

**GRANDANGOLO IN
RADIOTERAPIA
ONCOLOGICA: NUOVE
EVIDENZE E PRATICA
CLINICA**

POLMONE



XXXIII CONGRESSO NAZIONALE AIRO

AIRO2023

BOLAGNA,
OTTOBRE 2023
AI CONGRESSI



TRENTESIMO ANNIVERSARIO

Sara Ramella
Università Campus Bio-Medico di Roma
Fondazione Policlinico Campus Bio-Medico

I have the following real or perceived conflicts of interest that relate to this presentation:

Affiliation / Financial interest	Commercial company
Honoraria or consultation fees:	Astra Zeneca, Merk (MSD)
Participation in a company sponsored bureau:	Genetec, Gentili, Merk (MDS), Roche
Other support / potential conflict of interest:	Investigator for Astra Zeneca, Roche, Merk (MSD), Amgen

GRANDANGOLO IN RADIOTERAPIA ONCOLOGICA: NUOVE EVIDENZE E PRATICA CLINICA POLMONE

- ✓ NSCLC (Early Stage and Locally Advanced)
- ✓ SCLC (Limited Stage and PCI)



2023 World Conference
on Lung Cancer

SEPTEMBER 9-12, 2023 | SINGAPORE



Stereotactic Ablative Radiotherapy With or Without Immunotherapy for Early-Stage or Isolated Lung Parenchymal Recurrent Node-Negative NSCLC: An Open-Label, Randomized, Phase 2 Trial

I-SABR Study

Chang JY, Lin SH, Dong DL, Liao ZX, Gandhi S, Gay CM, Zhang JJ, Chun SG, Elamin YY, Frank FV, Blumenschein G, Cascone T, Le XN, Pozadzides JV, Tsao A, Verma V, Welsh J, Chen AB, Altan M, Mehran RJ, Vaporciyan AA, Swisher SG, Balter PA, Fujimoto J, Wistuba II, Feng L, Lee JJ and Heymach JV

**The University of Texas MD Anderson Cancer Center
Houston, TX 77025
USA**

Stereotactic Ablative Radiotherapy With or Without Immunotherapy for Early-Stage or Isolated Lung Parenchymal Recurrent Node-Negative NSCLC: An Open-Label, Randomized, Phase 2 Trial

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Schema

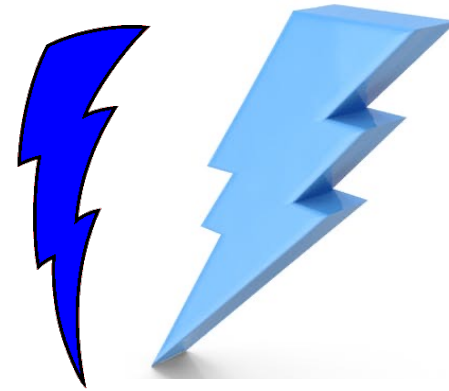
Staging:
Histologic confirmed
Diagnostic CT
PET/CT of lungs, mediastinum, adrenals
Brain MRI or CT (if indicated)
Invasive mediastinal staging (if indicated)
Pulmonary function tests
Lab tests

Stratification by:
Performance status (0-1 vs. 2)
Tumor size (≤ 3 cm vs. 3.1-5 cm vs. 5.1-7 cm)
Histology (squamous vs. non-squamous)
Lung cancer history (stage I vs. recurrence)

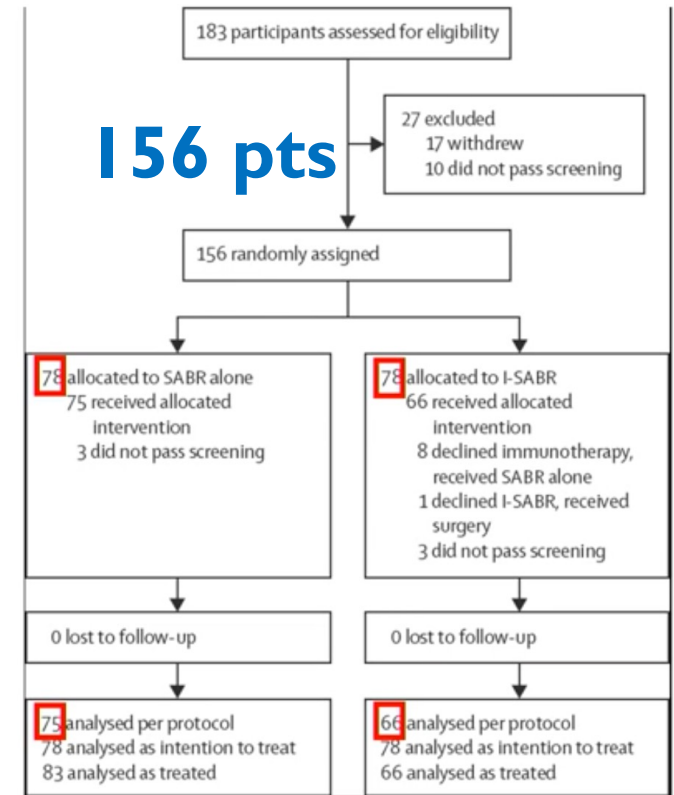
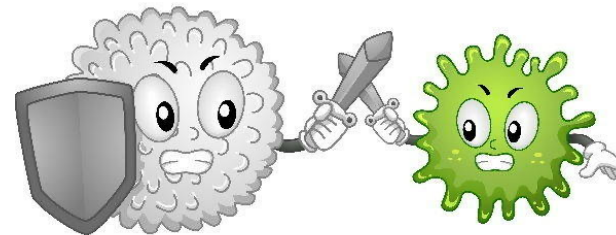
Randomized

SABR Only
50 Gy in 4 fx
OR
70 Gy in 10 fx

I-SABR
Nivo (480 mg) **same day or 36 H 1st fx**
SABR: 50 Gy in 4 fx OR 70 Gy in 10 fx
Nivo q4wk for **12 weeks**
(4 doses total)

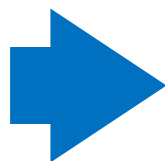


Follow-up:
H&P, labs, CT q3mo for 2 years
PET/CT at 9 months
PFT, EKG at 12 months
Collect tissues, blood/stool before, during and after TX
Image-based radiomic modeling



I-SABR STEREOTACTIC ABLATIVE RADIOTHERAPY +/- IMMUNOTHERAPY

**86-89% <3cm
cT1**



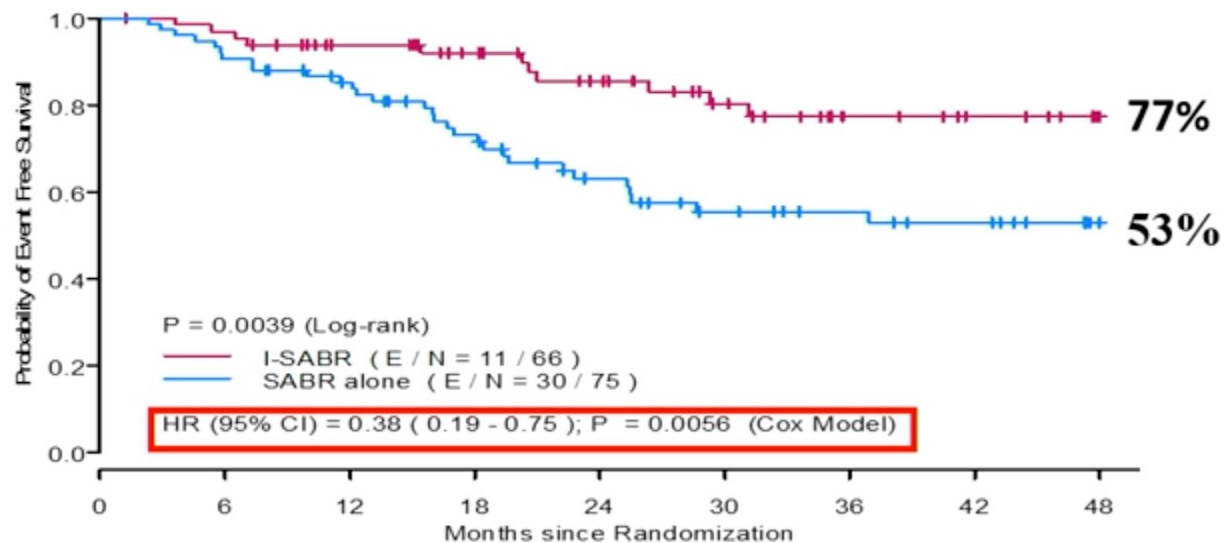
	SABR (n=75)	I-SABR (n=66)
Sex		
Female	41 (55%)	46 (70%)
Male	34 (45%)	20 (30%)
Race		
White	64 (85%)	62 (94%)
Any other race	11 (15%)	4 (6%)
Age, years		
	72 (66-78)	72 (66-75)
Smoking status		
Never	7 (9%)	7 (11%)
Current or previous	68 (91%)	59 (89%)
Eastern Cooperative Oncology Group performance status score		
0-1	68 (91%)	62 (94%)
2	7 (9%)	4 (6%)
Tumour histology		
Non-squamous carcinoma	61 (81%)	55 (83%)
Squamous cell carcinoma	14 (19%)	11 (17%)
Tumour size, cm		
Median	1.7 (1.3-2.2)	2.0 (1.4-2.6)
≤2 cm	51 (68%)	35 (53%)
>2 to ≤3 cm	16 (21%)	22 (33%)
>3 to ≤5 cm	8 (11%)	9 (14%)
Volume of gross tumour volume, mL		
	4.2 (2.4-9.1)	6.4 (2.5-15.1)
Lung cancer history		
Newly diagnosed	63 (84%)	50 (76%)
Recurrent	12 (16%)	16 (24%)
Single lesion		
	74 (99%)	62 (94%)
Two lesions		
	1 (1%)	4 (6%)

