

ONCOLOGY KNOWLEDGE HUB · TEACHING SLIDES

Lung Cancer

A mini review for clinicians

For postgraduate residents, medical students and practising clinicians

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Learning objectives

- Recognise how lung cancer presents, and the traps that delay diagnosis in India
- Separate tuberculosis from cancer and manage incidental nodules
- Plan one biopsy that diagnoses, stages and allows biomarker testing
- Choose surgery, SBRT or chemoradiation by stage and fitness
- Match systemic therapy to drivers and PD-L1 (no doses)
- Manage small cell lung cancer as an emergency; plan survivorship

Roadmap

- 1 Burden and biology
- 2 Presentation and the TB trap
- 3 Screening and nodules
- 4 Diagnosis and staging
- 5 Biomarkers
- 6 Surgery and radiotherapy
- 7 Systemic therapy
- 8 Algorithms
- 9 Small cell lung cancer
- 10 Survivorship, evidence and cases

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Burden and biology

Lung cancer in India

- About 80,000 new cases and nearly as many deaths a year (GLOBOCAN 2022)
- About three in four patients are diagnosed at stage III–IV
- Patients are often a decade younger than in Western series
- A substantial share never smoked, especially women
- Adenocarcinoma has overtaken squamous carcinoma

Causes and risk factors

Risk factors

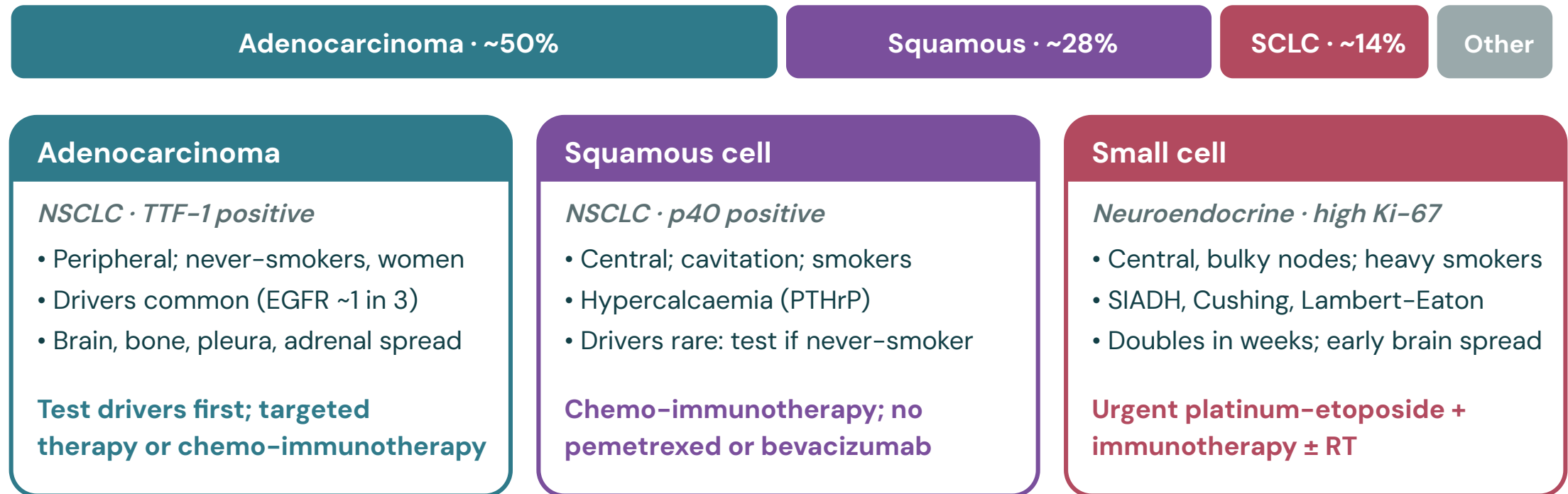
- Tobacco: cigarettes, bidis, hookah; second-hand smoke
- Biomass smoke: wood, dung, crop residue
- Outdoor air pollution (PM2.5)
- Occupation: asbestos, silica, diesel, arsenic, chromium, radon
- COPD, lung fibrosis, old TB scars
- Family history (modest), prior chest radiotherapy, HIV

Not causes

- Inherited tumour drivers: EGFR and ALK are somatic
- Lung biopsy (it does not spread cancer)
- Having had a normal chest X-ray
- Stopping smoking (risk falls steadily after quitting)

Three working types

Approximate share in Indian hospital series; adenocarcinoma has overtaken squamous, and "other" includes large-cell and NSCLC-NO:



Histology and drivers, not just stage, decide treatment

Types at a glance

Type	Typical patient	Backbone
Adenocarcinoma	Peripheral; never-smokers, women	Driver-matched drug or chemo-IO
Squamous	Central; smokers	Chemo-IO; no pemetrexed
Small cell	Central, bulky; heavy smokers	Platinum-etoposide + IO ± RT
Large cell / NOS	Mixed	Avoid NOS: use IHC sparingly

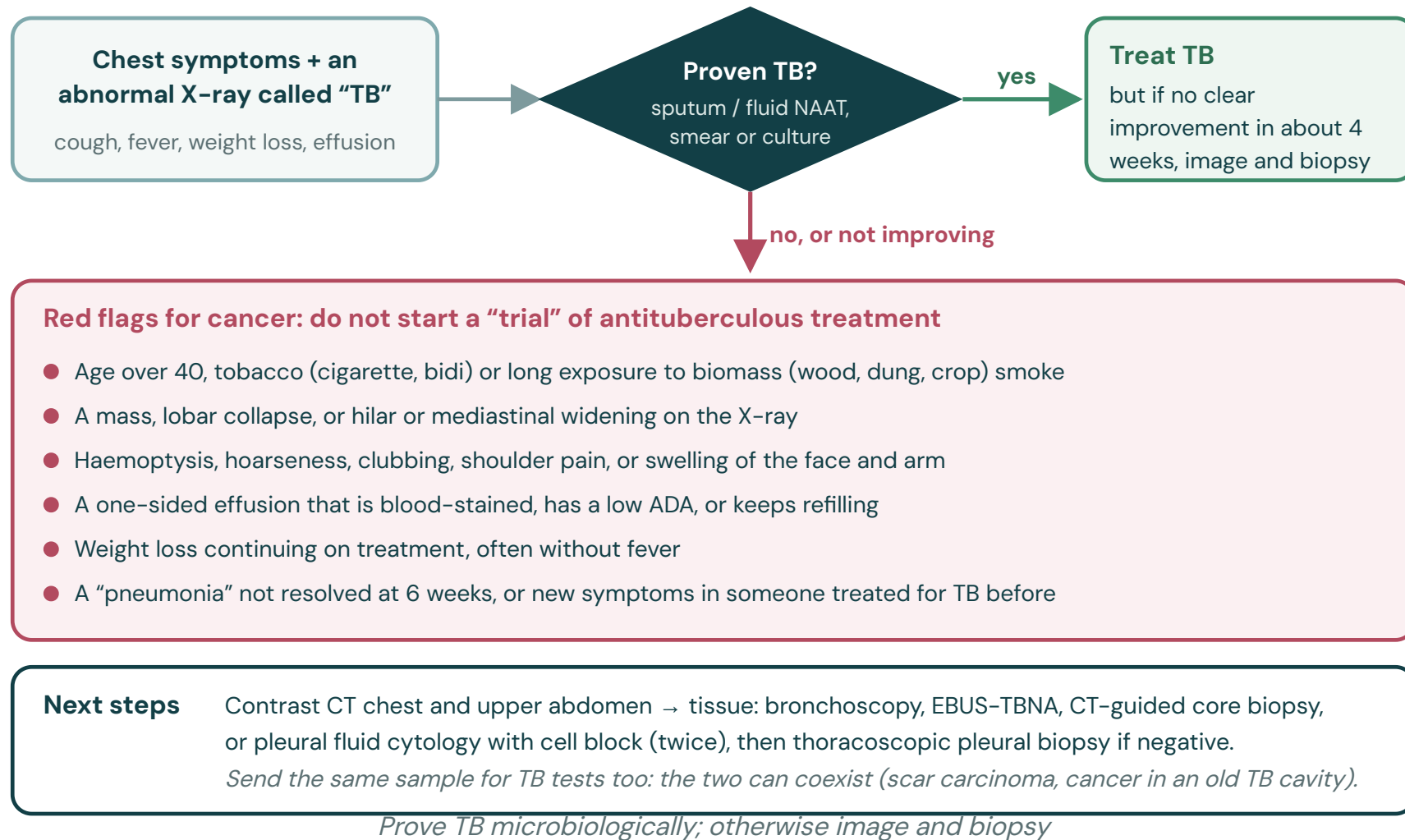
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Presentation and the TB trap

How lung cancer presents

- Cough over 3 weeks, haemoptysis, breathlessness, weight loss
- Hoarseness, stridor, dysphagia, SVC obstruction, effusion
- Pancoast: shoulder pain, C8–T1 weakness, Horner syndrome
- Paraneoplastic: hypercalcaemia, SIADH, Cushing, Lambert–Eaton, clubbing
- First presentation with brain, bone, liver or adrenal metastases
- Incidental nodule on CT

Tuberculosis or cancer?



Common traps

- ATT on an X-ray alone, without NAAT, smear or culture
- A lymphocytic effusion with low ADA called tubercular
- Non-resolving pneumonia in a smoker
- Reassurance from a normal chest X-ray
- “Young, female, never smoked” used to exclude cancer
- Shoulder pain treated as frozen shoulder; hoarseness not followed up

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Screening and nodules

Low-dose CT screening

- NLST: 20% fewer lung cancer deaths in heavy smokers
- NELSON: about 24% fewer deaths in men
- Eligible (USPSTF): 50–80 years, ≥ 20 pack-years, quit within 15 years
- Harms: false positives, overdiagnosis, radiation, biopsies
- Combine with smoking cessation and a nodule pathway

Screening in India: be cautious

- No Indian randomised trial; no national programme
- TB and fungal granulomas cause many false positives
- Offer only with shared decision-making and a follow-up pathway
- Never-smokers: not recommended outside research
- Chest X-ray, sputum cytology and tumour markers are not screening

The incidental nodule

Incidental nodule on CT in an adult aged 35 or over (not screening, no known cancer, not immunocompromised)

Solid nodule	Ground-glass (pure)	Part-solid
< 6 mm No routine follow-up (high risk: optional CT at 12 months)	< 6 mm No routine follow-up	< 6 mm No routine follow-up
6–8 mm CT at 6–12 months, then 18–24 months	≥ 6 mm CT at 6–12 months to confirm it persists, then every 2 years to 5 years	≥ 6 mm CT at 3–6 months; if persistent with a solid part ≥ 6 mm, treat as suspicious
> 8 mm CT at 3 months, PET-CT, or biopsy		

Benign signs: central, diffuse, laminated or popcorn calcification; fat within (hamartoma); stable solid size for 2 years.

