



# Recomendaciones de seguimiento

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# AGENDA

- Follow-up imaging
- Biomarkers for surveillance
- Long-term survivors
- Second primary tumors



# Follow-up imaging

# Lung Cancer Surveillance After Definitive Curative-Intent Therapy: ASCO Guideline

Bryan J. Schneider, MD<sup>1</sup>; Nofisat Ismaila, MD<sup>2</sup>; Joachim Aerts, MD, PhD<sup>3</sup>; Caroline Chiles, MD<sup>4</sup>; Megan E. Daly, MD<sup>5</sup>;

14 relevant studies to  
inform the evidence base  
for this guideline.

**Recommendation 1.1.** Patients should undergo surveillance imaging for recurrence every 6 months for 2 years (Type: Informal consensus; Evidence quality: Low; Strength of recommendation: Moderate).

**Recommendation 1.2.** Patients should undergo surveillance imaging for detection of new primary lung cancers annually after the first 2 years (Type: Evidence based; Evidence quality: Intermediate; Strength of recommendation: Moderate).

**Recommendation 2.1.** Clinicians should use a diagnostic chest computed tomography (CT) that includes the adrenals, with contrast (preferred) or without contrast when conducting surveillance for recurrence during the first 2 years post treatment (Type: Informal consensus; Evidence quality: Low; Strength of recommendation: Moderate).

**Qualifying statement.** There is no evidence of added benefit for a CT of the abdomen and pelvis over a chest CT through the adrenals as a surveillance imaging modality for recurrence.

**Recommendation 2.2.** Clinicians should use a low-dose screening chest CT when conducting surveillance for new lung primaries after the first 2 years post treatment (Type: Evidence based; Evidence quality: Low; Strength of recommendation: Moderate).

**Recommendation 2.3.** Clinicians should not use <sup>18</sup>F-labeled fluorodeoxyglucose positron emission tomography (<sup>18</sup>F-FDG PET) as a surveillance tool (Type: Informal consensus; Evidence quality: Low; Strength of recommendation: Moderate).

**Recommendation 3.** Surveillance imaging may be omitted in patients who are clinically unsuitable for or unwilling to accept further treatment. Age should not preclude surveillance imaging. Consideration of overall health status, chronic medical conditions, and patient preferences is recommended (Type: Informal consensus; Evidence quality: Low; Strength of recommendation: Weak).

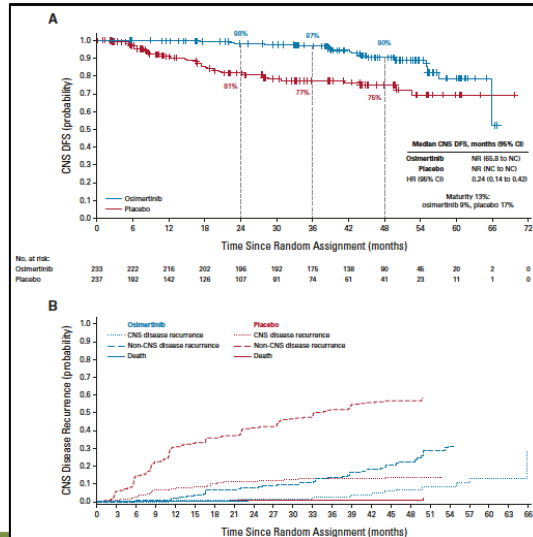
# Lung Cancer Surveillance After Definitive Curative-Intent Therapy: ASCO Guideline

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**Recommendation 5.1.** For patients with stage I-III NSCLC, clinicians should not use brain MRI for routine surveillance for recurrence in patients who have undergone curative-intent treatment (Type: Informal consensus; Evidence quality: Low; Strength of recommendation: Moderate).

- **Uncertainty:** driver mutations (EGFR, ALK...?)

ADAURA Trial



Roche Reports P-III Study (ALINA) Results of Alecensa (alectinib) for ALK-Positive Early-Stage Lung Cancer

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## LUNG CANCER SCREENING:

