Adjuvant / neoadjuvant Rx of potentially resectable EGFR mutated NSCLC

Navneet Singh MD DM FRCP (London)

Professor of Pulmonary Medicine &
Faculty-in-charge, Lung Cancer Clinic,
PGIMER, Chandigarh, India

Co-Chair, Treatment of Stage IV Non-Small Cell Lung Cancer (NSCLC)
Living Guideline Panel of American Society of Clinical Oncology (ASCO)

ns_chd@outlook.com

@ns_chd

http://linkedin.com/in/navneet-singh-160012

Disclosure

- Conflicts of Interest: None

Esteemed Panelists*

Sorted alphabetically by surname (last name) ; Details as provided by organizers

1.	Vasu Babu	Vijayawada	Medical Oncology
2.	Kunal Jobanputra	Mumbai	Medical Oncology
3.	Vanita Noronha	Mumbai	Medical Oncology
4.	Mansi Sharma	Delhi	Medical Oncology
5.	Vijay Sharnangat	Mumbai	Medical Oncology
6.	Ajay Kumar Singh	Mumbai	Medical Oncology

Most important question for this panel?

All panellists from same discipline in era of multidisciplinary Mx:

- Would we have some (? significant) differences of opinion?

OR

- Consensus will be the norm rather than the exception !

Adjuvant icotinib versus observation in patients with completely resected, EGFR-mutated, stage IB non–small cell lung cancer (GASTO1003, CORIN): A randomized phase II trial.

Ning Li, Bao-Xiao Wang, Wei Ou, Hena Shi, Dong Ji, Yan Yan, Shu-Quan Wang, Wu-Guang Chang, Teng-Fei Zhu, Si-Yu Wang; Sun Yat-sen University Cancer Center, Guangzhou, China; Sun Yat-Sen Memorial Hospital, Guangzhou, China; Betta Pharmaceuticals Co., Ltd., Hangzhou, China

Background: The role of adjuvant therapy in patients with completely resected stage IB non-small-cell lung cancer (NSCLC) remains to be determined. Icotinib is standard-of-care therapy for patients with advanced NSCLC harboring epidermal growth factor receptor (EGFR) mutation. This phase II study investigated whether adjuvant therapy with icotinib improves the clinical outcome compared with observation in patients with EGFR mutation-positive resected stage IB NSCLC. **Methods:** This phase II, open-label, randomized study (GASTO1003, CORIN) was conducted at Sun Yat-sen University Cancer Center. From May 2013 to December 2020, patients with completely resected, EGFR mutation-positive, stage IB (7th TNM staging for NSCLC) NSCLC without adjuvant chemotherapy according to physician and patient choices were enrolled. The patients were assigned in a 1:1 ratio to receive adjuvant therapy with icotinib (125mg, three times daily) for 12 months or to undergo observation. Therapy continued until disease progression or intolerable toxicity. The primary endpoint was disease-free survival (DFS). Secondary endpoints included overall survival (OS) and toxicity. Survival endpoints were assessed in the intention-to-treat population. **Results:** Three patients withdrew consent and were excluded. A total of 128 patients were enrolled and randomized, with 63 patients in the icotinib group and 65 patients in the observation group. Baseline characteristics were well balanced between the groups. The median duration of follow-up was 34.9 months. A total of 13 recurrence events occurred, including 2 in the icotinib arm and 11 in the observation arm. DFS was significantly longer among those in the icotinib arm than among those in the observation arm (hazard ratio: 0.20, 95% confidence interval, 0.04-0.89; P = 0.018). The 3-year DFS for the icotinib and observation arms were 95.3% and 86.7%, respectively. The OS data were immature with 3 deaths in the observation arm. The safety profile was consistent with the known safety profile of icotinib. Icotinib was well tolerated with no unexpected adverse events. No treatment-related death occurred. **Conclusions:** Adjuvant icotinib shows prolonged DFS and acceptable toxicity in patients with completely resected EGFR-mutated stage IB NSCLC. Ajuvant icotinib provides a treatment option for these patients. Clinical trial information: NCT02264210. Research Sponsor: Betta pharmaceuticals.

Salient features/issues:

1. Drug developed & being used currently in China
2. Study only included stage IB patients (no indication for CTx)
3. Impressive HR = 0.2
4. 3 yr DFS rates (95% vs. 87%)
5. DFS benefit + but OS data immature
6. No. of events low (n=13; 2 vs. 11)

86P **Aumolertinib as adjuvant therapy in postoperative EGFR-mutated non-small cell lung cancer**

Q. Zhang, C. He, T. He, Y. Wang, W. Lv, J. Hu

Department of Thoracic Surgery, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China

Background: Aumolertinib (HS-10296) is a novel, promising oral third-generation Epidermal Growth Factor Receptor (EGFR) tyrosine kinase inhibitor (TKI), which has demonstrated efficacy in tumours harbouring sensitive EGFR mutations and T790M resistance mutation. Aumolertinib has also been shown to have efficacy in CNS metastasis. However, the efficacy and safety of aumolertinib as adjuvant therapy in postoperative patients remains unknown.

Methods: Patients who underwent radical lung cancer surgery with EGFR-sensitizing mutations were enrolled and received aumolertinib 110 mg daily, the medication time (6months-36months) depended on pathology stage and physical conditions. The disease-free survival (DFS), safety and tolerability were evaluated.

Results: The study retrospectively analyzed 66 patients with pathologically confirmed adenocarcinoma, EGFR mutation-positive (exon 19 deletion or L858R), stage I—III NSCLC. At the data cutoff, all patients have no symptoms of tumor recurrence, 25(37.9%) patients have been followed up for over 1 year. At 12 months, 100% patients were alive and disease-free, patients'conditions were evaluated by chest CT, PET-CT, abdominal ultrasound, cranial MRI and other auxiliary examination. None of these patients have central nervous system disease. During aumolertinib therapy, 34.8% of patients had adverse treatment-related adverse events of any grade, but there was no grade $\geq$3 adverse events occurred, rash (15/66, 22.7%), mouth ulcer (7/66, 10.6%) and diarrhea (5/66, 7.6%) were common adverse reactions. No patients withdrew from therapy because of adverse drug reactions. Interestingly, we found aumolertinib was also effective in multiple primary lung cancer, among patients (5/66, 7.6%) who have multiple malignant lesions (ground -glass opacity, and $<$3cm), with aumolertinib treatment, 2 patients had reduction in size of lesions, and the other patients had no change in size.

Conclusions: This is the first study to demonstrate that aumolertinib has preliminary efficacy and a tolerable safety profile in patients with completely resected stage I-III NSCLC harboring EGFR mutations. This study is still in progress and further analyses are undergoing to determine longer-term outcomes.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

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Salient features/issues:

1. Drug developed & being used currently in China
2. 3rd generation TKI (~ osimertinib)
3. Study included stage I-III patients (no data if eligible patients received CTx)
4. Single arm (no comparator)
5. Small study (n=66); retrospective
6. 1-yr DFS rate = 100% !
7. DFS & OS data both immature

clinical trial updates

Updated Overall Survival and Exploratory Analysis From Randomized, Phase II EVAN Study of Erlotinib Versus Vinorelbine Plus Cisplatin Adjuvant Therapy in Stage IIIA Epidermal Growth Factor Receptor+ Non–Small-Cell Lung Cancer

Dongsheng Yue, MD[1]; Shidong Xu, MD[2]; Qun Wang, MD[3]; Xiaofei Li, MD[4]; Yi Shen, MD[5]; Heng Zhao, MD[6]; Chun Chen, MD[7]; Weimin Mao, MD[8]; Wei Liu, MD[9]; Junfeng Liu, MD[10]; Lanjun Zhang, MD[11]; Haitao Ma, MD[12]; Qiang Li, MD[13]; Yue Yang, MD[14]; Yongyu Liu, MD[15]; Haiquan Chen, MD[16]; Zhenfa Zhang, MD[1]; Bin Zhang, MD[1]; Changli Wang, MD[1]

abstract

Clinical trials frequently include multiple end points that mature at different times. The initial report, typically based on the primary end point, may be published when key planned co-primary or secondary analyses are not yet available. Clinical Trial Updates provide an opportunity to disseminate additional results from studies, published in JCO or elsewhere, for which the primary end point has already been reported.