SABR regimen		
50 Gy in four fractions	63 (84%)	59 (89%)
70 Gy in ten fractions	12 (16%)	7 (11%)
Number of nivolumab cycles		
Median	NA	4 (4-4)
≤2	NA	11 (17%)
>2	NA	55 (83%)
PD-L1 status		
<1%	34 (45%)	27 (41%)
≥1%	16 (21%)	15 (23%)
Unknown	25 (33%)	24 (36%)
Epidermal growth factor receptor status		
Wild type	22 (29%)	25 (38%)
Mutated	3 (4%)	1 (2%)
Unknown	50 (67%)	40 (61%)
Underwent endobronchial ultrasound		
Yes	50 (67%)	43 (65%)
No	25 (33%)	23 (35%)
Received brain MRI		
Yes	40 (53%)	34 (52%)
No	35 (47%)	32 (48%)

PATTERNS OF FAILURE	REVISED STAR 5y cumulative recurrence rate % (95CI)	SABR % 4y
Any local failure	6.3 (2.3-13.3)	13.3
Any regional failure	12.5 (6.4-20,8)	10.7
Any distant failure	8.8 (3.8-16.2)	16
Any recurrence or death	17.6 (10.1-26.7)	36

Primary endpoint: EFS

Per protocol



No. at Risk (No. of Event)

I-SABR	66 (0)	54 (4)	38 (4)	18 (3)	7 (0)
SABR	75 (0)	59 (11)	34 (14)	22 (4)	11 (1)

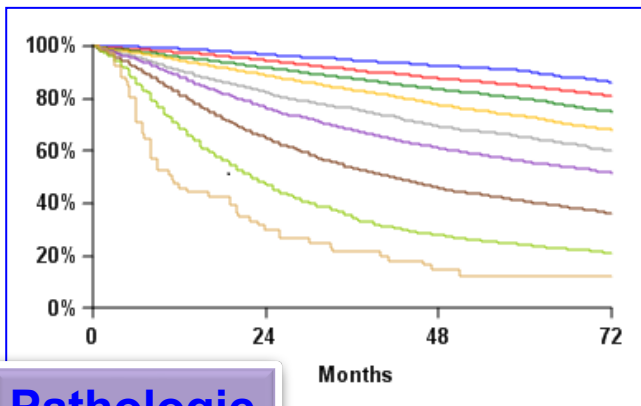
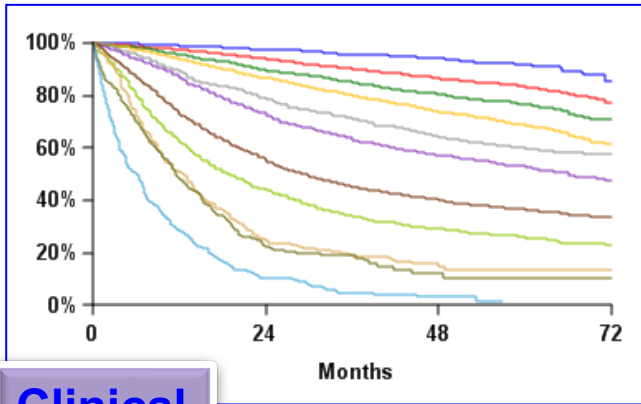
Toxicity

	Grade 2		Grade 3	
	SABR	I-SABR	SABR	I-SABR
Acute kidney injury	1
Adrenal insufficiency	1
Anorexia	1
Arthralgia	..	2
Blurred vision	..	1
Conjunctivitis	1
Diarrhoea	..	1
Dyspnoea	1
Fatigue	1	7	..	2
Hyperthyroidism	..	1	..	1
Hypoxia	1
Hepatitis (acute)	1
Myalgia	..	1
Oral mucositis	..	1
Oral dysesthesia	..	1
Pneumonia (infectious)	1
Pneumonitis	1	2
Pruritus	..	2
Rash	..	2	..	1
Xerophthalmia	..	1
Xerostomia	..	1

Data are number of events. No grade 4-5 adverse events occurred.
I-SABR=stereotactic ablative radiotherapy with immunotherapy.
SABR=stereotactic ablative radiotherapy.

Stage grouping for the TNM 8th edition

Goldstraw P et al. J Thorac Oncol 2016; 11: 39-51



	Events/N	MST	24 months	60 months
IA1	68/781	NR	97%	92%
IA2	505/3105	NR	94%	83%
IA3	546/2417	NR	90%	77%
IB	560/1928	NR	87%	68%

	Events/N	MST	24 months	60 months
IA1	139/1389	NR	97%	90%
IA2	823/5633	NR	94%	85%
IA3	875/4401	NR	92%	80%
IB	1618/6095	NR	89%	73%

I-SABR

EVENT FREE SURV 4y

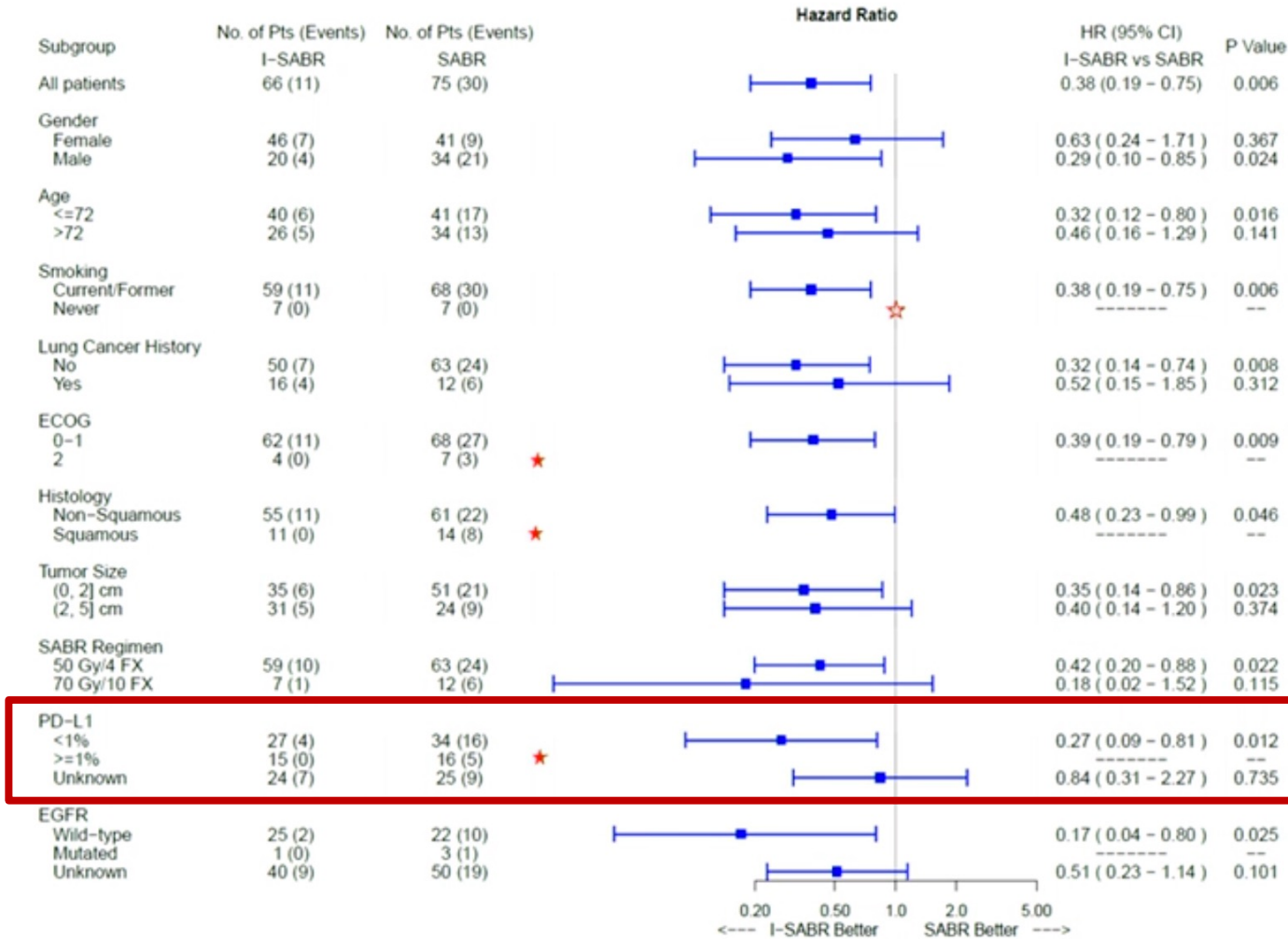
- SABR + IO 77%
- SABR 55%

Recurrent Lesion:

- SABR + IO 24%
- SABR 16%

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Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti



ONGOING PHASE III TRIALS:

- ✓ PACIFIC 4/RTOG 3515
- ✓ NCI
- ✓ ASTEROID

Right Tx for the right patient

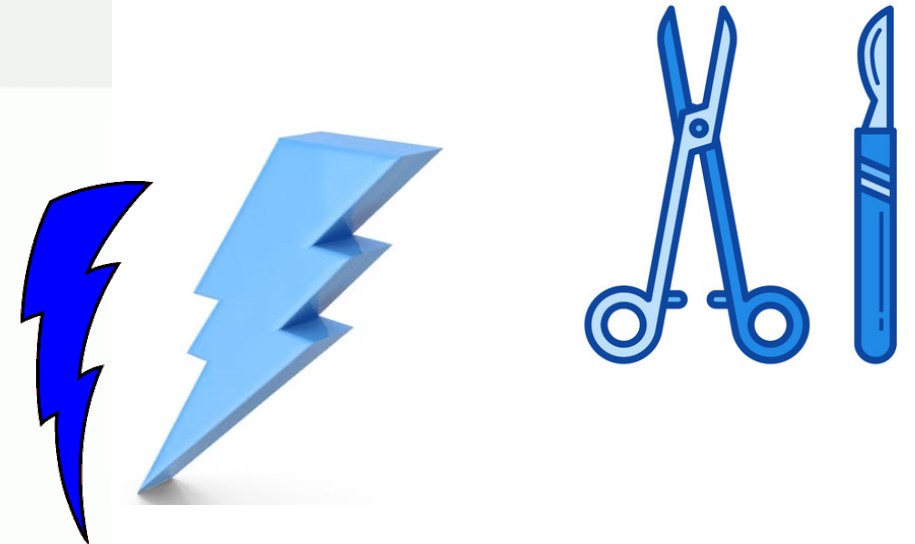
Surgical outcomes for early-stage NSCLC at facilities with SBRT programs (NCDB 2004 – 2015)

