM)		
pIA/pIB/pIIA/pIIIA/pIIB/pIV/unknown	455 (82.1%)/64/15/3/16/0/1	468 (84.8%)/46/18/1/17/1/2

Result 1. Overall survival (primary endpoint)

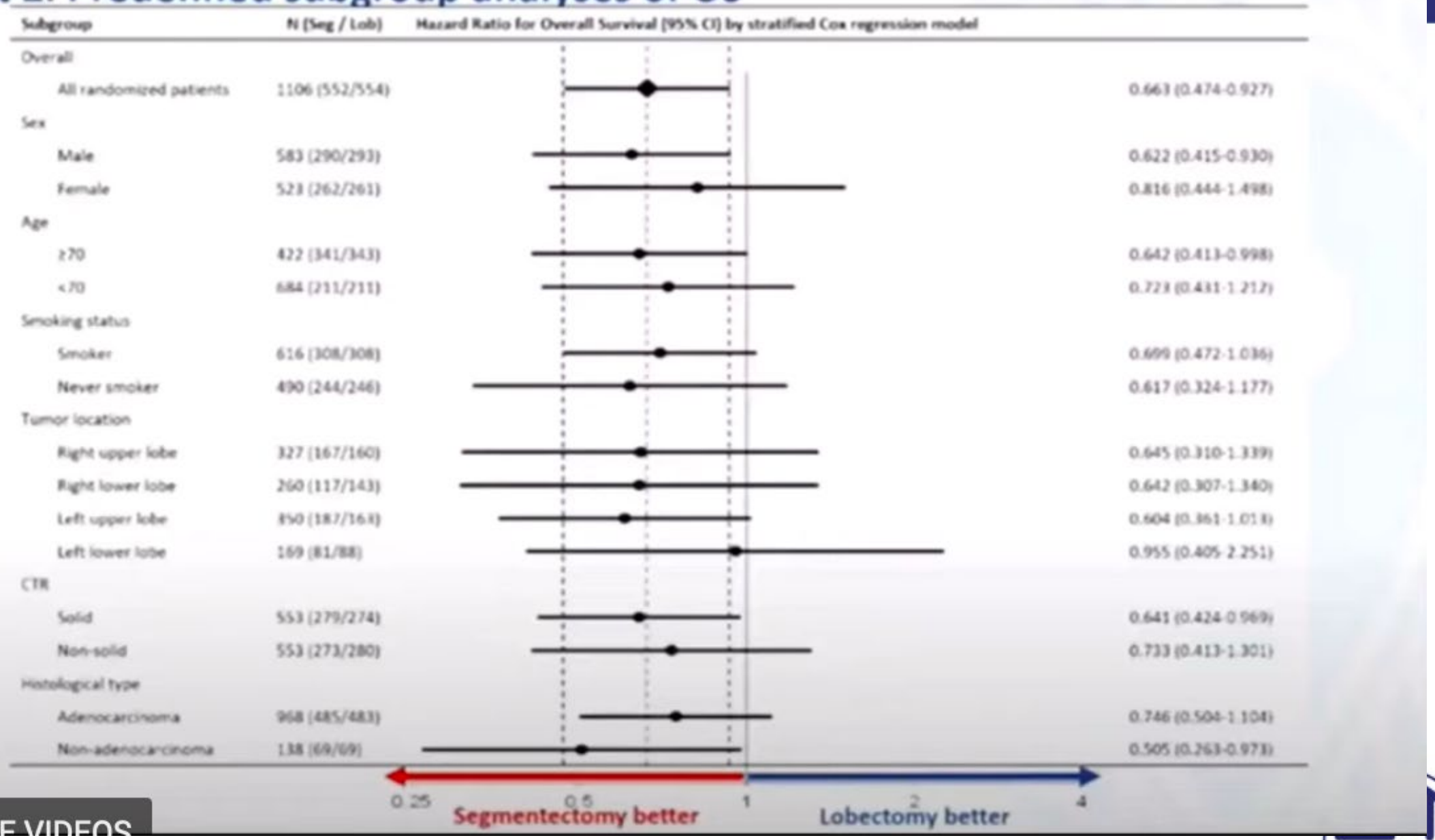


HR: 0.663
95% CI: 0.474–0.927
one-sided

P <0.0001 for non-inferiority
P = 0.0082 for superiority

MORE VIDEOS

Result 2. Predefined subgroup analyses of OS



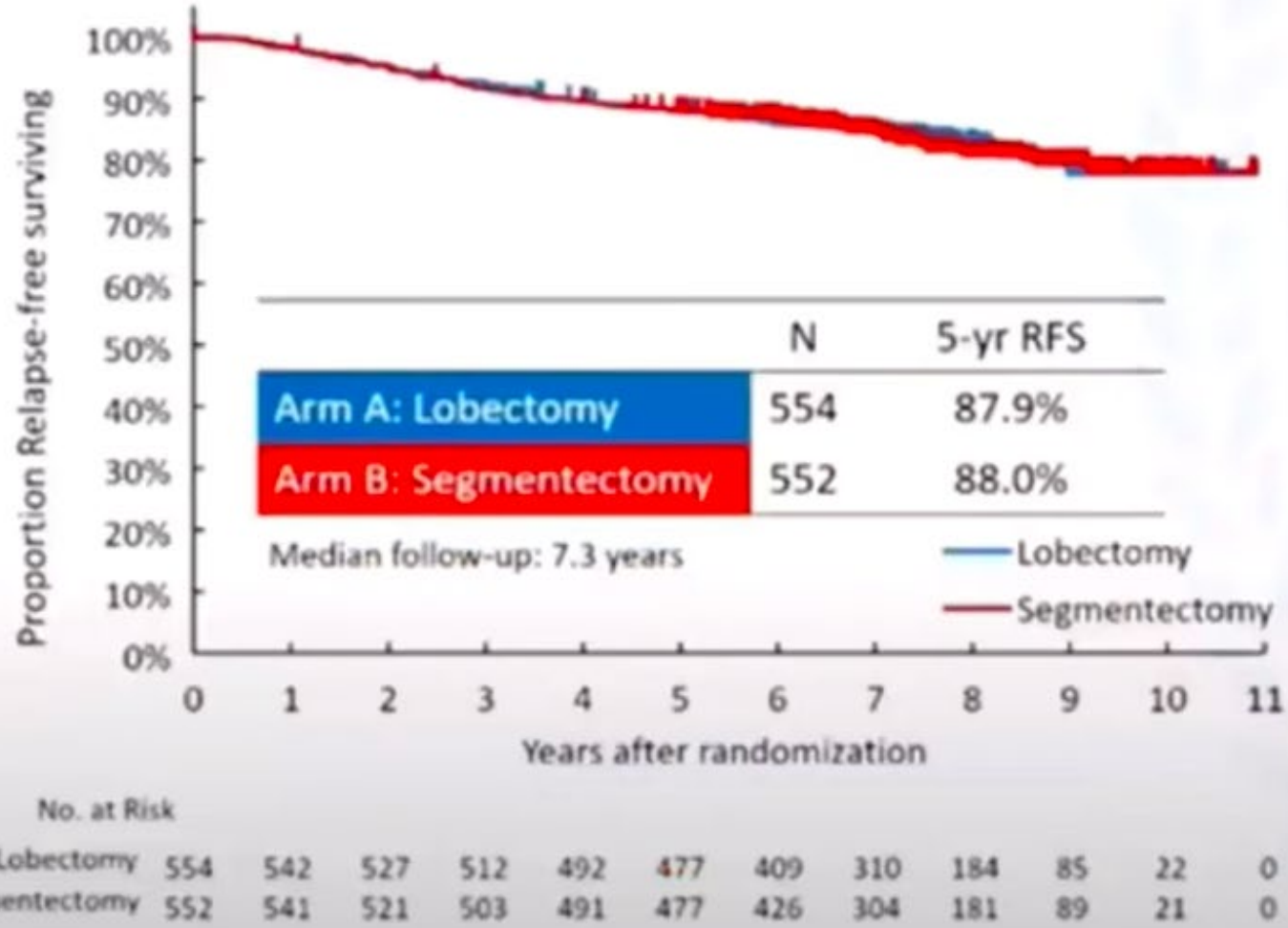
Result 3.
Postoperative respiratory function (key secondary endpoint)

FEV1.0 (mL)	Arm A: Lobectomy (N=554)	Arm B: Segmentectomy (N=552)	Difference	P value*
Post-op 6M	N=454	N=492		
Median	−13.1%	−10.4%	2.7%	<0.0001
Range	−63.8% to 53.5%	−48.6% to 27.9%		
Post-op 1Y	N=526	N=528		
Median	−12.0%	−8.5%	3.5%	<0.0001
Range	−57.1% to 49.6%	−37.0% to 30.0%		

Difference at post-op 1Y was smaller than expected criteria (10%).

FEV1.0, forced expiratory volume in 1.0 s.
*Wilcoxon's rank sum test p-value

Result 4. Relapse-free survival (RFS)



HR: 0.998
95% CI: 0.753–1.323
P = 0.9889

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Result 5. Recurrence pattern

- Proportion of local recurrence = loco-regional +/- distant recurrence among all enrolled patients.

Recurrence location	Arm A: Lobectomy (N=554)	Arm B: Segmentectomy (N=552)	P value*
Total	44 (7.9%)	67 (12.1%)	0.0214
Loco-regional	17 (3.1%)	38 (6.9%)	
Distant	14 (2.5%)	7 (1.3%)	
Loco-regional + distant	13 (2.3%)	20 (3.6%)	
Unclassified	0	2	
Proportion of local recurrence	30 (5.4%)	58 (10.5%)	0.0018

*Fisher's exact test

JCOG 0802 Segment vs Lobe Summary Clinical Stage 1A, <2 cm peripheral tumors

- Rule of “3%”
- OS 3% *BETTER* with segmentectomy: HR 0.663
  - 91% and 94% at 5 years
- RFS *same* but 5% higher locoregional recurrence with segment
  - 88% RFS for both
- Pulmonary function about 3% *BETTER* with segment at 6 and 12 mo
  - Does this matter?
- We all can’t wait for CALGB 140503 – Altorki Trial - to refute or substantiate this!

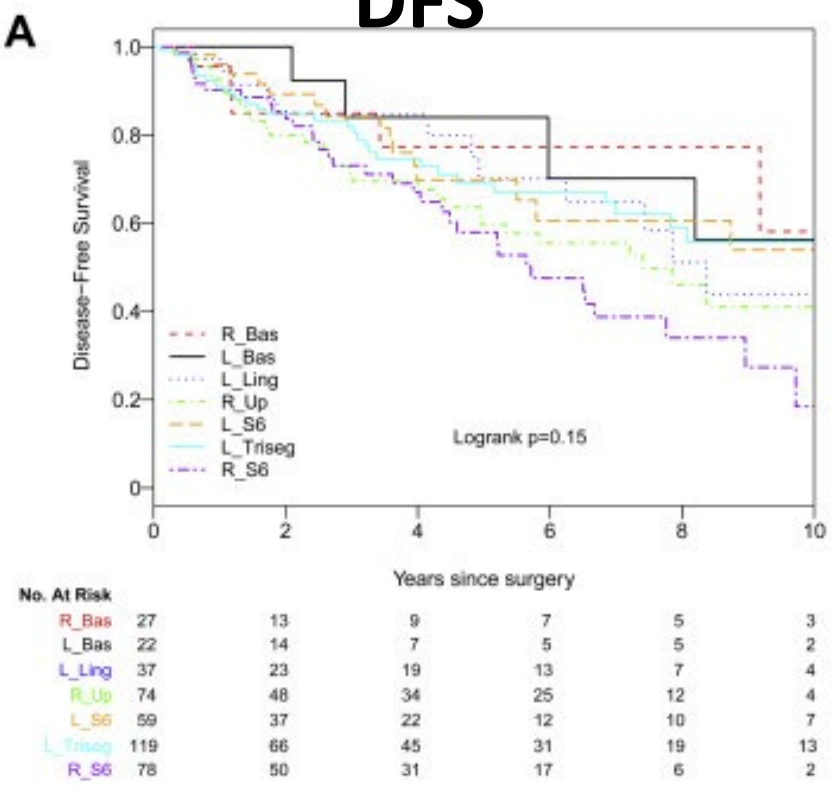
My interpretation of JCOG 0802: Segmentectomy new SOC for <2 cm, node negative, margin negative NSCLC