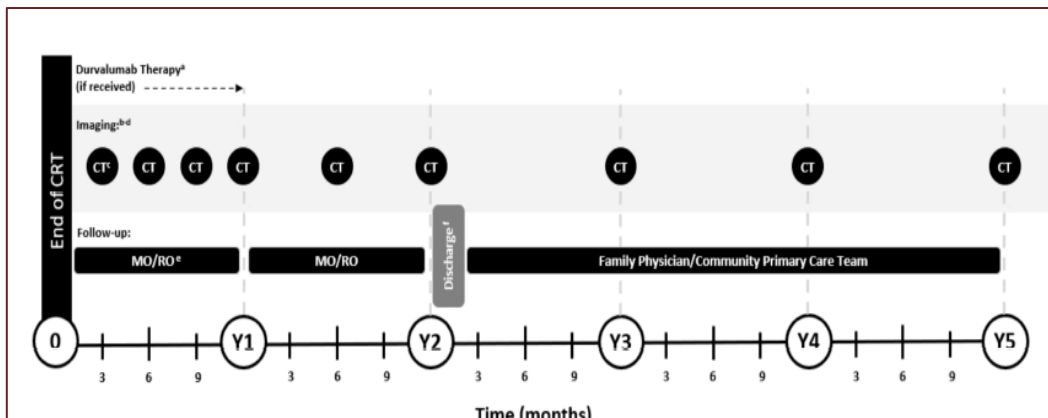
- A larger number of smaller tumors will be detected and treated with resection or SBRT.
- May a less frequent surveillance regimen be warranted in these patients with more emphasis on detection of second primaries an?.
- Chest CT annually?

Review

## Follow-Up Imaging Guidelines for Patients with Stage III Unresectable NSCLC: Recommendations Based on the PACIFIC Trial

Jenny J. Ko <sup>1,\*</sup>, Shantanu Banerji <sup>2</sup>, Normand Blais <sup>3</sup>, Anthony Brade <sup>4</sup>, Cathy Clelland <sup>5</sup>, Devin Schellenberg <sup>6</sup>, Stephanie Snow <sup>7</sup>, Paul Wheatley-Price <sup>8</sup>, Ren Yuan <sup>9</sup> and Barbara Melosky <sup>10</sup>

Expert working group recommendations for imaging and follow-up in stage III, unresectable NSCLC after treatment with CRT +/- durvalumab

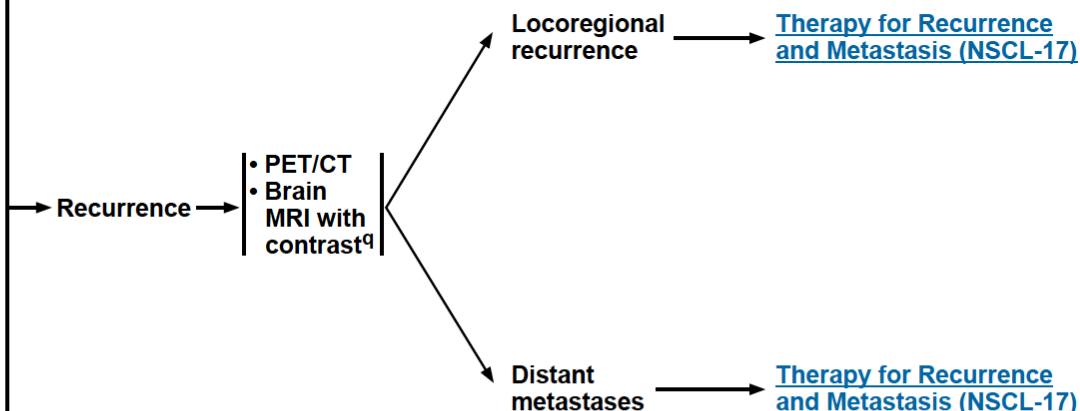


Brain MR is only recommended in the event of symptom presentation



### SURVEILLANCE AFTER COMPLETION OF DEFINITIVE THERAPY

- No evidence of clinical/radiographic disease
- Stage I–II (primary treatment included surgery ± chemotherapy)
    - H&P and chest CT<sup>jj</sup> ± contrast every 6 mo for 2–3 y, then H&P and a low-dose non-contrast-enhanced chest CT annually
  - Stage I–II (primary treatment included RT) or stage III or stage IV (oligometastatic with all sites treated with definitive intent)
    - H&P and chest CT<sup>jj</sup> ± contrast every 3–6 mo for 3 y, then H&P and chest CT ± contrast every 6 mo for 2 y, then H&P and a low-dose non-contrast-enhanced chest CT annually
      - ◊ Residual or new radiographic abnormalities may require more frequent imaging
  - Smoking cessation advice, counseling, and pharmacotherapy
  - PET/CT<sup>kk</sup> or brain MRI is not routinely indicated
  - [Cancer Survivorship Care \(NSCL-G\)](#)