- Facilities utilizing SBRT: from 3.3% to 77.5%
- Pts treated with SBRT: from 0.7% to 15.4%
- 90-day post-operative mortality: from 4.6% to 2.6%

90-day post-operative mortality:

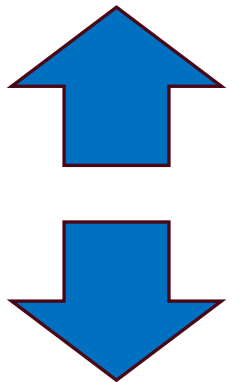
- facilities with > 6 years of SBRT experience (OR 0.84, $p = 0.003$)
- SBRT-to-Surgery volume ratios above 17% (OR 0.85, $p < 0.001$)

SBRT to improve patient selection for surgery



SBRT

OPERATIVE
MORTALITY





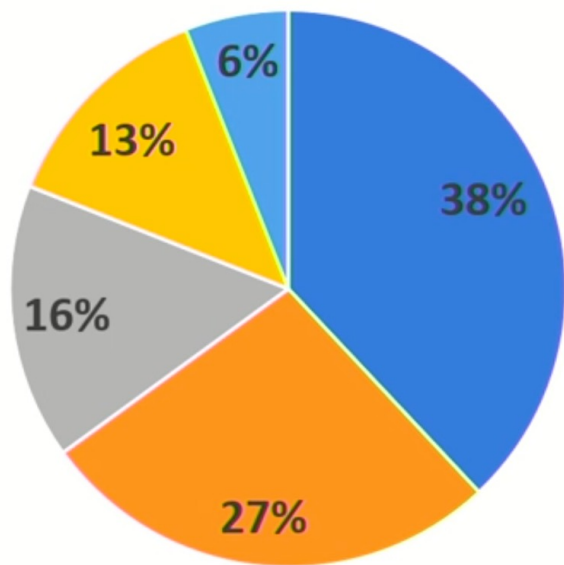
An International EORTC Survey on Resectability of Stage III Non-small Cell Lung Cancer

I. Houda¹, I. Bahce¹, C. Dickhoff¹, T.E. Kroese², S.G.C. Kroeze³, A.V. Mariolo⁴, M. Tagliamento⁵, L. Moliner⁶, M. Brandao⁷, J. Edwards⁸,
I. Opitz², C. Faivre-Finn⁹, D. de Ruysscher¹⁰, J. Remon¹¹, T. Berghmans⁷, A-M.C. Dingemans¹², B. Besse⁵, L.E.L. Hendriks¹⁰

¹Amsterdam University Medical Centers, location VU Medical Center, Amsterdam/NL, ²Universitätsspital Zürich, Zürich/CH, ³Kantonsspital Aarau AG, Aarau/CH, ⁴Curie-MontsourisThoracic Institute, Paris/FR, ⁵Gustave Roussy, Villejuif/FR, ⁶Institut Catala d'Oncologia, Barcelona/ES, ⁷Institut Jules Bordet, Bruxelles/BE, ⁸Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield/GB, ⁹The Christie NHS Foundation Trust, Manchester/GB, ¹⁰Maastricht University Medical Center, Maastricht/NL, ¹¹Centro Integral Oncológico Clara Campal HM Nou Delfos, Barcelona/ES, ¹²Erasmus University Medical Center, Rotterdam/NL



SURVEY - CONSENSUS SUMMARY AREAS OF CONTROVERSY IN RESECTABLE STAGE III NSCLC



- Thoracic surgeon
- Radiation oncologist
- Oncologist
- Pulmonologist
- Other

	NO	N1	N2 SINGLE	N2 MULTI	N2 BULKY	N2 INVASIVE
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	?	UNRESECTABLE ²	UNRESECTABLE
T3 size	NOT STAGE III DISEASE	RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE	UNRESECTABLE
T3 satellite	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE	UNRESECTABLE
T3 invasion	NOT STAGE III DISEASE	POTENTIALLY RESECTABLE	? ¹	?	UNRESECTABLE	UNRESECTABLE
T4 size	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE	?	UNRESECTABLE ²	UNRESECTABLE	UNRESECTABLE
T4 satellite	POTENTIALLY RESECTABLE	? ¹	?	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 invasion	? ¹	? ¹	?	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE

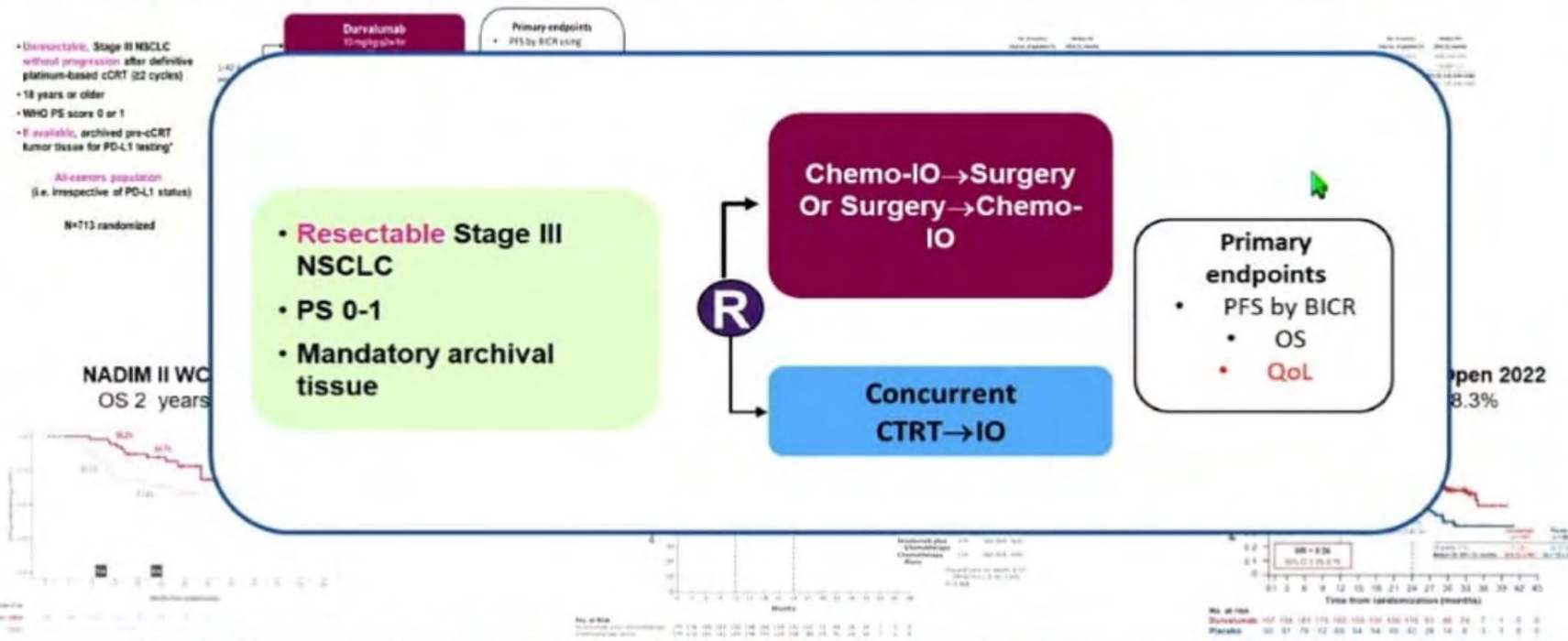
▪ TN-subgroups for stage III NSCLC; Some results may deviate from the results in the final consensus; ?, no consensus achieved; 1, no consensus achieved but considered as potentially resectable by thoracic surgeons; 2, consensus unresectable but no consensus in the group of thoracic surgeons.



IASLC  **2022 World Conference on Lung Cancer**
AUGUST 6-9, 2022 | VIENNA, AUSTRIA

2022 World Conference on Lung Cancer

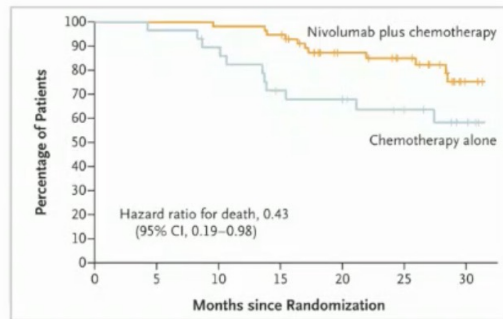
Is a surgical approach the best option for this patient? Surgical vs non surgical strategy?



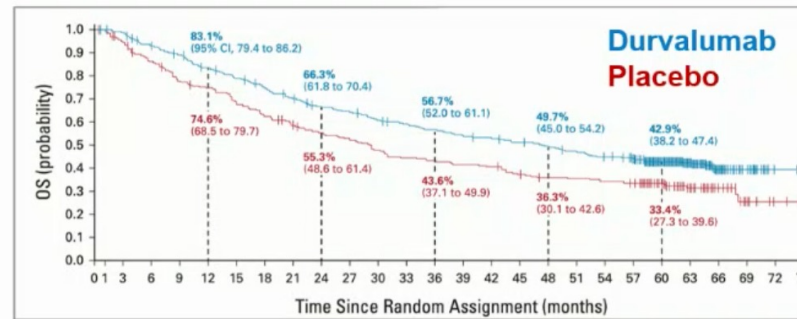
Courtesy of Corinne Faivre-Finn

Stage III NSCLC

Resectable stage III



Unresectable stage III



Study	Design	# of pts	pCR
CheckMate 816	C&IO - S	N = 358	24%
Keynote 671	C&IO - S - IO	N = 397	18%
CheckMate 77T	C&IO - S - IO	N = 461	25%
NADIM II	C&IO - S - IO	N = 86	37%

Study	Phase	IO	RCT	Median PFS
GEMSTONE 301	Phase III	Sugemalimab vs placebo	cCTRT or sCTRT	9 mo
LUN 14-179	Phase II	Pembro after cCTRT	cCTRT	18.7 mo