In India, healed TB and fungal granulomas are common and PET-avid: a PET-positive nodule still needs tissue before surgery or SBRT.

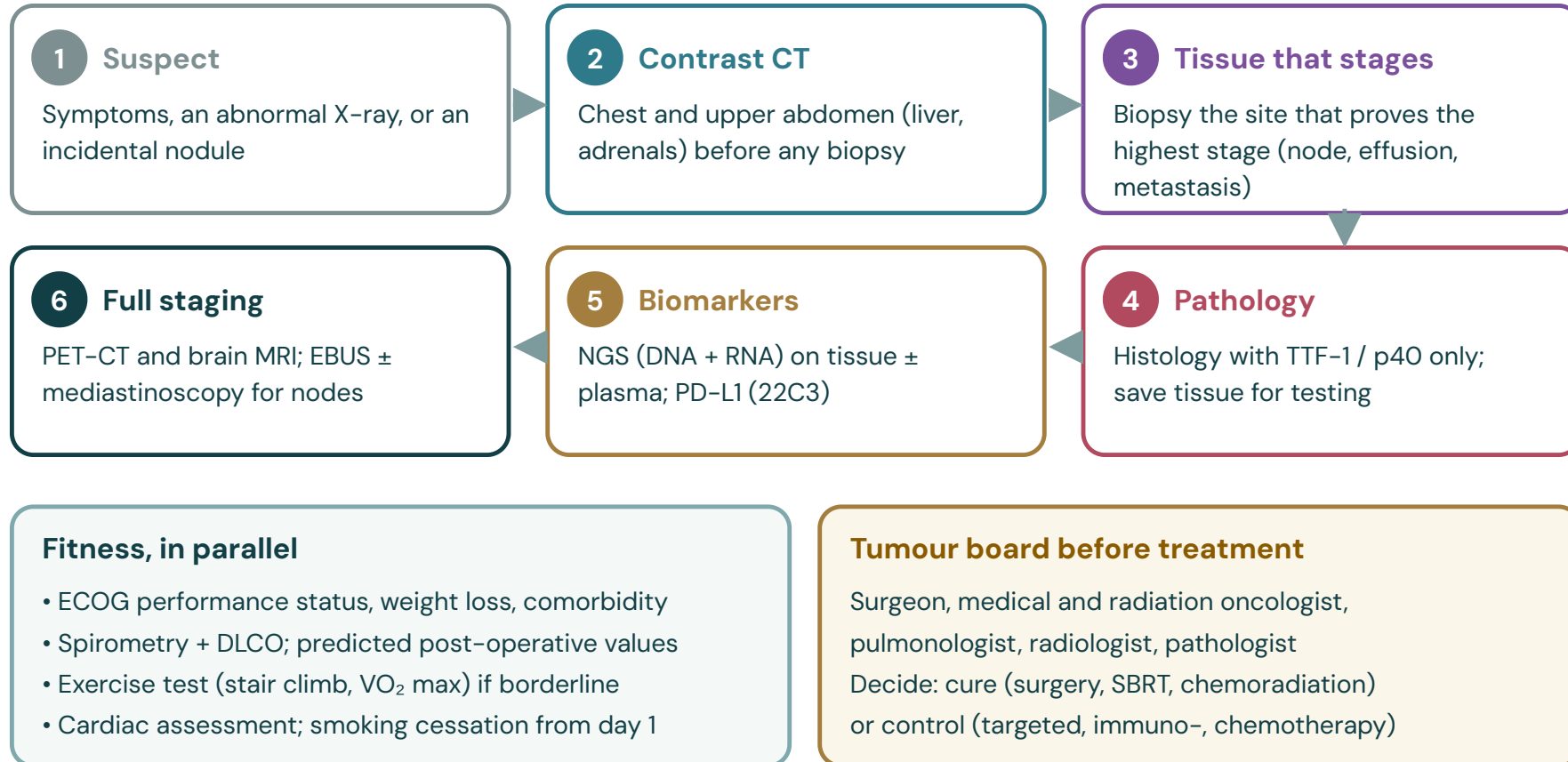
Screening (low-dose CT) uses Lung-RADS categories instead; nodules in known cancer are managed by the oncology team.

Fleischner Society 2017, simplified

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Diagnosis and staging

From suspicion to treatment plan



Do not start chemotherapy or immunotherapy in non-squamous NSCLC before the EGFR and ALK results, unless the patient is critically ill: the answer usually takes 1–2 weeks and changes the first treatment.
One biopsy for diagnosis, stage and biomarkers

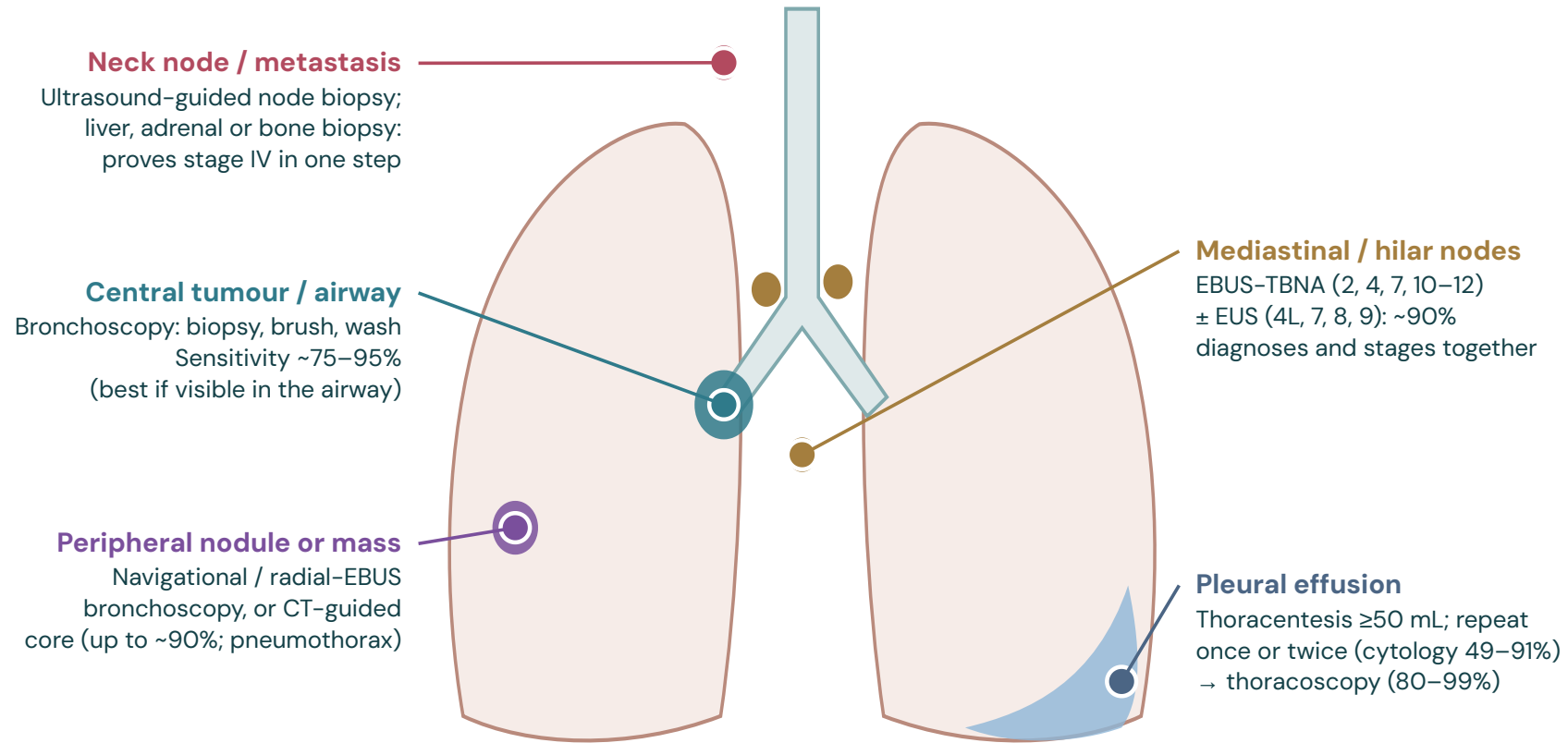
Tissue is precious

- CT before biopsy, so the biopsy can prove the highest stage
- EBUS-TBNA of a node gives diagnosis and N stage together
- Core biopsies and cell blocks work for NGS; smears often do not
- Minimal IHC: TTF-1, p40; avoid “NSCLC-NOS”
- Ask the pathologist to protect tissue for molecular tests

Staging tests

- PET-CT for anyone being considered for cure
- Confirm PET-positive nodes with EBUS: granulomas are PET-avid
- Brain MRI: stage III–IV (NCCN: from stage II), all small cell, any symptom
- Mediastinoscopy if EBUS is negative but suspicion remains
- Pleural effusion: cytology twice, then thoracoscopy

