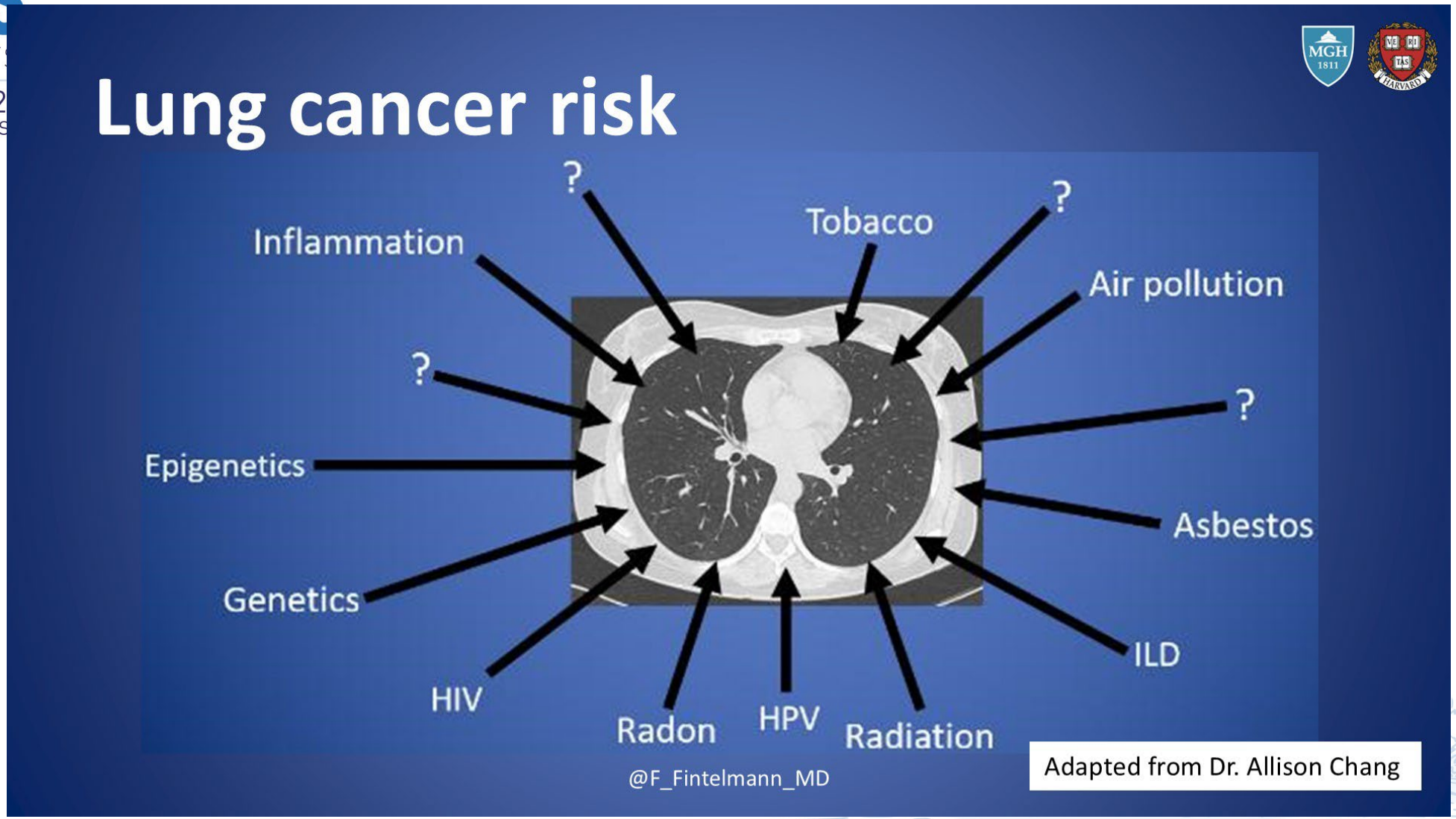
Lung Cancer UPDATES
ASCO HIGHLIGHTS
30 MAYO - 03 JUNIO 2025
Chicago, USA

Iniciativa científica de:
GECP lung cancer research

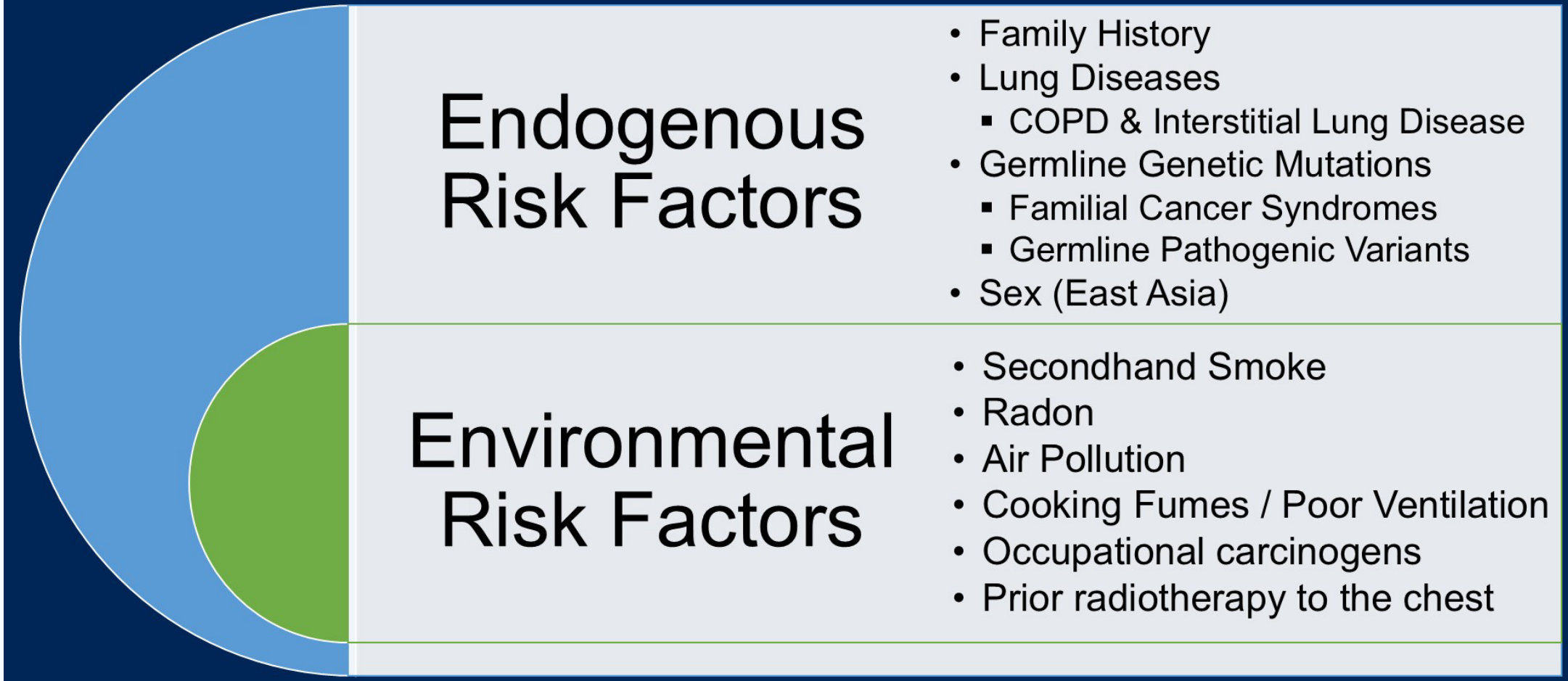
Diagnostico, cirugía y radioterapia

Mónica Antoñanzas Basa

Hospital Clínico San Carlos



Risk Factors for Lung Cancer in Non–Smokers



Screening NSCLC

Abstract 8002. Lung cáncer diagnosis rates (LCDR) in Lung Cancer Screening (LCS) and incidental Pulmonary Nodule (IPN)

- What is the cumulative Lung cáncer Diagnosis risk in LCS and IPN enrolles?
- DELUGE (Detecting Early Lung Cancer in Mississippi Delta: 2 cohortes

	LCS N= 8202	IPN N=24,858
Age, median (IQR) years*	65 (60 – 70)	64 (52 – 74)
Female sex*	51%	56%
Black race*	19%	29%
Uninsured / Medicaid*	1% / 4%	7% / 3%
Never smoked*	<1%	41%
COPD*	38%	17%
>1 nodule*	62%	33%
Nodule size, median (IQR)*	4 (2 – 6)	7 (5 – 10)

*P<.0001

Screening NSCLC

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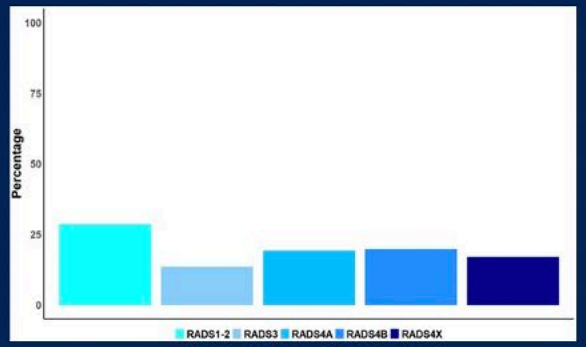
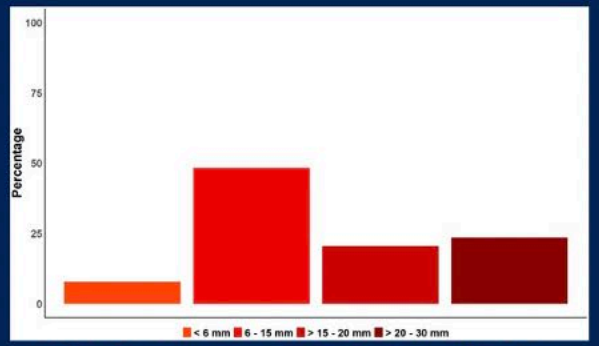
Patients Diagnosed with Lung Cancer

	LCS N= 401 (4.9%)	IPN 1139 (4.6%)
Age, median (IQR) years*	68 (63 – 72)	70 (63 – 76)
Female sex	54%	53%
Black race	18%	23%
Uninsured/Medicaid*	1%/4%	4%/2%
Never smoked*	0	10%
COPD*	54%	44%
>1 nodule*	61%	31%
Nodule size, median (IQR) mm*	10 (5 – 18)	15 (10 – 20)