The randomized, open-label, phase II EVAN study investigated the efficacy (disease-free survival [DFS] and 5-year overall survival [OS]) and safety of erlotinib versus vinorelbine/cisplatin as adjuvant chemotherapy after complete resection (R0) for stage III epidermal growth factor receptor (*EGFR*) mutation+ non–small-cell lung cancer. We describe the updated results at the 43-month follow-up. In EVAN, patients were randomly assigned (1:1) to erlotinib (n = 51) or vinorelbine/cisplatin (n = 51). The median follow-up was 54.8 and 63.9 months in the erlotinib and chemotherapy arms, respectively. With erlotinib, the respective 5-year DFS by Kaplan-Meier analysis was 48.2% (95% CI, 29.4 to 64.7) and 46.2% (95% CI, 27.6 to 62.9) in the intention-to-treat and per-protocol populations. The median OS was 84.2 months with erlotinib versus 61.1 months with chemotherapy (hazard ratio, 0.318; 95% CI, 0.151 to 0.670). The 5-year survival rates were 84.8% and 51.1% with erlotinib and chemotherapy, respectively. In whole-exome sequencing analysis, frequent genes with variants co-occurring at baseline were *TP53*, *MUC16*, *FAM104B*, *KMT5A*, and *DNAH9*. With erlotinib, a single-nucleotide polymorphism mutation in *UBXN11* was associated with significantly worse DFS ($P = .01$). To our knowledge, this study is the first to demonstrate clinically meaningful OS improvement with adjuvant erlotinib compared with chemotherapy in R0 stage III EGFR+ non–small-cell lung cancer.

J Clin Oncol 40:3912-3917.

Salient features/issues:

1. Study included stage IIIA
2. Erlotinib duration 2 yrs
3. Comparator = vinorelbine-cisplatin (? justified as SOC in current era of better tolerated & equally effective CTx drugs)
4. DFS benefit lost w/ time (2-yr 81% vs. 45% → 5-yr 48% vs. N/A)
5. OS (5-yr 85% vs. 51%) favored TKI arm [HR = 0.32]

original reports

Randomized Phase III Study of Gefitinib Versus Cisplatin Plus Vinorelbine for Patients With Resected Stage II-IIIA Non–Small-Cell Lung Cancer With *EGFR* Mutation (IMPACT)

Hirohito Tada, MD, PhD[1]; Tetsuya Mitsudomi, MD, PhD[2]; Toshihiro Misumi, PhD[3]; Kenji Sugio, MD, PhD[4]; Masahiro Tsuboi, MD, PhD[5], Isamu Okamoto, MD, PhD[6]; Yasuo Iwamoto, MD, PhD[7]; Noriaki Sakakura, MD, PhD[8]; Shunichi Sugawara, MD, PhD[9]; Shinji Atagi, MD, PhD[10]; Toshiaki Takahashi, MD, PhD[11]; Hidetoshi Hayashi, MD, PhD[12]; Morihito Okada, MD, PhD[13]; Hidetoshi Inokawa, MD, PhD[14]; Hiroshige Yoshioka, MD, PhD[15]; Kazuhisa Takahashi MD, PhD[16]; Masahiko Higashiyama MD, PhD[17]; Ichiro Yoshino MD, PhD[18]; and Kazuhiko Nakagawa MD, PhD[12]; for the West Japan Oncology Group

abstract

PURPOSE To investigate the efficacy of gefitinib as an adjuvant therapy for non–small-cell lung cancer patients with *EGFR* mutation.

PATIENTS AND METHODS IMPACT (WJOG6410L; University Hospital Medical Information Network Clinical Trials Registry: UMIN000006252), a randomized, open-label, phase III study, included patients with completely resected pathologic stage II-III non–small-cell lung cancer harboring *EGFR* mutations (exon 19 deletion or L858R) during September 2011 to December 2015. Patients were randomly assigned to receive gefitinib (250 mg once daily) for 24 months or cisplatin (80 mg/m^2 on day 1) plus vinorelbine (25 mg/m^2 on days 1 and 8; cis/vin) once every 3 weeks for four cycles. The primary end point was disease-free survival (DFS).

RESULTS Overall, 234 patients were randomly assigned. Among 232 eligible patients (116 each; excluding two who withdrew consent), the median DFS was 35.9 and 25.1 months in the gefitinib and cis/vin groups, respectively. However, Kaplan-Meier curves crossed around 4 years after surgery with no statistically significant difference (stratified log-rank $P = .63$; hazard ratio by stratified Cox proportional hazards model = 0.92; 95% CI, 0.67 to 1.28). Overall survival (OS) was also not different (stratified log-rank $P = .89$; hazard ratio = 1.03; 95% CI, 0.65 to 1.65), with the 5-year OS rates being 78.0% and 74.6% in the gefitinib and cis/vin groups, respectively. Treatment-related deaths occurred in 0 and three patients in the gefitinib and cis/vin groups, respectively.

CONCLUSION Although adjuvant gefitinib appeared to prevent early relapse, it did not prolong DFS or OS. However, similar DFS and OS may justify adjuvant gefitinib in the selected patient subsets, especially those deemed ineligible for platinum-doublet adjuvant therapy; however, this was not a noninferiority trial.

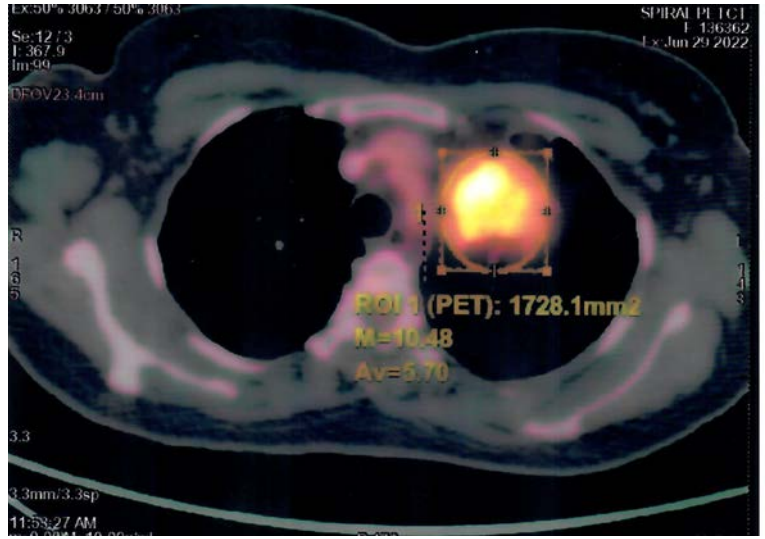
J Clin Oncol 40:231-241.

Salient features/issues:

1. Study included stage II-III
2. Gefitinib duration 2 yrs
3. Comparator arm = vinorelbine-cisplatin (? justified as SOC in current era of better tolerated & equally effective CTx drugs)
4. DFS (36 m vs. 25m) & OS (5-yr 78% vs. 75%) favored TKI arm
5. DFS benefit lost w/ time
6. no OS benefit

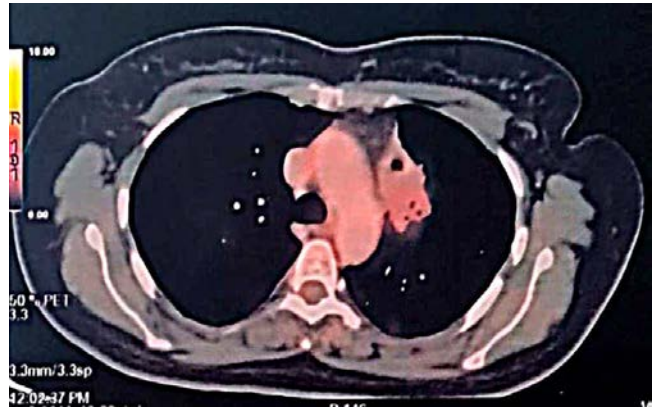
Real World Experience

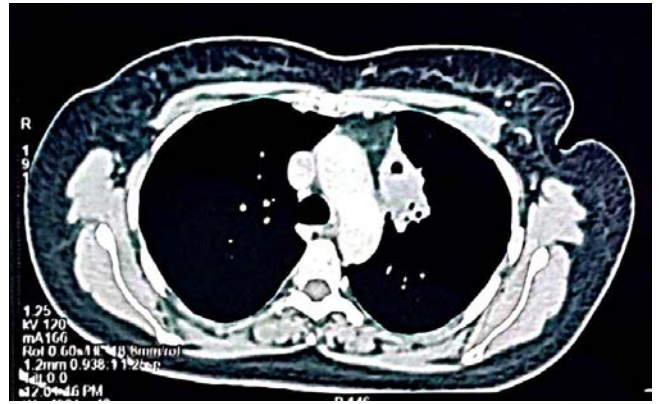
- Mrs. LS, 52 years, no smoking history, r/o Punjab presented with H/o cough x 6 months & hemoptysis x 2 months → HOV
- CECT Thorax: 4.5 x 4.0 cm LUL mass closely abutting mediastinum
- FOB: Lt VC palsy, LUL bronchus completely occluded with polypoidal growth → Endobronchial biopsy: adenocarcinoma NOS
- PET-CT → FDG avid (SUV_{max} 10.5) 6.0 x 5.8 x 5.1 cm LUL spiculated mass abutting mediastinal pleura & extending into Lt hilum with ill-defined interface with Lt Pul A.
- Clinical stage: T4N1M0 (IIIA) ECOG PS 0
- NACT (pemetrexed-cisplatin) started