# ADVANCED NSCLC

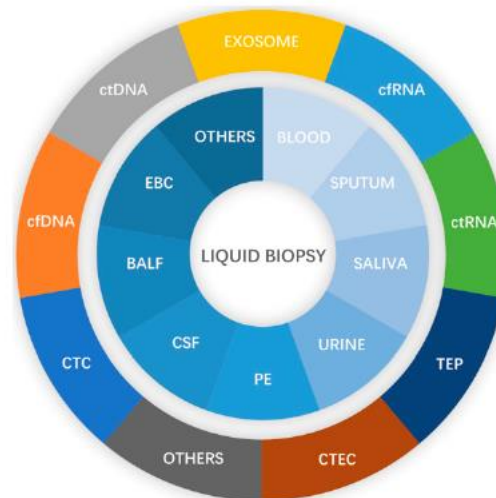
- **Response evaluation**
  - Recommended after two to three cycles of systemic therapy
  - Same initial radiographic investigation that demonstrated tumour lesions.
  - PET is not routinely recommended (high sensitivity, low specificity)
  - Use RECIST or iRECIST (pseudoprogression)
- **Follow-up**
  - Close follow-up (every 6-12 weeks) to allow for early initiation of a new line of therapy (it should also depend on individual retreatment options).
  - For patients who completed their scheduled ICI without signs of disease progression, follow-up CT scans should be made every 3-4 months. This interval can be increased for patients off therapy at 5 years.
  - Brain imaging for patients with EGFR, ALK,...?
  - **Early palliative care is strongly recommended (I,A).**



# Biomarkers for surveillance

# Liquid biopsy

Clinical application of liquid biopsy in  
NSCLC diagnosis and treatment



## EARLY DIAGNOSIS

Early warning and ancillary diagnosis



## PRECISE TREATMENT

Individualized medication guidance and  
drug resistance mechanism exploration



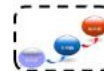
## DYNAMIC DETECTION

Real-time tracking of  
tumor progression and efficacy



## PROGNOSIS ASSESSMENT

Tumor prognosis and risk classification



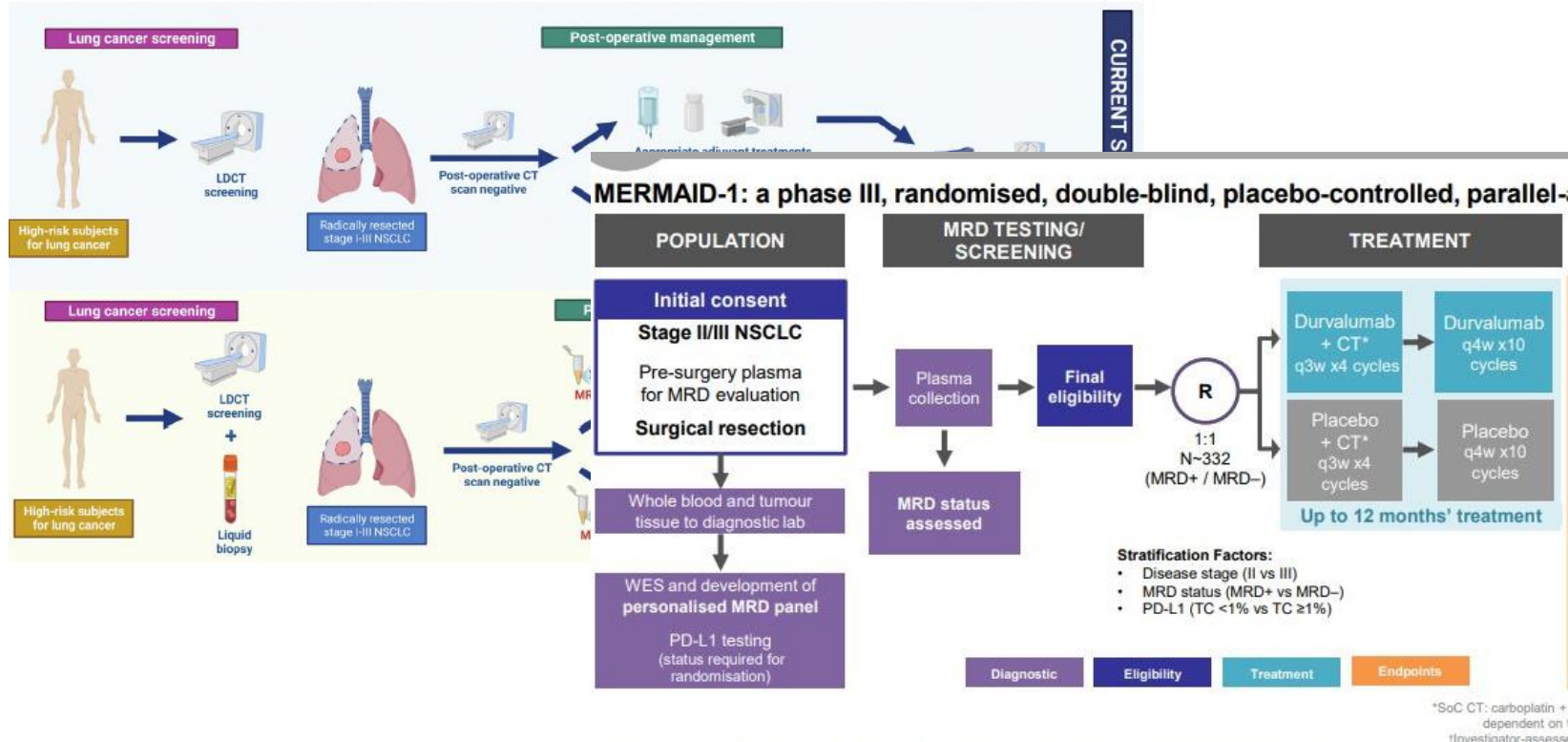
# Lung Cancer Surveillance After Definitive Curative-Intent Therapy: ASCO Guideline