*P<.01



LCS: T0 Lung-RADS distribution



IPN: Baseline nodule size distribution

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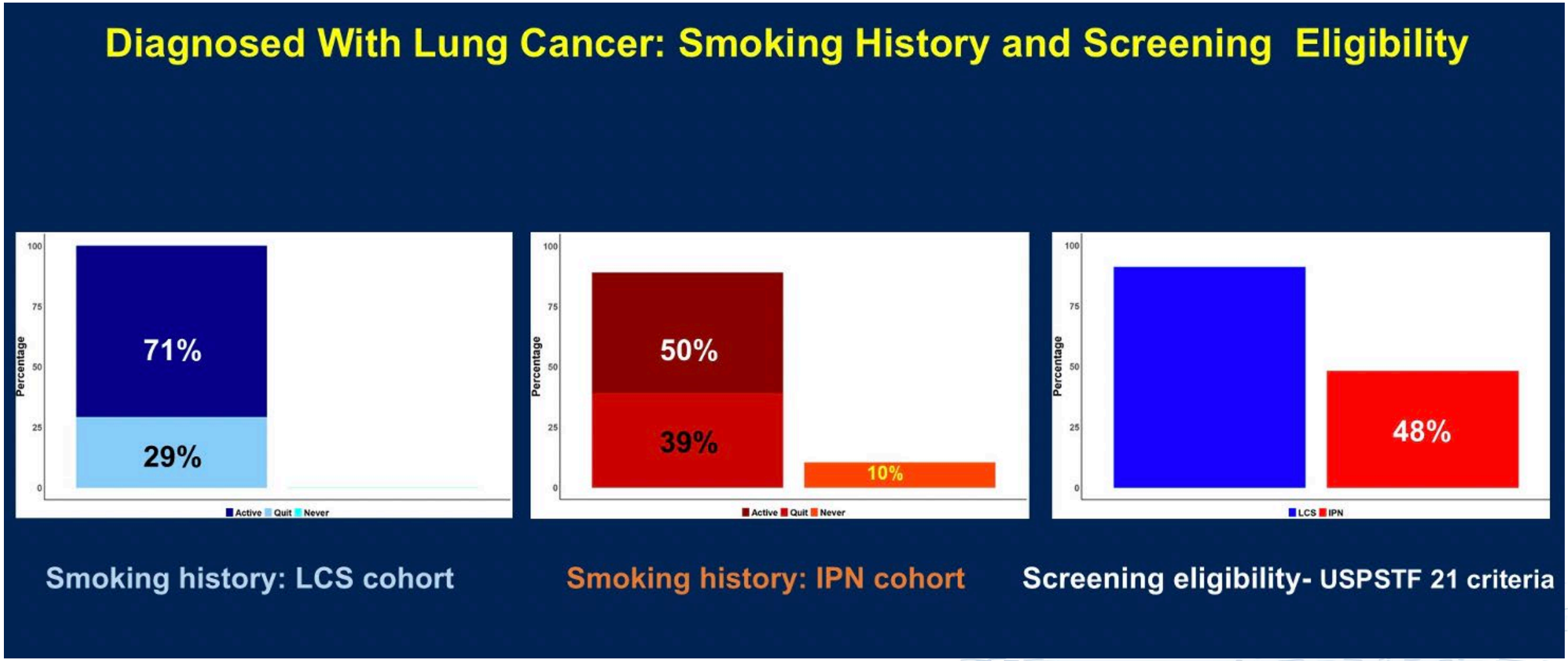

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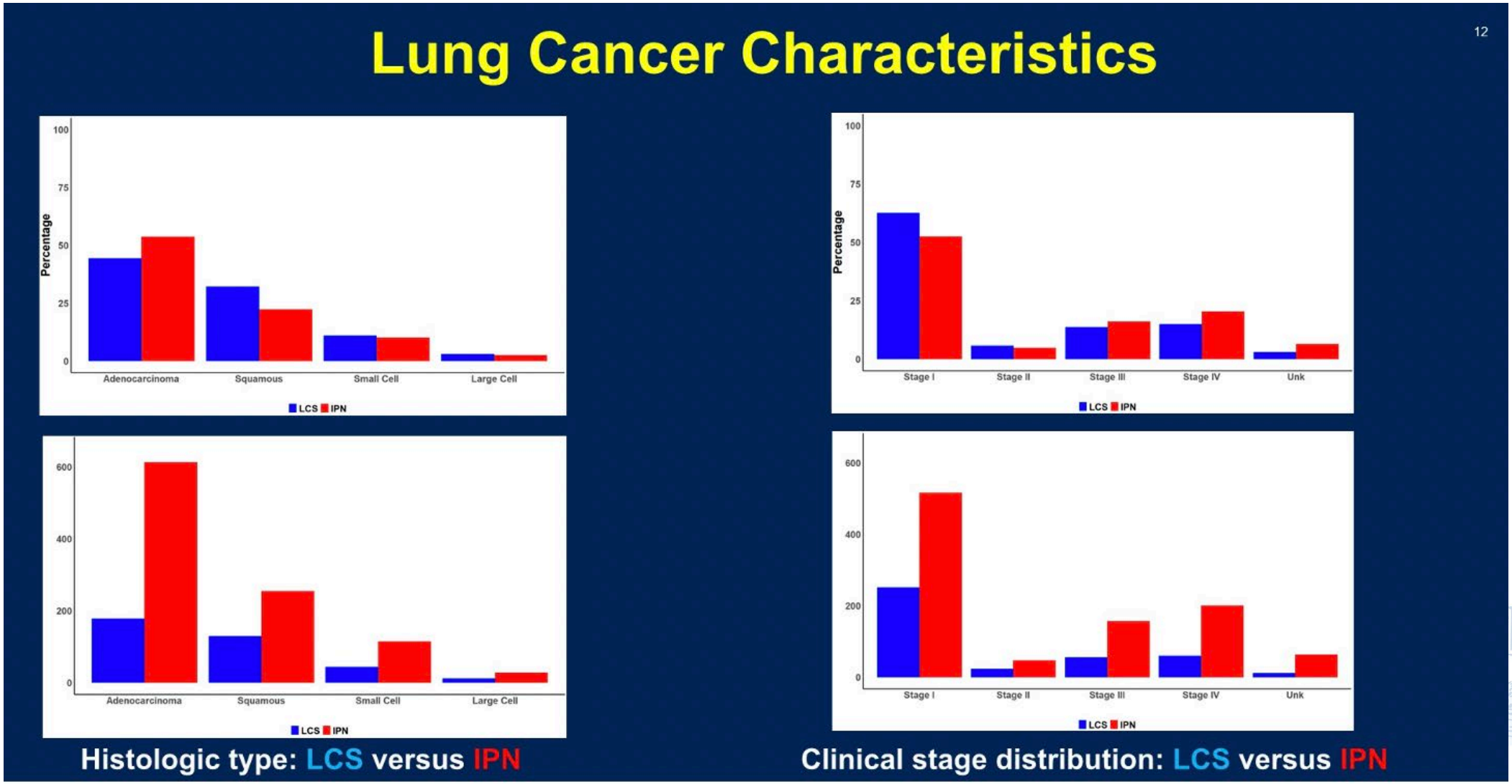

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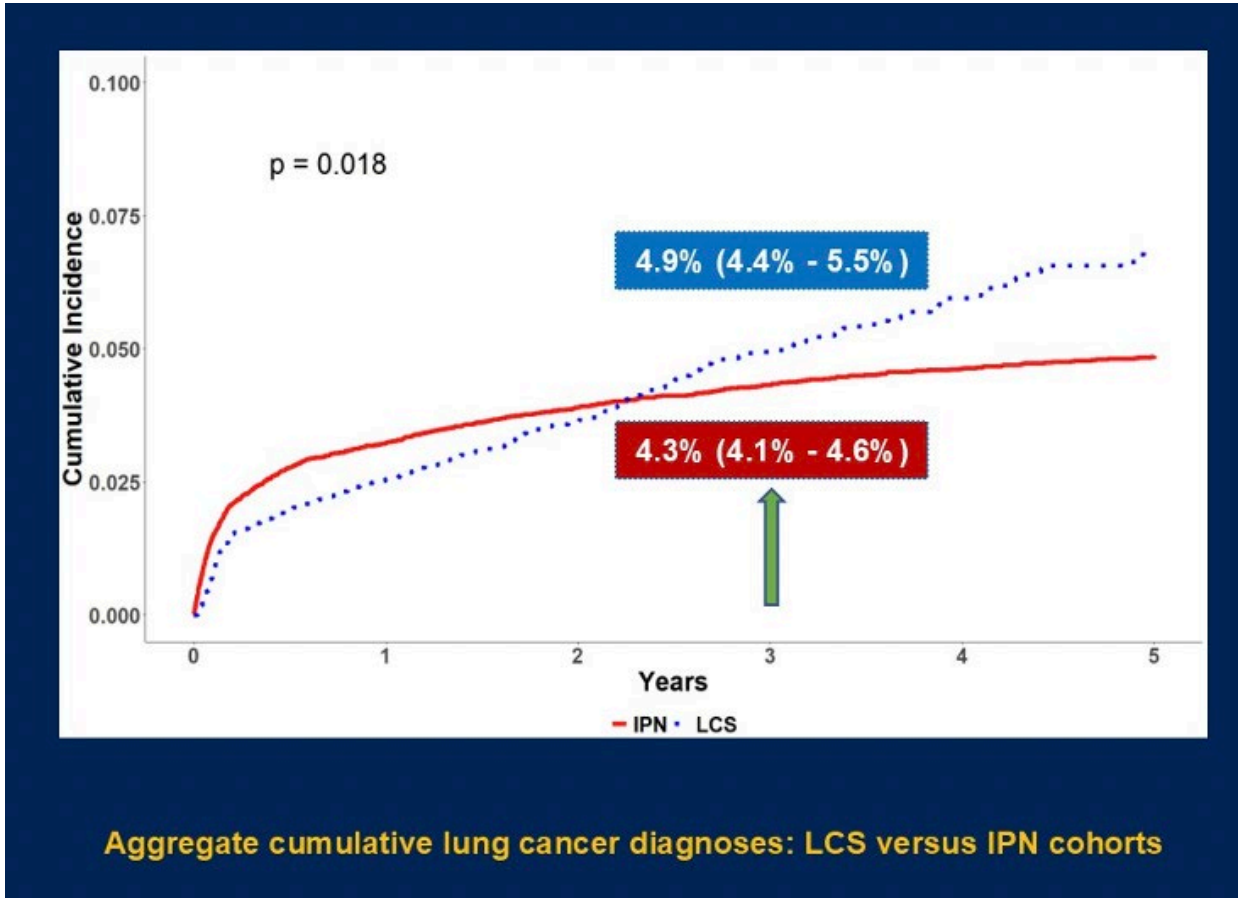

Aggregate cumulative lung cancer diagnoses: LCS versus IPN cohorts

Screening NSCLC

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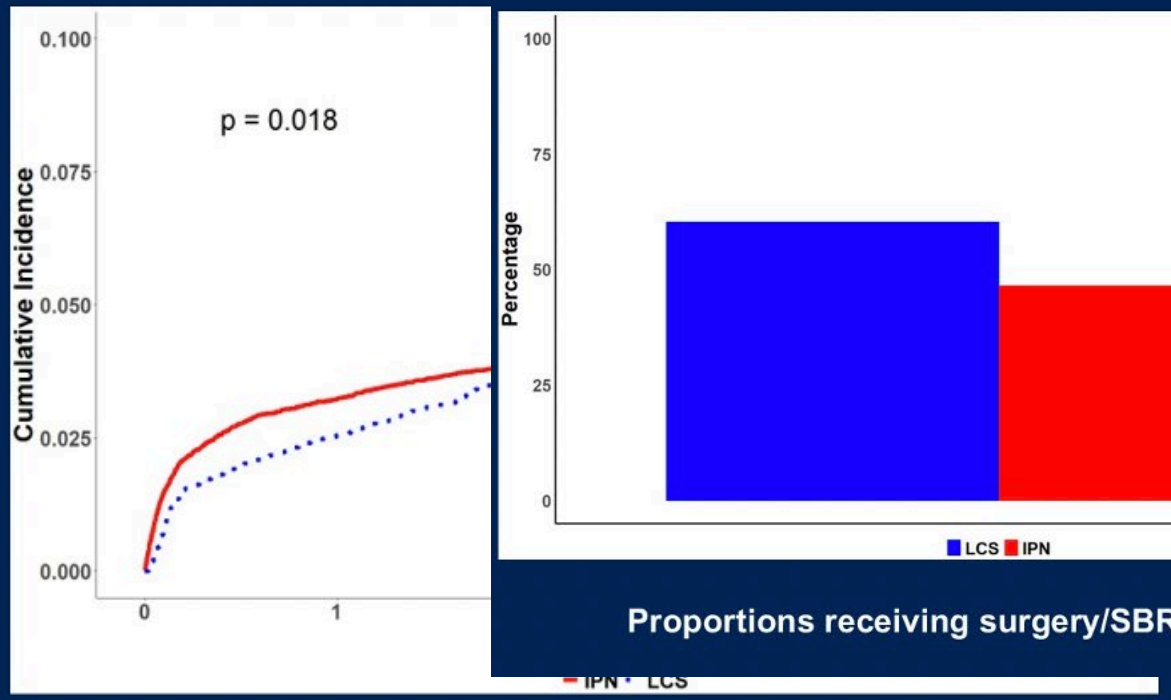
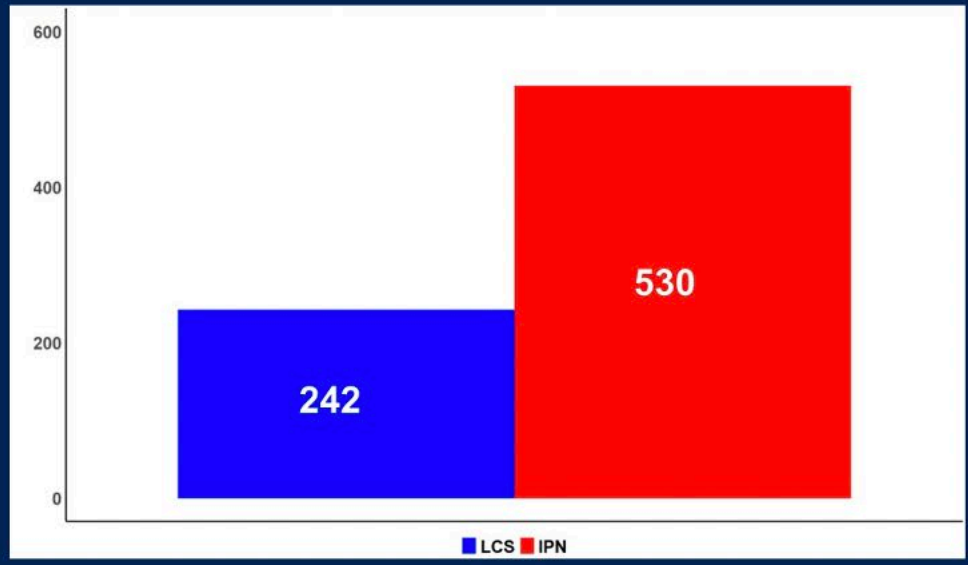