Real World Experience

- Reflex molecular testing (tissue): EGFR Exon 19 del M+ (others –ve)
- C2 onwards gefitinib added to chemotherapy
- Surgical opinion after C2 → 3+ cycles then reassess
- Tolerated Rx well (Dose intensity ≈ 95%; Grade 2 fatigue/anorexia)
- Repeat PET-CT (after C5) → FDG avid (SUV_{max} 7.0) 3.5 x 3.0 x 2.4 cm LUL ant. segment mass abutting mediastinum & extending into Lt hilum with ill-defined interface with Lt Pul A. Metabolic & radiological PR (RECIST – 42% ↓ ; WHO – 70% ↓)





Real World Experience

- Plan: surgical review (if R0/R1 feasible) else to shift to concurrent chemo-radiation
- Patient underwent thoracotomy and LUL lobectomy with sleeve resection of Lt main pulmonary A. + SLND
- Final Stage : G2 acinar predominant invasive adenocarcinoma ypT2a N0 (IB) [3.5 x 3.2 cm; all 8 LN -ve] R0 L0 V0 Pl0 STAS –ve. Residual tumor >10%
- Adjuvant osimertinib initiated

Adjuvant TKI for resected EGFR mutated NSCLC

- Which drug?
- Monotherapy OR combination?
- Which disease or patient characteristics define eligibility?
- For how long?
- Criteria for stopping treatment?
- What are preferred endpoints of efficacy?
- What is magnitude of outcomes that would make adjuvant TKI as the preferred treatment?

Trial	EVAN	IMPACT	ADJUVANT	ADAURA
Phase	II	III	III	III
Number	102	232	222	682
Stages	IIIA	II-III	II-IIIA	IB-IIIA
Drug	Erlotinib vs. Vin-Cis	Gefitinib vs. Vin-Cis	Gefitinib vs. Vin-Cis	Osimertinib vs. **Placebo**
Duration	2 years	2 years	2 years	**3 years**
DFS	5-yr 48% vs. NA **HR =0.38** 2-yr 81% vs. 45%	5-yr 32% vs. 34% HR = 0.92	5-yr 23% vs. 23%	3-yr 84% vs. 34% (II-IIIA) **HR = 0.23** 3-yr 85% vs. 44% (IB–IIIA) **HR = 0.27**
OS	84m vs. 61m 5-yr 85% vs. 51% **HR = 0.32**	Median NR 5-yr 78% vs. 75% HR = 1.03	76m vs. 63m 5-yr 53% vs. 51% HR = 0.92	N.A. (Immature)

Do you know when you were born?

- The Greatest Generation (born 1901–1927)
- The Silent Generation (born 1928–1945)
- Baby Boomers (born 1946–1964)
- Generation X (born 1965–1980)
- Millennials (born 1981–1996)
- Generation Z (born 1997–2012)
- Generation Alpha (born 2013–2025)

Adjuvant TKI for resected EGFR mutated NSCLC

- Which drug?
  - ❖ 1st Generation: Erlotinib / Gefitinib
  - ❖ 2nd Generation: Afatinib / Dacomitinib
  - ❖ 3rd Generation: Osimertinib
  - ❖ Generation ‘X’ : Amivantamab
  - ❖ Generation ‘Z’: Drugs Not Available locally (icotinib / aumolertinib)

Adjuvant TKI for resected EGFR mutated NSCLC

- Monotherapy Or Combination?
  - ❖ 1st Generation: Erlotinib / Gefitinib
  - ❖ 2nd Generation: Afatinib / Dacomitinib
  - ❖ 3rd Generation: Osimertinib
  - ❖ Generation ‘X’ : Amivantamab
- Combination with
  - ➢ Pemetrexed-Carboplatin?
  - ➢ VEGF inhibitor : Bevacizumab / Ramucirumab?

Adjuvant TKI for resected EGFR mutated NSCLC

- Which disease or patient characteristics define eligibility?
  - Disease Stage: IA / IB / II / IIIA / IIIB (T3N2 / T4N2)
  - Clinical Stage vs. Pathological Stage?
  - Type of mutation:
    - Common (Exon 19 Del & L858R)
    - Uncommon (other than Exon 20 Ins): L861Q / G719X / S768I
    - Exon 20 Ins
    - Dual mutations (including denovo T790M)

Adjuvant TKI for resected EGFR mutated NSCLC

- How long?
  - 2 years
  - 3 years
  - 5 years
  - Till disease relapse OR unacceptable clinical / financial toxicity

Adjuvant TKI for resected EGFR mutated NSCLC

- Endpoints for treatment efficacy?
  - ❖ DFS benefit
  - ❖ DFS + OS benefit
  - ❖ OS benefit irrespective of DFS benefit
  - ❖ DFS benefit but w/o worsening (?stable/improvement) in QOL/PROs
  - ❖ DFS benefit but w/o grade 3 drug related AEs
  - ❖ OS benefit even if a/w worsening / no improvement in QOL/PROs

Adjuvant TKI for resected EGFR mutated NSCLC

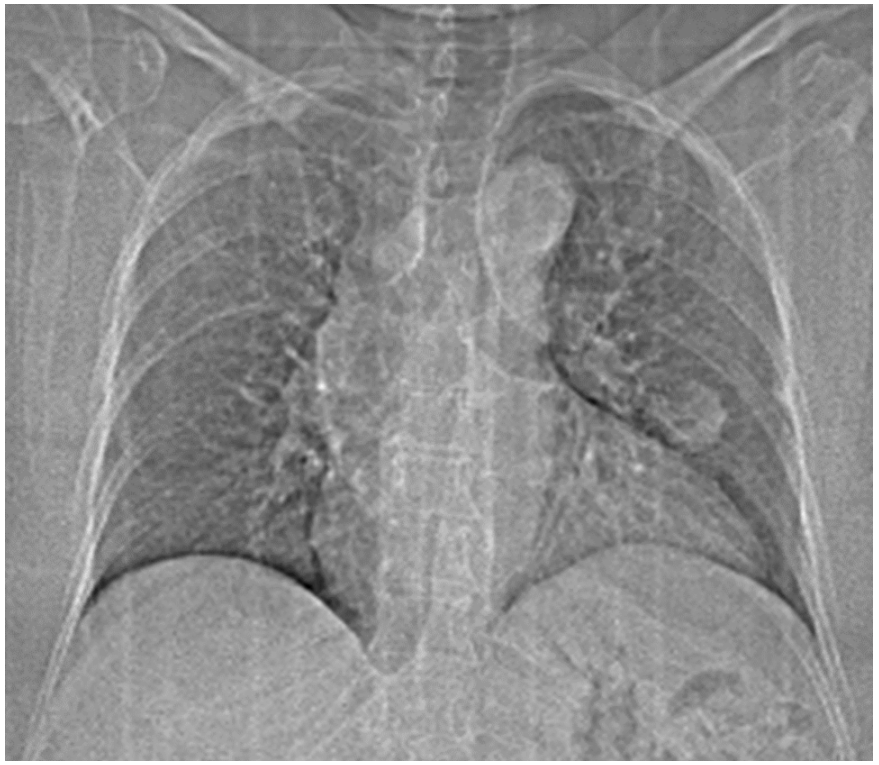
- Magnitude of benefit desired
  - ❖ Improvement in 5-year OS: ≥ 5% vs. ≥ 10% vs. ≥ 15%
  - ❖ DFS benefit sustained for ≥ 4 years
  - ❖ HR for DFS ≤ 0.33
  - ❖ Any other?