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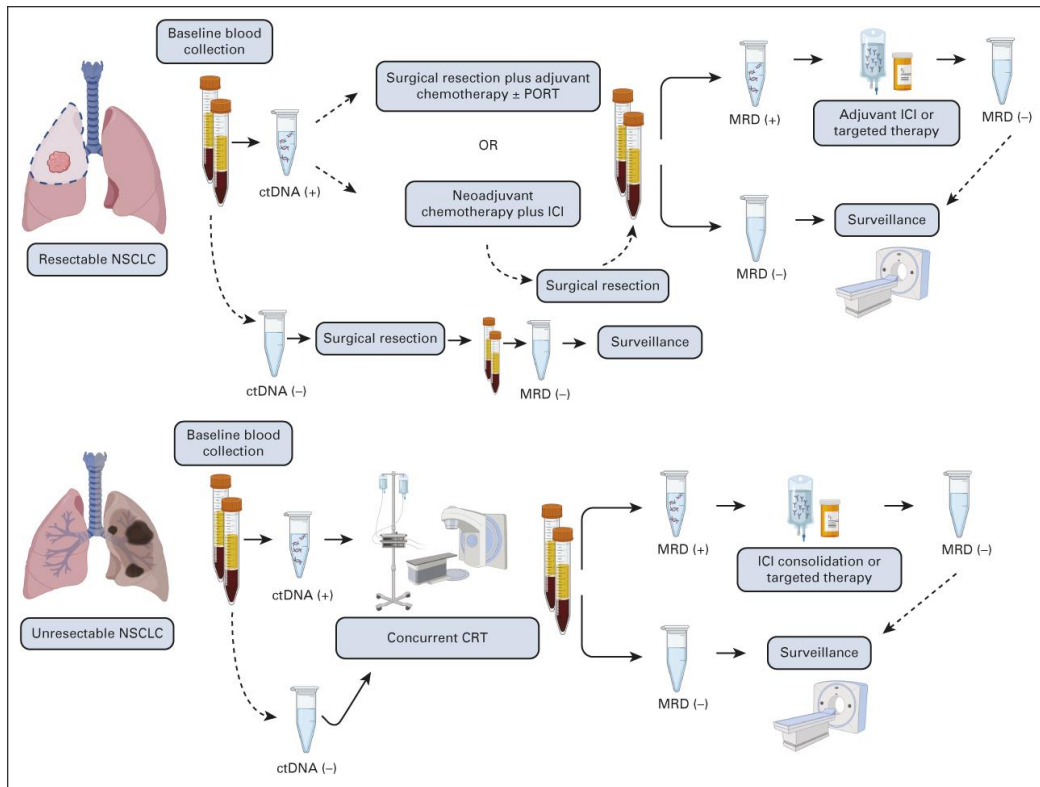
14 relevant studies to inform the evidence base for this guideline.

**Recommendation 4.** Clinicians should not use circulating biomarkers as a surveillance strategy for detection of recurrence in patients who have undergone curative-intent treatment of stage I-III NSCLC or SCLC (Type: Informal consensus; Evidence quality: Intermediate; Strength of recommendation: Moderate).

# Minimal residual disease (MRD) evaluation

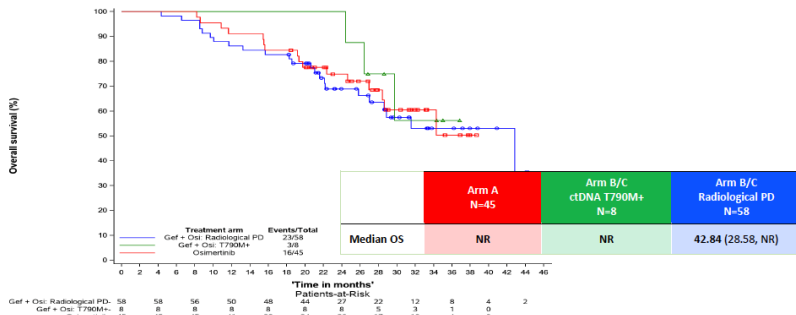


# Proposed clinical trial for e-NSCLC and LA-NSCLC



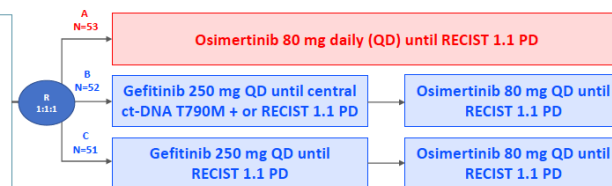
# Predicting progression in patients with advanced cancer

## Overall survival: Osimertinib vs. Sequential approach



## APPLE phase II trial: study design

- Advanced NSCLC.
- Del19, L858R *EGFR* mut.
- EGFR TKI naïve.
- ECOG PS 0-2.
- Stable BM allowed w/o steroids.