Matthias Guckenberger

Invited Discussant LBA61, 1292MO, LBA62 and 1293MO

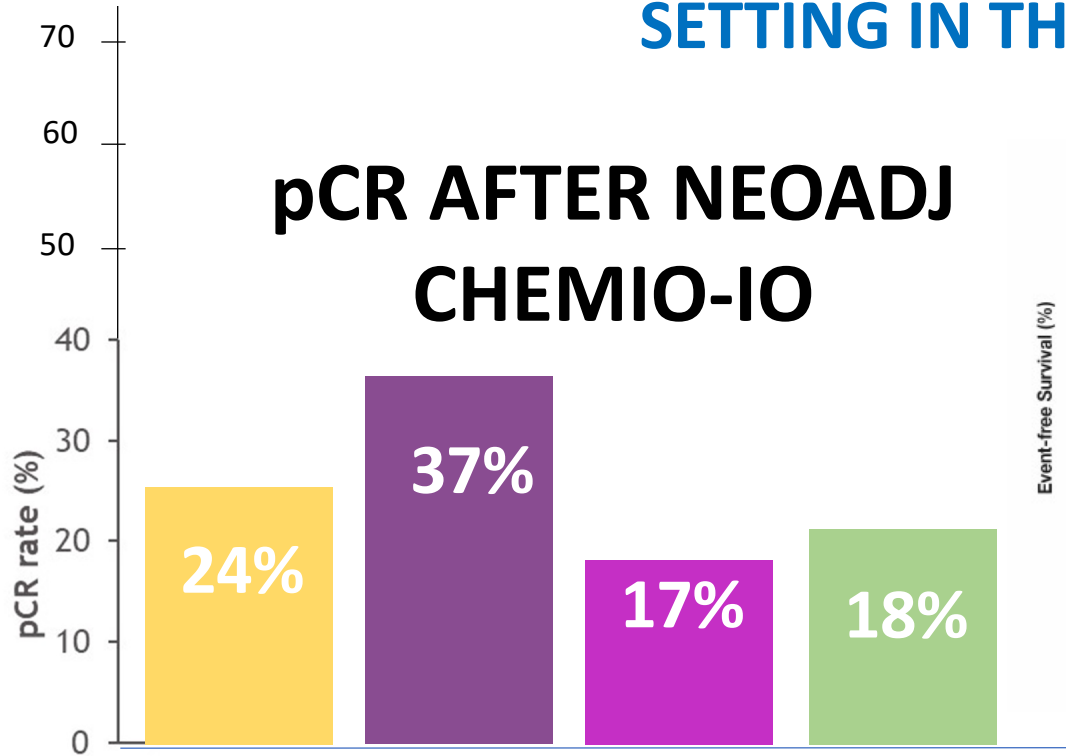
Exciting times in resectable & unresectable stage III NSCLC



REFERENCES: Provencio NEJM 2023; Forde NEJM 2022; Spigel JCO 2023; Zhou Lancet Oncol 2022; Durm Cancer 2020

IMPROVING pCR INTEGRATING RADIATION THERAPY IN NEOADJUVANT SETTING IN THE ERA OF IMMUNOTHERAPY

pCR AFTER NEOADJ CHEMIO-IO

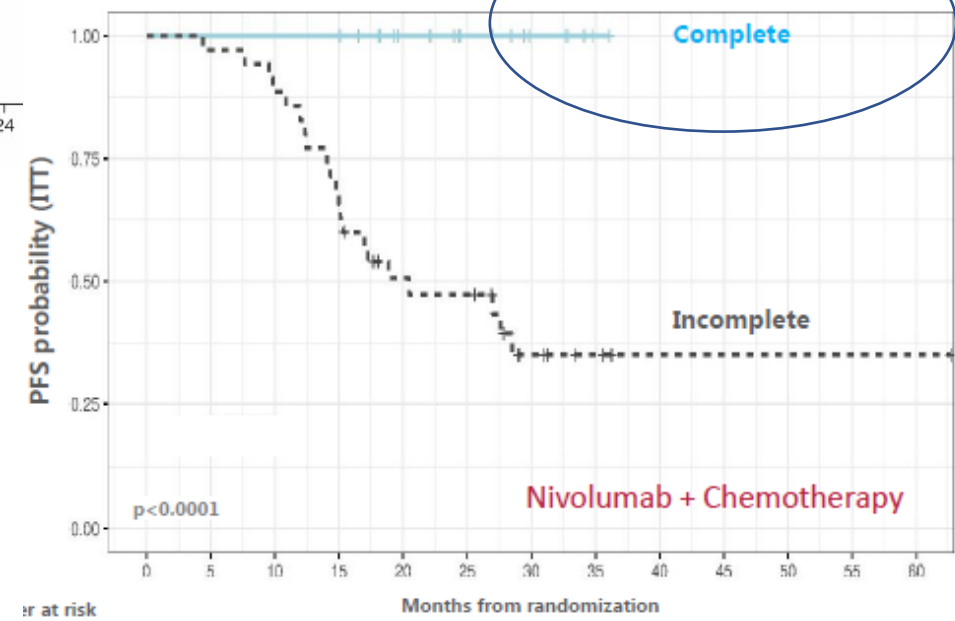
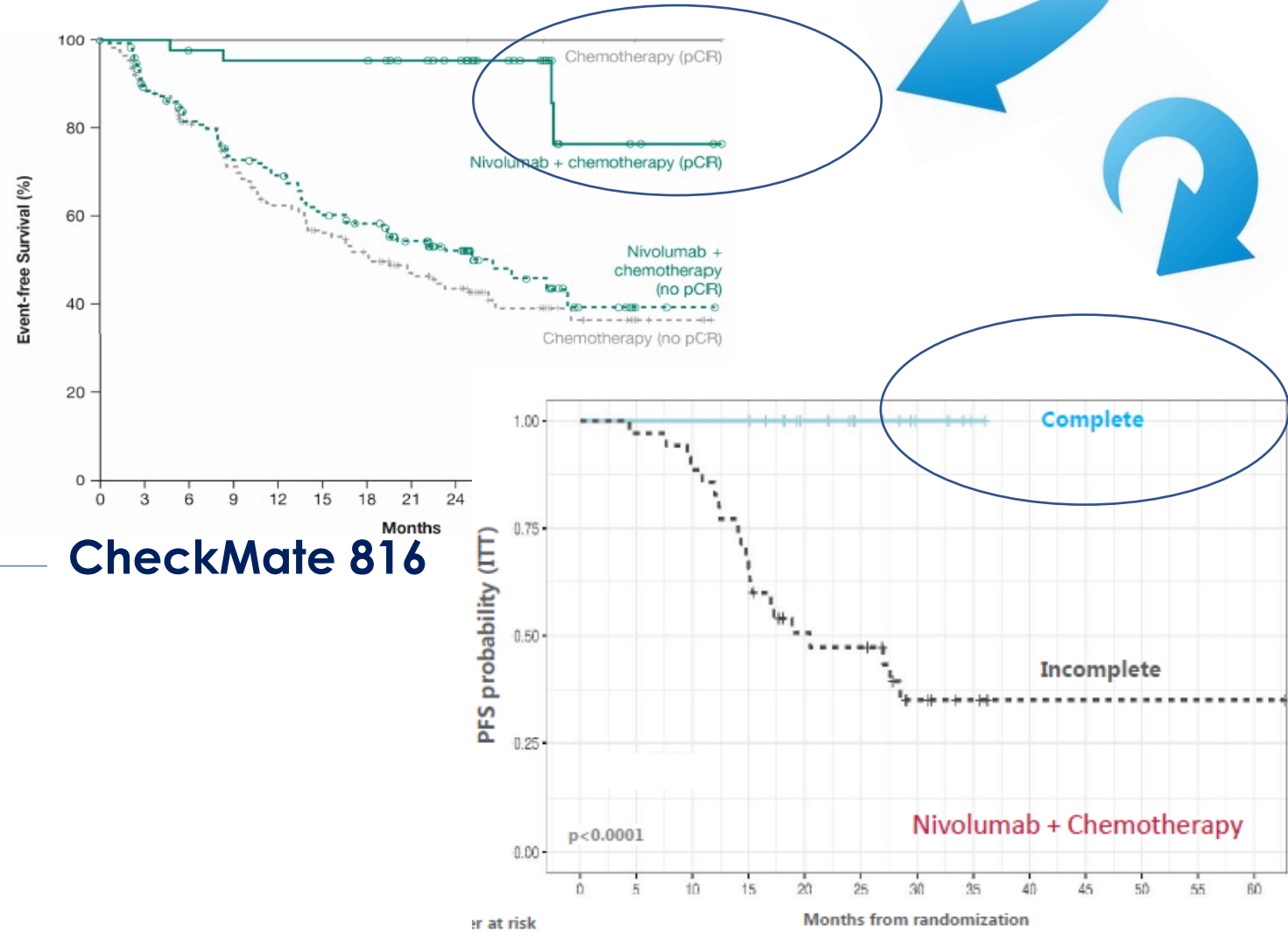