Which biopsy, for which lesion

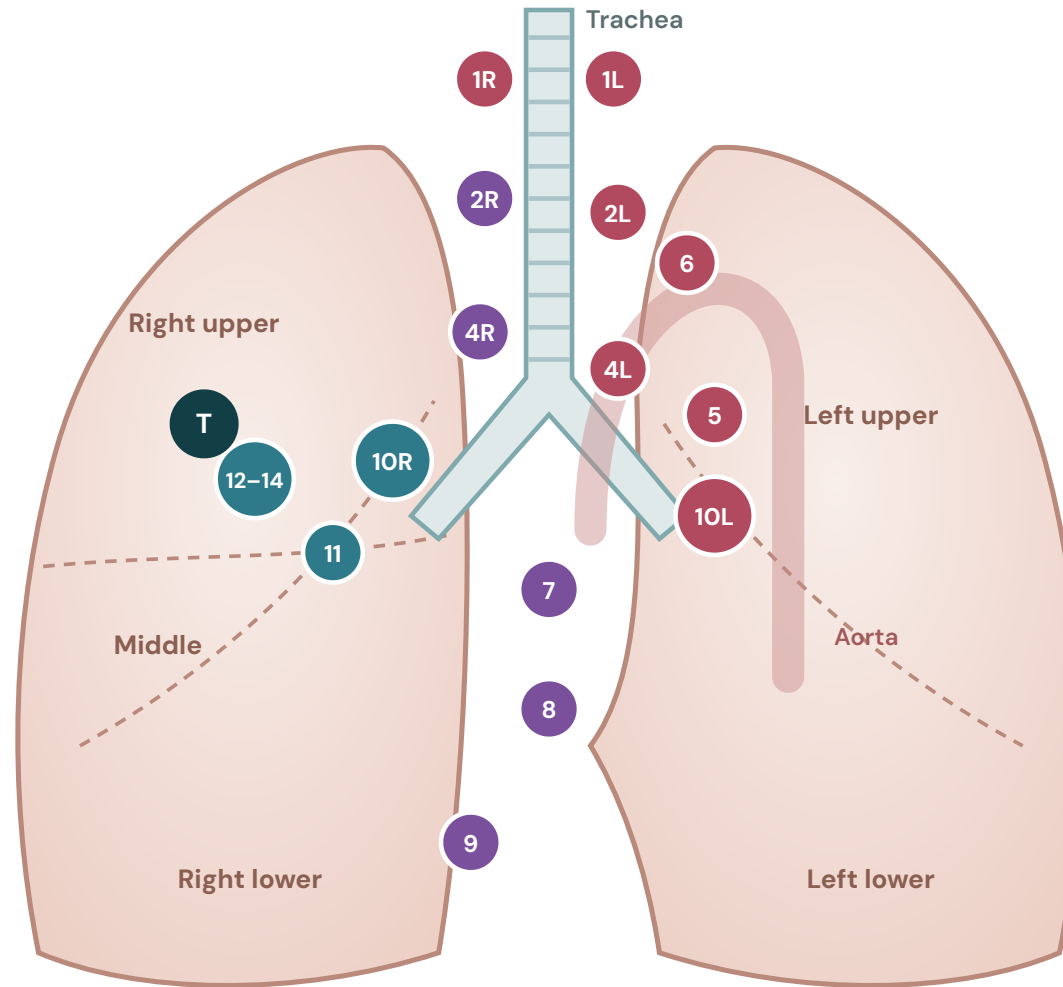


Rule: biopsy the site that proves the HIGHEST stage, with the least risk, and get enough tissue (core or cell block) for NGS and PD-L1.

Sputum cytology only for central tumours when nothing else is possible; it never stages.

One procedure: diagnosis, stage and enough tissue

Lobes and node stations



The N category depends on the side of the tumour

For a RIGHT-sided tumour

- N1** Hilar, interlobar, lobar (10–14), same side
- N2** Same-side mediastinal or subcarinal (2R, 4R, 7–9)
- N3** Opposite-side nodes, or any scalene or supraclavicular node (1)

**9th edition: N2a = one N2 station;
N2b = more than one N2 station.**

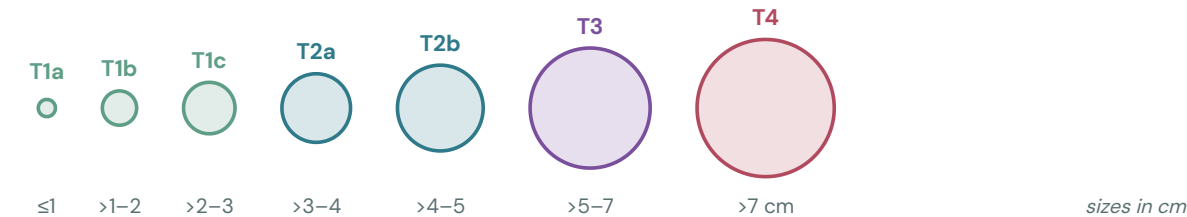
Reach of each test

- EBUS-TBNA: 2, 3p, 4, 7, 10–12
- EUS (oesophageal): 4L, 7, 8, 9 + adrenal
- Mediastinoscopy: 2, 4, 7
- VATS or anterior approach: 5, 6

*Left-sided tumour: 2L, 4L, 5, 6 become N2
right-sided stations become N3.*

TNM 9th edition at a glance

T: primary tumour (circles to scale)



Invasion upgrades T regardless of size

- T2** Main bronchus (not carina), visceral pleura, atelectasis to the hilum
- T3** Chest wall, parietal pleura or pericardium, phrenic nerve; separate nodule in the same lobe
- T4** Mediastinum, heart, great vessels, trachea, carina, oesophagus, vertebra, diaphragm, recurrent laryngeal nerve; separate nodule in a different lobe on the same side

N and M (9th edition changes in bold)

- N1** Ipsilateral hilar / intrapulmonary nodes
- N2a** **One ipsilateral mediastinal or subcarinal station**
- N2b** **Two or more N2 stations**
- N3** Contralateral mediastinal/hilar, or scalene/supraclavicular
- M1a** Other-lung nodule; pleural/pericardial spread or effusion
- M1b** Single extrathoracic metastasis
- M1c1** **Multiple metastases in one organ system**
- M1c2** **Metastases in several organ systems**

Stage groups (simplified)



IASLC/UICC 9th edition (from 2025). T categories are unchanged from the 8th; N2 and M1c are now subdivided. Check the full table before a final st

N2 split into N2a/N2b; M1c into M1c1/M1c2

Fitness for surgery

- FEV₁ and DLCO in everyone → predicted post-operative (ppo) values
- Both ppo ≥60%: low risk; 30–60%: stair climb ≥22 m / shuttle ≥400 m; <30%: CPET
- VO₂ max >20 low risk; 10–20 individualise; <10 → sublobar or SBRT
- Repeat after induction therapy
- ECOG, weight loss, cardiac assessment
- Smoking cessation and rehabilitation improve fitness

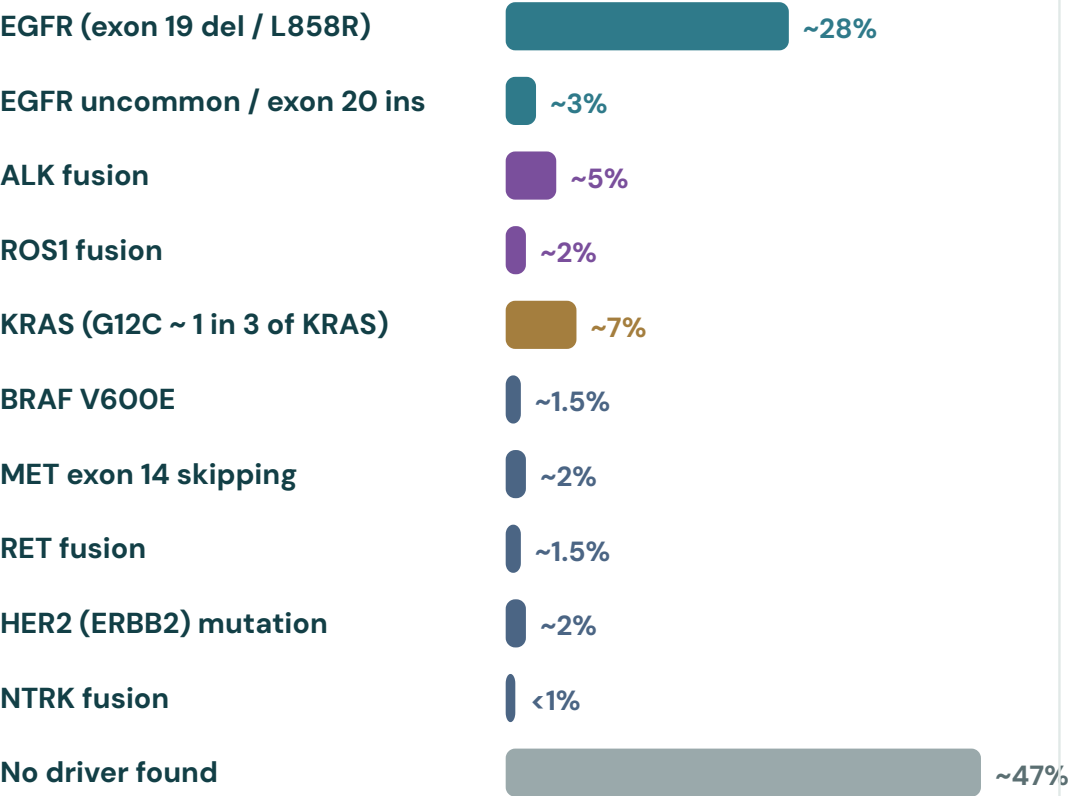
5 Biomarkers

Who and how to test

- All advanced non-squamous NSCLC
- Squamous in never- or light smokers, or the young
- EGFR and ALK (and PD-L1) in resected or resectable stage IB–III
- NGS with DNA and RNA preferred; plasma ctDNA if tissue is scant
- A negative plasma test does not exclude a driver

The driver map

Approximate frequency in Indian lung adenocarcinoma (varies by series, smoking and test)