Aggregate cumulative lung cancer diagnoses: LCS versus IPN cohorts

Rates of definitive local curative-intent treatment

Proportions receiving surgery/SBRT



Number of patients receiving surgery/SBRT

Screening NSCLC

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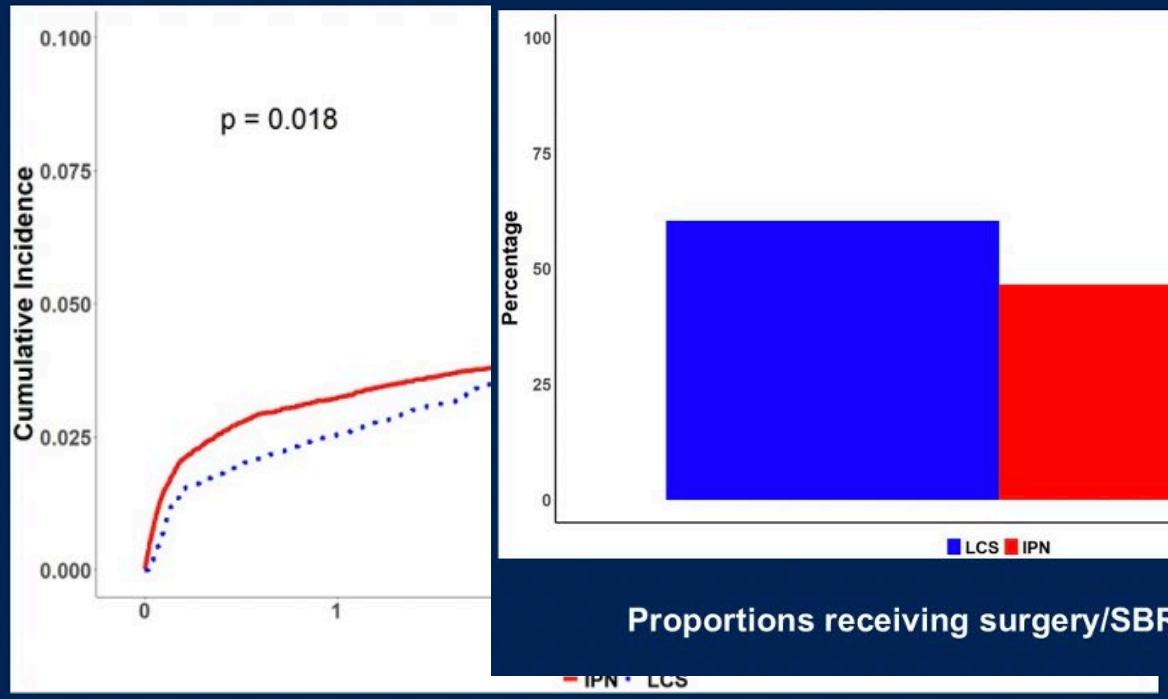

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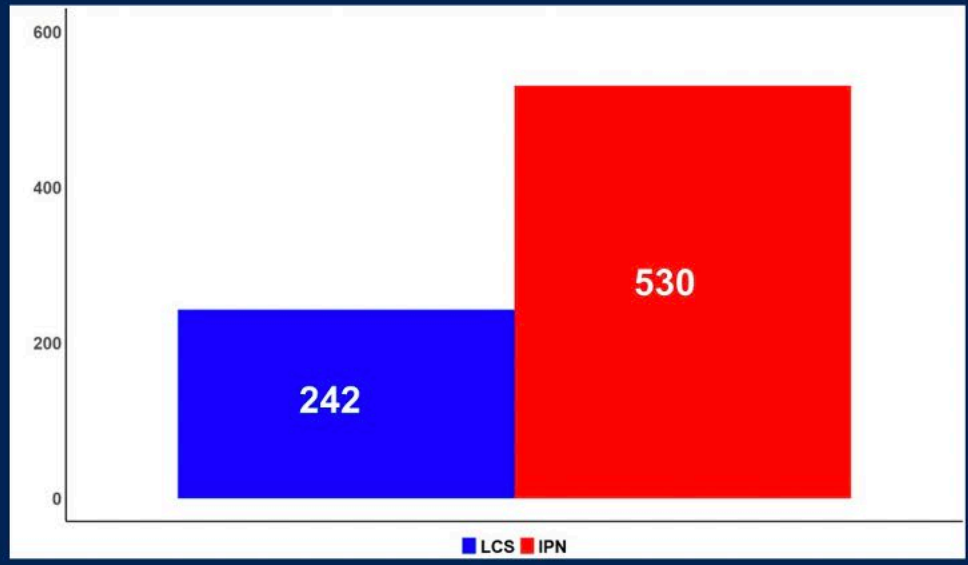
Proportions receiving surgery/SBRT



Number of patients receiving surgery/SBRT

LC specific mortality ↓ - NNS to prevent 1 LC death

↓ all cause mortality

Screening NSCLC

Abstract 8002. Lung cáncer diagnosis rates (LCDR) in Lung Cancer Screening (LCS) and incidental Pulmonary Nodule (IPN)

What do the detected lung cancer cases in DELUGE tell us?

LCS part

9% of LC did **NOT** fullfill USPSTF21 criteria but all associated with known risk factor, smoking

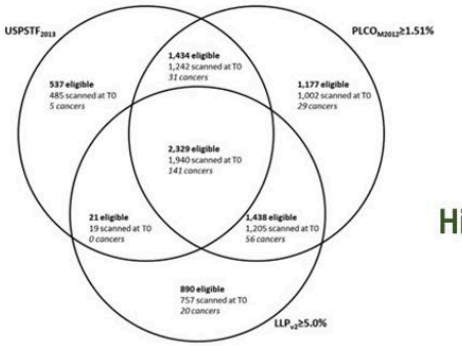
IPN part

52% of LC did **NOT** fullfill USPSTF21 criteria

10% of LC **NOT** associated with smoking

Other risk assess criteria? $PLCO_{M2012}$ ≥1.51%?

Other explanation for ↑ % LC detected in this region?



PLCOM2012: ↑ eligible participants & ↑ screen detected LC

History other cancer ?

PM2.5

Radon

Arsenic

Genetics ?

Screening NSCLC

Abstract 8002. Lung cáncer diagnosis rates (LCDR) in Lung Cancer Screening (LCS) and incidental Pulmonary Nodule (IPN)

DELUGE questions and how to move forward

Question	DELUGE
Did we **reach** the population at risk?	How many eligible were NOT screened (LCS) or evaluated (IPN)?
Optimizing nodule **risk assessment?**	LungRADS score & IPN size work What was false+ rate and how to ↓?
(Best) FU **interval**	USPSTF21 = yearly, IPN = Fleischer What was adherence and is this an optimal interval?
Evaluate & integrate **interventions to ↓ risk**	Was smoking cessation program incorporated? Other risk factors evaluated & addressed?

Factores de riesgo

Abstract 10573. NSCLC in BRCA germline carriers

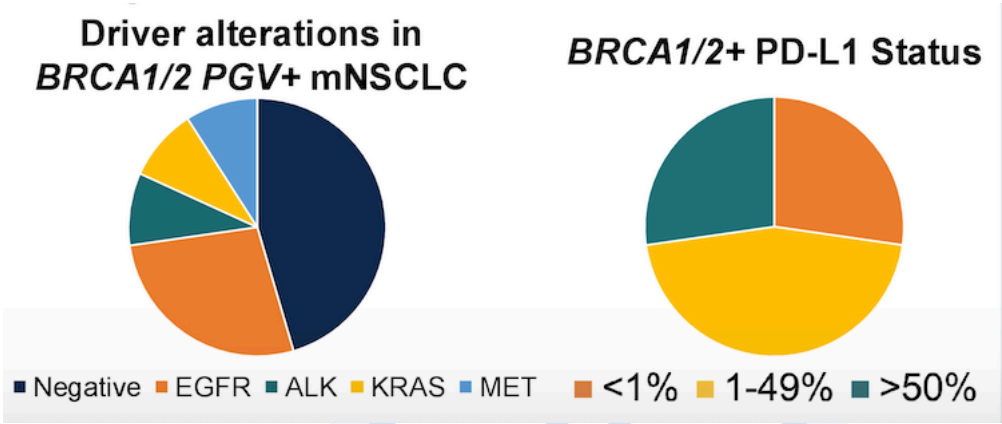
- Patients with pathogenic germline variants (PGVs) in BRCA1 and BRCA2 may have an increased risk of developing cáncer (estimate 5- 7%). Single institution

Results

	BRCA1/2 PGV (N=25)	PGV Negative (N=623)
Median age of onset, years	68 ± 14	67 ± 13
Female Sex	16 (64%)	319 (51%)
Never Smoker	**11 (44%)**	**99 (16%) p<0.01**
Stage I or II at diagnosis	14 (56%)	370/561 (66%)
Adenocarcinoma	17 (68%)	445 (71%)
Squamous cell	5 (20%)	120 (19%)

Recurrence: 3/14 (21.4%) *BRCA1/2* PGV patients with stage I-II NSCLC had recurrence within 5-years of definitive local therapy

Molecular Drivers: 6/11 (54.5%) of *BRCA1/2* PGV patients with stage III-IV NSCLC had actionable alterations (3 *EGFR*, 1 *ALK*, 1 *KRASG12C*, 1 *MET)*

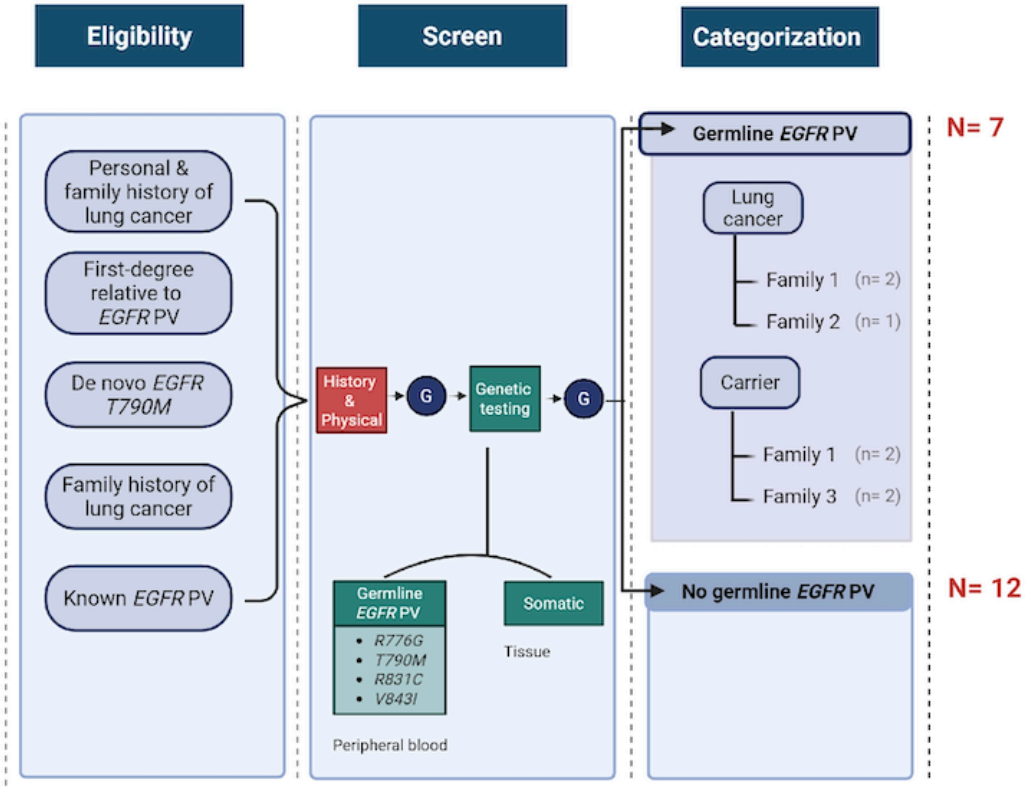


Among 11 *BRCA1/2* PGV patients with advanced stage III-IV disease, 6 had actionable genetic alterations, most commonly in EGFR (3/11).