### Stratification criteria:

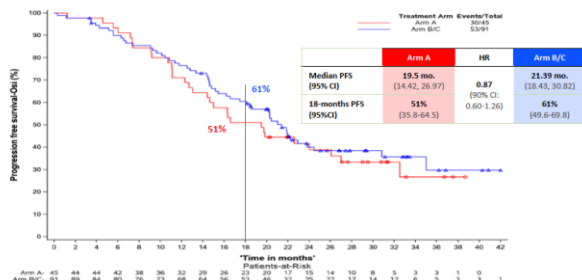
- EGFR* mutation subtype (Del19 vs. L858R)
- Brain metastases (present vs. absent)
- T790M at baseline (positive vs. negative)



**CENTRAL ct-DNA cobas *EGFR* Mutation Test v2, performed Q4W.**  
**Only applied as a predictive for making treatment decisions in arm B**

**RECIST 1.1 assessment with thorax, abdomen and brain CT-scans Q8W.**

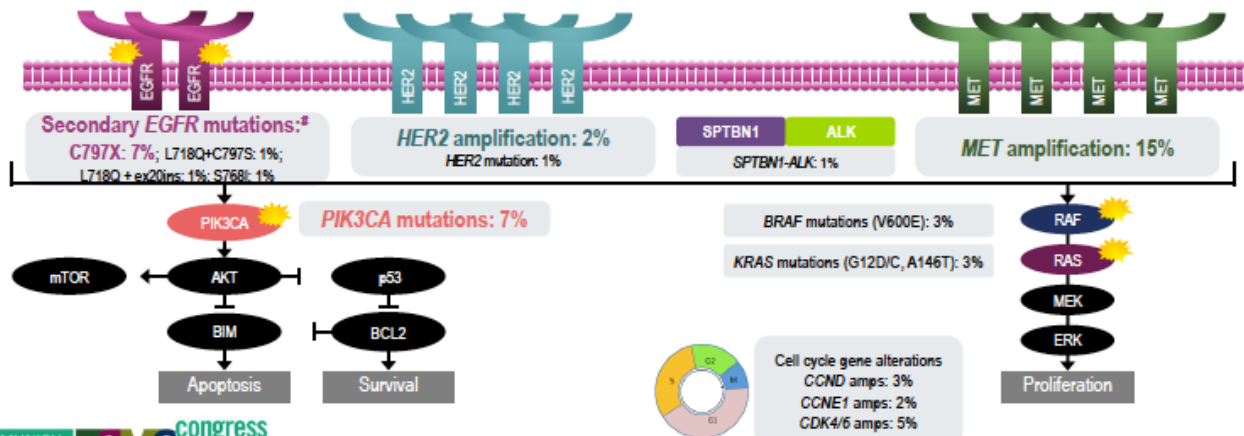
## Progression Free Survival on osimertinib



# To Identify Resistance Mutations in patients with advanced cancer

## RESULTS: CANDIDATE ACQUIRED RESISTANCE MECHANISMS WITH OSIMERTINIB (n=91)\*

- No evidence of acquired EGFR T790M
- The most common resistance mechanisms were **MET** amplification and EGFR C797S mutation
  - Other mechanisms included **HER2** amplification, **PIK3CA** and **RAS** mutations





# Long-term survivors

# Long-term survivors



## NCCN Guidelines Version 1.2023 Survivorship

[NCCN Guidelines Index](#)  
[Table of Contents](#)  
[Discussion](#)

### STANDARDS FOR SURVIVORSHIP CARE<sup>b</sup>

Care of the cancer survivor should include:

1. Surveillance for cancer spread or recurrence, and screening for subsequent primary cancers ([SURV-4](#))<sup>c</sup>
2. Monitoring long-term effects of cancer, including psychosocial, physical, and immunologic effects
3. Prevention and detection of late effects of cancer and therapy
4. Evaluation and management of cancer-related syndromes, with appropriate referrals for targeted intervention
5. Coordination of care between primary care providers and specialists to ensure that all of the survivor's health needs are met
6. Planning for ongoing survivorship care:<sup>d</sup>
  - ◇ Information on treatment received including all surgeries, radiation therapy (RT), and systemic therapies
  - ◇ Information regarding follow-up care, surveillance, and screening recommendations
  - ◇ Information on post-treatment needs, including information on acute, late, and long-term treatment-related side effects and health risks when possible ([NCCN Guidelines for Treatment of Cancer by Site](#))
  - ◇ Delineation of roles of all health care providers (including oncologists, primary care physicians [PCPs], and subspecialists) in long-term survivorship care with coordinated timing of care and transfer of care as appropriate
  - ◇ Promotion of adherence to healthy behavior recommendations ([HL-1](#))
  - ◇ Periodic assessment of ongoing needs and identification of appropriate resources