Publication pending, may be important nuances

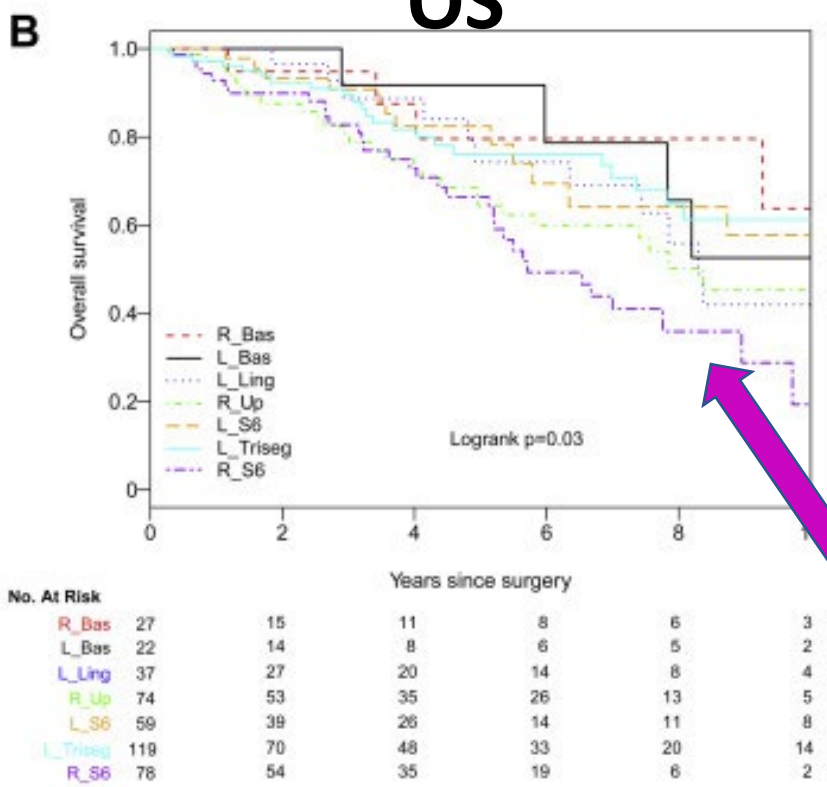
Segmentectomy – Do they all yield the same outcomes?
Annals of Thoracic Surgery
March 2021

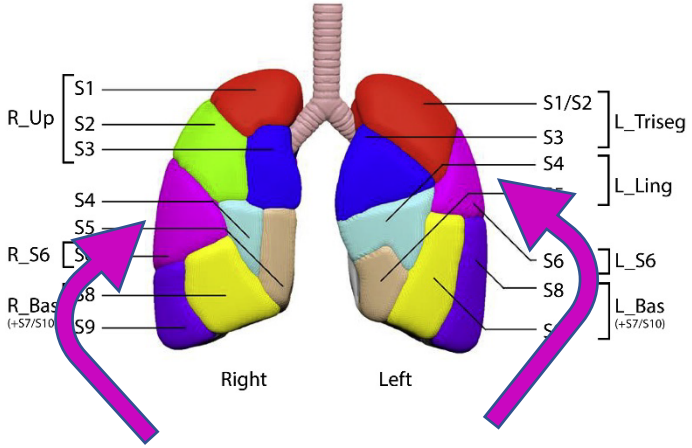
Intentional Segmentectomy for Clinical T1 N0 Non-small Cell Lung Cancer: Survival Differs by Segment

DFS



OS



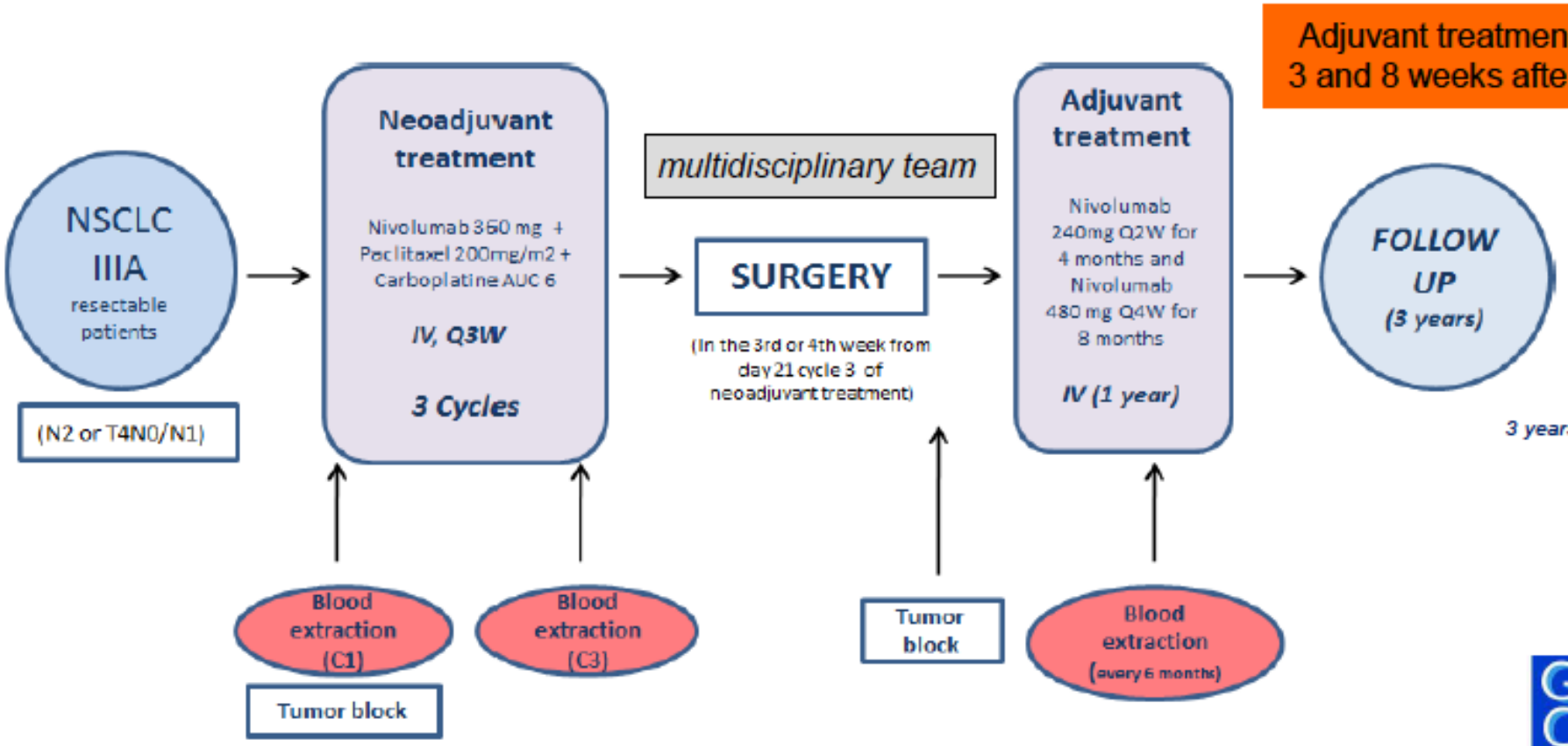


S6=superior segment (or should we rename it the ***INFERIOR*** segment?)

Gregory D. Jones, Raul Caso, Giye Choe, Kay See Tan, James G. Connolly, Joe Dycoco, Daniela Molena, Bernard J. Park, James Huang, Prasad S. Adusumilli, Matthew J. Bott, Robert J. Downey, William D. Travis, David R. Jones, Gaetano Rocco.
Intentional Segmentectomy for Clinical T1 N0 Non-small Cell Lung Cancer: Survival Differs by Segment,
The Annals of Thoracic Surgery, Volume 111, Issue 3, 2021,Pages 1028-1035,ISSN 0003-4975,
https://doi.org/10.1016/j.athoracsur.2020.05.166.

NADIM Trial – update
Presented at World Lung September 2021

NADIM: Study design & Flow-chart



- Phase II
- Single-arm
- Open-label
- Multicenter
- Resectable IIIA NSCLC
- 46 patients

GECP
Grupo Español de Cáncer de Pulmón
Spanish Lung Cancer Group

WCLC

- World Lung 2018 and 2019 and 2021

Nadim trial

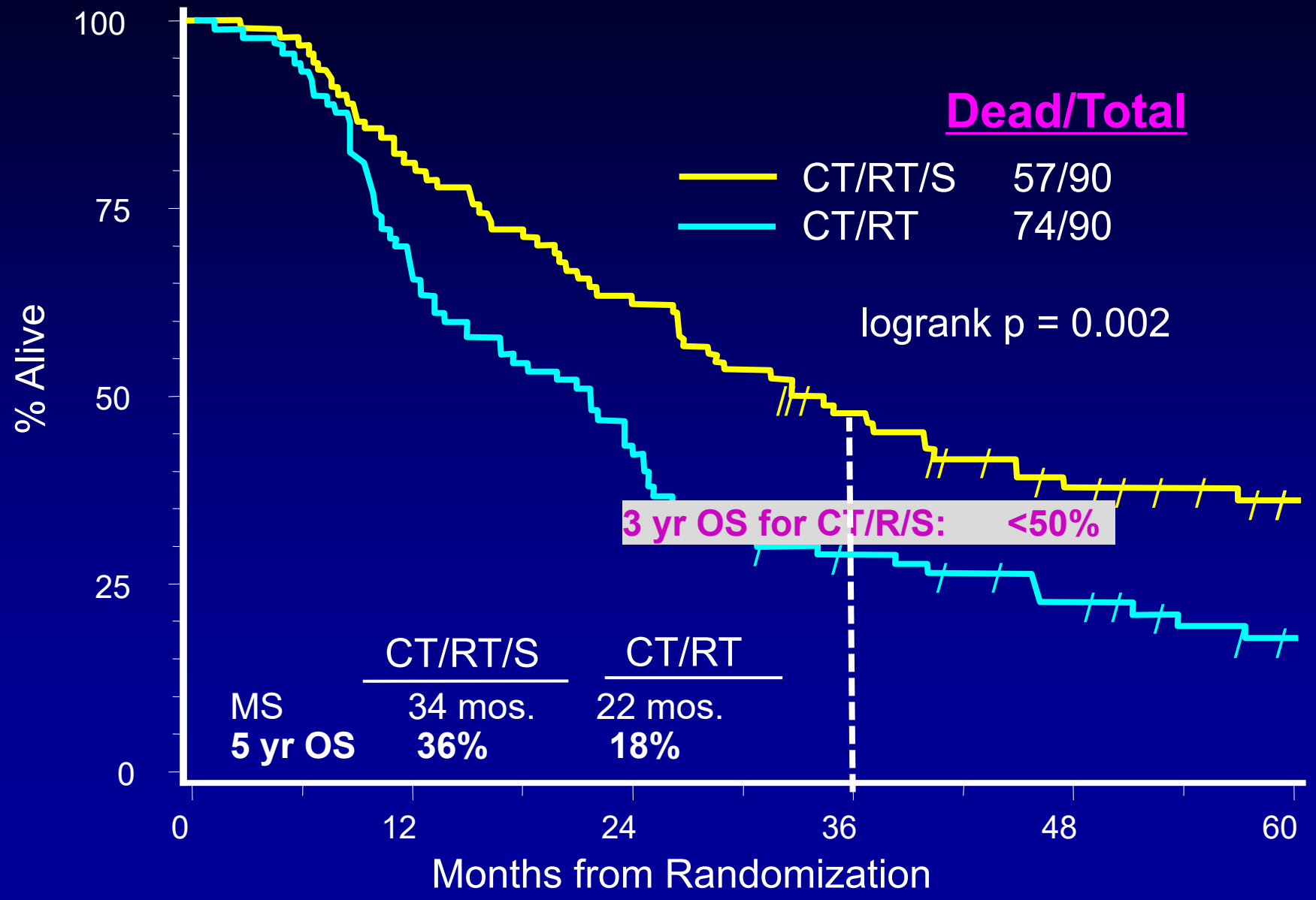
Patients with stage IIIA (N2 or T4N0) are potentially curable
but median overall survival has been only 15 months