Factores de riesgo

Abstract 10617. Familial Lung cáncer. Germline EGFR T790. 13 years

- Nineteen patients were enrolled between 2011 and 2024.
- Seven participants with *EGFR T790M* PV (3 NSCLC cancer, 4 carriers) were followed with serial computed tomography (CT).
- An AI model (3D nnUNet) was used to delineate lung nodules.
- Volumetric analyses were performed with ITK-SNAP.



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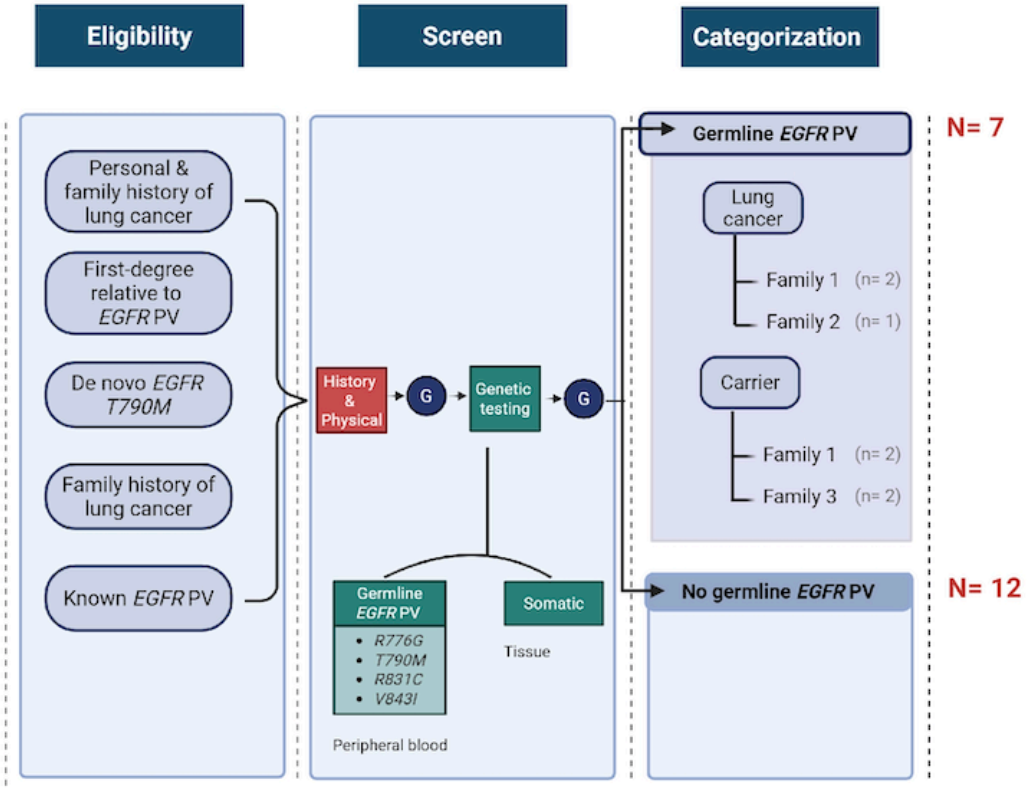

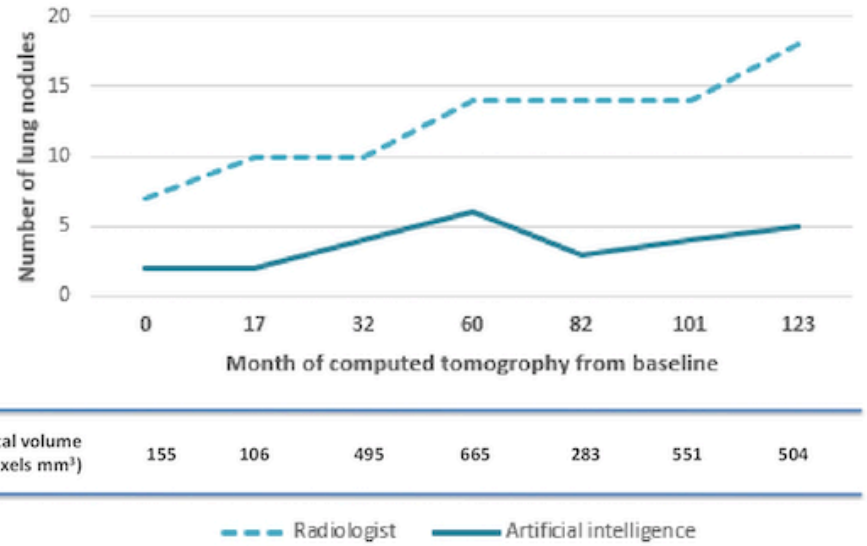

Figure 3: Number of nodules per radiologist & AI in index pt's son (no NSCLC, 10 yr f/u)

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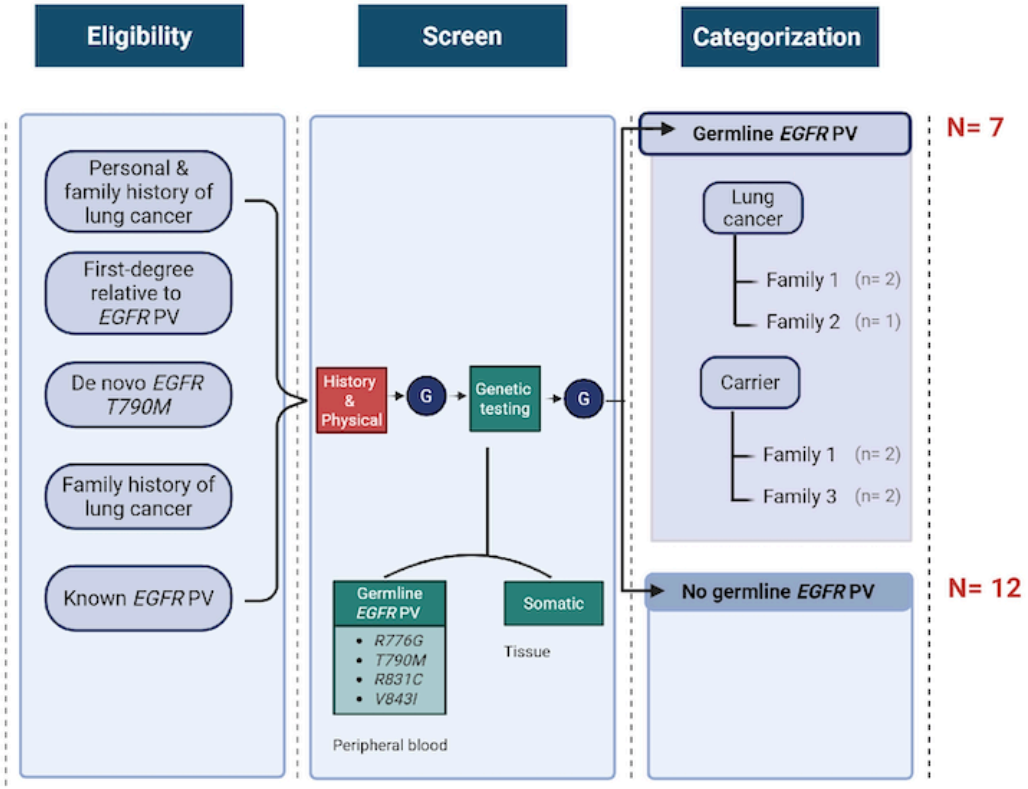