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NADIM II

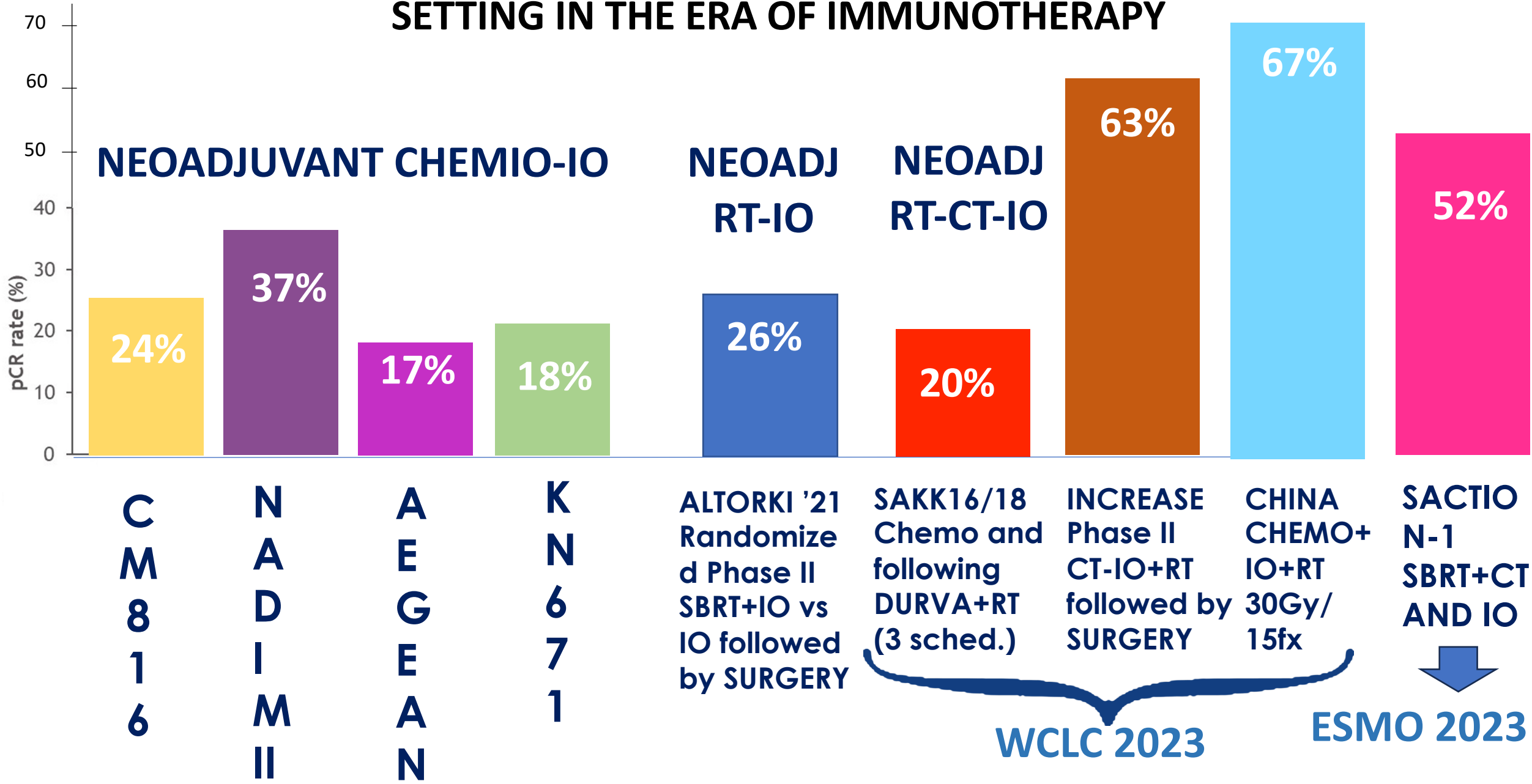
AIRO2023

Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti

	Trial Neoadj CT-IO	Checkmate 816	NADIM II	AEGEAN
1°	pCR	24%	37%	17%
2°	Resected non pCR	45%	49%	56%
3°	R1-R2 +Unresected	31%	14%	27%



IMPROVING pCR INTEGRATING RADIATION THERAPY IN NEOADJUVANT SETTING IN THE ERA OF IMMUNOTHERAPY



Surgery after neoadjuvant immuno-chemoradiotherapy in potentially resectable NSCLC: Results from the INCREASE trial

C. Dickhoff^{1,10,11}, D.J. Heineman¹, F.L. Schneiders^{2,10,11}, I. Houda³, J. Veltman³, S. Hashemi³, M. Franssen^{3,10,11}, T. Radonic^{4,10,11}, I.H. Bartelink⁵, L.J. Meijboom⁶, D.E. Oprea-Lager⁶, N. Bouwhuis⁵, T.D. de Gruij^{7,10,11}, S. Senan^{2,10,11}, I. Bahce^{3,10,11}

		n (%)
Sex (male:female)		10:15
Age (years, median (IQR))		64 (55-69)
Histology		
	Adenocarcinoma	12 (48%)
	Squamous cell carcinoma	7 (28%)
	Large-cell NOS	5 (20%)
	Large-cell neuroendocrine	1 (4%)
Tumor stage (8 th TNM edition)		
Stage IIB	T3N0	5 (20%)
Stage IIIA	T3N1	4 (16%)
	T4N0	12 (48%)
Stage IIIB	T4N1	3 (12%)
	T3N2	1 (4%)
Chest wall invasion		
	<i>Sulcus superior tumors</i>	7
	<i>Other</i>	4
Radiotherapy dose		
	50Gy	22 (88%)
	60Gy	3 (12%)

pCR 63% MPR73%

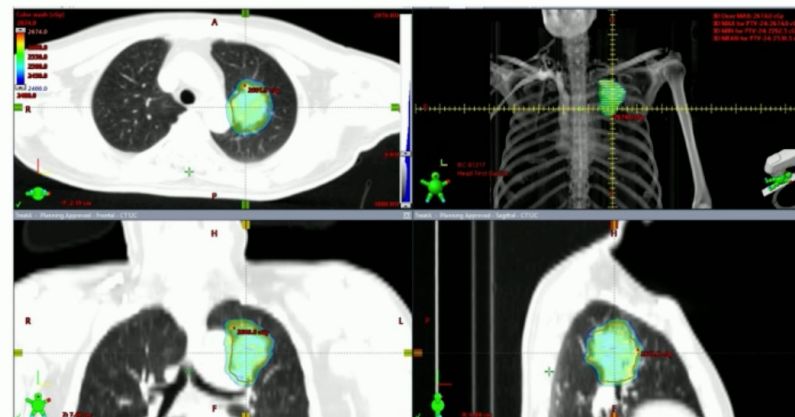
Stereotactic body radiation therapy with sequential immunotherapy as neoadjuvant therapy in resectable NSCLC (SACTION-1)

a single-arm, open-labelled, phase 2 trial

PI: Prof. Hong Yang



Details of SBRT



pCR 52.2%

cN1/2 ypN0 76%

✓ NSCLC

- ❖ Association IO and RT
- ❖ Best RT improves surgical outcomes
- ❖ IO-RT: Volumes?

POLMONE

- ✓ NSCLC (Early Stage and Locally Advanced)
- ✓ SCLC (Limited Stage and PCI)

ASTRO 2023 PAY IT FORWARD

PARTNERING WITH OUR PATIENTS

ASTRO 65TH ANNUAL MEETING
October 1-4, 2023

San Diego Convention Center, San Diego

High dose hyperfractionated thoracic radiotherapy versus standard dose for limited stage small-cell lung cancer: a multicentre, open-label randomised, phase 3 trial.

Jiayi Yu, Lilei Jiang, Lina Zhao, Xiaomin Wang, Xue Yang, Dan Yang, Mingfei Zhuo, Hanxiao Chen, Yidian Zhao, Fang Zhou, Quanfu Li, Zhengfei Zhu, Li CHU, Zhanshu Ma, Qifeng Wang, Yanli Qu, Huiming Yu, Rong Yu, Jun Zhao, Anhui Shi



Study Schema

LS-SCLC

ECOG 0-1
Age 18-70

Randomize

Platinum/ Etoposide x 4
RT beginning 0-42 days after cycle 1

54 Gy VMAT SIB
30 fractions, BID
3 weeks

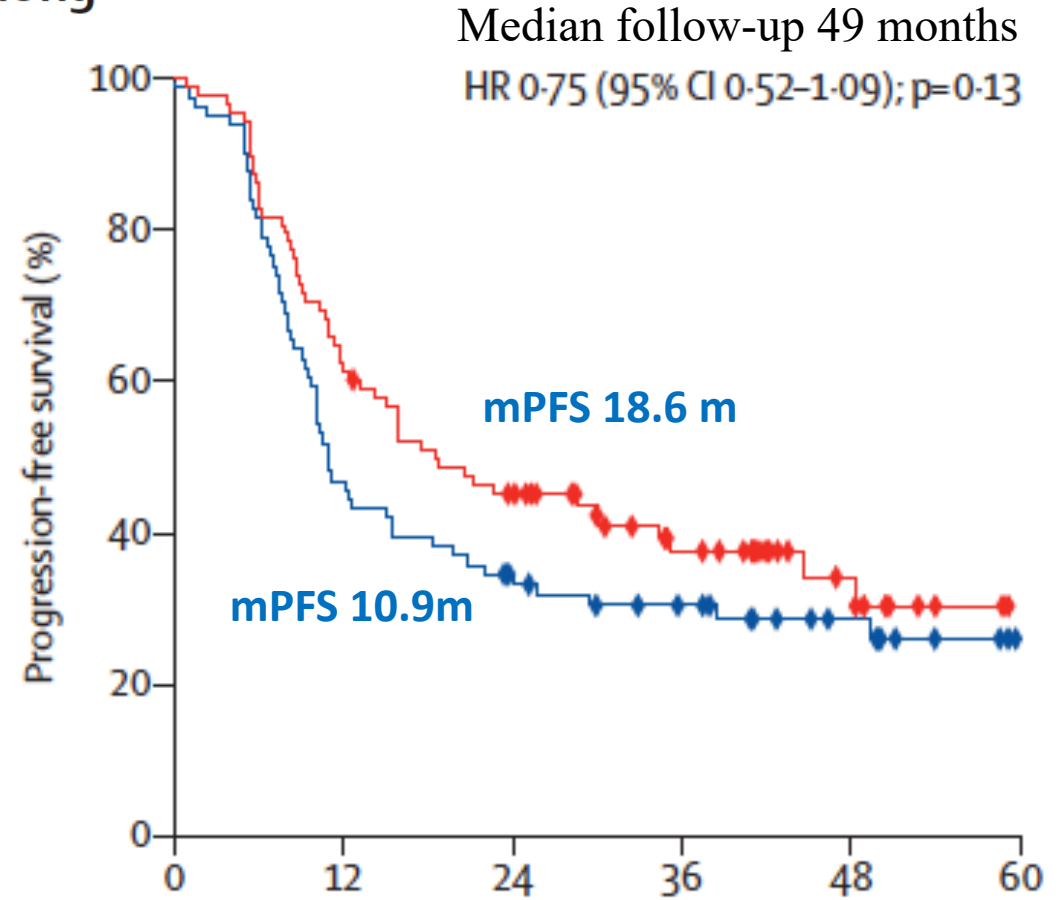
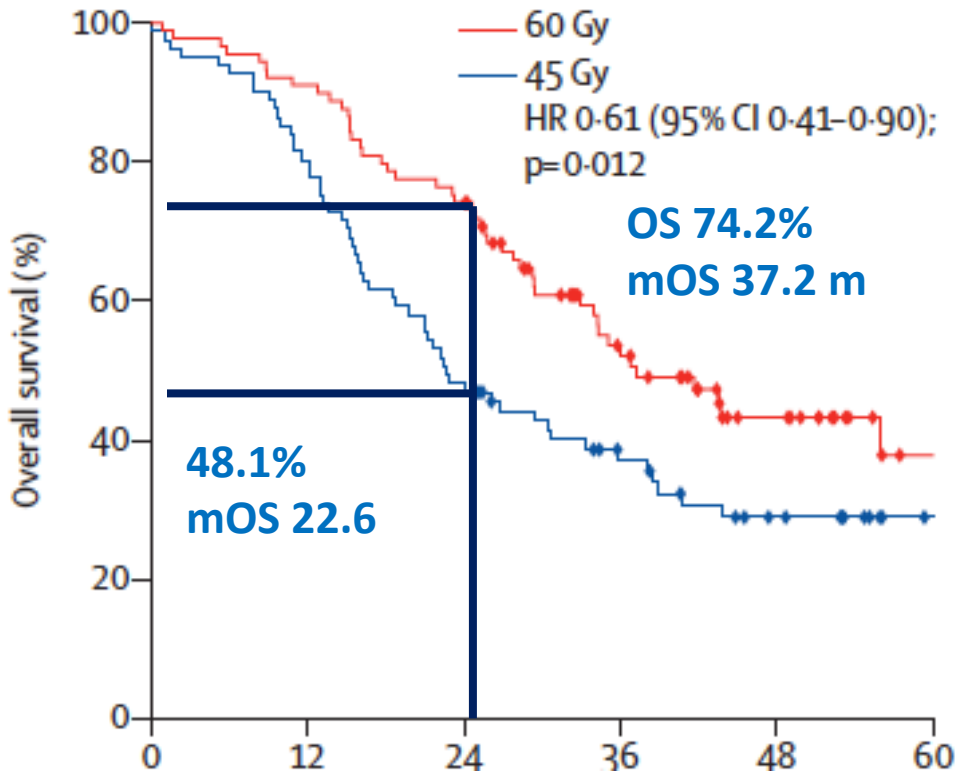
Staging: PET/CT, Brain MRI
+ PCI 25Gy in 10 fx