46 patients enrolled
41 went to surgery
85% major path response
61% path CR

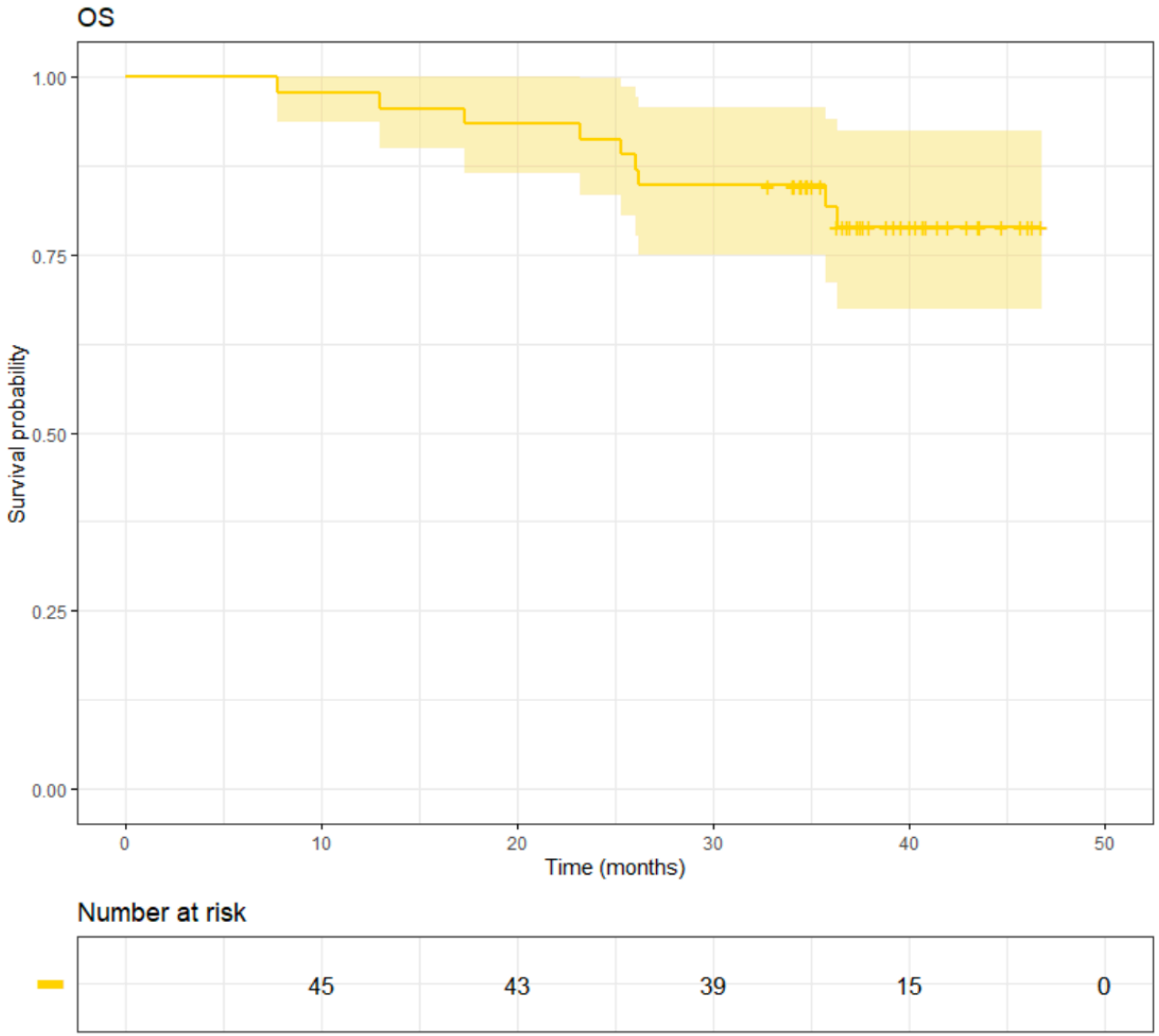
Historically - std chemo:
36-39 would go to surgery
major response not defined
2-12% path CR

- World Lung 2019

INT0139 OVERALL SURVIVAL OF THE LOBECTOMY SUBSET VERSUS MATCHED CT/RT SUBSET



RESULTS: OS



ITT population:

- **OS 81.9%** (95% CI: 66.8-90.6%) **at 36 months.**
- **OS 78.9%** (95%CI: 63.1-88.6%) **at 42 months.**

PP population:

- **OS 91.0%** (95%CI: 74.2-97.0%) **at 36 months.**
- **OS 87.3%** (95%CI: 69.3-95.1%) **at 42 months.**

PACIFIC Trial – 5 year survival data

PACIFIC 5 year Outcomes

JCO (online) 2/2/2022

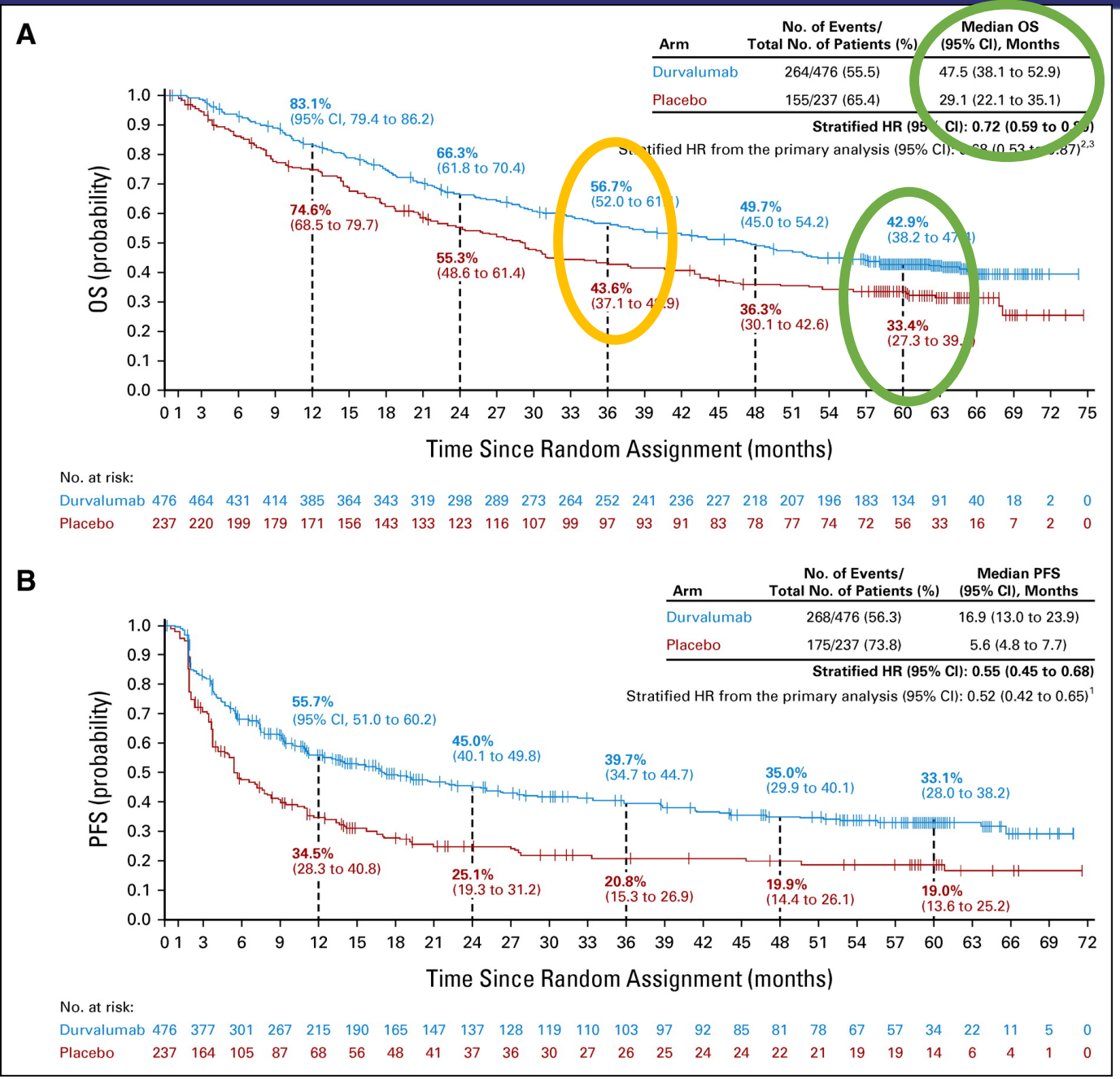


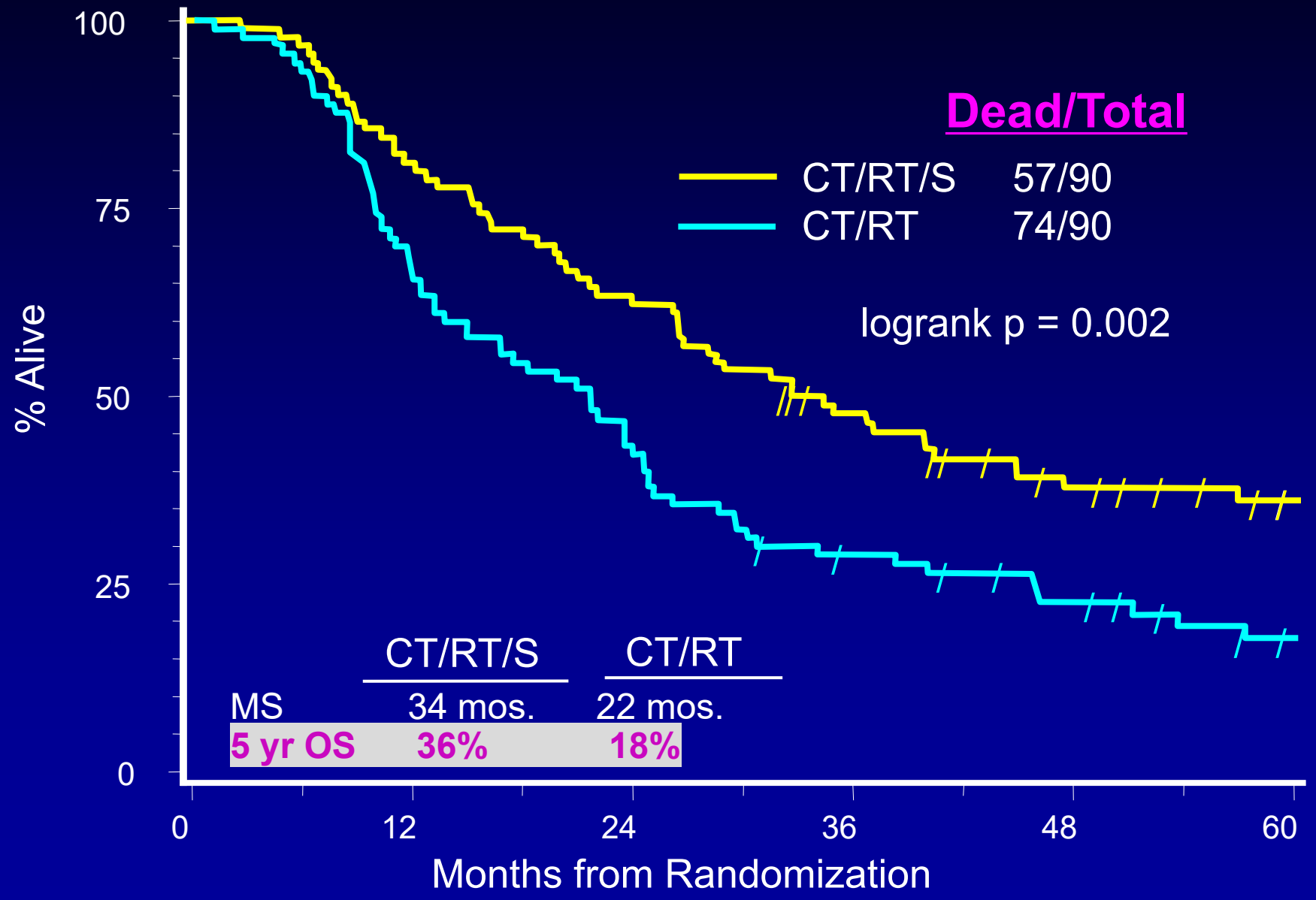
FIG 2. Updated (A) OS and (B) PFS (blinded independent central review) in the intent-to-treat population. The vertical dashed lines indicate yearly landmarks; the associated numerical values represent the OS and PFS rates at the landmark. OS was defined as time from random assignment until death from any cause. PFS was defined as time from random assignment to the date of the first documented event of tumor progression or death in the absence of disease progression. For PFS, patients who had not progressed or died at the time of the data cutoff were censored at the time of their last evaluable RECIST assessment; however, if the patient progressed or died after ≥ 2 missed visits, they were censored at the time of the latest evaluable RECIST assessment before the two missed visits.

HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

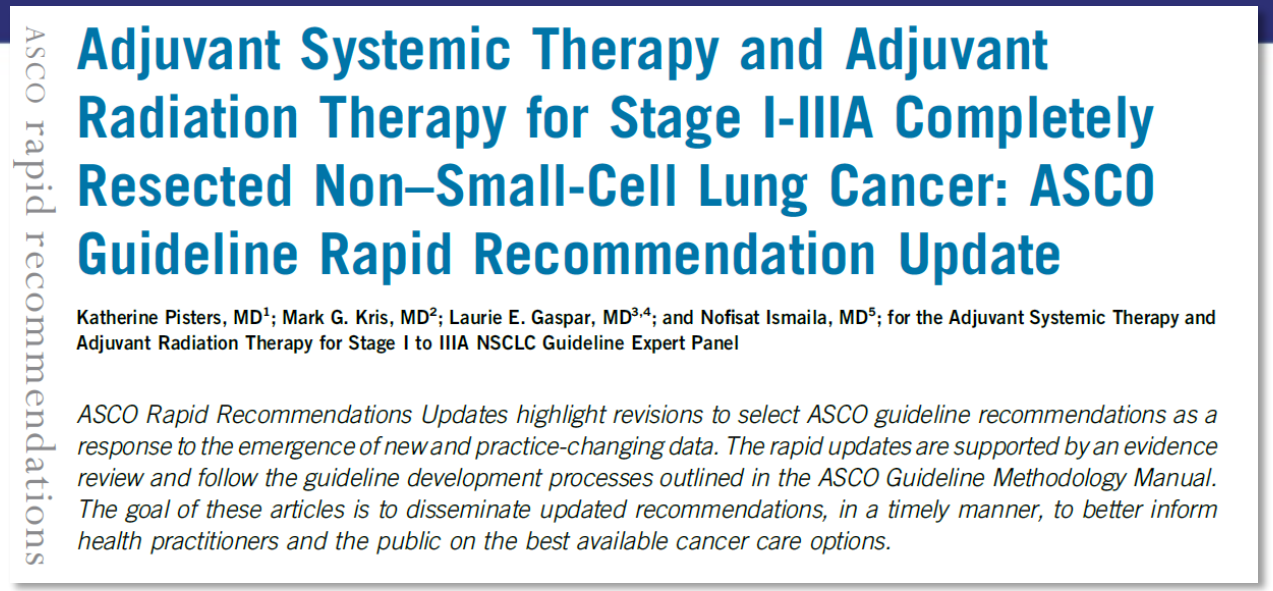
Published in: David R. Spigel; et al DOI: 10.1200/JCO.21.01308

https://ascopubs.org/doi/pdf/10.1200/JCO.21.01308

INT0139 OVERALL SURVIVAL OF THE LOBECTOMY SUBSET VERSUS MATCHED CT/RT SUBSET



ASCO Rapid Recommendations Update
Feb 15, 2022



ASCO rapid recommendations

Adjuvant Systemic Therapy and Adjuvant Radiation Therapy for Stage I-IIIA Completely Resected Non–Small-Cell Lung Cancer: ASCO Guideline Rapid Recommendation Update

Katherine Pisters, MD[1]; Mark G. Kris, MD[2]; Laurie E. Gaspar, MD[3,4]; and Nofisat Ismaila, MD[5]; for the Adjuvant Systemic Therapy and Adjuvant Radiation Therapy for Stage I to IIIA NSCLC Guideline Expert Panel

ASCO Rapid Recommendations Updates highlight revisions to select ASCO guideline recommendations as a response to the emergence of new and practice-changing data. The rapid updates are supported by an evidence review and follow the guideline development processes outlined in the ASCO Guideline Methodology Manual. The goal of these articles is to disseminate updated recommendations, in a timely manner, to better inform health practitioners and the public on the best available cancer care options.

https://pubmed.ncbi.nlm.nih.gov/35167335/

Stage IB (3<T<=4 cm N0M0)

1. Adjuvant osimertinib for EGFR mutations: Ex19del, L858R
2. Adjuvant platinum doublet +/- atezolizumab ***NOT*** recommended routinely

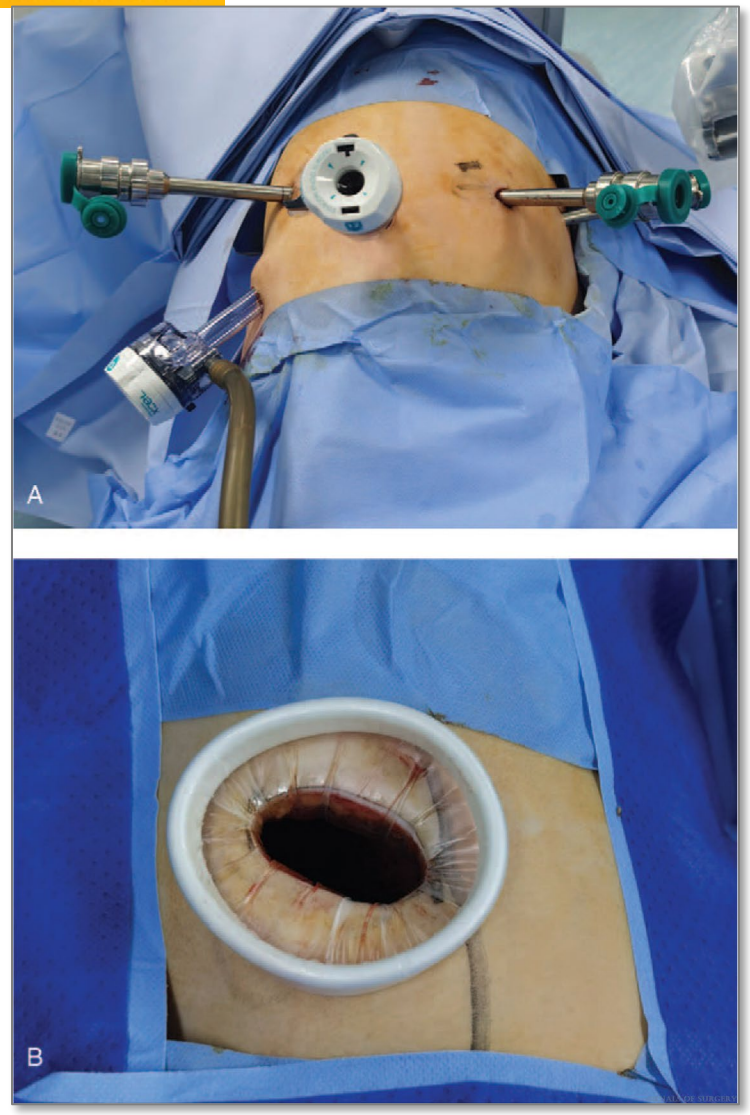
Stage IIA, IIB, IIIA

1. Adjuvant platinum doublet **recommended for all**, FOLLOWED BY:
2. Osimertinib if EGFR mutation
3. Atezolizumab if PDL1>=1% and EGFR negative

RVLob Randomized Trial
Annals of Surgery
February 2022

ANNALS OF SURGERY

Robotic Assisted vs. Video-Assisted Thoracoscopic Lobectomy: Short term results of a Randomized Clinical Trial: RVLob

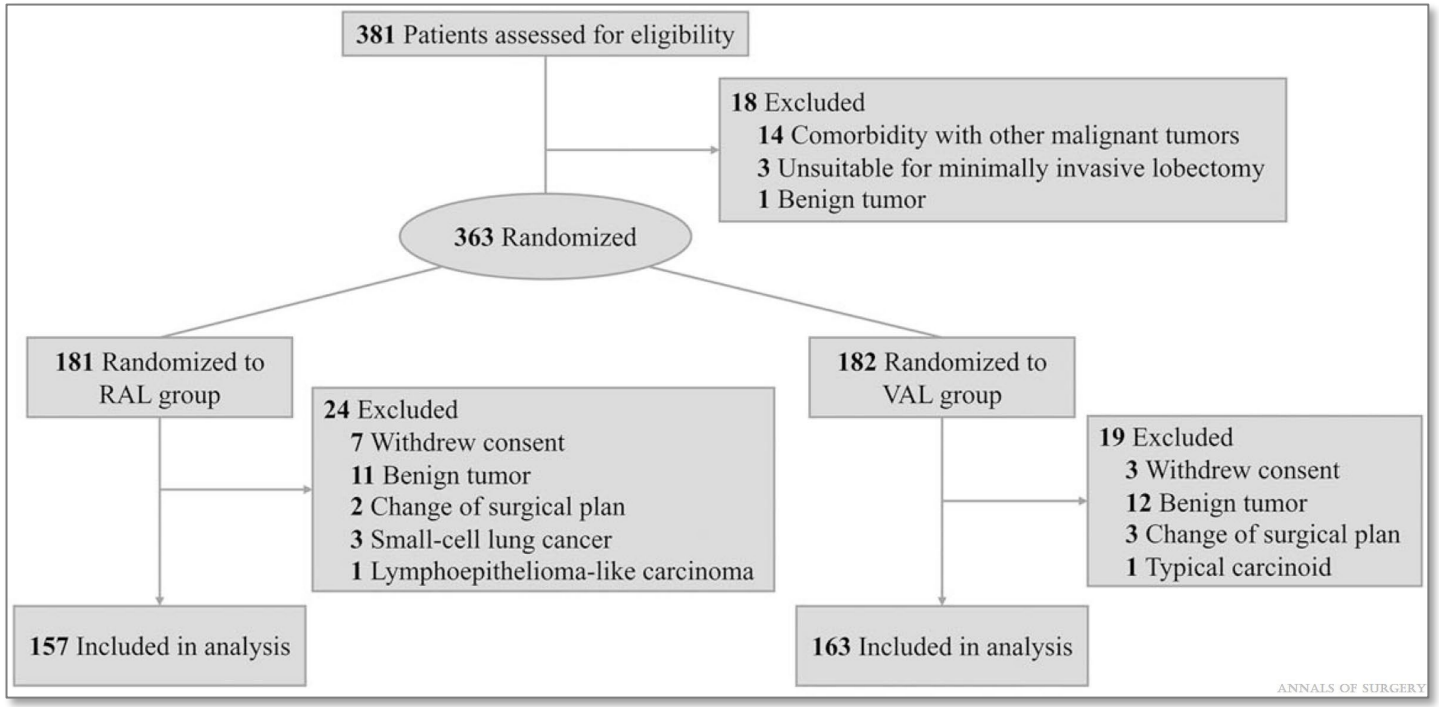


Jin, Runsen; Zheng, Yuyan; Yuan, Ye; Han, Dingpei; Cao, Yuqin; Zhang, Yajie; Li, Chengqiang; Xiang, Jie; Zhang, Zhengyuan; Niu, Zhenyi; Lerut, Toni; Lin, Jules; Abbas, Abbas E.; Pardolesi, Alessandro; Suda, Takashi; Amore, Dario; Schraag, Stefan; Aigner, Clemens; Li, Jian; Che, Jiaming; Hang, Junbiao; Ren, Jian; Zhu, Lianggang; Li, Hecheng