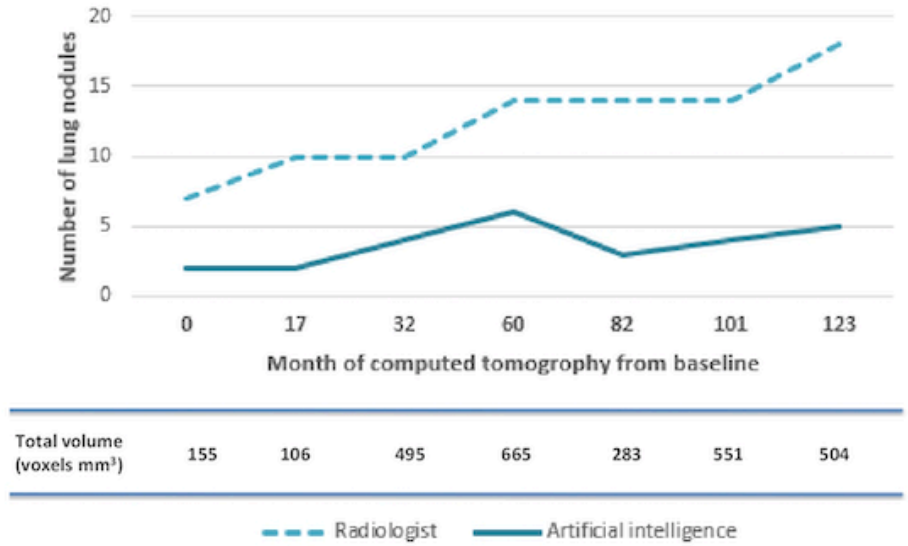


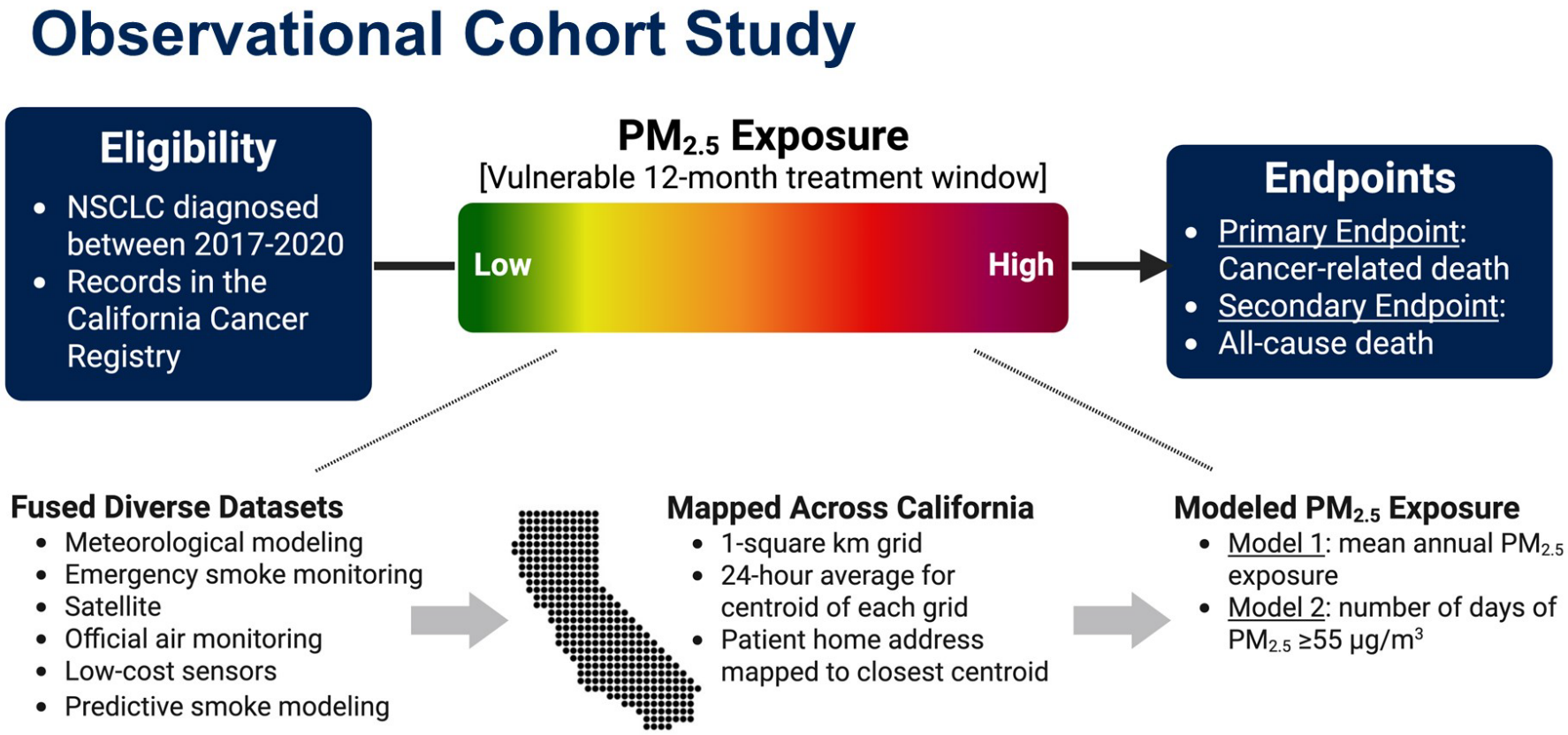
Figure 3: Number of nodules per radiologist & AI in index pt's son (no NSCLC, 10 yr f/u)

T790M carriers: Multiples bilateral GGOs 3º decade (remain dormant)
IA: monitor + LONG follow up

Factores de riesgo

Abstract 10520 Rapid Oral. Wild fire PM2.5 - NSCLC

- Ambient PM2.5 exposure from all sources including vehicle exhaust, power plants, agricultura and wildfire is associated with increased Lung cancer risk and may be associated with mortality.



PRESENTED BY: Surbhi Singhal, MD

Factores de riesgo

Abstract 10520 Rapid Oral. Wild fire PM2.5 - NSCLC

Hazard Ratio (HR) of Cancer-Related Death, Model 1

	Patients, n (%)	Mean Annual $PM_{2.5}$	
		Total Deaths, n	HR* (95% CI)
Total Cohort	18585	6097	1.198 (1.051-1.366)
Smoking History			
Never	5059 (27)	1565	1.362 (1.043-1.779)
Current or Former	13526 (37)	4532	1.168 (1.005-1.358)
NSCLC Stage			
I	7255 (39)	1024	1.313 (0.954-1.808)
II	1781 (10)	475	1.451 (0.922-2.285)
III	3568 (19)	1422	1.143 (0.872-1.497)
IV	5981 (32)	3176	1.209 (1.006-1.454)
Immunotherapy			
Not Given	14825 (80)	4348	1.190 (1.019-1.391)
Given	3702 (20)	1723	1.150 (0.894-1.480)

Higher mean annual $PM_{2.5}$ exposure was associated with 19.8% increased hazard of cancer-related death.

Association consistent for each subgroup

Factores de riesgo

Abstract 10520 Rapid Oral. Wild fire PM2.5 - NSCLC

	Patients, n (%)	$PM_{2.5}$ ≥55 μg/m³, AQI Unhealthy	
		Total Deaths, n	HR* (95% CI)
Total Cohort	18585	1730	0.933 (0.873-0.997)
Smoking History			
Never	5059 (27)	437	0.978 (0.858-1.115)
Current or Former	13526 (37)	1293	0.914 (0.846-0.987)
NSCLC Stage			
I	7255 (39)	301	1.022 (0.870-1.201)
II	1781 (10)	133	0.894 (0.699-1.142)
III	3568 (19)	416	1.003 (0.877-1.147)
IV	5981 (32)	880	0.888 (0.809-0.975)
Immunotherapy			
Not Given	14825 (80)	1231	0.961 (0.887-1.041)
Given	3702 (20)	491	0.878 (0.778-0.990)

For every 10 days with $PM_{2.5}$ ≥55 μg/m³, the hazard of death decreased by 7%.

Factores de riesgo

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Immunotherapy			
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Given	3702 (20)		

For every 10 days with $PM_{2.5}$ ≥55 μg/m³, the hazard of death decreased by 7%.

Higher ambient $PM_{2.5}$ exposure after non-small cell lung cancer (NSCLC) diagnosis is associated with increased risk of cancer-related death.

Paradoxically, higher wildfire-dominated $PM_{2.5}$ exposure was associated with improved survival particularly among patients with Stage IV disease and among those treated with immunotherapy, which warrants further investigation.

Factores de riesgo

Abstract poster 8050. Outcomes HIV Lung cáncer

Retrospective study 2005-2024

Figure 2. OS in HIV Negative and HIV Positive Patients

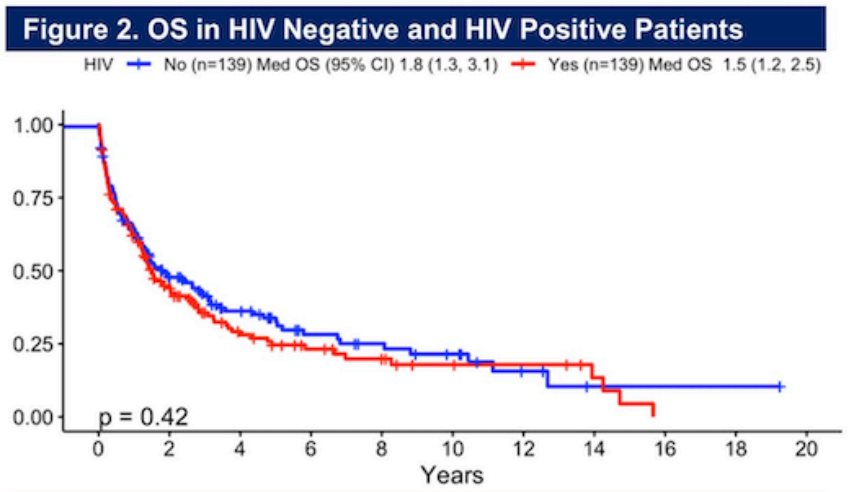


Figure 3. OS in Patients with Stage-Appropriate Treatment

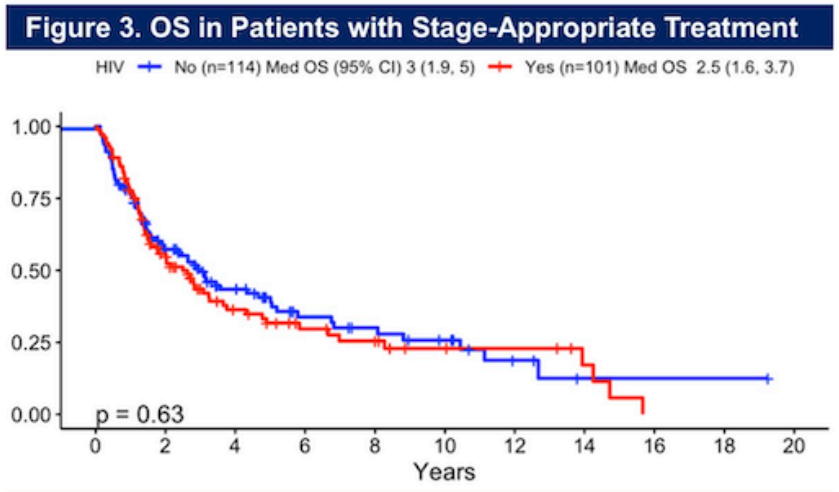


Figure 4. OS in Early Stage (Stage I/II)

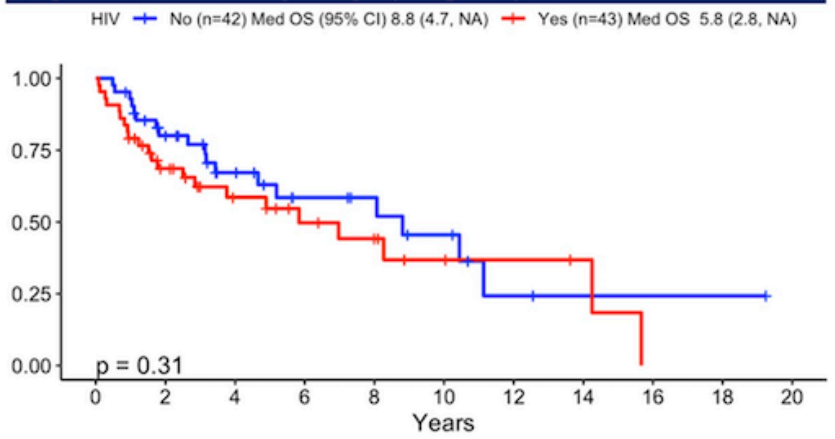
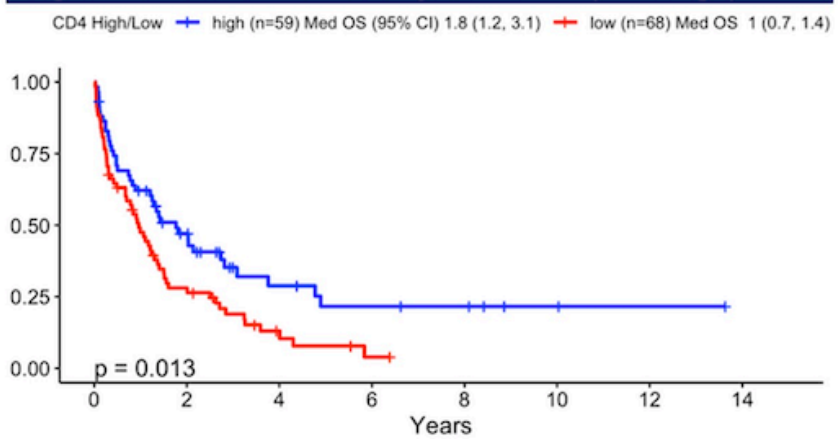


Figure 5. OS in HIV Positive by CD4 count (>400 high)

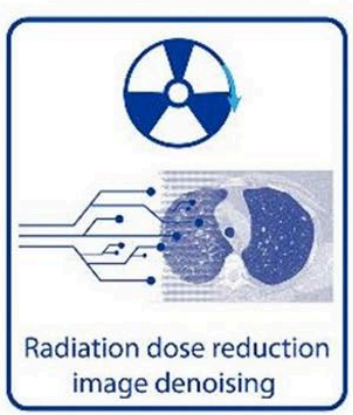


De los 97 pacientes que cumplían criterios de screening solo 7 lo realizaron

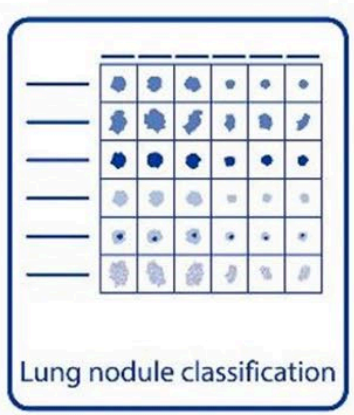
CD4 disminuidos < 400 : Peores resultados en OS