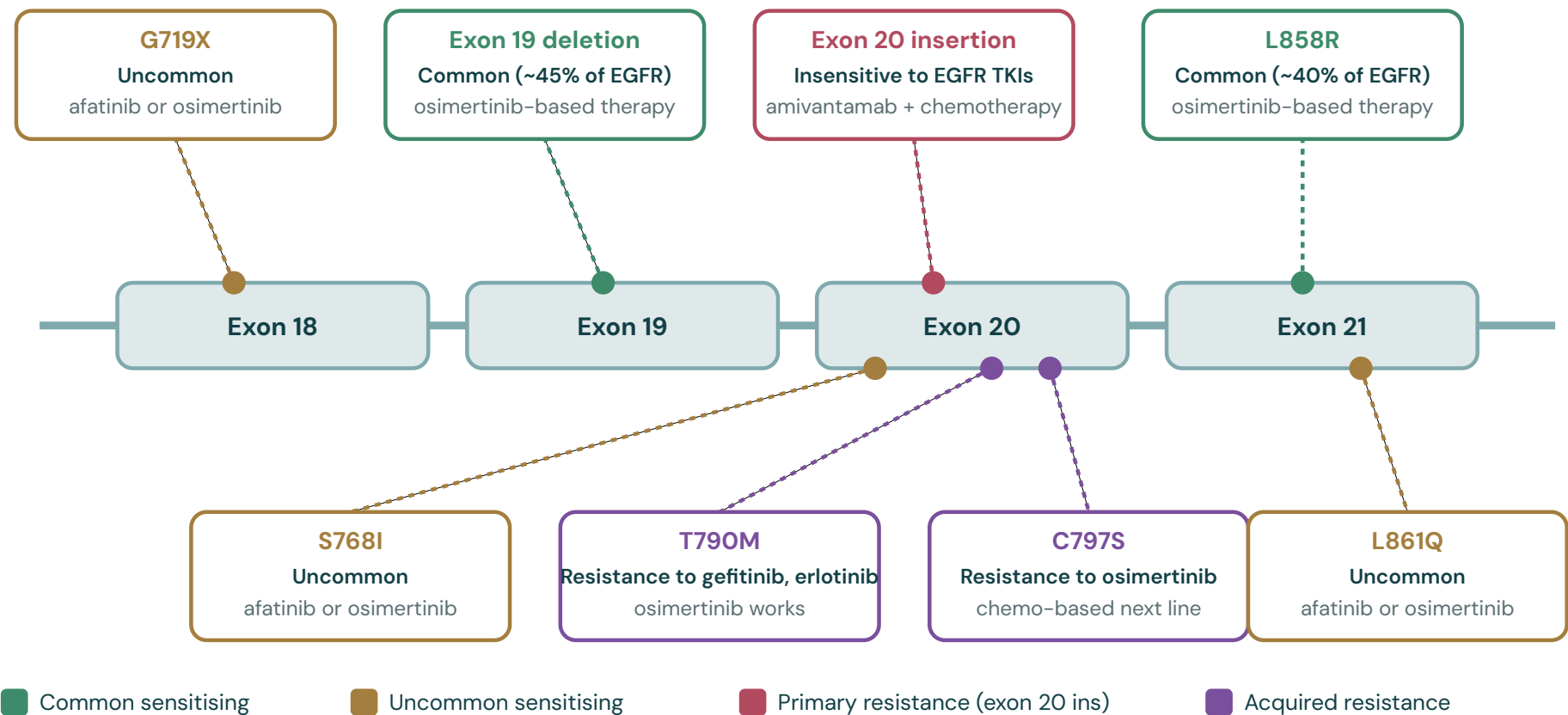
First-line matched option (no doses)

- osimertinib ± chemo · amivantamab-lazertinib
- afatinib or osimertinib · amivantamab + chemo (ex20)
- alectinib · lorlatinib · brigatinib
- taletrectinib · repotrectinib · entrectinib
- chemo-immunotherapy first; sotorasib / adagrasib later
- dabrafenib + trametinib · encorafenib + binimetinib
- capmatinib · tepotinib
- selpercatinib · pralsetinib
- zongertinib or trastuzumab deruxtecan (usually after chemo-I)
- larotrectinib · entrectinib, or chemo-IO
- PD-L1-guided immunotherapy ± chemotherapy

Test every non-squamous NSCLC, and squamous NSCLC in never- or light smokers. Gefitinib + chemotherapy is a proven, cheaper EGFR option.
EGFR PCR alone misses fusions, exon 20 insertions and other targets; use NGS with RNA where possible.
About half of Indian adenocarcinomas have an actionable driver

The EGFR mutation map

EGFR kinase domain: where the mutations sit and what they mean



Also at osimertinib progression: MET or HER2 amplification and small-cell transformation (re-biopsy). Plasma ctDNA can find many of these.
The exon predicts the drug

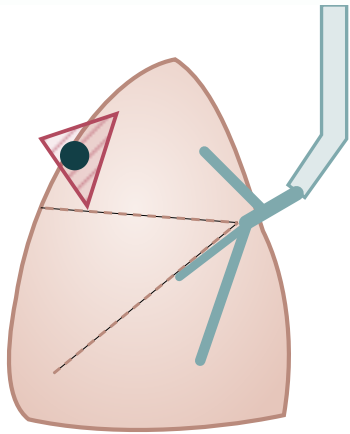
Test → consequence

Biomarker	What it changes
EGFR ex19del / L858R	Osimertinib-based therapy at every stage
ALK, ROS1, RET, MET ex14, BRAF, NTRK	Matched first-line TKI
KRAS G12C, HER2 mutation	Targeted drug after chemo-IO
PD-L1 TPS	IO alone (≥50%) vs chemo-IO
At TKI progression	MET, resistance mutations, SCLC transformation

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Surgery and radiotherapy

Types of lung resection



Wedge resection

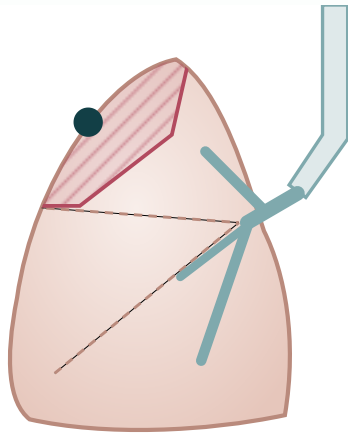
REMOVES

A small non-anatomical wedge with the nodule

KEEPS

The lobe and its airway

Peripheral ground-glass or small nodules; frail or elderly; diagnosis



Segmentectomy

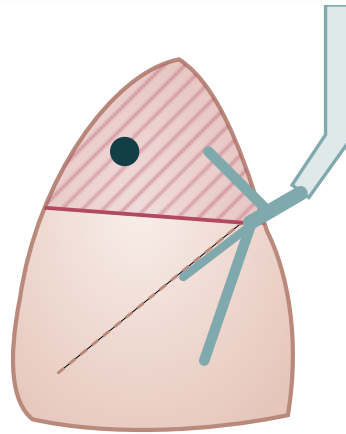
REMOVES

One or more anatomical segments with their bronchus and vessels

KEEPS

Rest of the lobe

Peripheral tumours ≤ 2 cm, node-negative (JCOG0802)



Lobectomy

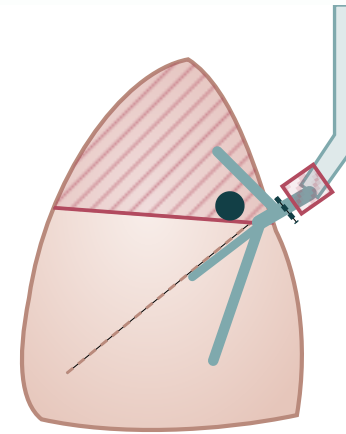
REMOVES

The whole lobe + hilar and mediastinal node dissection

KEEPS

Other lobes

Standard operation for fit patients with stage I–III



Sleeve lobectomy

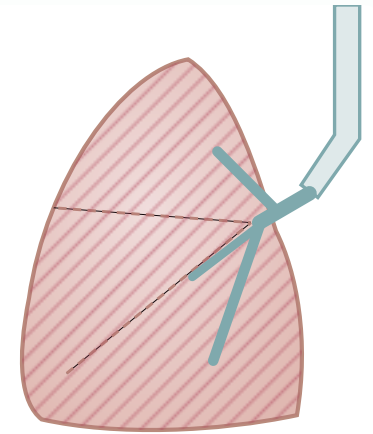
REMOVES

The lobe plus a cuff of main bronchus; airway rejoined

KEEPS

Lung below the cuff (avoids pneumonectomy)

Central tumours at the lobar origin



Pneumonectomy

REMOVES

The whole lung

KEEPS

Nothing on that side

Last resort for central tumours; highest risk (especially right side)

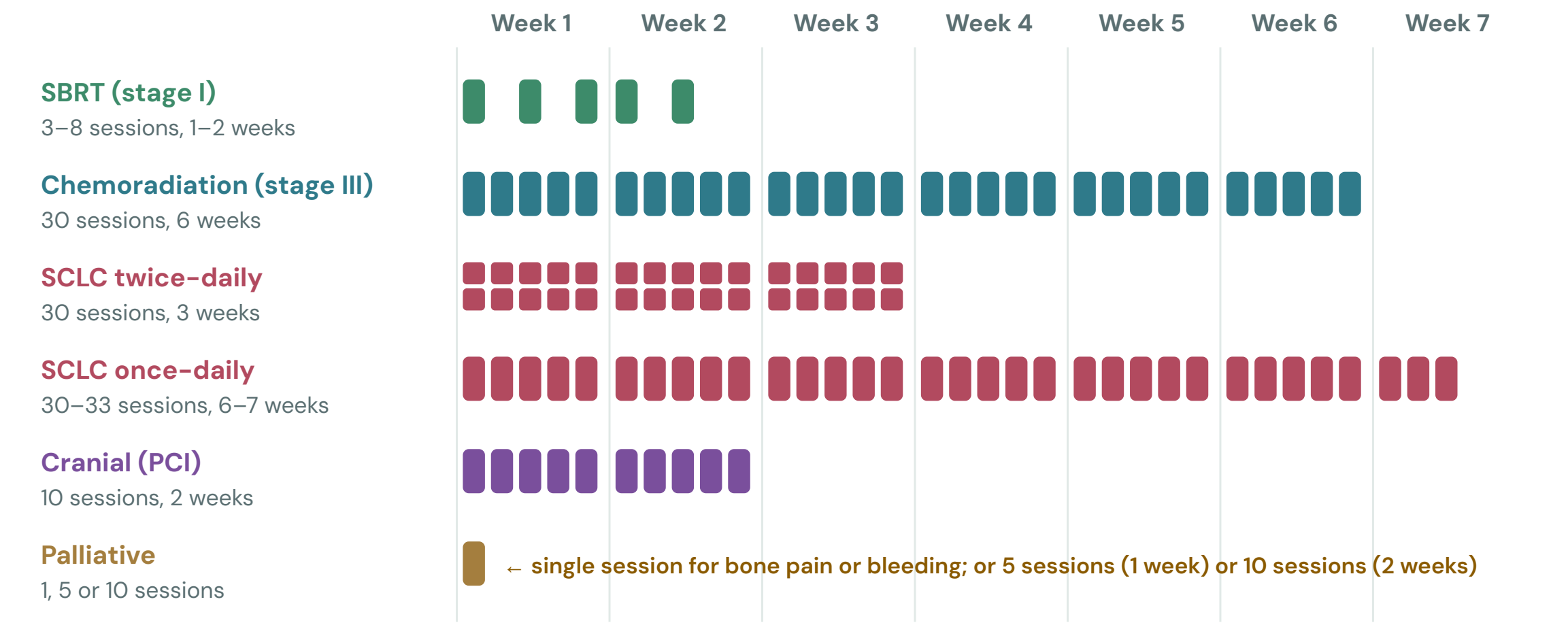
 Lung removed  Lung kept  Airway  Tumour  Bronchial join (sleeve)