Annals of Surgery275(2):295-302, **February 2022.**

doi: 10.1097/SLA.0000000000004922

https://journals.lww.com/annalsofsurgery/Fulltext/2022/02000/Robotic_assisted_Versus_Video_assisted.14.aspx



Robotic Assisted vs. Video-Assisted Thoracoscopic Lobectomy: Short term results of a Randomized Clinical Trial: RVLob

Jin, Runsen; Zheng, Yuyan; Yuan, Ye; Han, Dingpei; Cao, Yuqin; Zhang, Yajie; Li, Chengqiang; Xiang, Jie; Zhang, Zhengyuan; Niu, Zhenyi; Lerut, Toni; Lin, Jules; Abbas, Abbas E.; Pardolesi, Alessandro; Suda, Takashi; Amore, Dario; Schraag, Stefan; Aigner, Clemens; Li, Jian; Che, Jiaming; Hang, Junbiao; Ren, Jian; Zhu, Lianggang; Li, Hecheng

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https://journals.lww.com/annalsofsurgery/Fulltext/2022/02000/Robotic_assisted_Versus_Video_assisted.14.aspx

TABLE 2 - Perioperative Outcomes

Characteristic	Robotic-assisted Lobectomy (n = 157)	Video-assisted Lobectomy (n = 163)	P
Operation time [min], median (IQR)	110 (95–140)	120 (97.5–150)	0.25
Blood loss [mL], median (IQR)	100 (50–100)	100 (50–150)	0.04
Intraoperative blood transfusion, no. (%)	3 (1.9)	2 (1.2)	0.68
Postoperative hospital stay [d], median (IQR)	4 (4–5)	5 (4–5)	0.76
Chest tube duration [d], median (IQR)	3 (2–4)	3 (2–4)	0.97
Conversion to thoracotomy, no. (%)	7 (4.5)	9 (5.5)	0.86
Chest tube drainage [mL], median (IQR)	830 (550–1130)	685 (367.5–1160)	0.007
Postoperative complications, no. (%)	23 (14.6)	30 (18.4)	0.45
Clavien Dindo I-II	18 (11.5)	24 (14.7)	0.49
Pleural effusion	8 (5.1)	12 (7.4)	0.54
Pneumonia	4 (2.5)	1 (0.6)	0.21
Prolonged air leak	9 (5.7)	7 (4.3)	0.74
Recurrent air leak	0	1 (0.6)	>0.99
Hemorrhage	1 (0.6)	1 (0.6)	>0.99
Atrial fibrillation	0	1 (0.6)	>0.99
Ischemic stroke	0	1 (0.6)	>0.99
Hypoxemia	0	1 (0.6)	>0.99
Clavien Dindo III-IV	5 (3.2)	6 (3.7)	>0.99
Pleural effusion	2 (1.3)	2 (1.2)	>0.99
Pneumonia	0	1 (0.6)	>0.99

TABLE 2 - Perioperative Outcomes

Characteristic	Robotic-assisted Lobectomy (n = 157)	Video-assisted Lobectomy (n = 163)	P
Prolonged air leak	0	3 (1.8)	0.25
Recurrent air leak	1 (0.6)	1 (0.6)	>0.99
Hemorrhage	1 (0.6)	1 (0.6)	>0.99
Ischemic stroke	2 (1.3)	0	0.24
Hospitalization cost [$], median (IQR)	12821 (12145–13924)	8009 (7014–9003)	<0.001
Indirect cost [$], median (IQR)	5197 (5197–5205)	453 (445–453)	<0.001
Direct cost [$], median (IQR)	7624 (6491–8708)	7572 (6574–8550)	0.15
Visual analog scale			
Postoperative day 1, median (IQR)	2 (2–3)	3 (2–3)	0.08
Postoperative day 2, median (IQR)	2 (2–3)	2 (2–3)	0.13
Postoperative day 3, median (IQR)	2 (2–2)	2 (2–3)	0.60
Duration of extra analgetic [d], median (IQR)	0 (0–1)	0 (0–1)	0.11
Readmission, no. (%)	3 (1.9)	3 (1.8)	>0.99

IQR indicates interquartile range.

Robotic Assisted vs. Video-Assisted Thoracoscopic Lobectomy: Short term results of a Randomized Clinical Trial: RVLob

TABLE 3 - Lymph Node Dissection

Characteristic	Robotic-assisted Lobectomy (n = 157)	Video-assisted Lobectomy (n = 163)	*P*
Total number of lymph nodes, median (IQR)	11 (8–15)	10 (8–13)	0.02
Total number of lymph node stations, median (IQR)	6 (5–7)	5 (4–6)	<0.001
Number of N1 lymph nodes, median (IQR)	6 (4–8)	5 (3–7)	0.005
Number of N2 lymph nodes, median (IQR)	5 (4–8)	5 (3–7)	0.19
Nodal upstaging, no. (%)	12 (7.6)	20 (12.3)	0.23
Upstage, no. (%)			
cN0 to pN1	4 (2.5)	8 (4.9)	0.41
cN0 to pN2	6 (3.8)	7 (4.3)	>0.99
cN1 to pN2	2 (1.3)	5 (3.1)	0.45

IQR indicates interquartile range.

Jin, Runsen; Zheng, Yuyan; Yuan, Ye; Han, Dingpei; Cao, Yuqin; Zhang, Yajie; Li, Chengqiang; Xiang, Jie; Zhang, Zhengyuan; Niu, Zhenyi; Lerut, Toni; Lin, Jules; Abbas, Abbas E.; Pardolesi, Alessandro; Suda, Takashi; Amore, Dario; Schraag, Stefan; Aigner, Clemens; Li, Jian; Che, Jiaming; Hang, Junbiao; Ren, Jian; Zhu, Lianggang; Li, Hecheng

Annals of Surgery275(2):295-302, **February 2022.**

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https://journals.lww.com/annalsofsurgery/Fulltext/2022/02000/Robotic_assisted_Versus_Video_assisted.14.aspx

In conclusion, this was the first prospective RCT to compare RAL with VAL for the treatment of NSCLC. Both the robotic- and video-assisted techniques were demonstrated to be safe and feasible. RAL was associated with a higher number of LNs dissected; however, it also resulted in an increased amount of chest drainage and higher hospitalization costs. Further follow-up is ongoing to evaluate and compare the long-term efficacy of RAL and VAL.

RCT Level of Suction after VATS Lobe 2019

The effects of low suction on digital drainage devices after lobectomy using video-assisted thoracoscopic surgery: a randomized controlled trial†

Bo Laksáfoss Holbek[a,b,*], Merete Christensen[a], Henrik Jessen Hansen[a], Henrik Kehlet[b] and René Horsleben Petersen[a]

Cite this article as: Holbek BL, Christensen M, Hansen HJ, Kehlet H, Petersen RH. The effects of low suction on digital drainage devices after lobectomy using video-assisted thoracoscopic surgery: a randomized controlled trial†. Eur J Cardiothorac Surg 2019;55:673–81.

Key question

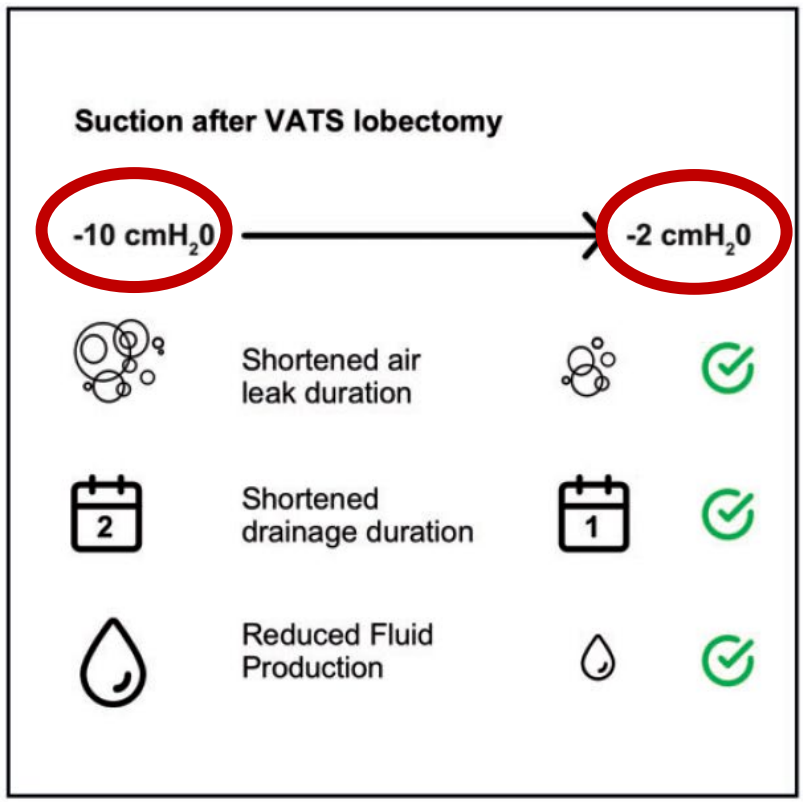
What is the optimal level of suction (-2 or -10 cmH_2O) on digital drainage devices after VATS lobectomy?

Key finding(s)

Suction of -2 cmH_2O reduces air leak duration, drainage duration and fluid output.

Take-home message

Drain suction should be kept to a minimum after VATS lobectomy.



The effects of low suction on digital drainage devices after lobectomy using video-assisted thoracoscopic surgery: a randomized controlled trial†

Bo Laksáfoss Holbek[a,b,*], Merete Christensen[a], Henrik Jessen Hansen[a], Henrik Kehlet[b] and René Horsleben Petersen[a]

Cite this article as: Holbek BL, Christensen M, Hansen HJ, Kehlet H, Petersen RH. The effects of low suction on digital drainage devices after lobectomy using video-assisted thoracoscopic surgery: a randomized controlled trial†. Eur J Cardiothorac Surg 2019;55:673–81.