AI use cases in Lung Screening


Screening eligibility


Radiation dose reduction
image denoising


Lung nodule detection


Lung nodule classification

Determining optimal
screening intervals

Opportunistic detection
of chronic disease

IA screening

Abstract 8055. LC- SHIELD study in never smokers

STUDY DESIGN

1) Never smokers (defined as lifetime exposure to less than 100 cigarettes)
2) 50 to 75 year old
3) One or more first-degree family members diagnosed with lung cancer
4) No personal history of malignancy
5) No recent CT thorax in recent two years
6) No history of pulmonary tuberculosis or chronic lung disease

Registration by scanning QR code

→ LDCT → Images analyzed by LungSIGHT

→ Longitudinal psychological assessment
→ Blood taking for translational analysis

→ **AI positive** (presence of lung nodule ≥5mm) → Formal Radiologist Reporting → Follow up LDCT in 3, 6, 12, 24 months depending on risk

→ AI negative → Follow up LDCT in 24 months

Retrospective validation by radiologist blinded to AI results

Sensitivity and Specificity for Detection of Lung Nodule ≥5mm (per subject basis)

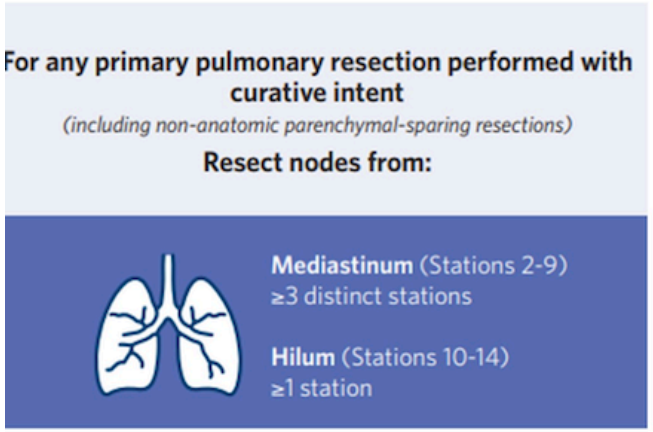
- Local data was used for iterative fine-tuning, optimizing the algorithm after analysis of first 181 cases.
- Sensitivity, specificity and concordance were evaluated in the validation cohort.

	AI-positive	Sensitivity	Specificity	Concordance
Before fine-tuning (n=181)	64%	88%	52%	67%
After fine-tuning (n=181)	43%	81%	85%	83%
Validation cohort (n=224)	39%	73%	77%	76%

LUNG SIGHT AI fist reader: High Lung cancer detedtion rate

Surgery

Abstract 11140. Lung cáncer quality surgery



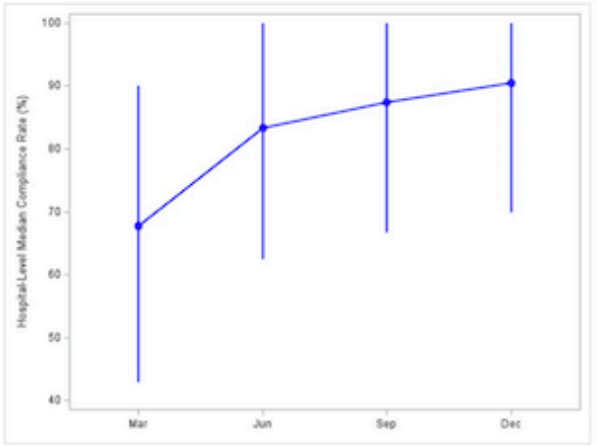
Objective: Increase compliance with Standard 5.8 ≥80% after participation in the Lung NODES national quality improvement (QI) collaborative

Compliance from 67% - 90%

Table 3. Adjusted multilevel analysis of factors associated with compliance

Characteristic	Compliance with Standard 5.8 OR (95% CI)	p-value
Data Collection Period		
Baseline (March)	Ref.	
Quarter 2 (June)	1.70 (1.49 – 1.94)	**<0.001**
Quarter 3 (September)	2.12 (1.85 – 2.42)	**<0.001**
Final (December)	2.50 (2.19 – 2.86)	**<0.001**
Surgical Approach		
Robotic assisted	1.38 (1.22 – 1.56)	**<0.001**
VATS	Ref.	
Resection		
Lobectomy	Ref.	**<0.001**
Segmentectomy	0.76 (0.65 – 0.89)	**<0.001**
Wedge	0.44 (0.40 – 0.48)	**<0.001**

Figure 2. Median hospital-level compliance increased from 67.8% at baseline to 90.5% post-participation



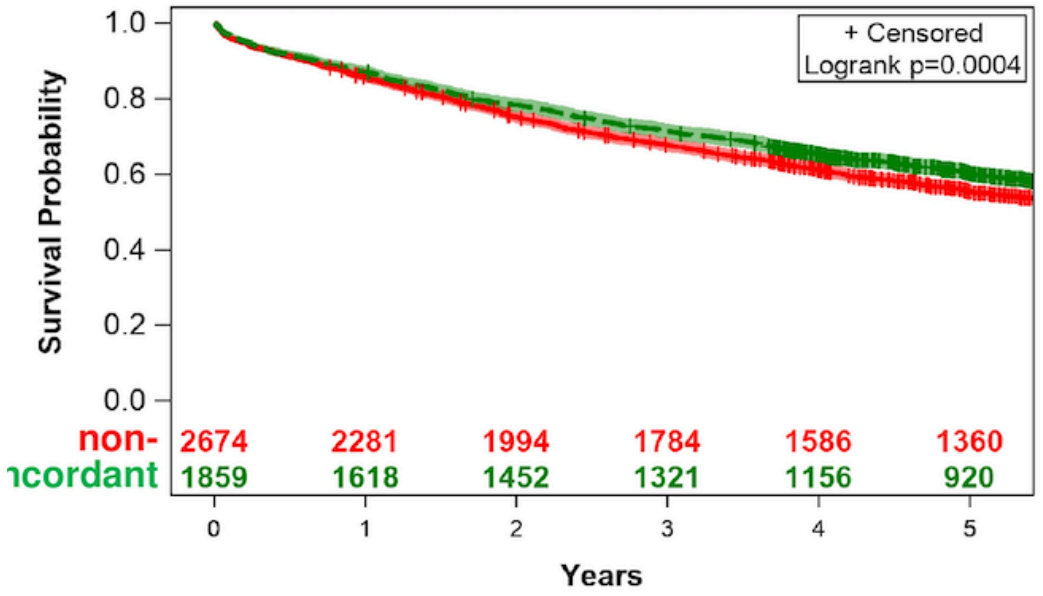
Surgery

Abstract poster 8067. Quality metric in Surgery CoC. N: 4536 patients

- Sampling of at least 3 mediastinal and at least 1 hilar lymph node stations during lung cancer resection was adopted by the American College of Surgeons (ACS) Commission on Cancer (CoC) as Operative Standard 5.8

Median OS was superior in concordant (7.6y) v non-concordant (6.1y) patients (p=0.0004, Fig. 1).

Fig 1. Overall survival by 3+1-concordance status



Conclusions

In this large, community, population-based surgical database,

CoC OS 5.8 "3+1" LN adherence for lung cancer resection was associated with:

- ↑ surgical complications
  but also
- ↑ nodal upstaging
- ↑ adjuvant treatment utilization
- ↑ **overall survival**

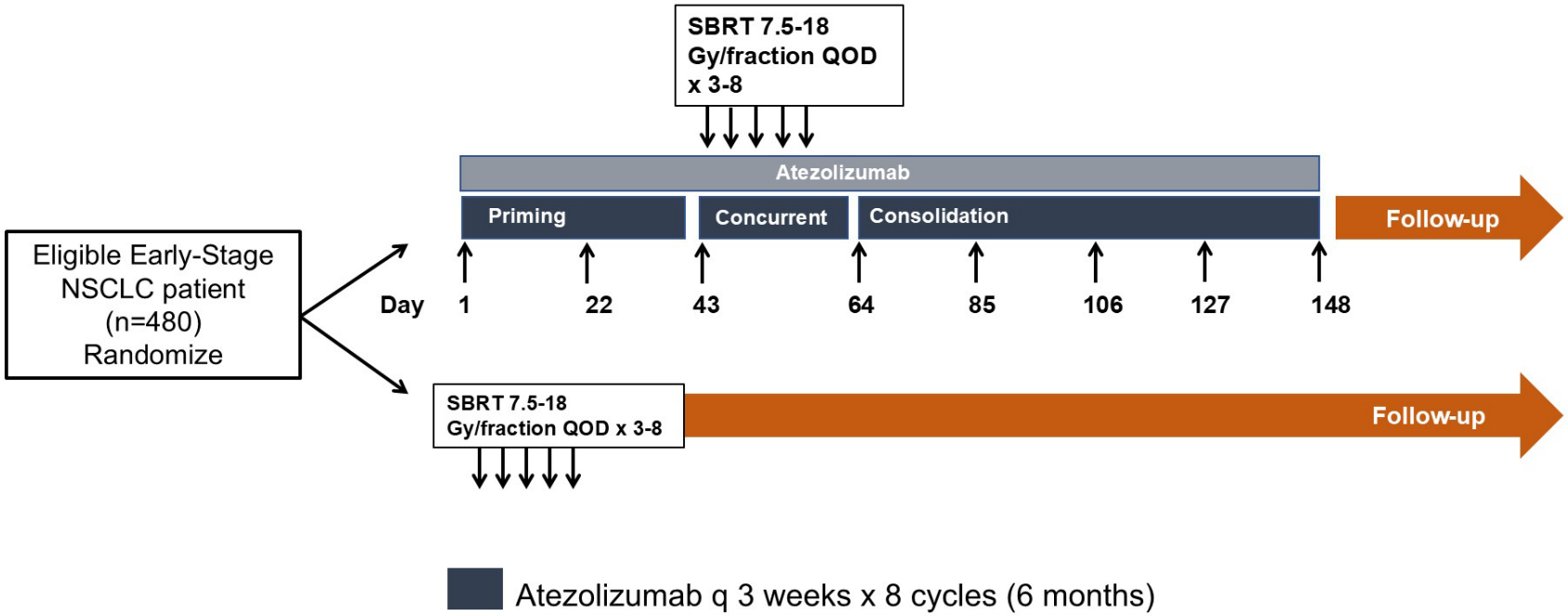
These findings:

- **likely represent real-world practice and outcomes**
- support the use of this quality metric for curative-intent lung cancer surgery.

Early Stage Radiotherapy

Oral Abstract 8003: SWOG/NRG S1914: Randomized phase III trial of induction/consolidation atezolizumab + SBRT versus SBRT alone in high risk, early-stage NSCLC.