# Long-term survivors



- Periodic assessment (at least annually)
- Shared coordination with PCP

Survivorship Concerns	Survivorship Care Survey
Cardiac Health	1. Do you have shortness of breath or chest pain after physical activities (eg, climbing stairs) or exercise? Yes/No 2. Do you have shortness of breath when lying flat, wake up at night needing to get air, or have persistent leg swelling? Yes/No
Anxiety, Depression, Trauma, and Distress	3. In the past two weeks, have you been bothered more than half the days by little interest or pleasure in doing things? Yes/No 4. In the past two weeks, have you been bothered more than half the days by feeling down, depressed, or hopeless? Yes/No 5. Has stress, worry, anger, fear of recurrence, or distress about effects of cancer treatment interfered with your life? Yes/No
Cognitive Function	6. Do you have difficulties with multitasking or paying attention? Yes/No 7. Do you have difficulties with remembering things? Yes/No 8. Does your thinking seem slow? Yes/No
Fatigue	9. Do you feel persistent fatigue despite a good night's sleep? Yes/No 10. Does fatigue interfere with your usual activities? Yes/No 11. How would you rate your fatigue on a scale of 0 (none) to 10 (extreme) over the past week? 0–10
Lymphedema	12. Since your cancer treatment, have you had any swelling, fatigue, heaviness, or fullness on the same side as your treatment that has not gone away? Yes/No
Pain	13. Have you had any pain in the past week? Yes/No 14. How would you rate your pain on a scale of 0 (none) to 10 (extreme) over the past week? 0–10
Hormone-Related Symptoms	15. Have you been bothered by hot flashes/night sweats? Yes/No 16. Have you been bothered by other hormone-related symptoms (ex, vaginal dryness, erectile dysfunction, urinary incontinence)? Yes/No
Sexual Health	17. Do you have any concerns regarding your sexual function, sexual activity, sexual relationships, or sex life? Yes/No 18. Are these concerns causing you distress? Yes/No
Fertility	19. Do you have concerns about fertility or family planning? Yes/No
Sleep Disorder	20. Are you having problems falling asleep, staying asleep, or waking up too early? Yes/No 21. Are you experiencing excessive sleepiness (ie, sleepiness or falling asleep in inappropriate situations or sleeping more during a 24-hour period than in the past)? Yes/No 22. Have you been told that you snore frequently or that you stop breathing during sleep? Yes/No
Healthy Lifestyle	23. Do you engage in regular physical activity or exercise, such as brisk walking, jogging, weight/resistance training, bicycling, swimming, etc.? Yes/No ► 23a. If you answered "Yes," how often? 24. Excluding white potatoes, do you eat at least 2½ cups of fruits and/or vegetables each day? Yes/No 25. Do you have concerns about your weight? Yes/No 26. Do you take vitamins or other supplements? Yes/No
Immunizations and Infections	27. Have you received your flu vaccine this flu season? Yes/No 28. Are you up to date on your vaccines? Yes/No/Don't know
Employment/ Return to Work	29. Do you have concerns about how cancer and/or cancer therapy has affected your ability to work? Yes/No

# Long-term survivors

- Very limited literature to address the concerns of lung cancer survivors.
- **Long term toxicities:** Potential impact of treatments on patient's health:
  - current comorbidities
  - risk of new long-term complications
  - Long-term toxicities of immunotherapy are unknown.
- **QoL evaluation** → sedentary lifestyle and decreased physical activity is associated with decreased QoL, as well as decreased symptom control.
- **Return to their careers** (younger, higher household income, lower fatigue score, a stable relationship and vocational training).
  - lung cancer survivors → high risk of unemployment.
- **Smoking cessation** → improve outcome, lower incidence of second primary tumour

## NCCN Guidelines Version 3.2023 Non-Small Cell Lung Cancer

### CANCER SURVIVORSHIP CARE

#### NSCLC Long-Term Follow-up Care

- Cancer Surveillance (See [NSCL-16](#))
  - Immunizations
    - ▶ Annual influenza vaccination
    - ▶ Herpes zoster vaccine
    - ▶ Pneumococcal vaccination with revaccination as appropriate
    - ▶ COVID vaccination as per the guidance of the CDC
    - ▶ Hepatitis vaccination
  - [See NCCN Guidelines for Survivorship](#)
- #### Counseling Regarding Health Promotion and Wellness<sup>1</sup>
- Maintain a healthy weight
  - Adopt a physically active lifestyle (regular physical activity: 30 minutes of moderate-intensity physical activity on most days of the week)
  - Consume a healthy diet with emphasis on plant sources
  - Limit consumption of alcohol if one consumes alcoholic beverages