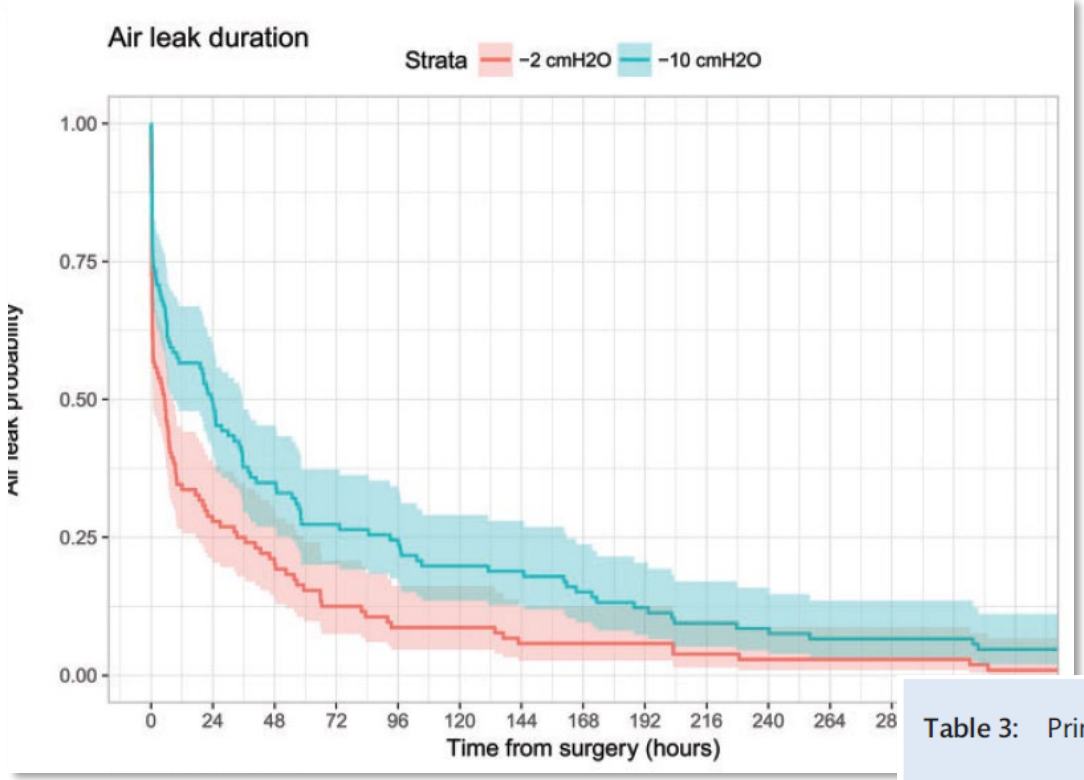


Table 3: Primary and secondary outcomes

Variables	−2 cmH_2O ($n = 111$)	−10 cmH_2O ($n = 111$)	*P*-value
Drainage duration (h)	27.4 (23.3–71.2)	47.5 (24.5–117.8)	0.047
Time to air leak cessation (<20 ml/min) (h)	5.2 (0.3–34.2)	23.7 (0.8–90.8)	<0.001
Time to fulfilment of drain removal criteria[a] (h)	17.2 (12.3–46.2)	35.7 (12.8–102.8)	<0.001
Prolonged air leak >5 days	16 (14.4)	27 (24.3)	0.089
Additional drain due to expanding subcutaneous emphysema	2 (1.8)	4 (3.6)	0.68
Pneumothorax after drain removal	46 (41.8)	55 (49.5)	0.31
Size of pneumothorax (mm)	15.5 (8.0–25.5)	15.0 (8.0–23.5)	0.59
Pneumothorax/SCE requiring drain reinsertion	10 (9.0)	6 (5.4)	0.44
Drainage duration of reinserted drain	2.0 (2.0–2.8)	3.0 (2.0–5.5)	0.27
Fluid accumulation requiring thoracentesis	2 (1.8)	2 (1.8)	1.00
Total drain fluid (ml)	566.0 (329.0–1155.0)	795.0 (454.2–1605.0)	0.007
Length of in-hospital stay	2.0 (2.0–5.8)	3.0 (2.0–9.0)	0.18

Values are expressed as *n* (%) or median (interquartile range).
[a]Drain removal criteria are: air leak consistently below 20 ml/min for at least 12 h with non-bloody, non-chylous fluid.
SCE: subcutaneous emphysema.

Circulating Tumor Cells for Lung Cancer Screening

AIR Study

Circulating tumour cells as a potential biomarker for lung cancer screening: a prospective cohort study

Charles-Hugo Marquette, Jacques Boutros, Jonathan Benzaquen, Marion Ferreira, Jean Pastre, Christophe Pison, Bernard Padovani, Faiza Bettayeb, Vincent Fallet, Nicolas Guibert, Damien Basille, Marius Ilie, Véronique Hofman*, Paul Hofman*, on behalf of the AIR project Study Group†

- 654 patients 2015-2017, met NLST criteria AND have COPD
- ISET Rarecells CTC assay (Isolation by size of epithelial tumor cell technique) + LDCT + clinical exam
- Nodule >= 5 mm considered “positive”
- Sensitivity was only 26.3% BUT highly specific when positive
- “one dimensional” approach currently not adequate

Lancet Respir Med 2020;
8:709–16

AIR Study

Circulating tumour cells as a potential biomarker for lung cancer screening: a prospective cohort study

Charles-Hugo Marquette, Jacques Boutros, Jonathan Benzaquen, Marion Ferreira, Jean Pastre, Christophe Pison, Bernard Padovani, Faiza Bettayeb, Vincent Fallet, Nicolas Guibert, Damien Basille, Marius Ilie, Véronique Hofman, Paul Hofman*, on behalf of the AIR project Study Group†*

Research in context

Evidence before this study

Low-dose chest CT lung cancer screening has been shown to reduce lung cancer mortality. However, implementation of this screening is hampered by the high number of false positives. To improve the performance of screening tools, tumour-derived blood biomarkers have been tested in patients at risk, particularly as part of screening programmes. Some biomarkers, such as circulating free DNA, microRNA, protein panels, or circulating tumour cells (CTCs) have shown promising results. In a previous observational study, we detected CTCs using the isolation by size of epithelial tumour cells technique (ISET), long before lung cancer was diagnosed radiologically. We carried out a literature search in MEDLINE through PubMed and Embase from their inception date to June 1, 2015, with the keywords "lung cancer", "early detection", "screening", "predictive", "biomarker", "circulating tumour cell", and "liquid biopsy". At the time of initiation of this study there were no published data regarding the use of CTCs as a biomarker for lung cancer screening.

Added value of this study

The AIR study is a prospective, multicentre, cohort study done in 21 university centres in France and is the largest cohort trial to test the performance of ISET as a lung cancer screening tool. However, this technique was not sufficiently reliable to recommend use for lung cancer screening, detection of interval cancers, characterisation of pulmonary nodules or prediction of the occurrence of lung cancer. The rate of lung cancer detection in our population was high, compared with other cohorts, reaching as high as 3·1% prevalent lung cancers and 2·8% 1-year incident lung cancers.

Implications of all the available evidence

The detection of lung cancer using blood biomarkers is still in progress. Many teams have tested various biomarkers with mixed results. It is likely that biological signatures alone will not be sufficient for screening. The solution might lie in integrating a triple clinical, biological, and radiological signature into lung screening programmes. Patients with chronic obstructive pulmonary disease have a particularly high risk of developing lung cancer and should be given special attention in screening programmes.

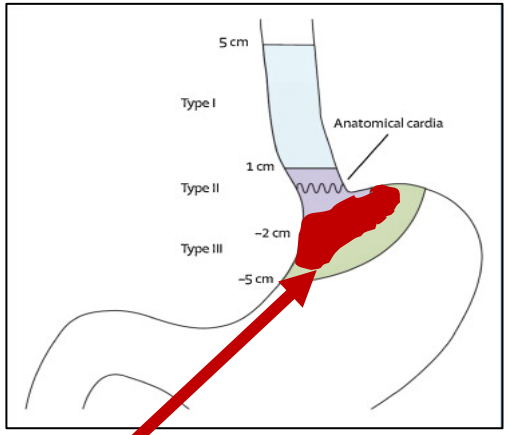
Lancet Respir Med 2020; 8:709–16

Key Esophageal Papers

Neo-AEGIS: Phase 3 RCT CROSS vs FLOT NCT01726452 Reported ASCO 2021

377 patients Adeno of Eso/GEJ

- Carbo Taxol + 41 GY (CROSS) vs. Docetaxel, 5FU, Leucovorin, Oxaliplatin (FLOT) or MAGIC
- 3 year survival 56% and 57%
- NONINFERIORITY of periop chemo vs. CROSS
- *Useful for GEJ when not sure if Siewert 2 vs 3*



	Arm A (Magic/FLOT)	Arm B CROSS
R0 (negative margins)	82%	95%
ypN0	44.5%	60.1%
Tumor regression grade 1 & 2	12.1%	41.7%
Pathologic complete response	5%	16%
Neutropenia (Gr 3/4)	14.1%	2.8%
Neutropenic sepsis	2.7%	0.6%
Postoperative in-hospital deaths	3%	3%
Postoperative Pneumonia/ARDS	20%/0.6%	16%/4.3%
Anastomotic Leak	12%	11.7%
Clavien-Dindo > III<V	23.6%	22%

(Abstract Only)

DOI:10.1200/JCO.2021.39.15_suppl.4004 *Journal of Clinical Oncology* 39, no. 15_suppl (May 20, 2021) 4004-4004.

https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.15_suppl.4004

Neo-AEGIS continued

- MAGIC: Epirubicin, Cis, 5FU
- 157 had MAGIC, 27 had FLOT
- less pCR, RO due to no radiation
- Potential benefit of avoiding radiation
  - Easier on patient
  - More aggressive systemically
  - Removes concern about anastomosis in radiation field
  - Esophagitis non issue?

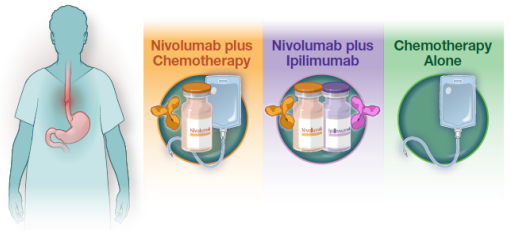
- Use of nivo postop – tbd, we are doing it regardless of periop strategy

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma

Doki Y et al. DOI: 10.1056/NEJMoa2111380



CLINICAL PROBLEM

In patients with advanced esophageal squamous-cell carcinoma, first-line chemotherapy is associated with poor overall survival. Incorporating immune checkpoint inhibitors, such as nivolumab and ipilimumab, into first-line treatment might improve clinical outcomes.

CLINICAL TRIAL

Design: A randomized, open-label, global phase 3 trial compared the efficacy and safety of both an immune checkpoint inhibitor in combination with chemotherapy and a dual immune checkpoint inhibitor combination with chemotherapy alone in previously untreated patients with advanced esophageal squamous-cell carcinoma.

Intervention: 970 adults with unresectable advanced, recurrent, or metastatic disease were assigned to nivolumab plus chemotherapy (fluorouracil and cisplatin), nivolumab plus ipilimumab, or chemotherapy alone. The primary end points were overall survival and progression-free survival.

RESULTS

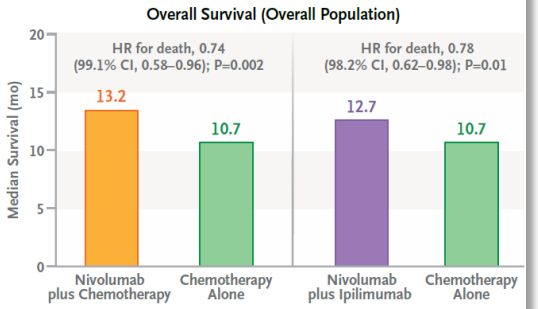
Efficacy: After a 13-month minimum follow-up, median overall survival was significantly longer with nivolumab plus chemotherapy and with nivolumab plus ipilimumab than with chemotherapy alone. The benefits were seen among patients with tumor-cell programmed death ligand 1 (PD-L1) expression of 1% or greater and in the overall population. A significant progression-free survival benefit was seen only with nivolumab plus chemotherapy among patients with PD-L1 expression of 1% or greater.

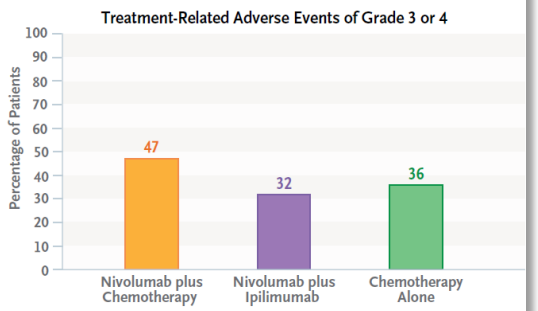
Safety: The safety profiles of the nivolumab-containing regimens were consistent with those of the individual components of each regimen. Grade 3 or 4 treatment-related adverse events were more common with nivolumab plus chemotherapy than with the other two regimens.

LIMITATIONS AND REMAINING QUESTIONS

- The open-label design of the trial may have influenced causality assessments of adverse events.
- Whether nivolumab plus chemotherapy and nivolumab plus ipilimumab are associated with similar outcomes — and whether one regimen is better than the other for certain subgroups of patients — is unknown.

Links: Full Article | NEJM Quick Take





CONCLUSIONS

In patients with previously untreated, advanced esophageal squamous-cell carcinoma, treatment with nivolumab plus chemotherapy and treatment with nivolumab plus ipilimumab were both superior to chemotherapy alone with respect to overall survival. No new safety signals emerged with either regimen.