SWOG/NRG S1914 Schema



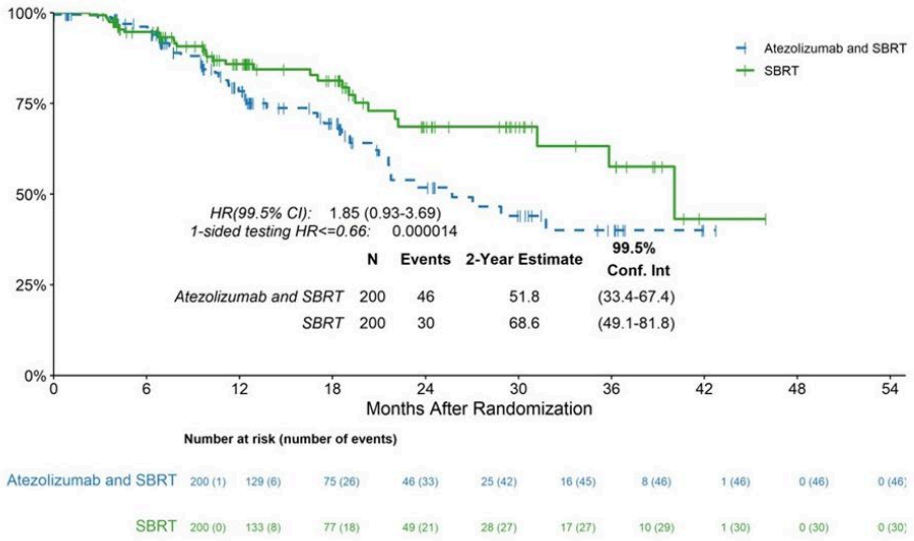
Tumor > 2cm
Tumor SUV max > 6.2
Moderately or poorly differentiated or undifferentiated histology
INOPERABLES

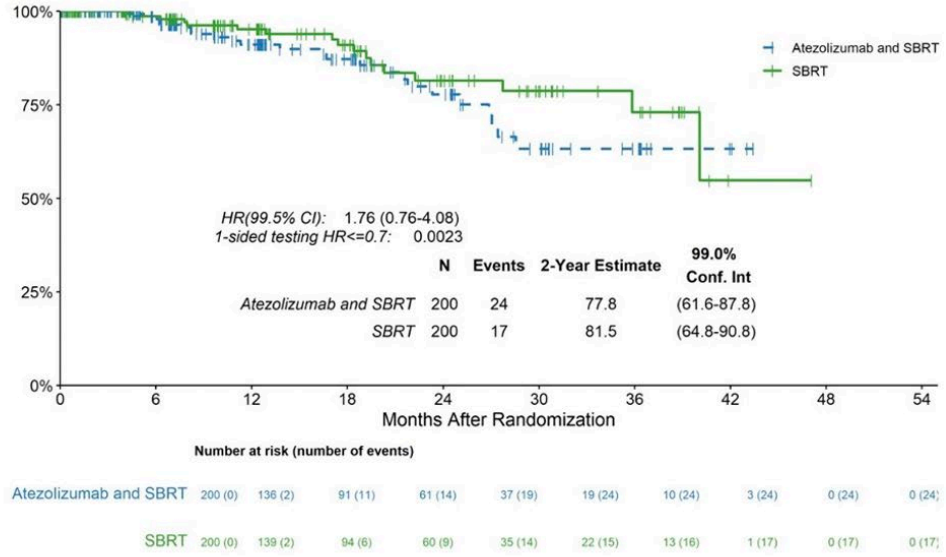
Early Stage Radiotherapy

Oral Abstract 8003: SWOG/NRG S1914: Randomized phase III trial of induction/consolidation atezolizumab + SBRT versus SBRT alone in high risk, early-stage NSCLC.

Futility Analysis of PFS and OS

Data as of Aug 28, 2024





With 76 PFS events:
HR=0.66 rejected at 0.0025 level
*Width of HR CI is 99.5% to be consistent with level of testing (0.0025)

With 41 deaths:
HR=0.70 rejected at 0.005 level
*Width of HR CI is 99% to be consistent with level of testing (0.005)

Futility met for both PFS and OS

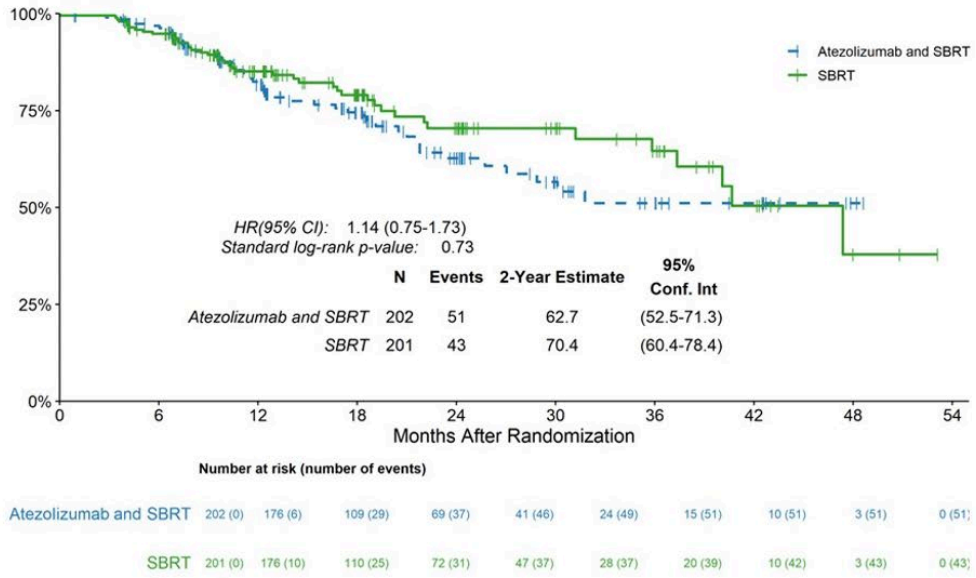
FU (in months) for 362 alive pts:
Median: 9.9 months, IQR: 4.1-18.5, Range: 0.03-47.0

Early Stage Radiotherapy

Oral Abstract 8003: SWOG/NRG S1914: Randomized phase III trial of induction/consolidation atezolizumab + SBRT versus SBRT alone in high risk, early-stage NSCLC.

Updated PFS and OS

Data as of April 1, 2025

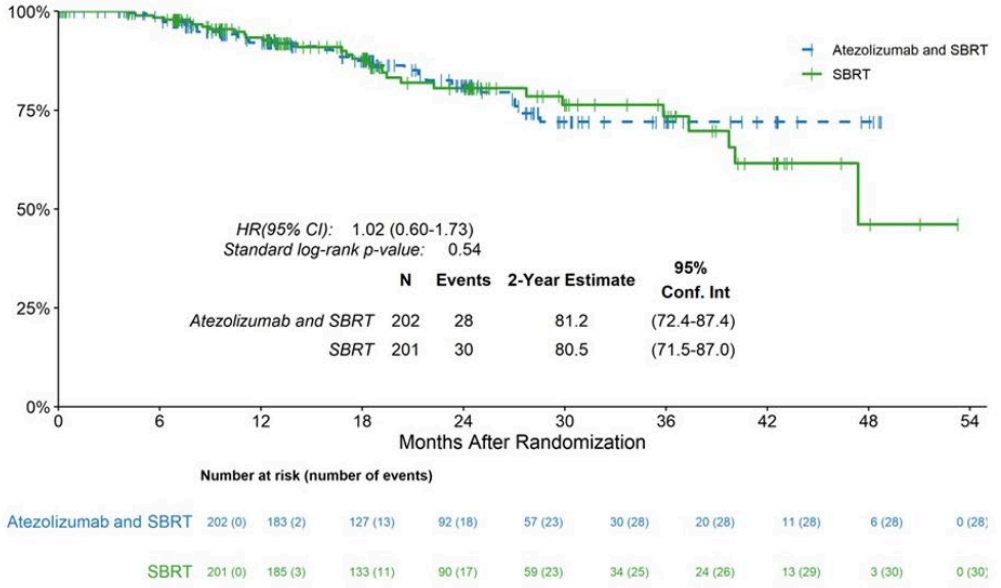


Analysis on 94 PFS events

* If continued to full information, primary analysis at 225 PFS events

FU (in months) 345 for alive pts:

Median: 13.8 months, IQR: 9.4-24.6, Range: 0.1-53.3



Analysis on 58 deaths

* If continued to full information, primary analysis at 245 deaths or 36 months of follow-up

Early Stage Radiotherapy

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Updated PFS and OS

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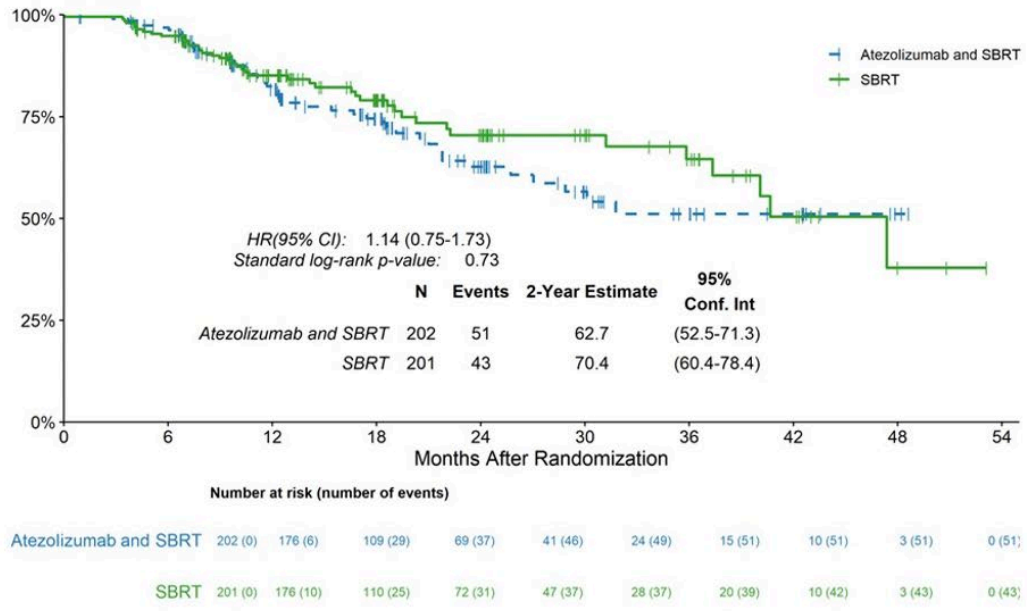

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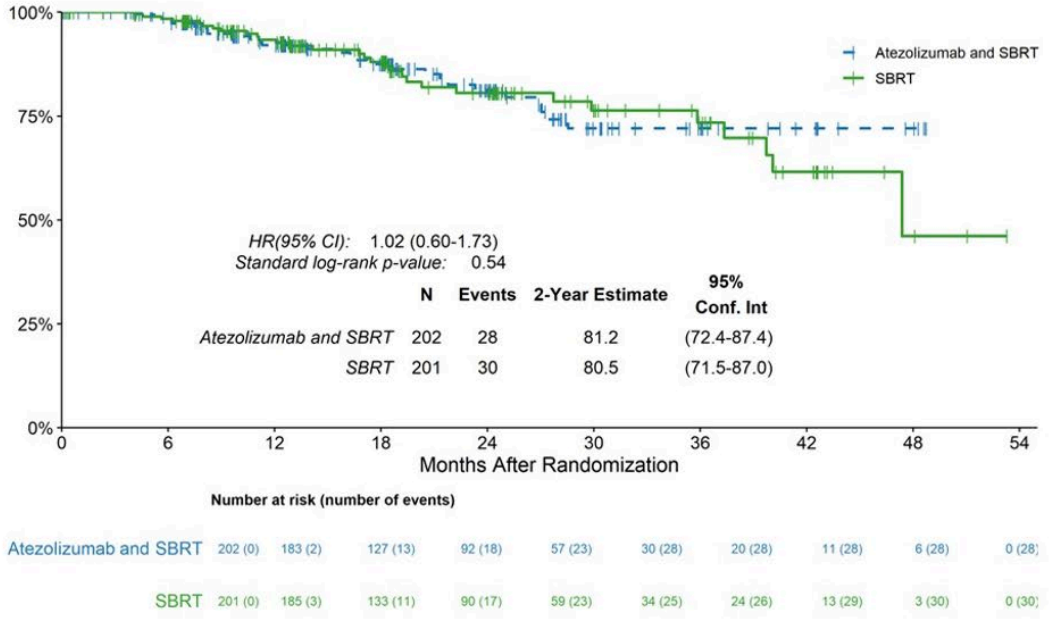
Quizas



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Early Stage Radiotherapy

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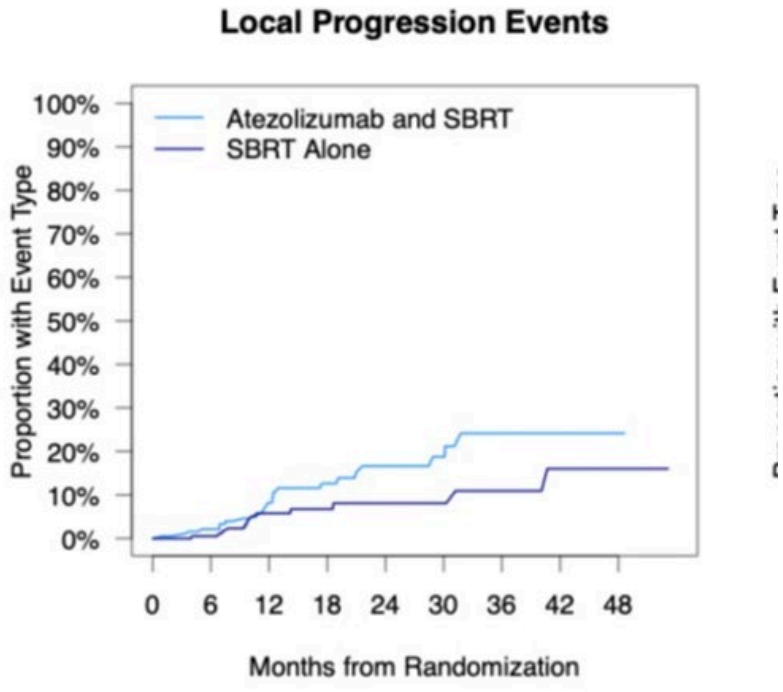


Aunque era población de alto riesgo : Pocos eventos en rama control: Dosis altas y coorecto plan de SBRT

No datos sobre PDL1 ni TMB: planeado

5% local failures: Overcalling fibrosis?