#### Additional Health Monitoring

- Routine blood pressure, cholesterol, and glucose monitoring
- Bone health: Bone density testing as appropriate
- Dental health: Routine dental examinations
- Routine sun protection

#### Resources

- National Cancer Institute Facing Forward: Life After Cancer Treatment  
<https://www.cancer.gov/publications/patient-education/facing-forward>

#### Cancer Screening Recommendations<sup>2,3</sup>

These recommendations are for average-risk individuals and high-risk patients should be individualized.

- Colorectal Cancer:  
[See NCCN Guidelines for Colorectal Cancer Screening](#)
- Prostate Cancer:  
[See NCCN Guidelines for Prostate Cancer Early Detection](#)
- Breast Cancer:  
[See NCCN Guidelines for Breast Cancer Screening and Diagnosis](#)

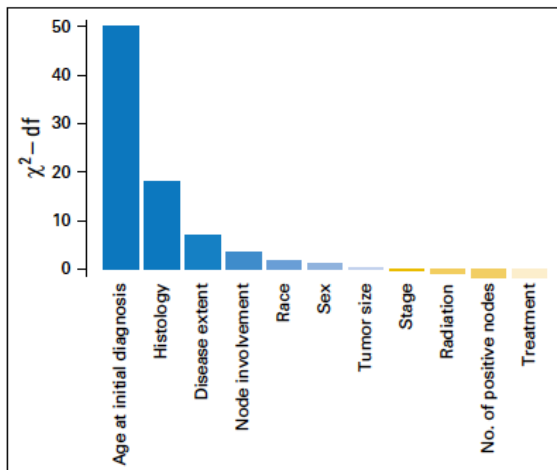


# Second primary tumors

# Second primary lung cancer (SPLC)

- Survivors of LC high risk of SPLC: x4-6 initial primary LC
- No consensus screening guidelines for survivors of LC who are at a high risk of SPLC
- SEER (1988-2003): 20,032 IPLC → 10-year risk of SPLC among survivors was 8.36%

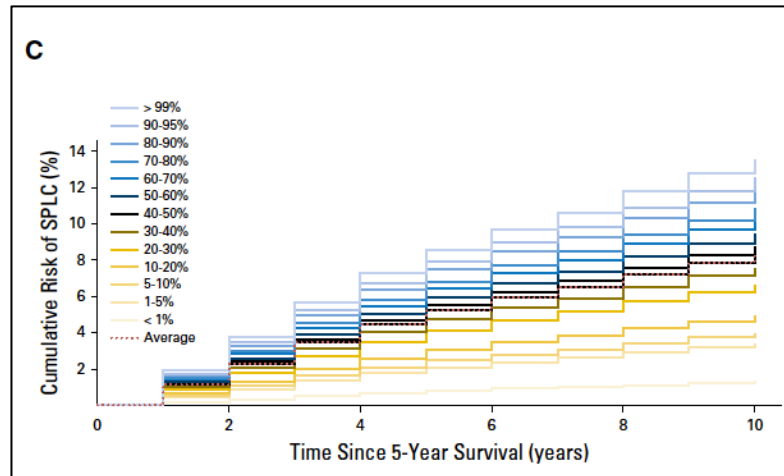
## Risk Stratification for Second Primary Lung Cancer



**Table 2.** Factors Associated With Second Primary Lung Cancer (SPLC) Risk Among Survivors of Lung Cancer Included in the Final Prediction Model for SPLC Risk

Factor	HR <sub>s</sub>	95% CI	P
<b>Histology of IPLC</b>			
AD (reference)	1.00		
SQ	1.06	0.91 to 1.24	.4600
LC	1.15	0.90 to 1.48	.2600
SC	1.22	0.96 to 1.56	.1100
Other*	0.79	0.67 to 0.93	< .001
<b>Age at diagnosis of IPLC, years</b>			
70-75 (reference)	1.00		
0-44	0.54	0.36 to 0.83	< .001
45-49	1.04	0.76 to 1.42	.8000
50-54	1.00	0.77 to 1.30	1.0000
55-59	1.25	1.00 to 1.56	.0520
60-64	1.45	1.19 to 1.76	< .001
65-69	1.24	1.02 to 1.51	< .001
70-74	0.59	0.43 to 0.81	< .001
75-79	0.44	0.26 to 0.76	< .001
≥ 85	0.15	0.02 to 1.06	.0570
<b>Extent of IPLC†</b>			
Localized (reference)	1.00		
Regional	0.85	0.74 to 0.98	< .001
Distant	0.54	0.36 to 0.82	< .001