Checkmate 648

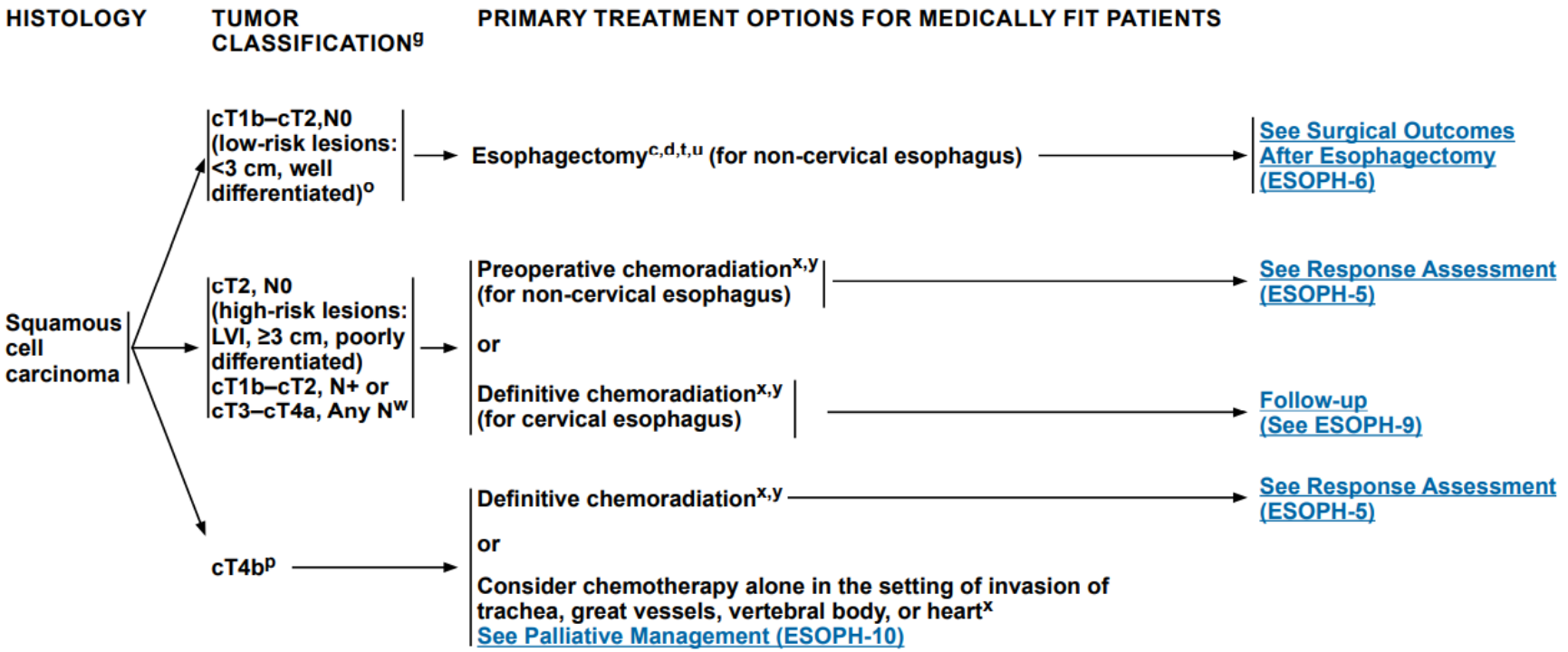
NEJM 2/3/2022

UNRESECTABLE SCCA
NIVO + CHEMO or NIVO+IPI
better than chemotherapy alone

**important for airway invasive cases*

Esophageal and Esophagogastric Junction Cancers

Discussion



[c] See Principles of Pathologic Review and Biomarker Testing (ESOPH-B).
[d] See Principles of Surgery (ESOPH-C).
[g] See Staging (ST-1) for tumor classification.
[o] Preclinical staging cannot establish the number of positive nodes.
[p] For select patients, consider endoluminal stenting when appropriate. See Principles of Palliative/Best Supportive Care (ESOPH-H).
[t] Transhiatal or transthoracic, or minimally invasive; gastric reconstruction preferred.
[u] Feeding jejunostomy for postoperative nutritional support, generally preferred.
[w] Histologic confirmation of suspected positve node is desirable.
[x] See Principles of Systemic Therapy (ESOPH-F).
[y] See Principles of Radiation Therapy (ESOPH-G).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Key Mesothelioma Papers

SMART Trial

Surgery for malignant pleural mesothelioma after radiotherapy (SMART): final results from a single-centre, phase 2 trial

B C John Cho, Laura Donahoe, Penelope A Bradbury, Natasha Leighl, Shaf Keshavjee, Andrew Hope, Prodipto Pal, Michael Cabanero, Kasia Czarnecka, Karen McRae, Ming-Sound Tsao, Marc de Perrot

	Grade 3	Grade 4
Any grade 3 or 4 complications	33 (34%)	14 (15%)
Atrial fibrillation	24 (25%)	0
Pneumonia	1 (1%)	4 (4%)
Venous thromboembolism	3 (3%)	1 (1%)
Orthostatic hypotension	4 (4%)	0
Empyema	2 (2%)	2 (%)
Chylothorax	2 (2%)	1 (%)
Haemothorax	0	3 (3%)
Fluid retention	2 (2%)	0
Diaphragmatic dehiscence	0 (%)	2 (%)
Wound dehiscence or infection	2 (2%)	0
Hiccups	2 (2%)	0
Gastrointestinal bleeding	0	1 (1%)
Platypnoea-orthodeoxia syndrome	0	1 (1%)
Clostridium difficile colitis	1 (1%)	0
Renal dysfunction	1 (1%)	0

Data are n (%). Patients were counted for each complication.

Table 2: Grade 3 and 4 complications within 30 days of extrapleural pneumonectomy

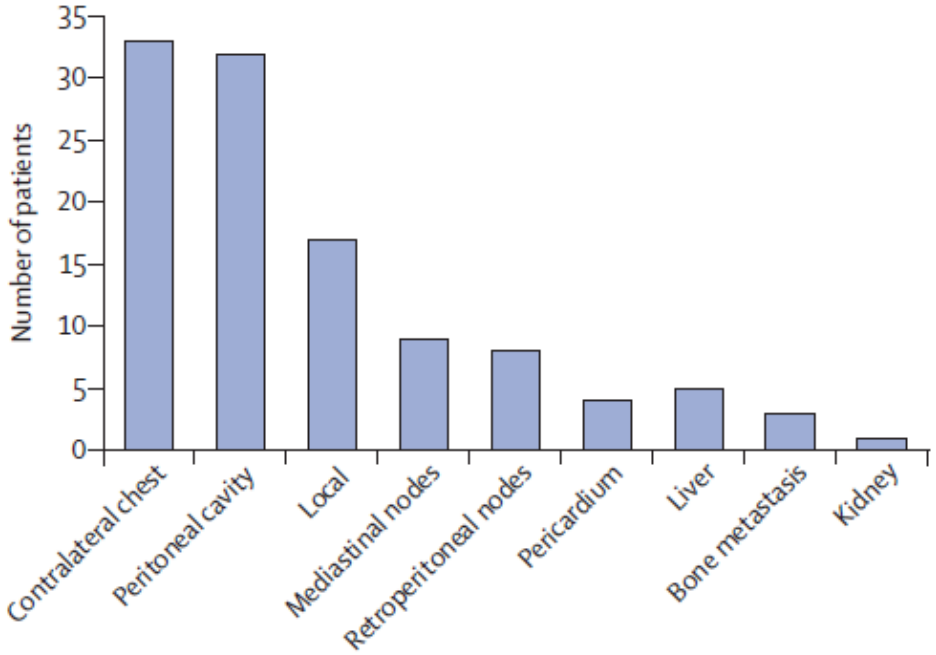


Figure 2: Site of first disease recurrence in 72 patients
Site of first disease recurrence in all 72 patients with at least one disease recurrence.

Lancet Oncol 2021; 22: 190–197
Published Online
January 12, 2020
https://doi.org/10.1016/S1470-2045(20)30606-9

Surgery for malignant pleural mesothelioma after radiotherapy (SMART): final results from a single-centre, phase 2 trial

B C John Cho, Laura Donahoe, Penelope A Bradbury, Natasha Leighl, Shaf Keshavjee, Andrew Hope, Prodipto Pal, Michael Cabanero, Kasia Czarnecka, Karen McRae, Ming-Sound Tsao, Marc de Perrot

Research in context

Evidence before this study

No curative treatment for malignant pleural mesothelioma is available because of an absence of consensus and generally poor outcomes reported in trials and case reports, despite many attempts. We searched PubMed, for large (>50 patients), prospective, multimodal clinical trials of radical surgery for malignant pleural mesothelioma published from Jan 1, 2000, to April 30, 2020, using the search terms "malignant pleural mesothelioma" and "surgery" and "clinical trial" or "prospective study". We found 11 studies. We reviewed their results, specifically their complication rates, operative mortality rates, and overall survival. We found their outcomes were relatively heterogeneous and generally poor (overall survival <20 months).

Added value of this study

Treating patients with malignant pleural mesothelioma with extrapleural pneumonectomy is controversial because the intervention is associated with morbidity and has poor clinical benefit. Our results show that the combination of radiotherapy followed by extrapleural pneumonectomy, although morbid, was clinically feasible compared with extrapleural pneumonectomy alone. We report one of the highest median overall survival results for patients with malignant pleural mesothelioma in a large surgical series using extrapleural pneumonectomy. Of note, we found that patients with node-negative disease and patients with epithelioid malignant pleural mesothelioma had the best improvement to overall survival.

Implications of all the available evidence

Surgery for mesothelioma after radiotherapy (SMART) resulted in an improvement to median overall survival, but it requires surgical and radiation expertise to achieve optimal results. SMART should not be adopted outside of expert centres with large surgical experience.

Podcast Recommendations

Lung Cancer Update Podcast

IASLC

Lung Cancer Considered
IASLC

STS podcasts:

Resilient Surgeon
Same Surgeon, Different Light
Beyond the Abstract
Webinar series

Gastrointestinal Cancer Update Podcast

A Spotify Original
Parcast
dare to lead
with Brené Brown

Behind the Knife

to go

CTSNet To Go
CTSNet

Other Surgery “Stuff”

Will email links to this and all papers

COVID related papers

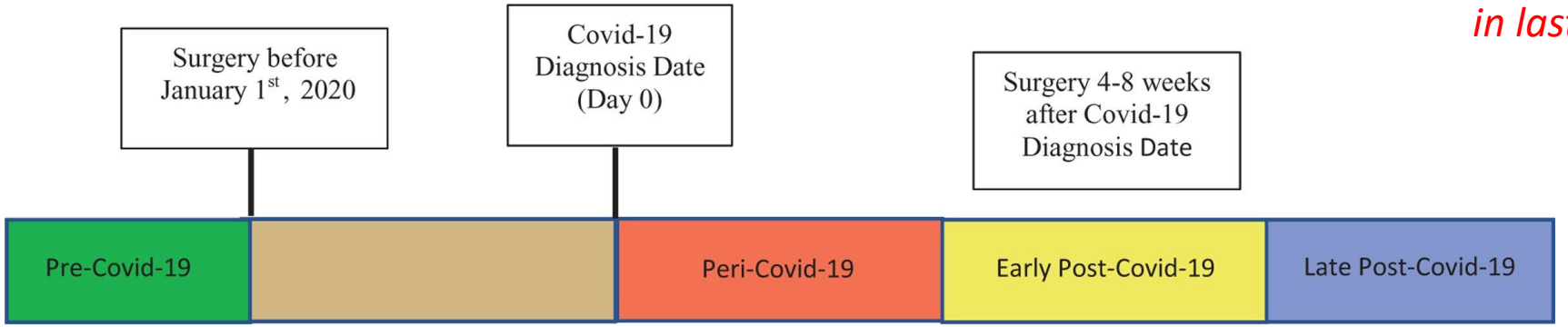
ORIGINAL ARTICLE

The Risk of Postoperative Complications After Major Elective Surgery in Active or Resolved COVID-19 in the United States

John Z. Deng, BS, Janine S. Chan, BS,† Alexandra L. Potter,‡ Ya-Wen Chen, MD,§ Harpal S. Sandhu, MD, FRCSC,||¶ Nikhil Panda, MD, MPH,§ David C. Chang, PhD, MPH, MBA,§ and Chi-Fu Jeffrey Yang, MD#✉*

Annals of Surgery 275(2):242-246, February 2022.