Lung-sparing when oncologically adequate

Surgery: key evidence

- Lobectomy + nodal dissection is standard for fit patients
- JCOG0802: segmentectomy for ≤ 2 cm peripheral N0 (better OS, more local recurrence)
- CALGB 140503: sublobar resection non-inferior for ≤ 2 cm N0
- Sleeve lobectomy is preferred to pneumonectomy
- Single-station N2: perioperative therapy + surgery; bulky N2: chemoradiation

Radiotherapy schedules



Each block = one session (Mon–Fri); twice-daily = two sessions at least 6 hours apart. SBRT is usually given on alternate days.
Sessions and weeks by setting

Radiotherapy: indications

- SBRT for inoperable stage I: ~90% local control
- Concurrent chemoradiation for unresectable stage III (dose escalation harmful)
- No routine PORT for pN2 RO (Lung ART)
- Palliative RT: haemoptysis, bone pain, SVCO, cord compression
- Brain: SRS for few metastases; TKI first if EGFR/ALK and asymptomatic

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Systemic therapy

Early and locally advanced NSCLC

Setting	Option (no doses)
Stage II–III resectable, no driver	Perioperative chemo–IO (surgery–first acceptable)
Resected IB–IIIA, no driver	Cisplatin doublet → atezolizumab/pembrolizumab
Resected, EGFR+	Chemo → osimertinib 3 years (ADAURA)
Resected, ALK+	Alectinib 2 years (ALINA)
Resectable II–III, no driver	Perioperative chemo–IO
Unresectable III	CRT → durvalumab; EGFR+: osimertinib

Perioperative immunotherapy

- CheckMate 816, KEYNOTE-671, AEGEAN, CheckMate 77T
- Pathological complete response ~17–25% vs 2–4%
- Event-free survival HR about 0.6
- KEYNOTE-671: overall survival gain
- Test EGFR and ALK before starting

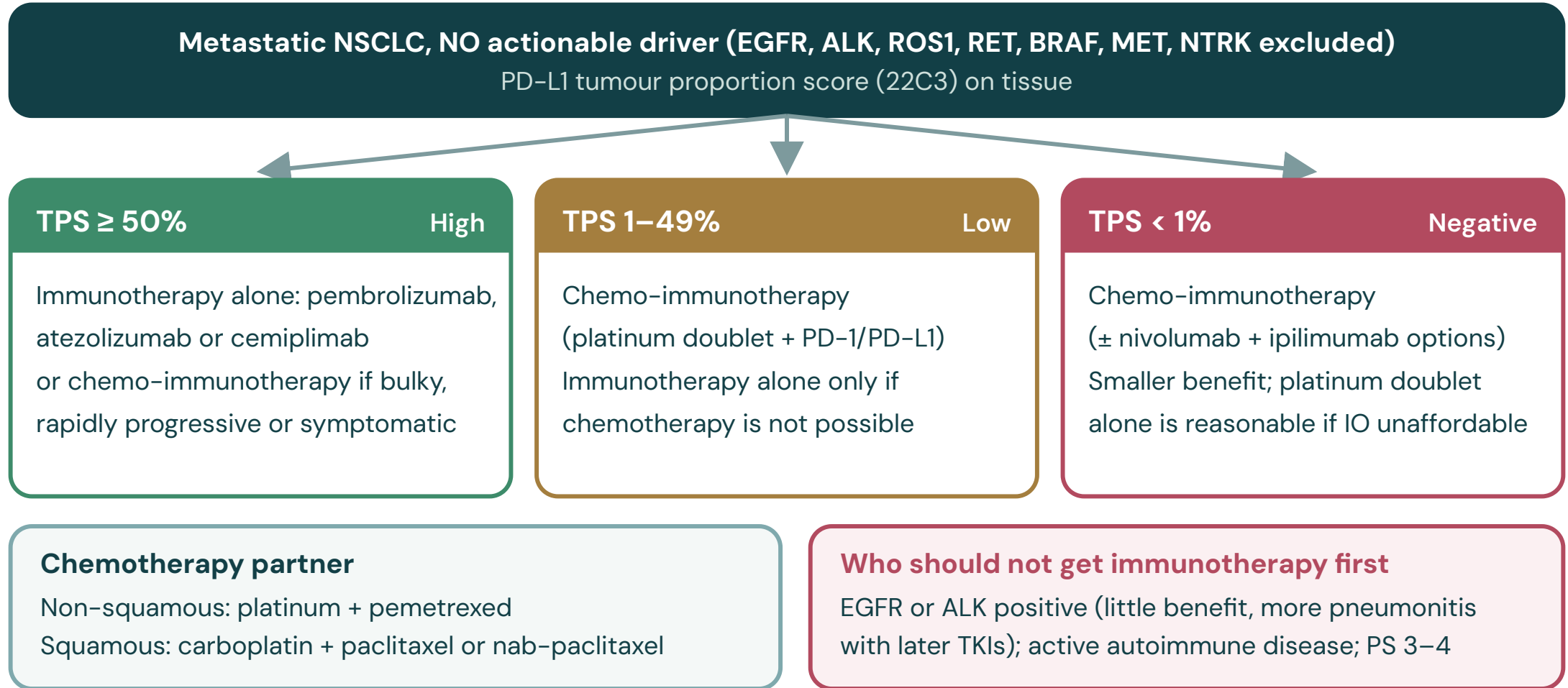
EGFR-mutant metastatic NSCLC

- FLAURA: osimertinib beat older TKIs, including survival
- FLAURA2: + chemotherapy: median OS 47.5 vs 37.6 months
- MARIPOSA: amivantamab + lazertinib beat osimertinib
- Tata Memorial: gefitinib + chemo beats gefitinib (affordable)
- Exon 20 insertions: amivantamab + chemotherapy (PAPILLON)

ALK and other drivers

- ALK: alectinib (ALEX), lorlatinib (CROWN), brigatinib
- Lorlatinib: ~60% progression-free at 5 years; lipids, mood effects
- RET: selpercatinib beat chemo-IO (LIBRETTO-431)
- ROS1: taletrectinib or repotrectinib; KRAS G12C: sotorasib after chemo-IO
- HER2 mutation: zongertinib or trastuzumab deruxtecan; adjuvant selpercatinib for RET

No driver: PD-L1 guides

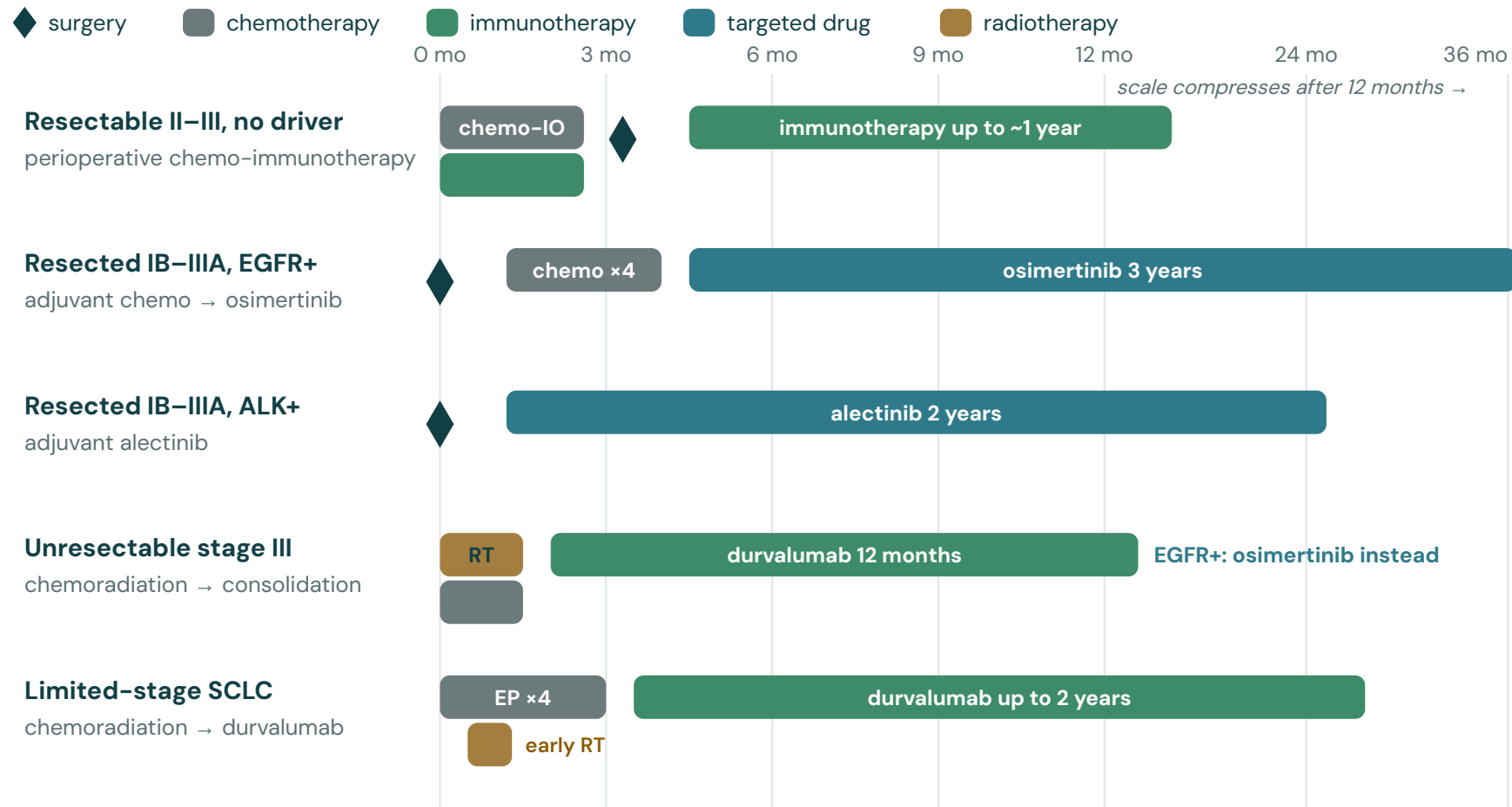


Performance status and tempo matter as much

Immunotherapy evidence

- KEYNOTE-024: pembrolizumab, 5-year survival ~32% vs 16% (PD-L1 $\geq$ 50%)
- KEYNOTE-189 / 407: chemo + pembrolizumab, any PD-L1
- KEYNOTE-042: benefit driven by $\geq$ 50% subgroup
- Avoid IO before osimertinib: pneumonitis risk
- Early palliative care (Temel) improves quality of life

Curative-intent calendars



Durations as in the pivotal trials (CheckMate 77T, KEYNOTE-671, AEGEAN, ADAURA, ALINA, PACIFIC, LAURA, ADRIATIC).