45 Gy VMAT
30 fractions, BID
3 weeks

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Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti

High-dose versus standard-dose twice-daily thoracic radiotherapy for patients with limited stage small-cell lung cancer: an open-label, randomised, phase 2 trial



Gronberg, Lancet Oncology 2021

SURVIVAL DATA OF LD-SCLC IN RANDOMIZED TRIALS

	<i>TURRISI 1999</i> <i>Once Daily 45Gy/ Twice Daily 45Gy</i>	<i>CONVERT 2017</i> <i>Once Daily 66Gy/ Twice Daily 45Gy</i>	<i>NORWEGIAN 2021</i> <i>Twice Daily 60Gy/ Twice Daily 45Gy</i>
Median OS	19/23m	25/30m	37.2/22.6m
2-year OS	41/47%	51/56%	72/48%
5-year OS	16%	31/34%	-

Baseline Characteristics

	54 Gy group (n=108)	45 Gy group (n=116)	P value
Age, years			
Median	60(33-70)	62(35-70)	0.804
Sex			
Female	49(45.4)	53(45.7)	0.962
Male	59(54.6)	63(54.3)	
ECOG performance status			
0	65(60.2)	70(60.3)	0.981
1	43(39.8)	46(42.2)	
2	0	0	
Smoking history			
Never smoker	41(38.0)	45(38.8)	0.898
Current or former smoker	67(62.0)	71(61.2)	
Disease stage			
II	14(13.0)	17(14.7)	0.714
III	94(87.0)	99(85.3)	
Weight loss 6 months before study, No. (%)			
≤5.00%/6 months	92(85.2)	98(84.5)	0.884
> 5.00%/6 months	16(14.8)	18(15.5)	

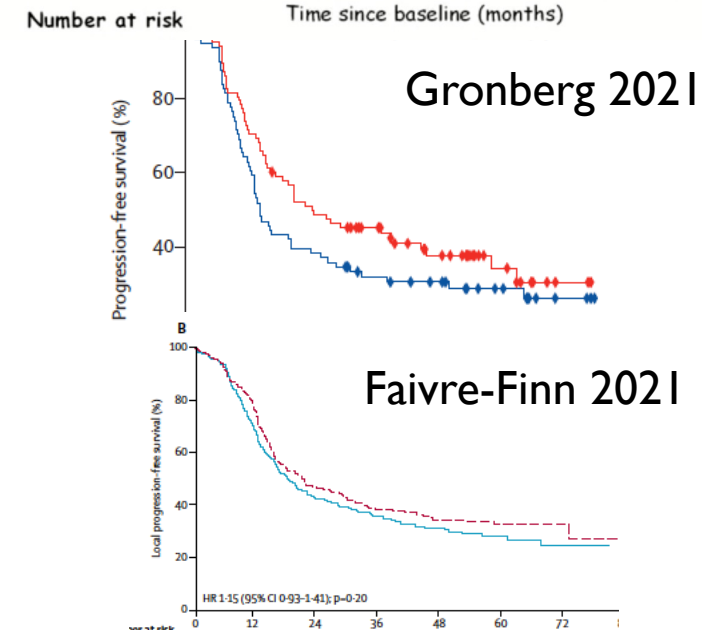
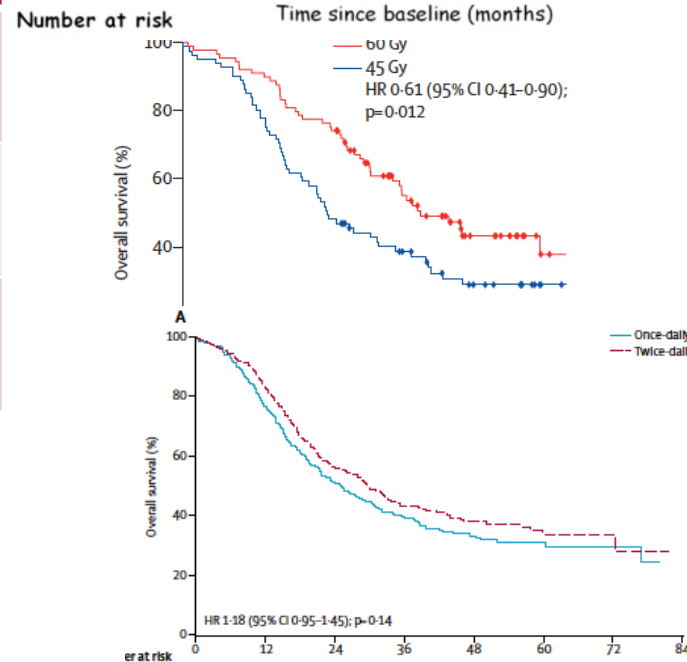
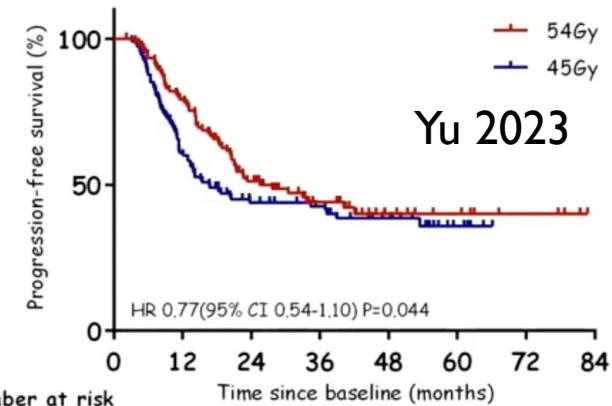
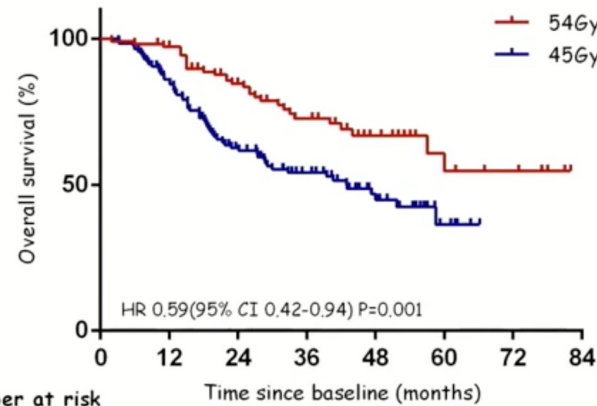
ESOPHAGITIS	GI-G2	G3	G4-5
BID 45Gy	40.5%	12%	0%
BID 54Gy	42%	13%	0%

PNEUMONITIS	GI-G2	G3	G4-5
BID 45Gy	21%	6%	0%
BID 54Gy	19%	4.6%	0%

M FUP 45m	Median OS	Median PFS	2y OS
BID 45Gy	43.1 months	16.7 months	53.5%
BID 54Gy	62.4months	30.5 months	77.7%

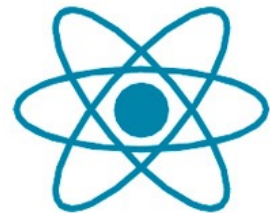
Overall Survival & Progression-free Survival

	CHINA ASTRO 2023	NORVE GEAN 2021	CONVERT 2017
Never smokers	38-38%	1-3%	1-2%
PCI	81-82%	85-85%	81-84%%
IMRT/ VMAT	100%	-	16-17%





ONGOING STUDIES EVALUATING IMMUNOTHERAPY IN LS-SCLC PATIENTS



Study name (start date)	Phase	Arm I	Arm II	Arm III	Primary endpoints
NRG LU005	II/III	ChemoRT: etoposide + cisplatin or carboplatin q21 days x3 cycles with either BID or daily radiation therapy	ChemoRT + IO: treatment as in Arm I + atezolizumab IV on day 1 or 2 of each chemo cycle and then every 3 weeks x17 cycles	N/A	PFS, OS
ETOP STIMULI	II	ChemoRT: etoposide + cisplatin or carboplatin q21 days x4 cycles with either BID or daily radiation therapy	ChemoRT + IO: treatment as in Arm I followed by q3 week nivolumab + ipilimumab x4 cycles then q2 week nivolumab x1 year	N/A	PFS, OS
ADRIATIC	III	ChemoRT + IO: ChemoRT as in Arm III followed by Durvalumab and placebo saline solution IV q4 weeks x4 followed by durvalumab monotherapy q4 weeks	ChemoRT + IO: ChemoRT as in Arm III followed by durvalumab and tremelimumab IV q4 weeks x4 followed by durvalumab monotherapy q4 weeks	ChemoRT: etoposide + platinum-based chemo q21 days x4 cycles with either BID or daily radiation therapy then two placebo saline solutions (IV) q4 week x4, followed by placebo saline solution monotherapy q4 weeks	PFS, OS