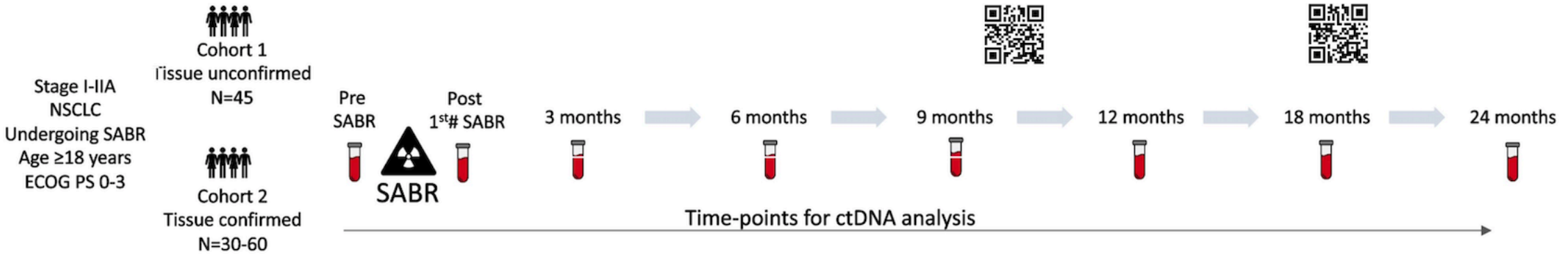
Early Stage Radiotherapy

Varios estudios similares

Trial (NCT ID)	Phase	Sample Size	Immunotherapy (Agent & Duration)	Status (Completion)
I-SABR (NCT03110978) – SABR ± nivolumab	II (RCT)	156	Nivolumab 480 mg IV, q4w × 4 cycles (≈4 months)	Results published 2023 ✅ Yes Improvement of 4-year EFS
KEYNOTE-867 (NCT03924869) – SBRT ± pembrolizumab	III (RCT)	448	Pembrolizumab (anti–PD-1) up to 1 year, q3w weeks	❌ No Terminated early for futility – n=448 no EFS/OS benefit and higher toxicity).
PACIFIC-4 / RTOG 3515 (NCT03833154) – SBRT ± durvalumab	III (RCT)	~630	Durvalumab 1500 mg IV, q4w × up to 26 cycles (24 months)	Closed to accrual (Enrollment ~630 completed by mid-2024; primary completion expected ~2026).

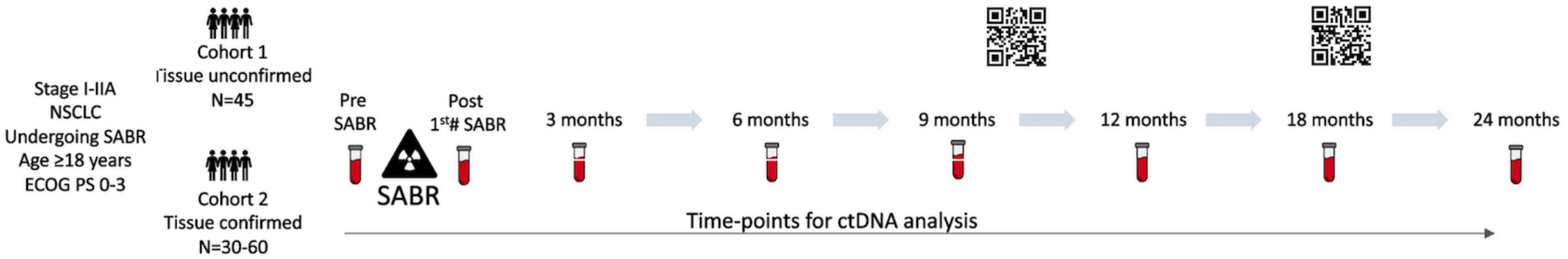
Early Stage Radiotherapy

Abstract Poster 3044. SABR DETECT trial. ctdNA pre and post SBRT in presumed NSCLC



Early Stage Radiotherapy

Abstract Poster 3044. SABR DETECT trial. ctdNA pre and post SBRT in presumed NSCLC



SHIELDING ULTRA MRD panel of hotspot regions in 2365 cancer-related genes with ultra-high sensitivity was used for ctDNA analysis (mutation + fragment profile + CNV

Early Stage Radiotherapy

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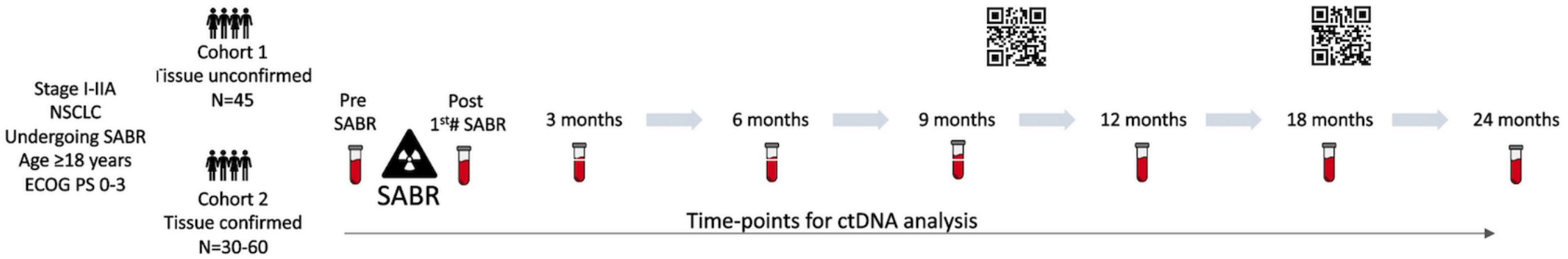

SHIELDING ULTRA MRD panel of hotspot regions in 2365 cancer-related genes with ultra-high sensitivity was used for ctDNA analysis (mutation + fragment profile + CNV

The ctDNA detection rate in pre-SABR samples was 22.7% versus 27.3% in post-SABR samples (Table 2). 37.9% of patients had detectable ctDNA either before or after SABR.

Early Stage Radiotherapy

Abstract Poster 3044. SABR DETECT trial. ctDNA pre and post SBRT in presumed NSCLC

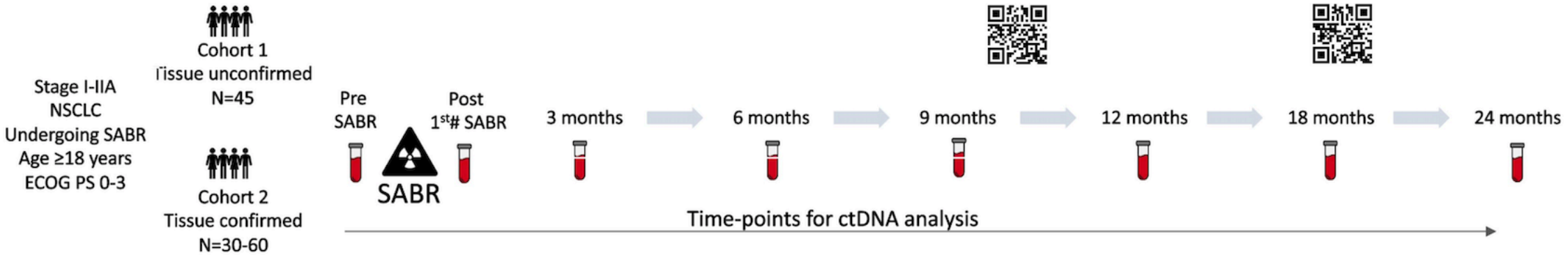

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Table 2 – ctDNA detection rates (N=66)		
Pre-SABR	**Post-SABR**	**n (%)**
detected	detected	8 (12.1%)
not detected	detected	10 (15.2%)
detected	not detected	7 (10.6%)
not detected	not detected	41 (62.1%)

Brain SRS

Abstract 2024. Irradiated tumor volumen as predictor of local recurrence and radionecrosis in BM treated with SRS

Study Population and Data Collection

- Retrospective cohort study of 431 lung patients with BM treated with single fraction Gamma-Knife, 2009- 2020, all-comers cohort from Stockholm region
- ^{11}C-methionine PET-CT: LNR >2 as threshold

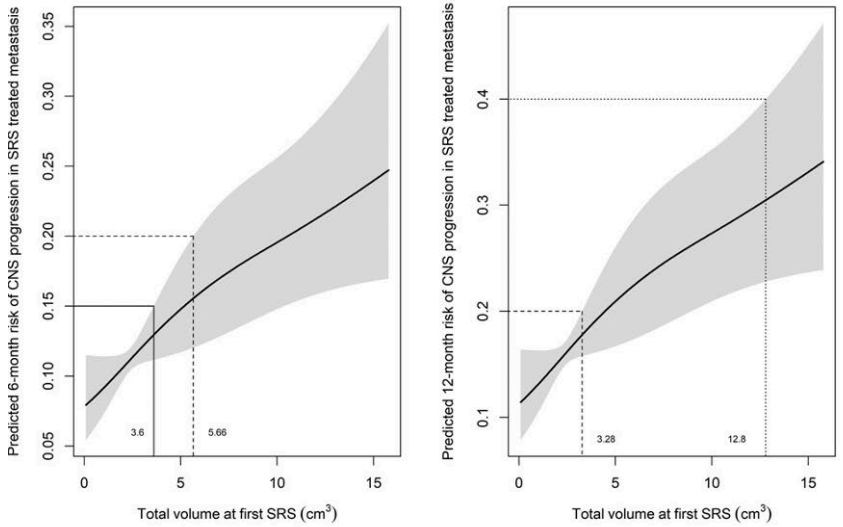
Karolinska Comprehensive Cancer Center

Statistical Analysis

- Cox regression models (penalized splines for non-
- Risk predictions at 6 and 12 months
- Sensitivity/specificity of PET-CT vs MRI
- Software: R version 4.2.2 with relevant packages

Results

Predicted 6- and 12-month risk of LC vs total volume of BM



Diagnostic performance of MET-PET vs MRI for RN & LR

- Sensitivity: 0.9091
- **Specificity: 0.6**
- Accuracy: 0.8519
- Positive predictive value: 0.9091
- Negative predictive value: 0.6

Brain SRS

Abstract 2024. Irradiated tumor volumen as predictor of local recurrence and radionecrosis in BM treated with SRS

- Larger irradiated tumor volumes were correlated with ↑ RN or LR risk
- ↓ volumes can lead to RN & LR, not evident at 6m, but emerging by 12m post-SRS
- ^{11}C-methionine PET-CT: ⊘ significant advantages in distinguishing LR from RN