PCI or brain-MRI surveillance follows limited-stage SCLC.

Plan the whole year at the start

After osimertinib progression

- Re-biopsy or ctDNA at progression
- MET amplification, EGFR C797S, HER2 amplification
- Small-cell transformation → platinum–etoposide
- Platinum–pemetrexed ± amivantamab (MARIPOSA-2)
- Immunotherapy alone does not work after EGFR-TKI failure

Brain metastases

- About 1 in 10 advanced NSCLCs at diagnosis
- Severe mass effect: neurosurgery first
- EGFR, ALK, RET, ROS1: brain-penetrant TKI first, MRI at 6–8 weeks
- MET ex14, KRAS G12C, BRAF: radiotherapy, then systemic therapy
- No driver: radiotherapy (SRS or HA-WBRT); systemic first if asymptomatic

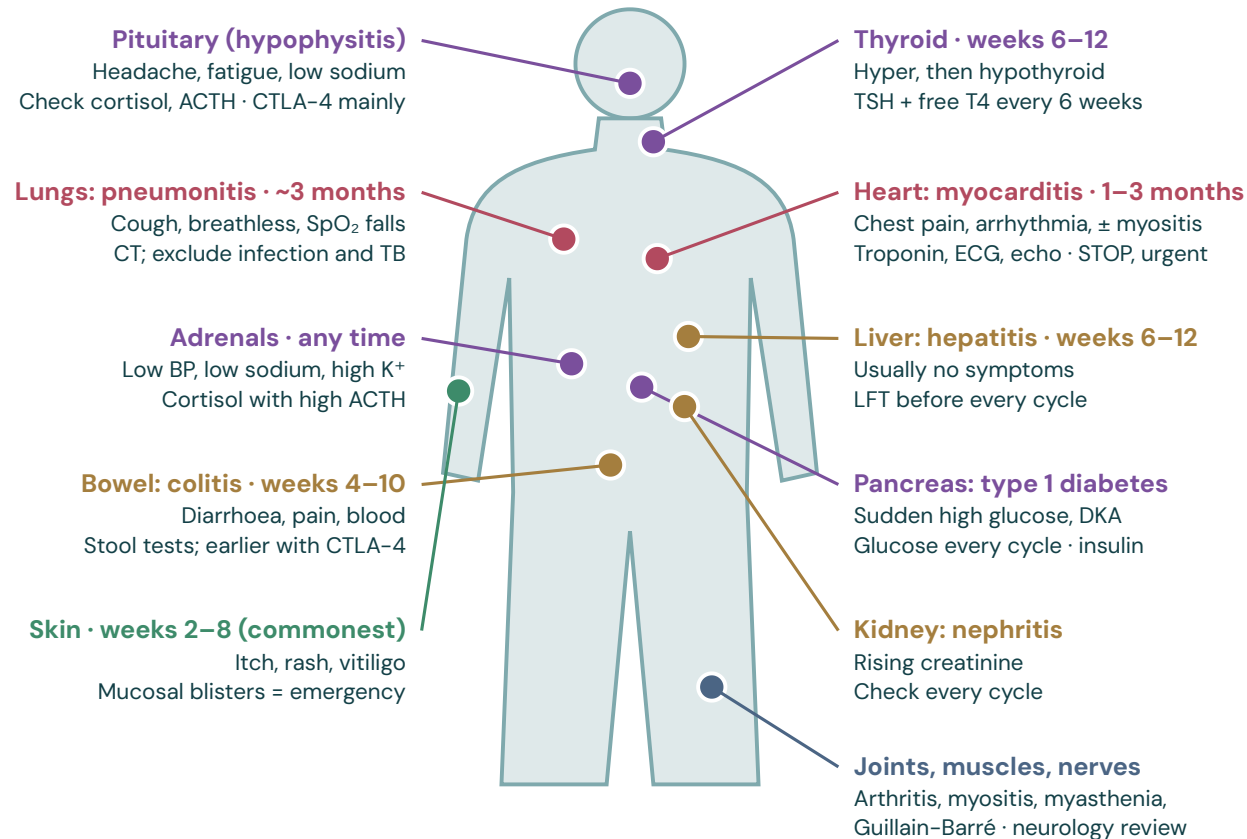
Oligometastatic disease

- Usually 1–3 (at most 5) metastases, good PS
- At least ~3 months of systemic therapy, then treat every site
- Randomised phase 2 evidence: Gomez et al., SABR–COMET
- Decide in a tumour board; brain MRI and PET first
- Oligoprogression on a TKI: treat the site, continue the drug

Later lines (no driver)

- After IO alone: platinum doublet; rechallenge only if ≥ 6 months off IO
- After chemo-IO: pemetrexed if unused, else docetaxel $\pm$ ramucirumab (REVEL)
- HER2 IHC 3+ or c-MET overexpression: targeted ADCs
- Oligoprogression: local therapy, continue current drug
- Treat every 6–12 weeks with imaging; stop for toxicity

Immune side effects at a glance



Rose: can be life-threatening, act today · Gold: common, monitor blood tests · Purple: endocrine, often permanent, replace hormone

Timing is typical, not fixed: side effects can appear months after the last dose. Give every patient an immunotherapy alert card.

Where, when and the first test

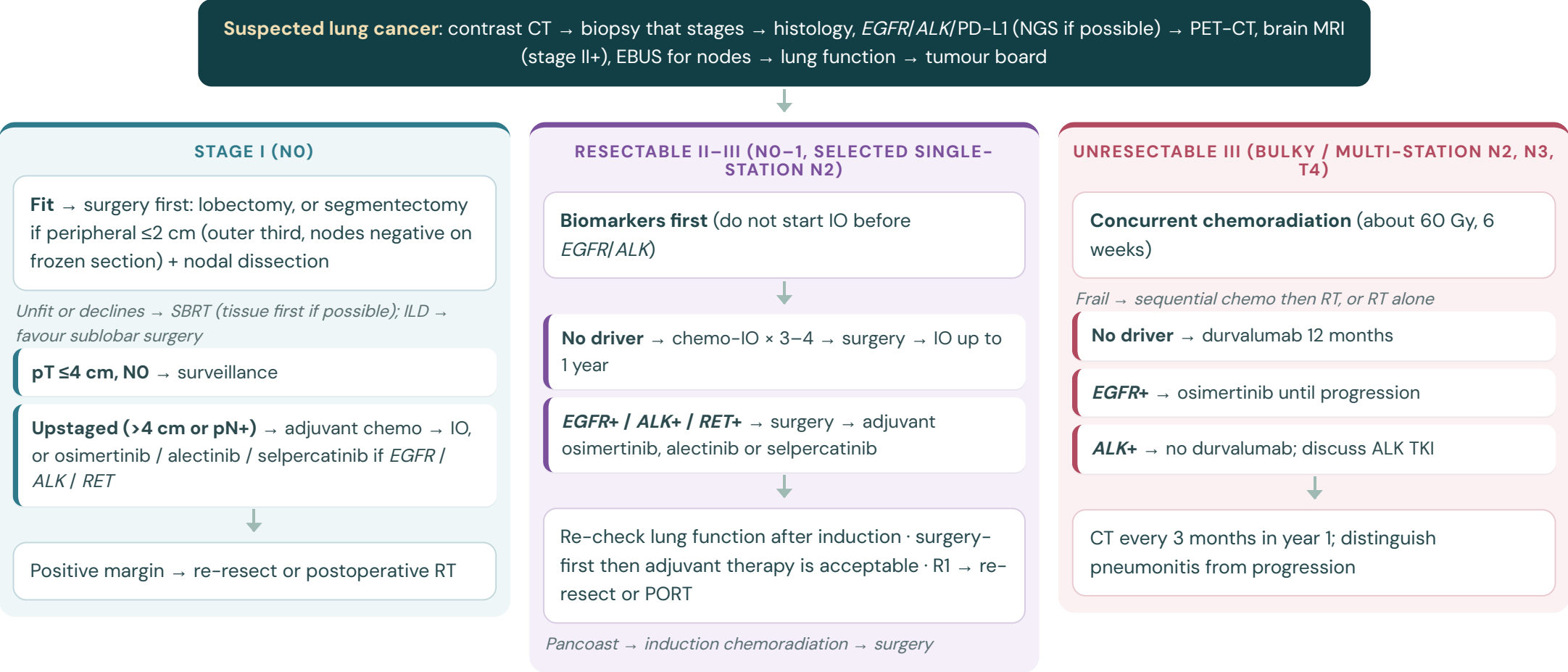
Emergencies in lung cancer

- SVC obstruction: biopsy first; stent for severe symptoms
- Spinal cord compression: steroids, same-day MRI, RT or surgery
- Massive haemoptysis: airway, bronchial artery embolisation
- Hypercalcaemia, SIADH: correct carefully
- Febrile neutropenia, immune pneumonitis: same-day assessment