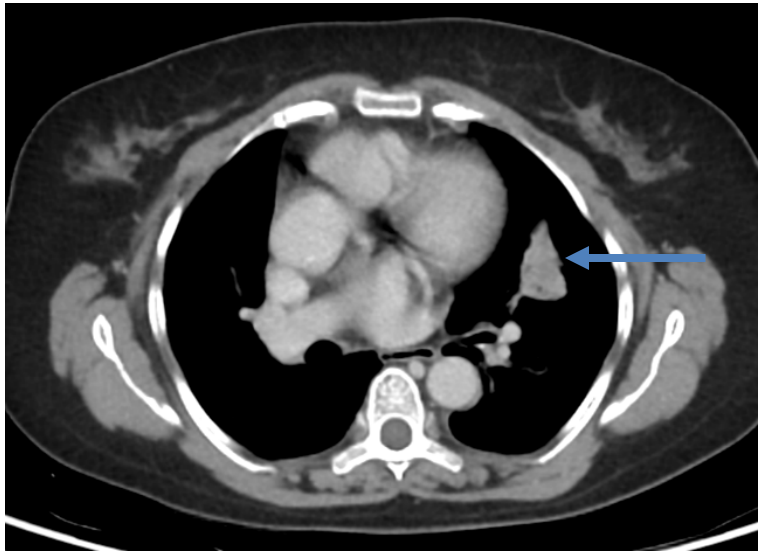
What is ‘resectable’ NSCLC?

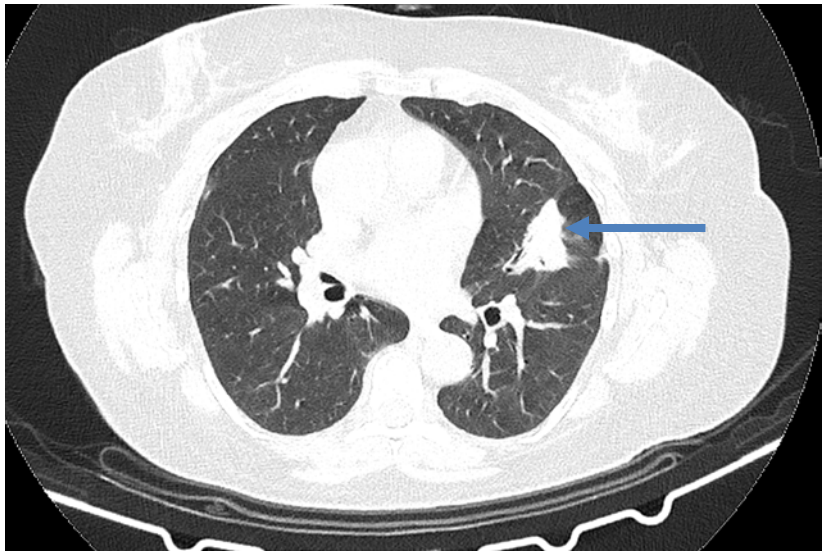
1. No evidence of extra-thoracic metastases
2. No evidence of intra-thoracic metastases
3. N3 disease has been ruled out
4. N2 disease is not bulky or multi-station
5. Primary lesion is amenable to R0 resection

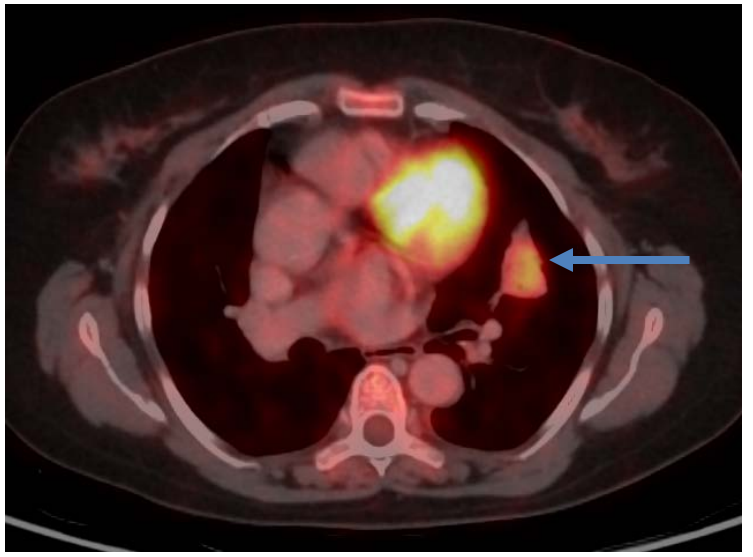
Real World Experience

- Mrs. AB, 57 years, no smoking history, r/o Himachal Pradesh
- No respiratory complaints
- Incidentally detected to have LUZ nodule on Chest radiograph while undergoing pre-operative evaluation for uterine fibroids in March 2022.
- Following hysterectomy, referred to Pulmonology / Lung Cancer Clinic

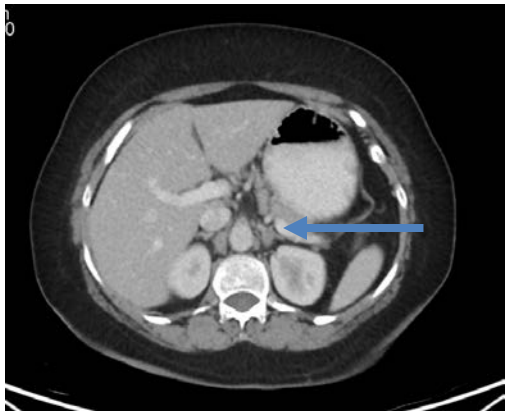


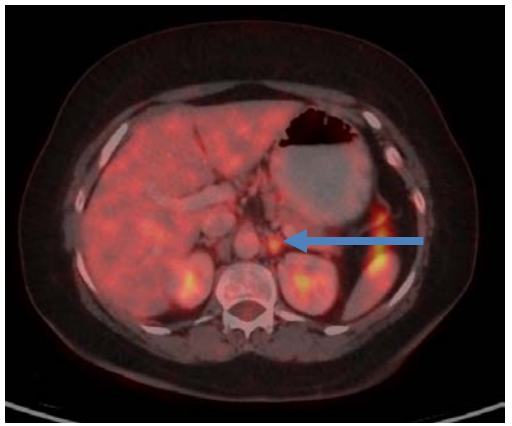


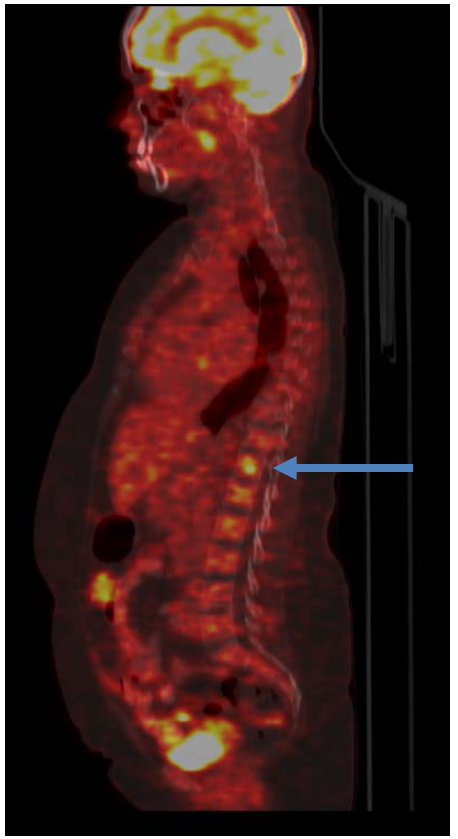




- HRCT thorax → PET-CT scan : 3.0 x 2.0 cm LUL FDG avid (SUV_{max} 6.8) spiculated lesion in LUL lingular segment; non-FDG avid sub-cm pleural based GGNs (2) in LLL; Faintly FDG avid sub-cm 2R/4R/6 LN; FDG avid (SUV_{max} 5.0) sub-cm nodular lesion in Lt adrenal gland; FDG avid (SUV_{max} 7.6) in D12 vertebra.
- PET guided biopsy from LUL (same scan)→ Adenocarcinoma (lepidic predominant)