Higgins, Translational Lung Cancer Research, Vol 8, Suppl 2 September 2019

SURVIVAL DATA OF LD-SCLC IN LD-SCLC TRIALS

	<i>TURRISI</i> 1999 <i>Once Daily</i> 45Gy/ <i>Twice Daily</i> 45Gy	<i>CONVERT</i> 2017 <i>Once Daily</i> 66Gy/ <i>Twice Daily</i> 45Gy	<i>NORWEGIAN</i> 2021 <i>Twice Daily</i> 60Gy/ <i>Twice Daily</i> 45Gy	<i>STIMULI</i> 2022 <i>RTCT</i> <i>followed by</i> <i>nivo-</i> <i>ipi/RTCT</i>	<i>WELSH trial</i> 2020 <i>RTCT (twice</i> <i>daily) +</i> <i>pembro</i>
Median OS	19/23m	25/30m	37.2/22.6m	NR/32.1m	39m
2-year OS	41/47%	51/56%	72/48%	63/66%	65.8%
5-year OS	16%	31/34%	-	-	

ASTRO 2023
PAY IT FORWARD
PARTNERING WITH OUR PATIENTS

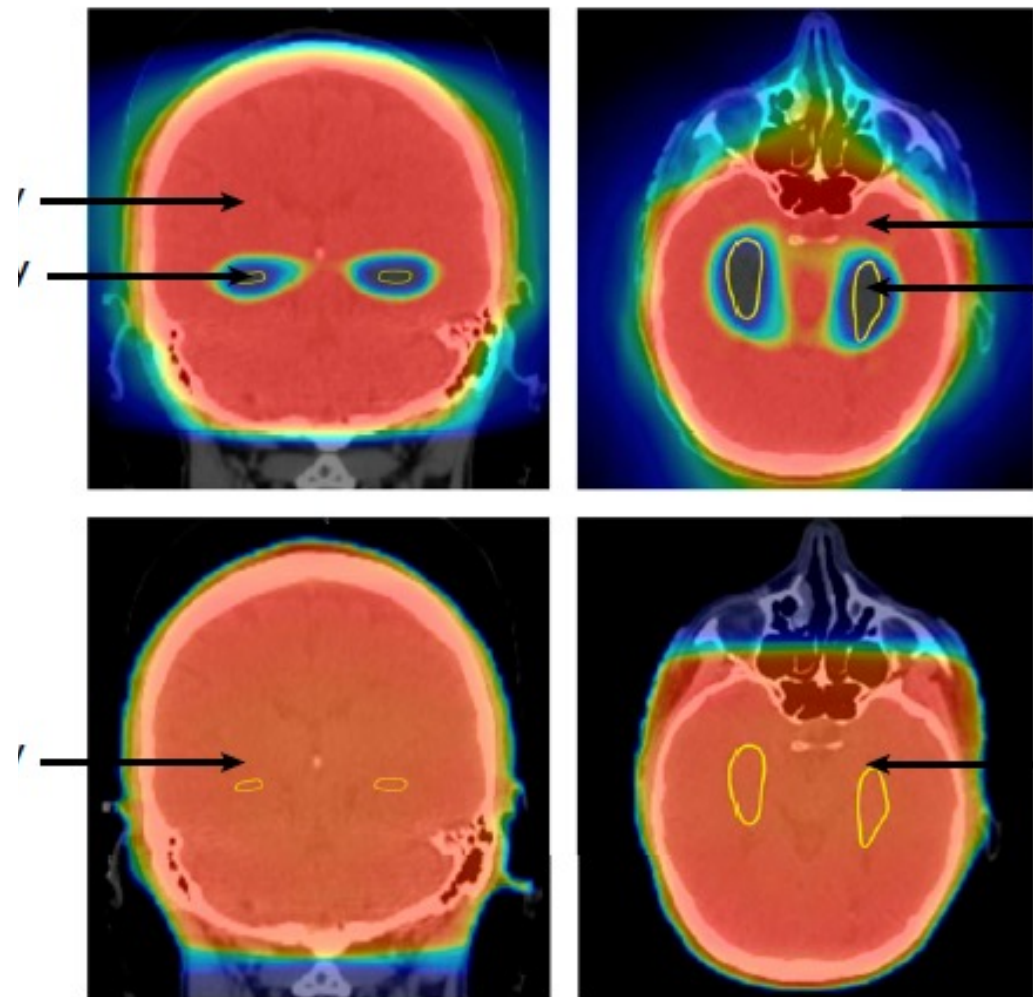
NRG ONCOLOGY
Advancing Research. Improving Lives.™

Primary endpoint results of NRG CC003:

Phase IIR/III trial of prophylactic cranial irradiation with or without hippocampal avoidance for small cell lung cancer

Vinai Gondy, MD*, Stephanie Pugh, PhD, Minesh P. Mehta, MD*, Jeffrey S. Wefel, PhD, Wolfgang A. Tome, PhD, Alex Y. Sun, MD, Gregory M. M. Videtic, MD, Benjamin Lok, MD, Harold A. Yoon, MD, John H. Heinzerling, MD, Albert S. DeNittis, MD, Ronald C. McGarry, MD, Kiran Devisetty, MD, Vijayananda Kundapur, MD, Abraham Wu, MD, Rebecca Paulus, BS, Lisa A. Kachnic, MD

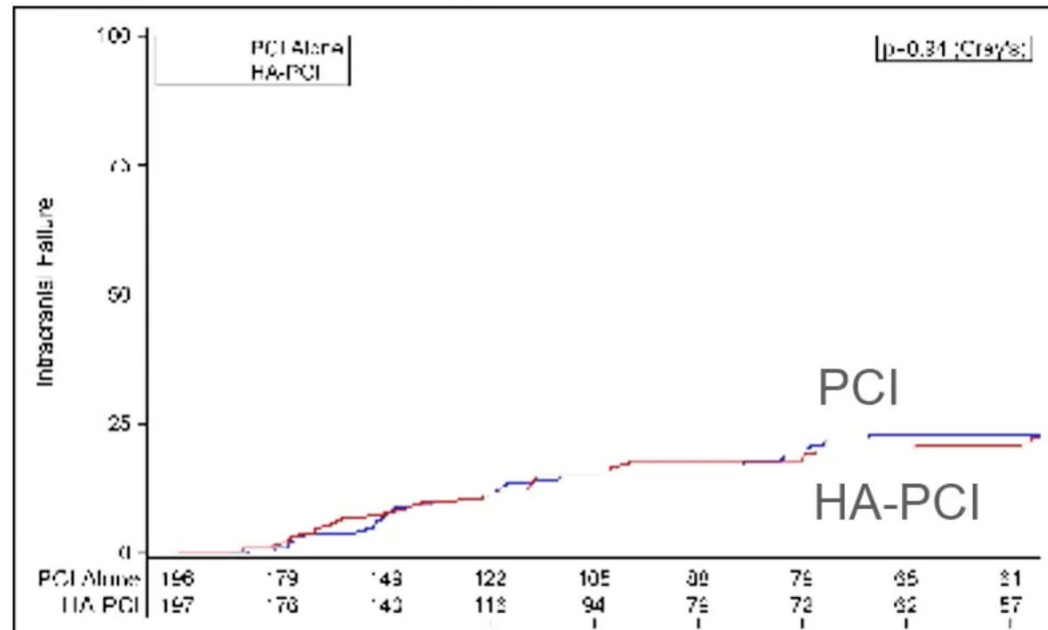
*Co-Principal Investigators contributed equally to this work.



Primary Endpoints

- Phase IIR: Intracranial Relapse
 - Non-inferiority met ($p < 0.0001$)
 - 12-month: PCI 14.8% vs. HA-PCI 14.2%
 - Adjusted HR=0.93, 95% CI: 0.61-1.43, $p=0.75$
 - Extensive stage and Memantine usage predicted higher risk of intracranial relapse
 - Stage: HR=2.47, 95% CI: 1.57-3.91, $p=0.0001$
 - Memantine: HR=1.60, 95% CI: 1.04-2.46, $p=0.033$

Intracranial Relapse



SECONDARY ENDPOINT

- Hippocampal avoidance prevents first failure in any cognitive test
 - 23% relative risk reduction

Variable	HR	95% CI	p value
Treatment arm (HA-PCI vs. PCI [RL])	0.77	0.61-0.98	0.033

Hippocampal Avoidance During Whole-Brain Radiotherapy Plus Memantine for Patients With Brain Metastases: Phase III Trial NRG Oncology CC001

	HA-WBRT+M	WBRT	
Executive function at 4 months	23.3%	40.4%	p= .01
Learning at 6 months	11.5%	24.7%	p= .049
Memory at 6 months	16.4%	33.3%	p =.02



HIPPOCAMPAL SPARING RADIOTHERAPY

AUTHORS	TRIAL	CONCLUSIONS
N. Rodriguez De Dios, et al J Clin Oncol. 2021 Oct 1;39(28):3118-3127.	Phase III Trial of Prophylactic Cranial Irradiation with or without Hippocampal Avoidance for SMALL-CELL LUNG Cancer	Sparing the hippocampus during PCI better PRESERVES COGNITIVE FUNCTION in patients with sclc. No differences were observed with regard to brain failure, OS, and QoL compared with standard PCI.
J Belderbos et al J Thorac Oncol. 2021 May;16(5):840-849.	OC-0503 Phase III trial of Prophylactic Cranial Irradiation with or without Hippocampus Avoidance in SCLC	This randomized trial DID NOT FIND a lower probability of cognitive decline in patients with SCLC receiving HA-PCI compared with conventional PCI. No increase in brain metastases at 2 years was observed in the HA-PCI arm.