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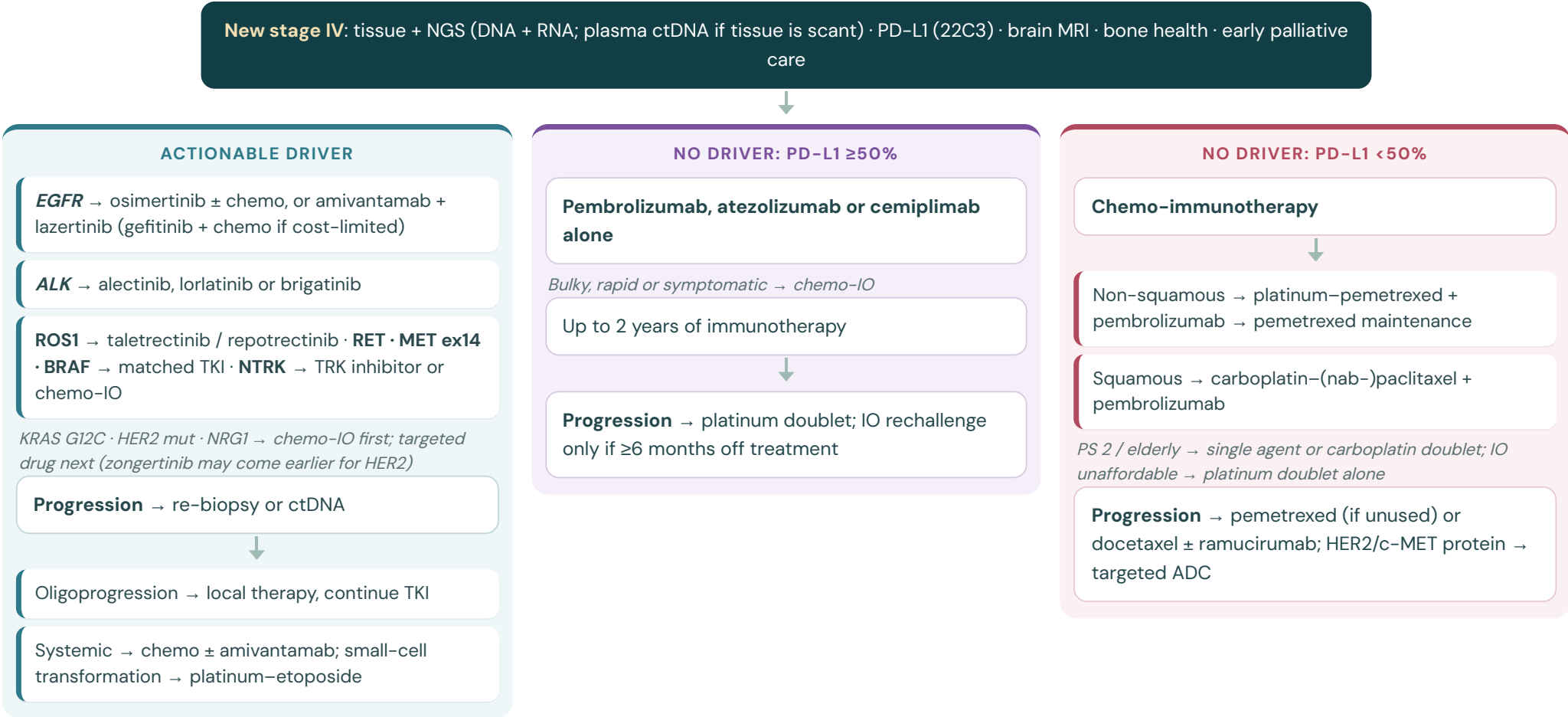
Management algorithms

Algorithm 1: non-metastatic NSCLC



All patients: smoking cessation from the first visit; tumour board before treatment; lung-sparing surgery when oncologically adequate. Confirm PET-positive nodes with EBUS before calling a tumour unresectable.

Algorithm 2: metastatic NSCLC



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Small cell lung cancer

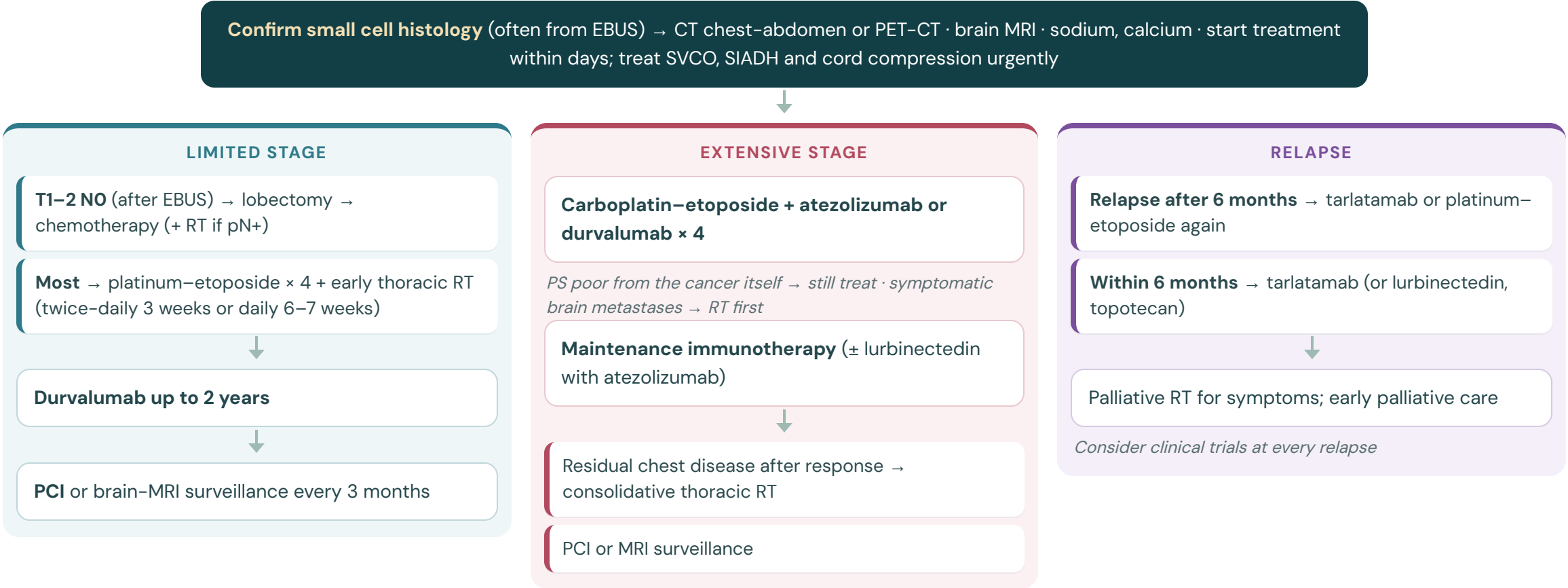
Small cell: what is different

- 15% of lung cancers; nearly all in heavy smokers
- Doubles in weeks: treat within days
- SIADH, Cushing, Lambert–Eaton
- Brain metastases common: MRI at diagnosis
- Poor PS from the cancer is not a reason to withhold treatment

Small cell: treatment

Setting	Option
Limited (T1–2 N0)	Lobectomy → chemotherapy
Limited	EP + early thoracic RT → durvalumab (ADRIATIC)
Extensive	Carboplatin–etoposide + atezolizumab/durvalumab
Relapse >6 months	Tarlatamab or platinum rechallenge
Relapse ≤6 months	Tarlatamab, lurbinectedin, topotecan

Algorithm 3: small cell lung cancer



Small cell lung cancer can double in weeks: arrange treatment within days of diagnosis, and refer patients with poor performance status rather than excluding them.

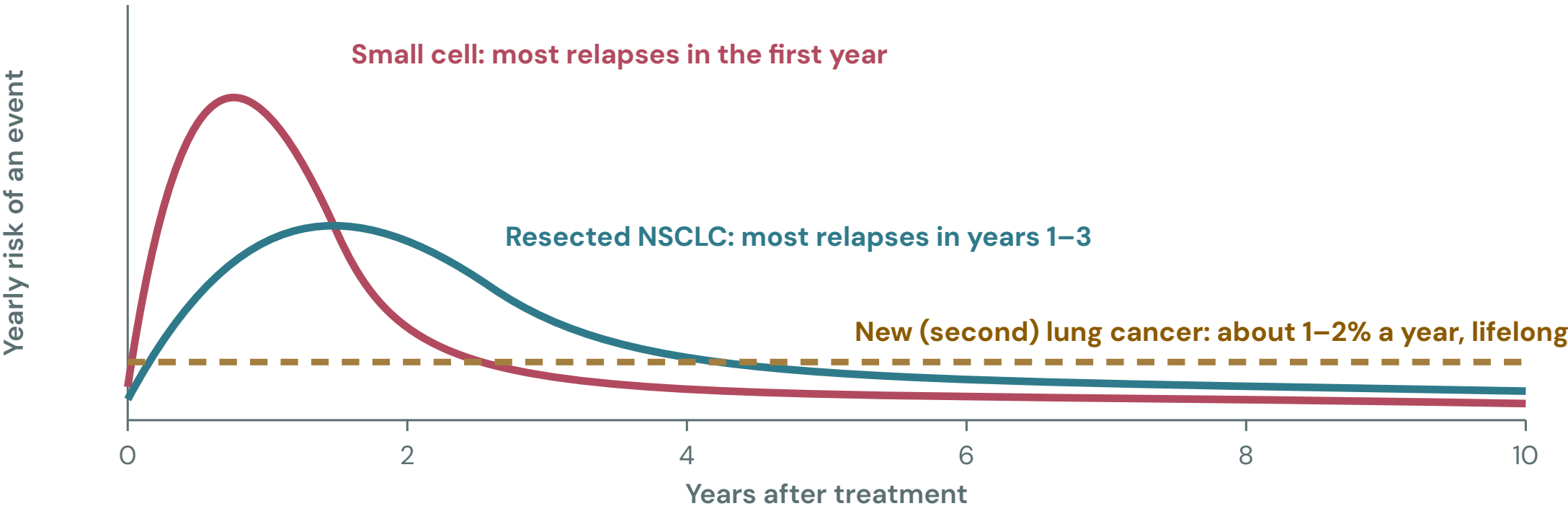
Radiotherapy in small cell

- Thoracic RT early: twice daily 3 weeks or daily 6–7 weeks (CONVERT)
- PCI after response in limited stage, or MRI surveillance
- Extensive stage: MRI surveillance is valid (Takahashi)
- Consolidative thoracic RT for residual disease (CREST)
- Palliative RT for SVCO, bone, brain