Real World Dilemma

- Stage ? T1c N3 M1c (IVB)
- In view of primary lesion being resectable and doubt about involvement of mediastinal lymph nodes and extra-thoracic metastases, the plan as discussed with and agreed by patient/family was:

1. PET guided biopsy from adrenal / vertebral lesions
2. If both in #1 came out as negative → to do a staging EBUS-TBNA
3. If #2 ruled out N3 disease → surgical resection
4. Simultaneously send ddPCR liquid biopsy for EGFR mutations (while tissue was being processed for reflex molecular testing)

Real World Experience

- Patient took second opinion(s) and got MRI brain + spine (-ve) & abdomen (one lesion each in both adrenal glands – Lt 1.7 x 1.2 cm).
- Chemotherapy started (pemetrexed-cisplatin)
- Assessment for PET guided biopsy done (after C1) → D12 vertebra (marrow) uptake resolved; Lt adrenal nodule 0.8 x 0.6 cm → biopsy deemed to be technically not feasible
- ALK (D5F3 IHC) –ve; ROS1 screening (D4D6 IHC) –ve ; PD-L1 (SP263 IHC) <1% ; liquid biopsy ddPCR (for EGFR mutations) –ve
- EGFR RT-PCR (tissue) : exon 19 deletion
- Plan discussed w/ pt/family: inability to exclude metastatic disease → Rx changed to pemetrexed + carboplatin + gefitinib (w.e.f. C2)

Real World Experience

- After C3 (C2 of Pem-Carbo-Gef) → gr 2 mucositis / transaminitis
- Unwilling for further chemotherapy → shifted to afatinib
- Repeat PET-CT (3 months from Dx): Non-FDG avid 3.0 x 1.5 cm LUL lingula nodule; no metabolically active lesion elsewhere.
- Underwent VATS guided LUL lobectomy + SLND in July 2022
- Final Stage : G2 acinar predominant adenocarcinoma ypT1b N0 (IA2) [2.0 x 1.8 cm; all 14 LN -ve] R0 L0 V0 STAS –ve
- Rx plan (discussed in institutional MD meeting & agreed to by pt /family: afatinib continued (can't afford osimertinib).
- 4m post-op doing fine: repeat imaging planned at 6m

What is ‘resectable’ NSCLC?

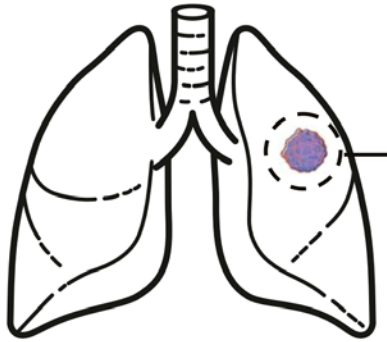
1. No evidence of (widespread) extra-thoracic or intra-thoracic metastases (by imaging + cytological and/or histopathological sampling)
2. N3 disease has been ruled out (by imaging + endoscopic and/or surgical sampling)
3. N2 disease is not bulky or multi-station (either upfront OR after neoadjuvant treatment)
4. Primary lesion is deemed amenable to R0 resection (either upfront OR after neoadjuvant treatment)

Approval

ADAURA

Osimertinib

Stage IB-IIIA HR 0.20



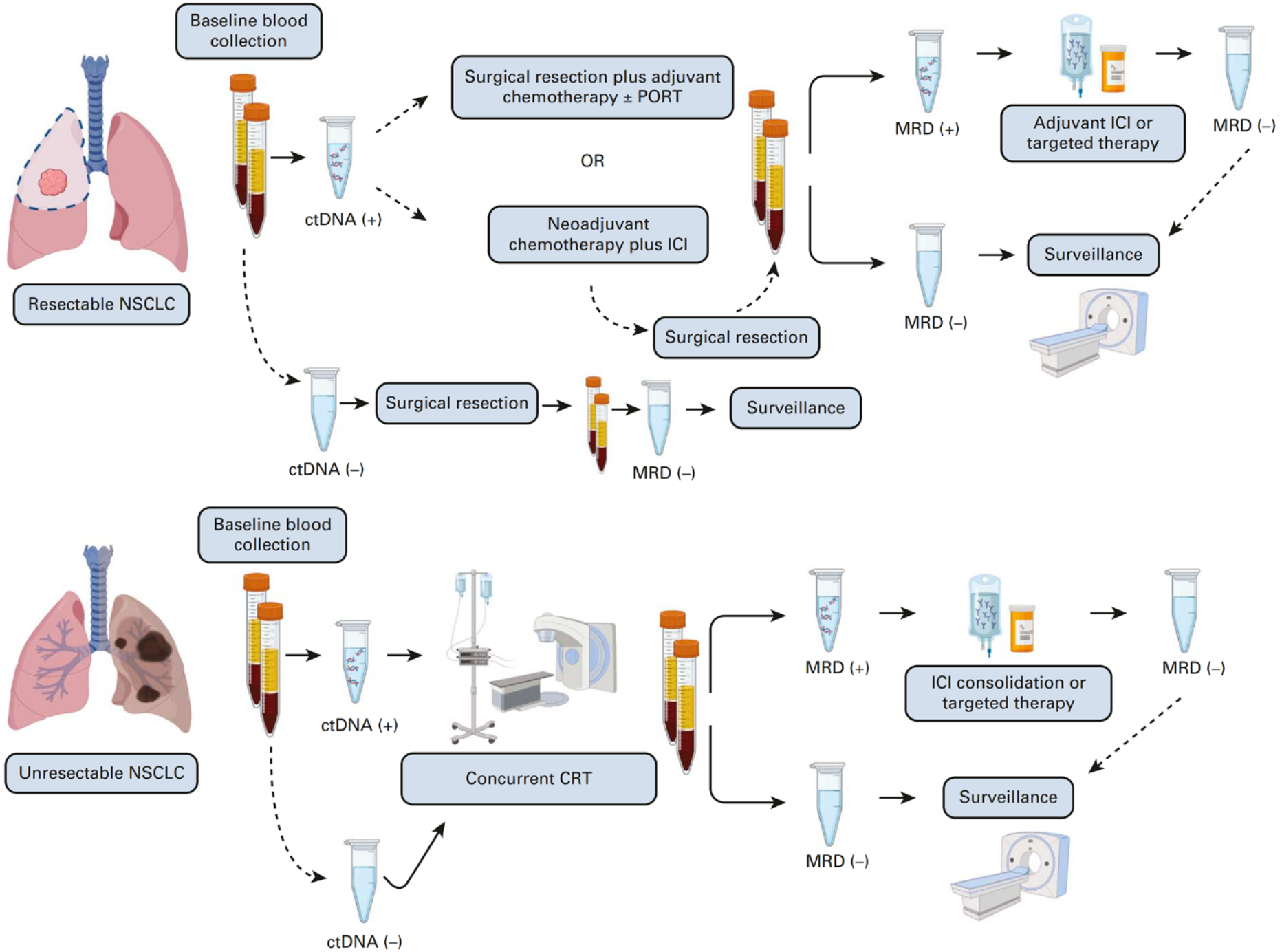
Localized NSCLC after definitive operation
EGFR 19del or *L858R*

IMPACT	ADJUVANT	EVIDENCE	EVAN
Phase III Stage II-IIIA Gefitinib *v* chemotherapy	Phase III Stage II-IIIA (N1-2) Gefitinib *v* chemotherapy	Phase III Stage II-IIIA Icotinib *v* chemotherapy	Phase II Stage IIIA Erlotinib *v* chemotherapy
DFS: 35.9 *v* 25.1 months *P* = .63, HR = 1.28	DFS: 30.8 *v* 19.8 months *P* = .001, HR = 0.56	DFS: 47.0 *v* 22.1 months *P* < .0001, HR = 0.36	DFS: 42.4 *v* 21.2 months *P* < .0063, HR = 0.327
5-year OS: 78.0% *v* 74.6% *P* = .89, HR = 1.03	5-year OS: 53.2 % *v* 51.2% *P* = .674, HR = 0.92	5-year OS: not reached	5-year OS: 84.8 % *v* 51.1% *P* = .0015, HR = 0.318