✓ SCLC

❖ Total Dose/Time

❖ Association IO+RT

❖ IMRT/VMAT for patient's OS and QoL



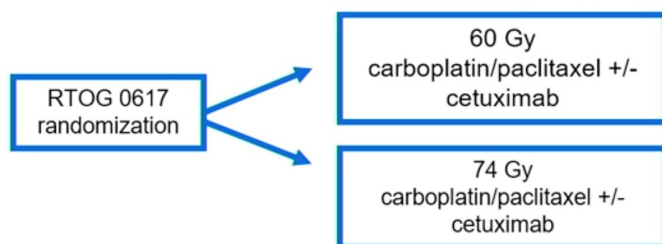
Long-term outcomes by radiation technique for locally-advanced non-small cell lung cancer:

A secondary analysis of NRG Oncology-RTOG 0617 at 5-years

Stephen Chun, Chen Hu, Ritsuko Komaki, Robert Timmerman, Steven Schild, Jeffrey Bogart, Michael Dobelbower, Walter Bosch, Vivek Kavadi, Samir Narayan, Puneeth Iyengar, Clifford Robinson, Jan Rothman, Adam Raben, Mark Augspurger, Robert MacRae, Rebecca Paulus, Jeffrey Bradley

World Conference on Lung Cancer
September 11, 2023

Methods – Planned secondary analysis of NRG-RTOG 0617 stratification

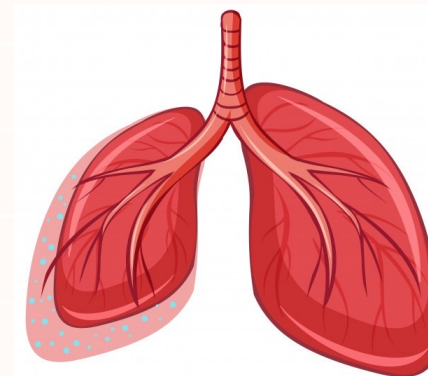


Compared IMRT and 3D-CRT outcomes

- Stratified: 3D-CRT 53%, IMRT 47% in both 60/74Gy dose arms (N = 482)
- Median follow-up 5.2 years
- Endpoints
 - 5-year overall survival, PFS, local failure, DMFS
 - Severe late Grade ≥ 3 toxicities
 - Development of secondary malignancies

Results – Severe Long-term Toxicity Profile

Grade ≥ 3 Adverse Event	Radiation Technique Comparison		Univariate logistic regression Lung V5Gy
	IMRT	3D-CRT	
<u>Pneumonitis</u>	<u>3.5%</u>	<u>8.2%</u>	OR = 1.02 (95% CI: 0.99-1.05) p = 0.13
	<u>p = 0.03</u>		
Esophagitis	13.2%	15.3%	OR = 1.01 (95% CI: 0.996-1.03)
	p = 0.50		
Weight loss	3.9%	3.1%	
	p = 0.63		
Cardiovascular	5.3%	8.2%	
	p = 0.20		
Neurologic	5.7%	5.9%	
	p = 0.93		
Hematologic	58.8%	50.2%	
	p = 0.06		

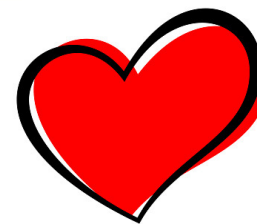


Results – Association of heart doses and survival (unadjusted univariate analysis)

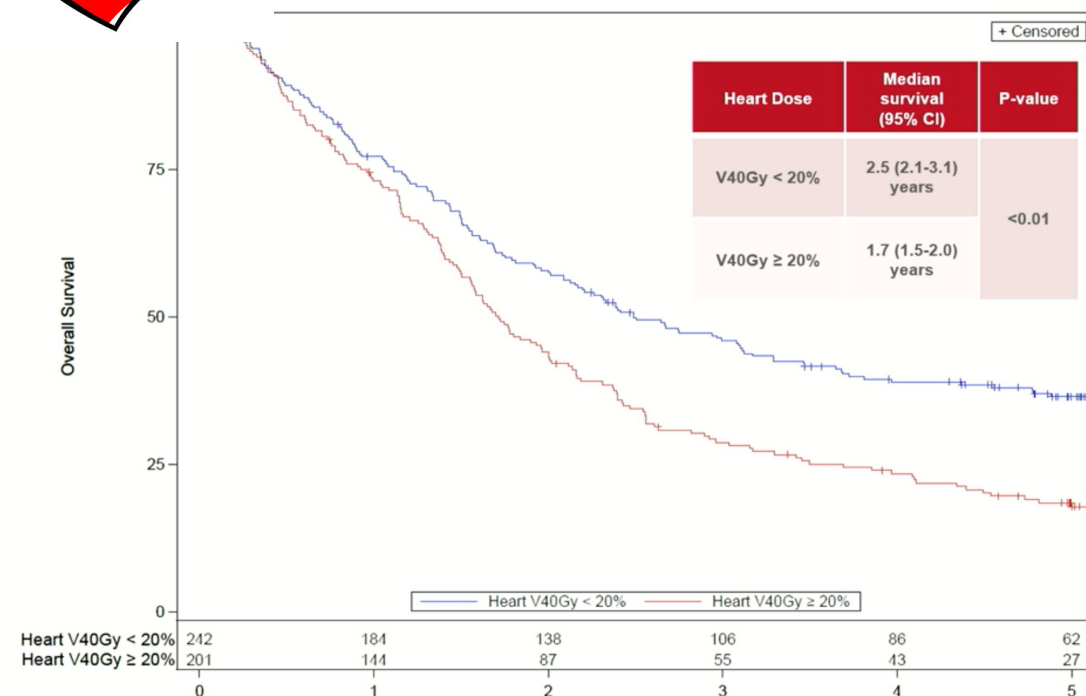
Heart Dose	Comparison	HR (95% CI)	P-value
V20Gy	Continuous	1.012 (1.01-1.02)	< 0.01
V40Gy		1.016 (1.01-1.02)	< 0.01
V60Gy		1.027 (1.01, 1.04)	< 0.01

CONCLUSION

Strongest evidence supporting IMRT/VMAT
in LA-NSCLC and it should be used
standardly in this setting

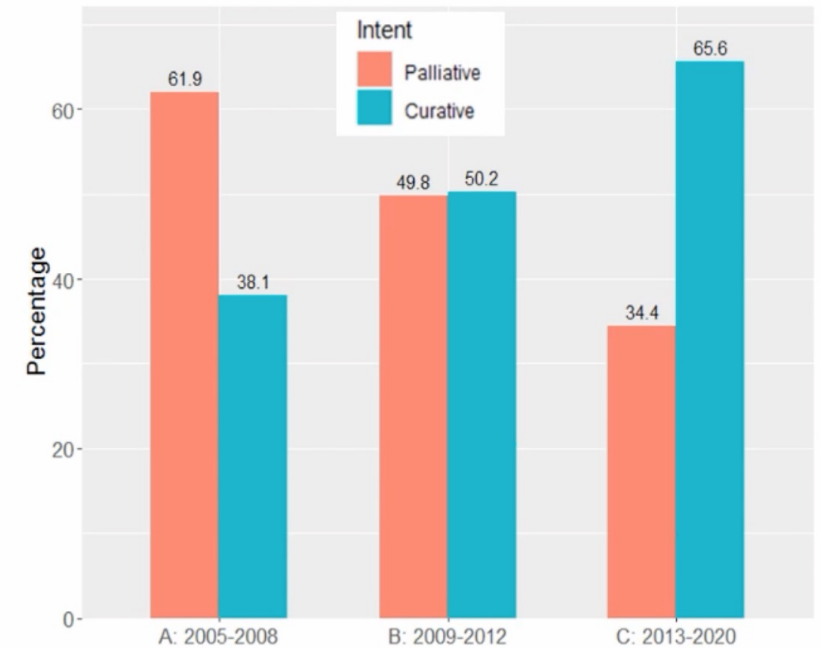
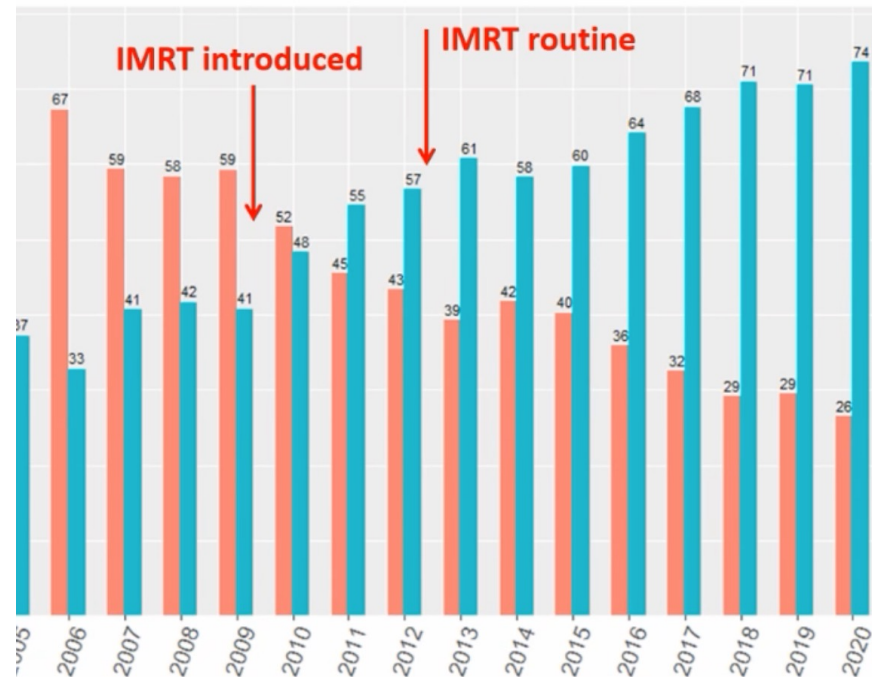


Overall survival by heart V40Gy



«L'EVOLUZIONE AL SERVIZIO DEI PAZIENTI»

Proportion of patients receiving curative intent radiotherapy



Whole cohort, n= 12499

Fornacon-Wood, Chan et al. *Frontiers in Oncology*, in press

AIRO2023

Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti



«IO SONO, PERCHE' SIAMO» UBUNTU

Thank
you