## PREDICTING MODEL SPLC



lung, extra-lung, synchronous, metachronic

# Second primary lung cancer (SPLC)

**Mujer 54a**  
**2010 CPNM LA**

**QT-RT NA → CIR**  
**yRP**

**2018 ADK pulm IVa**

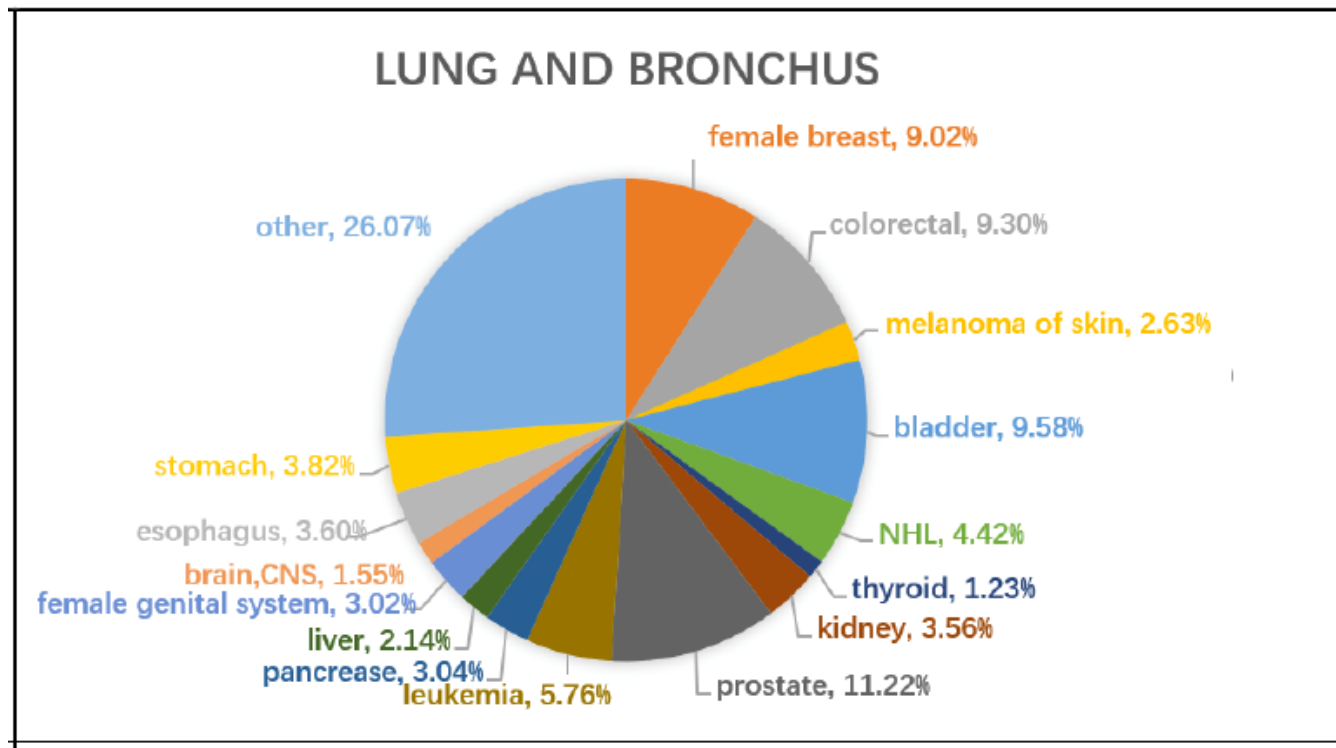
**IO → RC**

**2023**

**Progresión ganglionar supra/infra**  
**diafragmática**

**Biopsia: SCLC**

# Other second primary cancer



# Second primary cancer

**Mujer 55a**  
**2018 CPNM EGFR +**  
**Osimertinib → RC**

**2021**  
**CDI mama D**  
**CIR + RT + HT**



# To wrap up

- **Follow-up imaging**
  - Early: every 6m x2y, then annually (low dose CT)
  - LA: every 3m x1st y, every 6m x2nd y, then annually
  - Advanced:
    - Close follow-up (every 6-12 weeks)
    - After completion IO: every 3-4 months
    - Brain MRI: uncertain for patients with driver mutations
- **Biomarkers for surveillance:** ctDNA, MDR, to predict progression, to Identify resistance mutations .



# To wrap up

- **Long-term survivors**
  - Long-term toxicities, uncertain with IO
  - QoL
  - Smoking cessation
  - Health promotion
  - Immunization
  - Screening for second primary tumors



# Muchas gracias por vuestra atención!