Role of first-generation EGFR-TKI

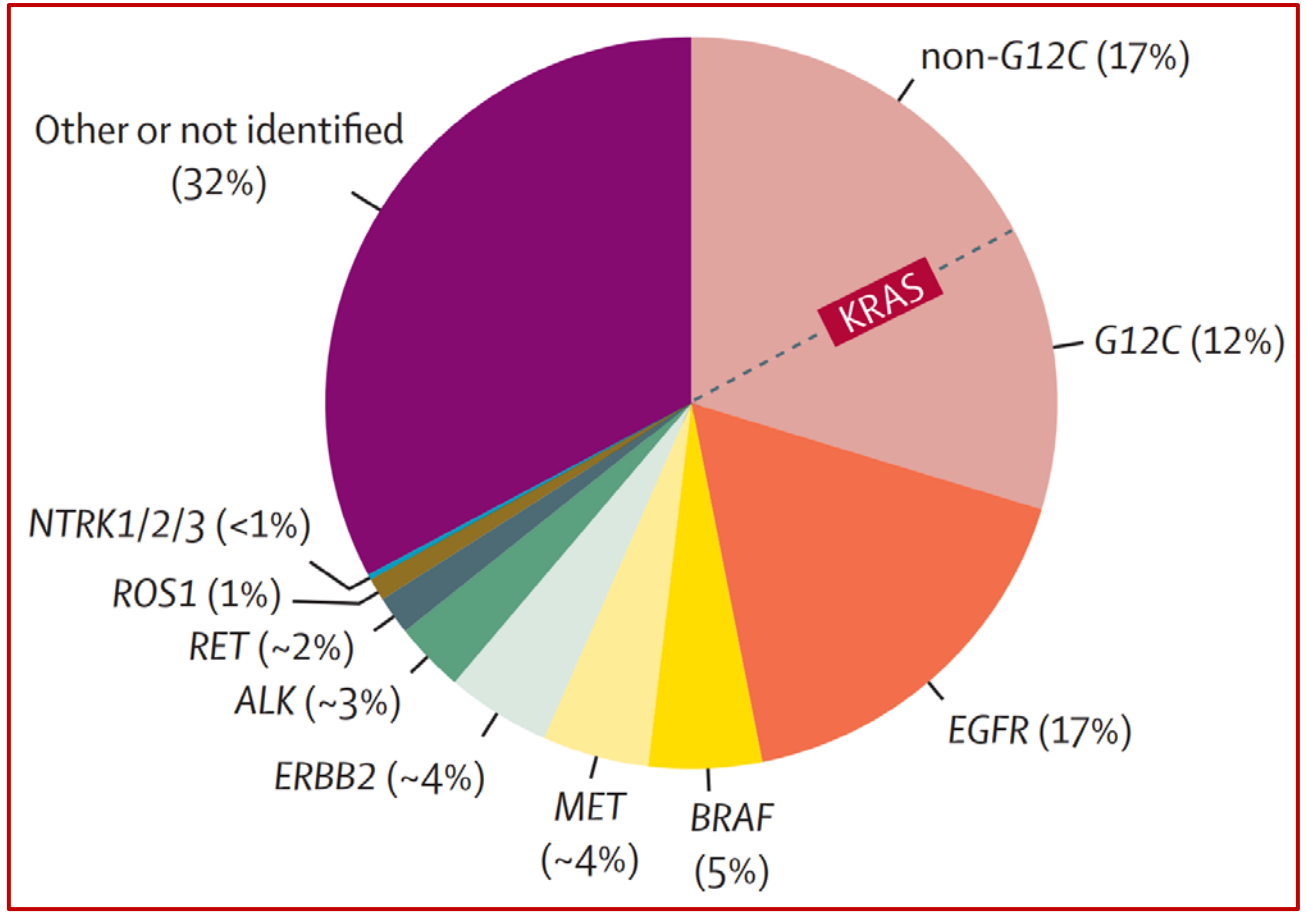
Accessibility of osimertinib	Prolonged OS	Comparison with chemotherapy	Future scenarios
Drug accessibility in certain districts Economic burden	The OS has actually been improved compared with the chemotherapy era EGFR-TKIs rechallenge after relapse contributed to the prolonged OS	Non-inferior OS data of first-generation TKI Meaningful DFS benefit with or without chemotherapy in ADAURA Toleration Willingness	Optimal duration of adjuvant EGFR-TKI: 3-year or 5-year? Rechallenge TKI after relapse Genomic profile MRD-guided tailored therapy

Liu SY et al. J Clin Oncol 2022; 40(3): 217–20

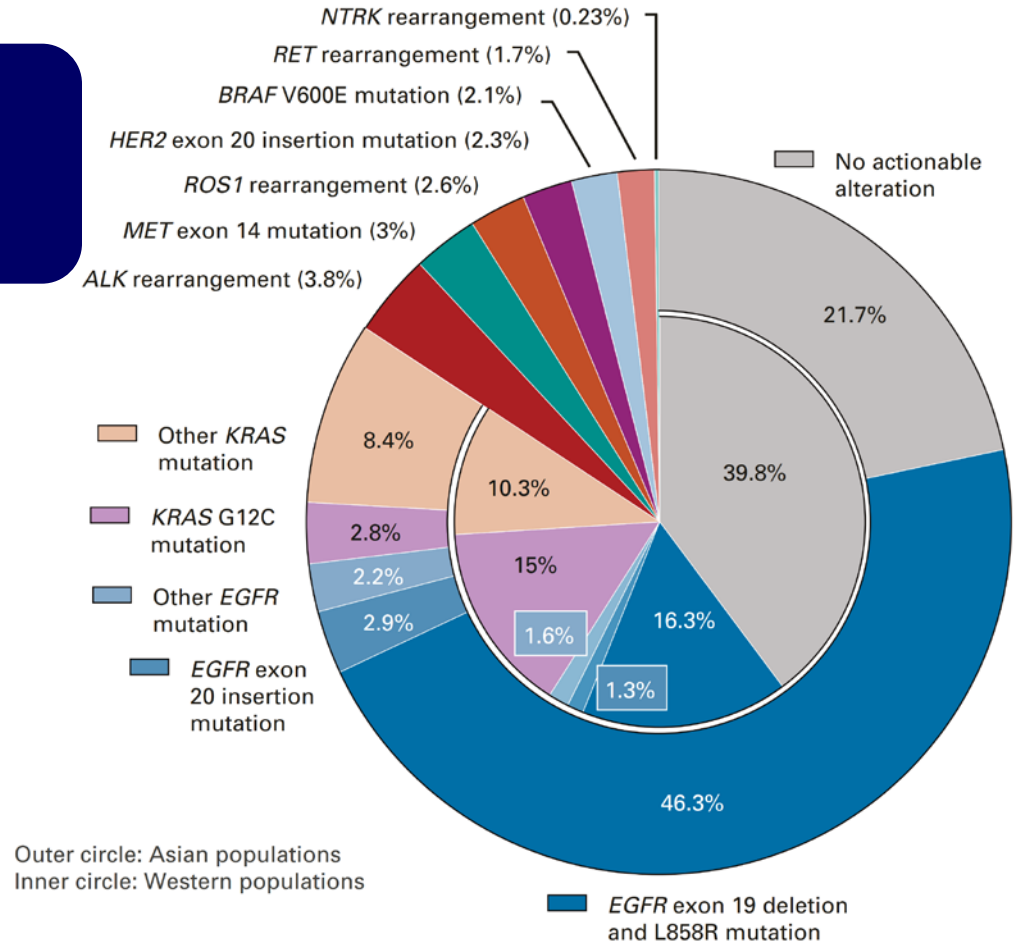


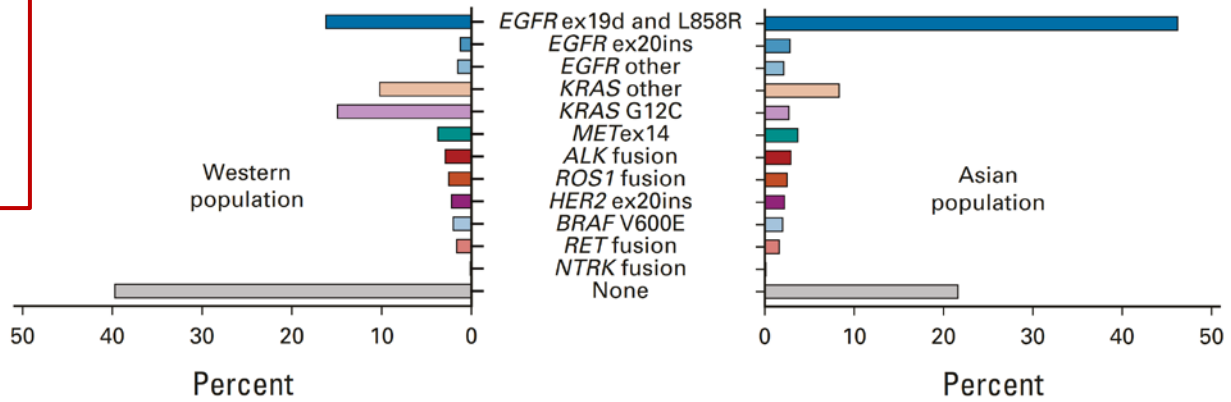
Pellini B et al. J Clin Oncol 2022; 40(6): 567–75

Beyond EGFR targeted Rx?