Most read, most emailed An Surg Paper in last 60 days



Postoperative pneumonia	33 (1.3%)	57 (7.3%)	11 (2.5%)	23 (1.4%)	<0.001
Postoperative respiratory failure	62 (2.4%)	57 (7.3%)	11 (2.5%)	45 (2.8%)	<0.001
Any postoperative complication	270 (10.3%)	131 (16.8%)	52 (11.7%)	183 (11.2%)	<0.001

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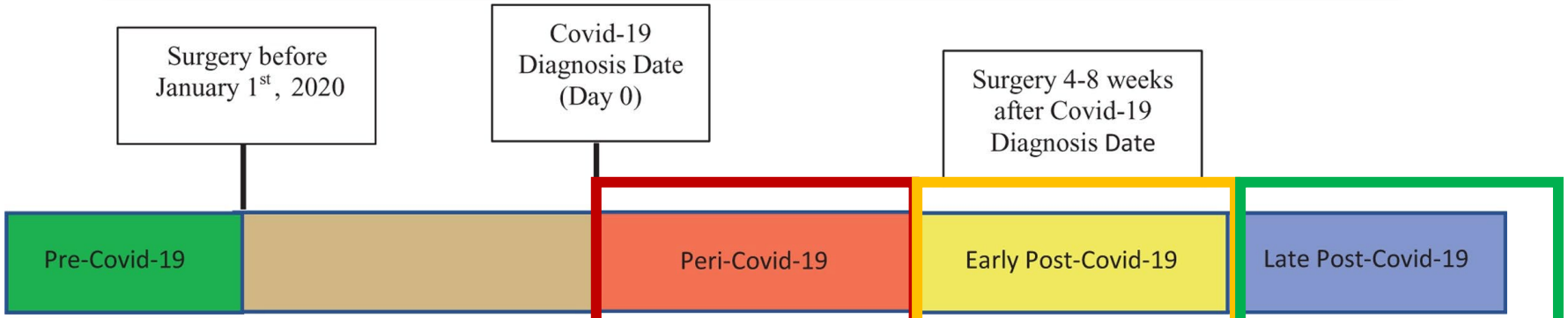
Annals of Surgery 275(2):242-246, February 2022.

Conclusions: Major, elective surgery 0 to 4 weeks after SARS-CoV-2 infection is associated with an increased risk of postoperative complications. Surgery performed 4 to 8 weeks after SARS-CoV-2 infection is still associated with an increased risk of postoperative pneumonia, whereas surgery 8 weeks after Covid-19 diagnosis is not associated with increased complications.



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Any postoperative complication	270 (10.3%)	131 (16.8%)	52 (11.7%)	183 (11.2%)	<0.001

Tracheostomy and Covid – VERY highly read

Outcomes After Tracheostomy in COVID-19 Patients

Chao, Tiffany N. MD*; Harbison, Sean P. MD†; Braslow, Benjamin M. MD†; Hutchinson, Christoph T. MD‡; Rajasekaran, Karthik MD*; Go, Beatrice C. BS§; Paul, Ellen A. BSE*; Lambe, Leah D. BSN, RN, CEN||; Kearney, James J. MD*; Chalian, Ara A. MD*; Cereda, Maurizio F. MD¶; Martin, Niels D. MD†; Haas, Andrew R. MD, PhD‡; Atkins, Joshua H. MD, PhD¶; Rassekh, Christopher H. MD*

Annals of Surgery: September 2020 - Volume 272 - Issue 3 - p e181-e186
doi: 10.1097/SLA.0000000000004166

Novel Percutaneous Tracheostomy for Critically Ill Patients With COVID-19

Check for updates

Luis Angel, MD, Zachary N. Kon, MD, Stephanie H. Chang, MD, Samaan Rafeq, MD, Saketh Palasamudram Shekar, MD, Brian Mitzman, MD, Nancy Amoroso, MD, Ronald Goldenberg, MD, Kimberly Sureau, NP, Deane E. Smith, MD, and Robert J. Cerfolio, MD

Division of Pulmonary and Critical Care Medicine, Department of Medicine, New York University Langone Health, New York, New York; and Department of Cardiothoracic Surgery, New York University Langone Health, New York, New York

https://www.annalsthoracicsurgery.org/article/S0003-4975(20)30603-2/fulltext

Skin Prep

The Comparative Efficacy of Chlorhexidine Gluconate and Povidone-iodine Antiseptics for the Prevention of Infection in Clean Surgery

A Systematic Review and Network Meta-analysis

Ryckie G. Wade, MSc,†✉ Nicholas E. Burr, MBBS,‡§ Gordon McCauley, MBBS,*† Grainne Bourke, MB,*† and Orestis Efthimiou, PhD¶*

Annals of Surgery. 274(6):e481-e488, December 2021.

Chlorhexidine better than iodine prep

Surgical Professional Issues

The Resilience Bank Account: Skills for Optimal Performance

Michael Maddaus, MD

Department of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota

The day-to-day life of a cardiothoracic surgeon and other high-stakes occupations is riddled with chronic stress punctuated by acute, sometimes life-threatening, crises. Additional stress from the realms of a surgeon's personal life can add to the silent burden surgeons often carry. The tolls paid for poor management of the cumulative stress load can impact surgeons and their patients, leading to errors of clinical judgment, burnout, early departures from practice, health issues, and substance abuse. This article reviews 6 individual skills or habits that can, when proactively integrated into a daily routine, make the difference. The idea of investing in a resilience bank account is suggested as a metaphor for the reserve building and cumulative positive impact of these habits over time.

(Ann Thorac Surg 2020;109:18-25)

SURGICAL PERSPECTIVE

Safe and Supported Pregnancy

A Call to Action for Surgery Chairs and Program Directors

Michaela C. Bamdad, MD, MHS,✉ David T. Hughes, MD, and Michael Englesbe, MD

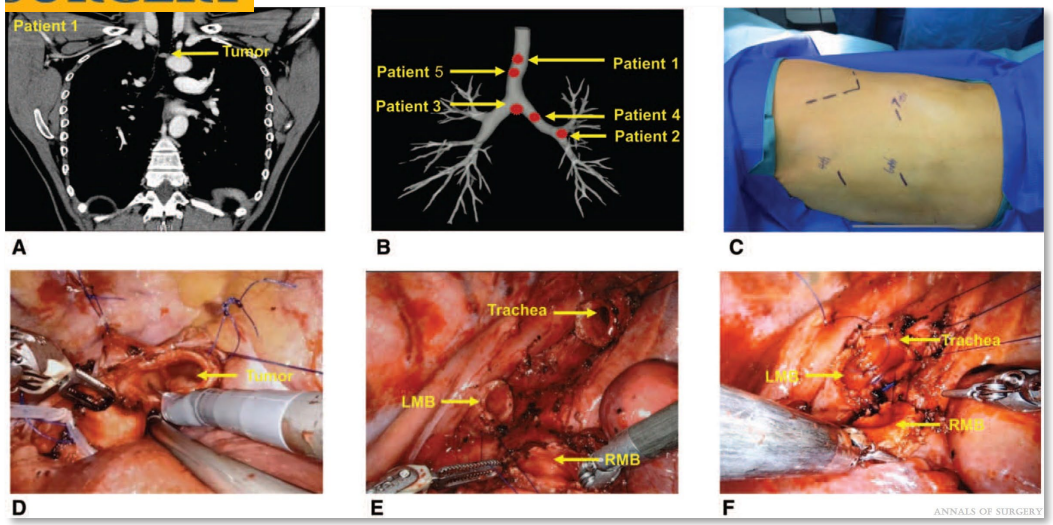
Annals of Surgery. 275(1):e1-e2, January 2022.

1. Prenatal Health Maintenance: Pregnant residents must be able to freely attend prenatal visits, without stigma or pushback. It is expressly not the responsibility of the pregnant resident to ask favors or arrange trades to attend medical appointments, but rather coverage is built into the schedule in the same manner as case and clinic assignments.
2. Maintaining Health and Well-being while Operating: Pregnant residents are supported in leaving the operating room during non-critical portions of the case to eat, drink, attend bodily needs, or rest, all of which are important in maintaining maternal and fetal health.
3. Special Considerations for Work Hours and Rotation Schedules: To minimize disruptions to sleep and circadian rhythm for residents in their third trimester, work shifts are limited to 12 hours and restricted to daytime work only. For rotations with overnight home call, alternative schedules are available. Some rotations may not be conducive to these restrictions and may necessitate schedule changes for pregnant residents and their peers.
4. Support for Non-Birthing Parents: Schedule accommodations are also available to non-birthing parents, including protected time to attend milestone prenatal and pediatric appointments, as well as a 2-week transition period after returning to work from parental leave of absence, during which the resident can choose schedule alterations that best fit their family's needs.
5. Culture of Support and Equity: Departmental leadership establishes a culture where pregnancy during clinical and research periods of training is fully supported. Discriminatory behavior about family planning or parental status is not tolerated.

Miscellaneous

ANNALS OF SURGERY

[Nonintubated Robotic-assisted Thoracic Surgery for Tracheal/Airway Resection and Reconstruction: Technique Description and Preliminary Results]



FULL TEXT ARTICLE

Management of Oligometastatic Disease in Advanced Non–Small Cell Lung Cancer

Howard West MD

Clinics in Chest Medicine, 2020-06-01, Volume 41, Issue 2, Pages 249-258, Copyright © 2020 Elsevier Inc.

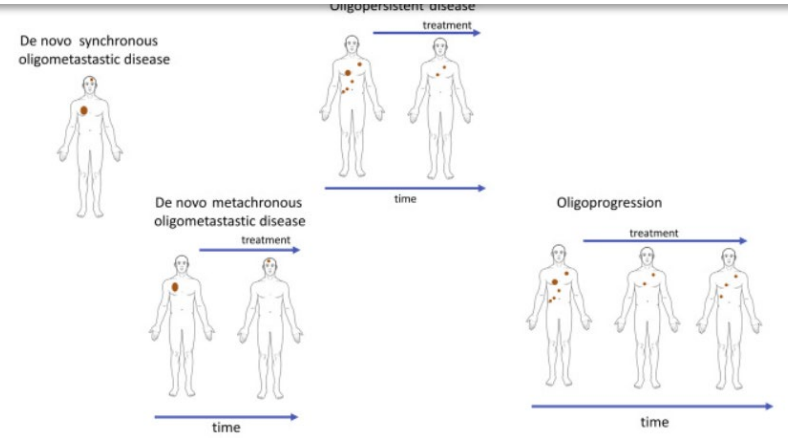


Fig. 1

Clinical settings representing variants of oligometastatic disease (OMD) in which local therapy may be appropriate.

Neoadjuvant atezolizumab and chemotherapy in patients with resectable non-small-cell lung cancer: an open-label, multicentre, single-arm, phase 2 trial

Catherine A Shu, Justin F Gainor, Mark M Awad, Codruta Chiuzan, Claud M Grigg, Aliyah Pabani, Robert F Garofano, Mark B Stoopler, Simon K Cheng, Abby White, Michael Lanuti, Frank D'Ovidio, Matthew Bacchetta, Joshua R Sonett, Anjali Saqi, Naiyer A Rizvi

Management of Ground-Glass Opacities in the Lung Cancer Spectrum

Check for updates

Yang Zhang, MD,* Fangqiu Fu, MD,* and Haiquan Chen, MD

Department of Thoracic Surgery, Fudan University Shanghai Cancer Center, Shanghai, China; Institute of Thoracic Oncology, Fudan University, Shanghai, China; State Key Laboratory of Genetic Engineering, School of Life Sciences, Fudan University, Shanghai, China; and Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

BMJ Open

Mesothelioma and Radical Surgery 2 (MARS 2): protocol for a multicentre randomised trial comparing (extended) pleurectomy decortication versus no (extended) pleurectomy decortication for patients with malignant pleural mesothelioma