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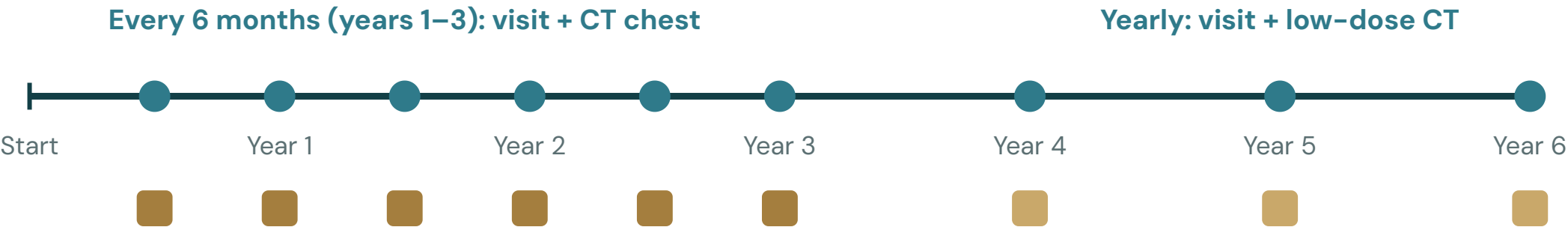
Survivorship, evidence and cases

When relapses happen



Relapse early; second cancers lifelong

Follow-up rhythm



- Clinic visit: symptoms, weight, smoking status, late effects, thyroid and cortisol after immunotherapy
- CT chest (contrast in years 1–3 if high risk); then low-dose CT once a year

Not routine when well: PET-CT, tumour markers (CEA, CYFRA 21-1), bone scan, brain MRI in NSCLC.
Small cell: closer review (every 2–3 months in year 1); brain MRI every 3 months in year 1 if no PCI was given.

CT every 6 months for 2–3 years, then yearly low-dose CT

Survivorship care

- Stop all tobacco (quitline 1800-11-2356): second primaries fall by >80%
- Reduce household biomass smoke
- Thyroid and cortisol after immunotherapy
- TB reactivation: test new cavities or effusions
- Rehabilitation, vaccines, nutrition, mental health

Landmark trials

Trial	Lesson
NLST / NELSON	LDCT screening saves lives in heavy smokers
IPASS	The biomarker selects targeted therapy
PACIFIC	Consolidation after chemoradiation
ADAURA	Test EGFR in every resected NSCLC
KEYNOTE-671	Perioperative chemo-IO improves survival
ADRIATIC	IO after CRT in limited small cell

Case 1: never-smoker on ATT for 5 months

- 46 y woman, biomass exposure; sputum NAAT never done
- Low-ADA exudate; cytology adenocarcinoma; EGFR ex19del
- Three small asymptomatic brain metastases
- Osimertinib ± chemotherapy (or gefitinib + chemo if cost-limited)
- No IO while EGFR result pending

Case 2: 1.8 cm nodule, COPD, past TB

- Biopsy before treatment: PET cannot exclude granuloma
- ppo FEV₁/DLCO ~40%: exercise testing
- Segmentectomy if fit; otherwise SBRT
- No adjuvant therapy for stage IA
- Serial CT: fibrosis versus recurrence

Case 3: single-station N2, no driver

- EBUS: station 7 positive only (N2a)
- NGS negative; PD-L1 60%
- Chemo-IO × 3–4 → lobectomy → IO up to 1 year
- No PORT for RO pN2
- Bulky multi-station N2 → chemoradiation instead

Case 4: unresectable IIC squamous

- EBUS confirms contralateral N3
- Concurrent chemoradiation over 6 weeks
- Durvalumab 12 months (PACIFIC)
- EGFR-positive equivalent → osimertinib (LAURA)
- CT every 3 months; watch for pneumonitis

Case 5: PD-L1 80%, bone metastases

- No driver on NGS
- Single-session RT for bone pain; bone agent
- Pembrolizumab alone (KEYNOTE-024)
- IO unaffordable → platinum–pemetrexed
- Quitline and early palliative care

Case 6: young ALK⁺ man with seizures

- “TB” effusion without microbiology
- ALK IHC positive; four brain metastases
- Lorlatinib or alectinib; radiosurgery often deferred
- Levetiracetam rather than enzyme inducers
- Plan work, fertility, family: long survival is common

Case 7: SVC O and SIADH, small cell

- Correct sodium slowly; stent if severe
- EBUS diagnosis within days
- Carboplatin–etoposide + atezolizumab/durvalumab
- Maintenance IO; thoracic RT; MRI surveillance or PCI
- Relapse ≤ 6 months: tarlatamab (DeLLphi-304)

Practice pearls for Indian clinics

- Never start a “trial” of ATT for a mass or unexplained effusion
- Plan one biopsy for diagnosis, stage and NGS
- Wait for EGFR/ALK before IO in non-squamous NSCLC
- PET-positive is not proof: confirm with EBUS or biopsy
- Discuss cost on day one: generics, PM-JAY, assistance programmes
- TKIs can restore performance status: do not deny testing

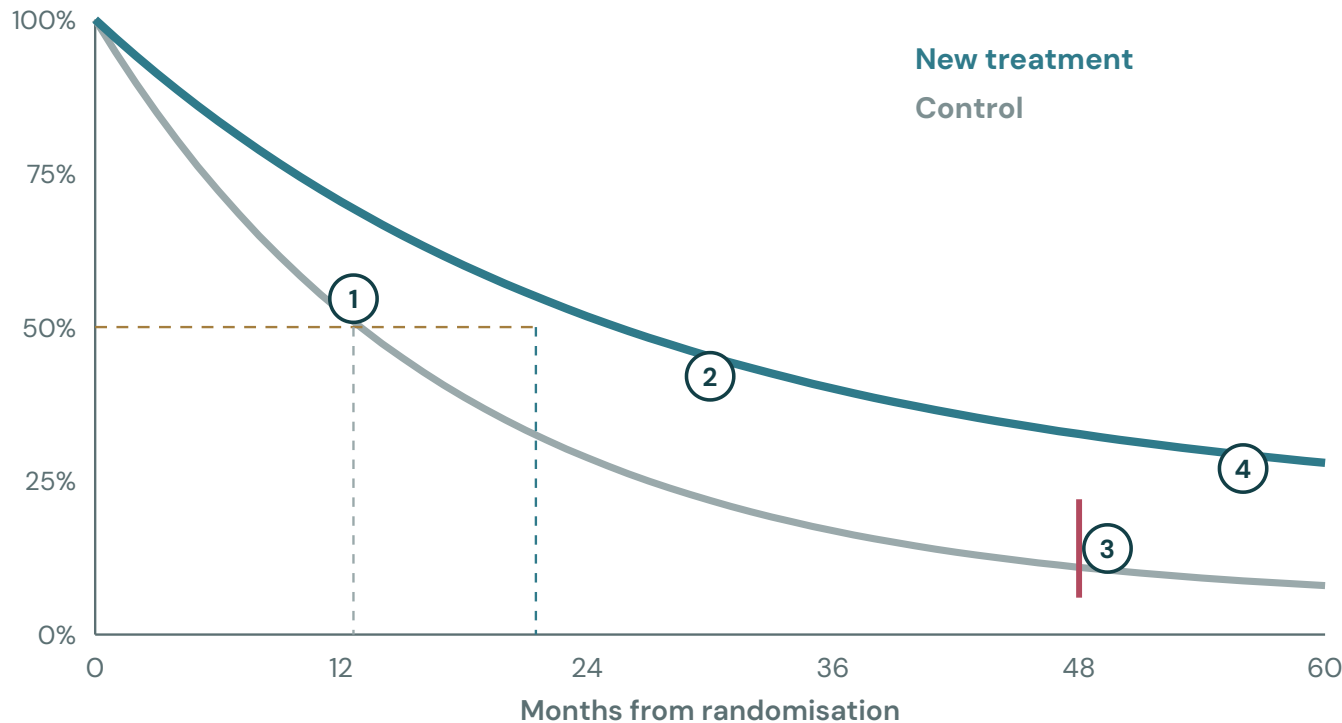
Special situations

- ILD: high cancer risk and high treatment toxicity; favour sublobar surgery
- ILD: immunotherapy and RT case by case with a pulmonologist
- Multiple primaries / multifocal GGOs: curative intent, lung-sparing
- Relapse <6 months after adjuvant therapy: treat as second line
- Re-stage if treatment is delayed ≥ 8 weeks

Absolute benefit and access

- Separate progression-free from overall survival
- Weigh intensified regimens against toxicity and cost
- Gefitinib + chemotherapy: proven, affordable EGFR option
- Chemotherapy alone remains valid when IO is unaffordable
- Prioritise drugs with overall-survival benefit

Reading a survival curve



- 1 Median**
The time at which half the patients have had the event. A median gain of a few months can hide a long tail of survivors.
- 2 Hazard ratio**
Relative risk of the event at any moment (0.70 = 30% lower risk). It is not an absolute difference.
- 3 Absolute difference**
The vertical gap at a fixed time (here about 20 points at 4 years). $NNT = 100 \div \text{gap}$.
- 4 The tail**
A plateau suggests some patients gain long-term control: the typical immunotherapy pattern.
- 5 Crossover and PFS**
If control patients get the new drug later, overall survival differences shrink; a PFS gain alone may not mean longer life.

Median, HR, absolute gap, tail, crossover

Take-home messages

- Prove TB before treating it; image and biopsy early
- Histology + stage + drivers + PD-L1 decide treatment
- Test EGFR/ALK at every stage before immunotherapy
- Lung-sparing surgery, SBRT and chemoradiation all cure
- Small cell is an emergency
- Stopping tobacco is part of treatment

THANK YOU

Questions and discussion

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Full mini review, algorithms, MCQ bank and case vignettes: drharitha.co.in/professionals

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