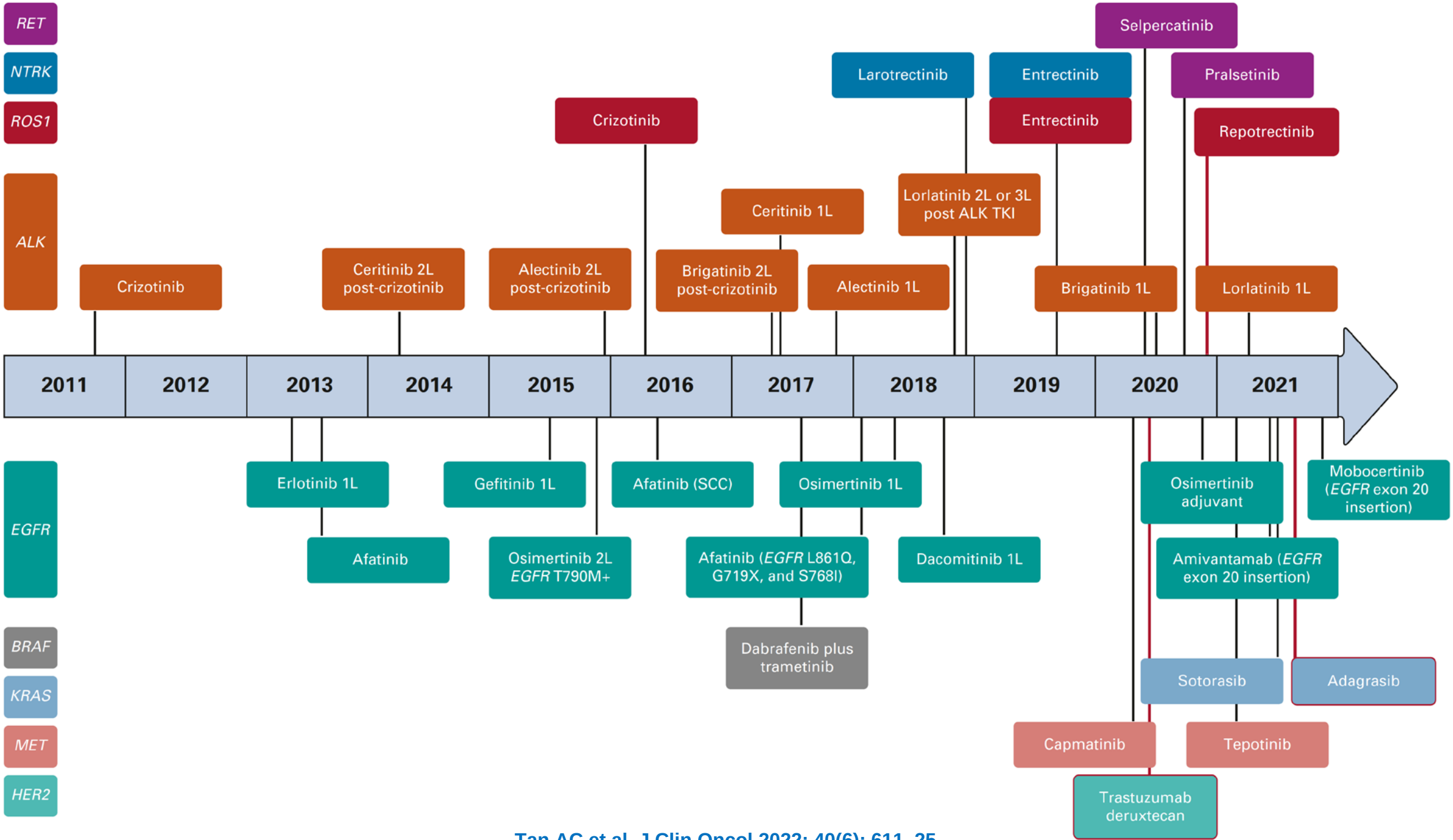


Thai AA et al. Lancet 2021 398: 535–54

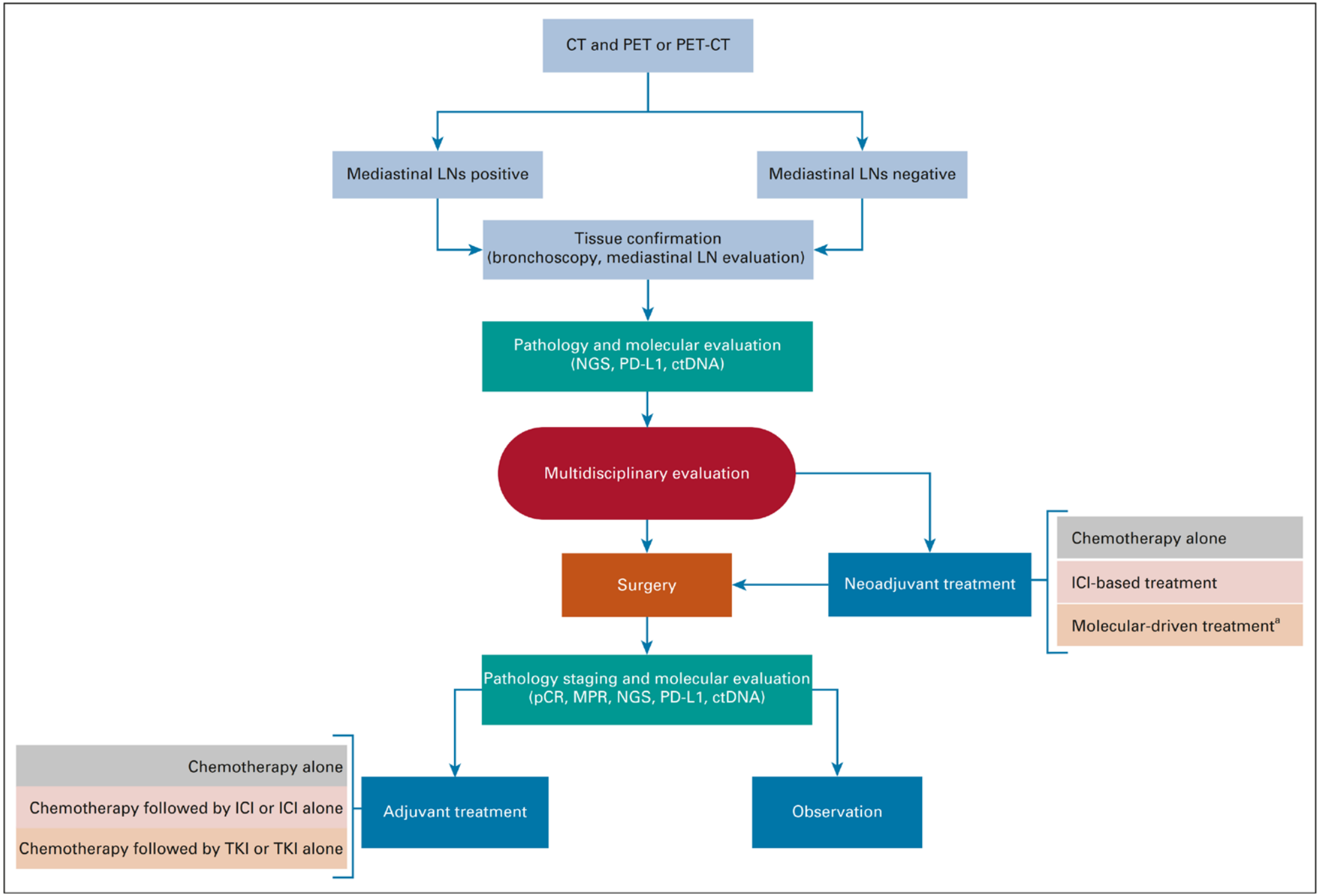




Tan AC et al. J Clin Oncol 2022; 40(6): 611–25



Tan AC et al. J Clin Oncol 2022; 40(6): 611–25

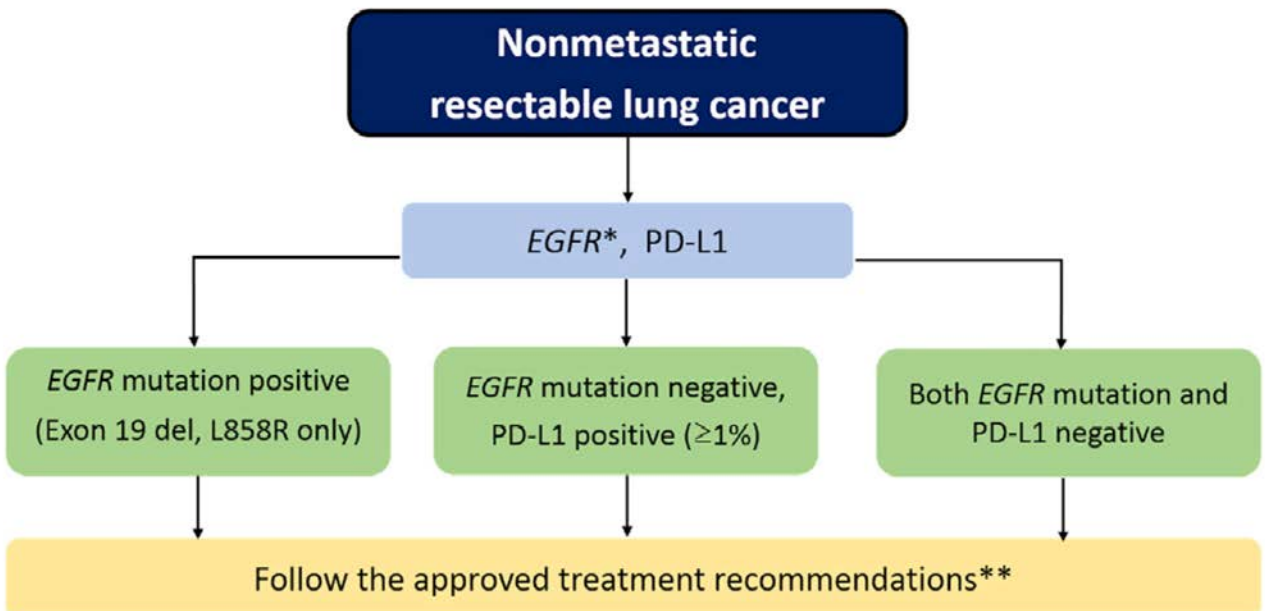


Passaro A, et al. J Clin Oncol 2022; 40(25): 2871-77

ORIGINAL ARTICLE

Expert Consensus Recommendations on Biomarker Testing in Metastatic and Nonmetastatic NSCLC in Asia

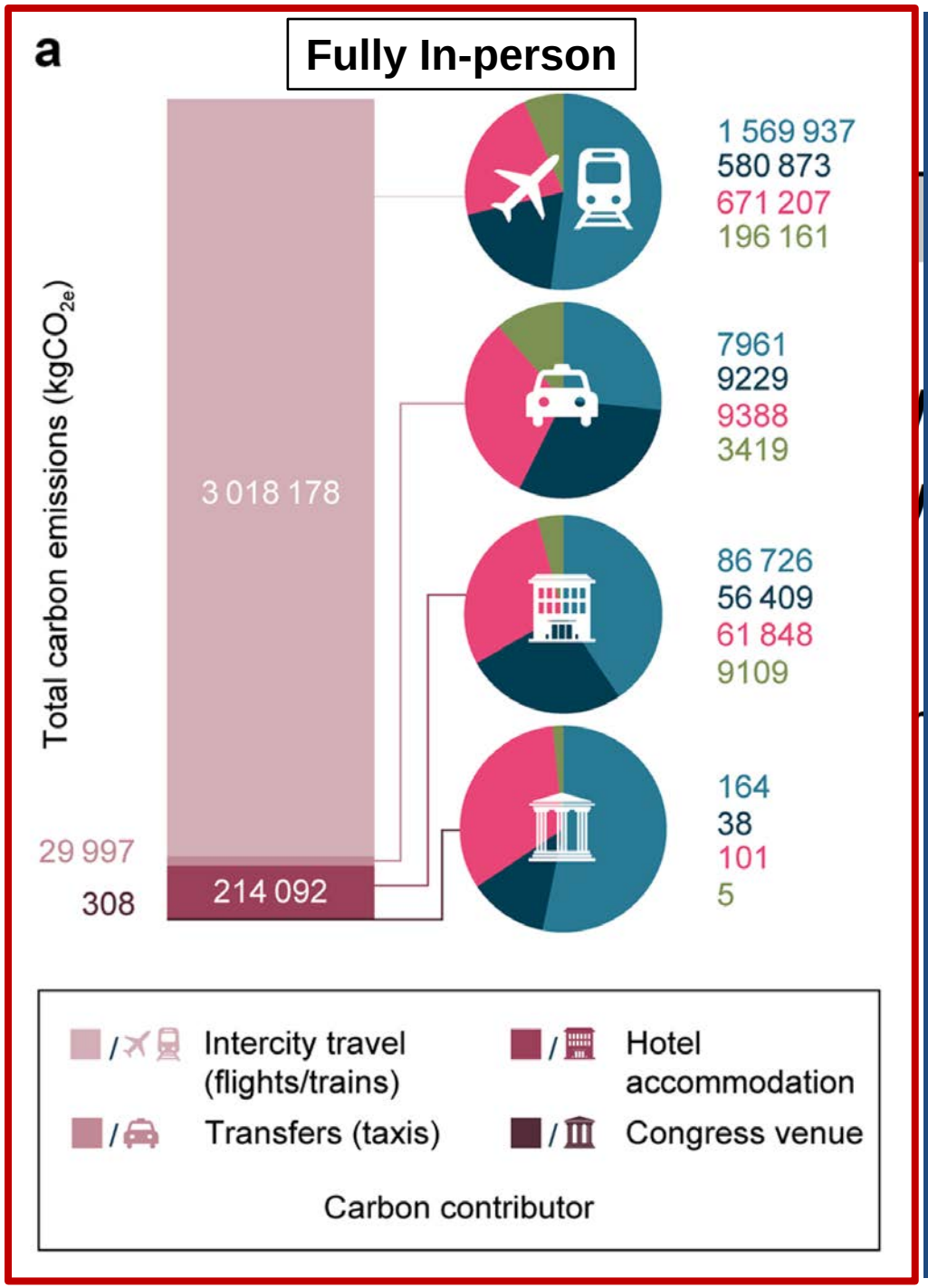
Tetsuya Mitsudomi, MD, PhD,[a,*] Daniel Tan, MRCP, PhD,[b] James Chih-Hsin Yang, MD, PhD,[c] Myung-Ju Ahn, MD, PhD,[d] Ullas Batra, MD, DM, ECMO,[e] Byoung-Chul Cho, MD, PhD,[f] Gerardo Cornelio, MD,[g] Tony Lim, FRCPath, FRCPA,[h] Tony Mok, MD, FRCPC, FASCO,[i] Kumar Prabhash, MD, DM, ECMO,[j] Thanyanan Reungwetwattana, MD, MSc,[k] Sheng-Xiang Ren, MD,[l] Navneet Singh, MD, DM,[m] Shinichi Toyooka, MD, PhD Yi-Long Wu, MD,[o] Pan-Chyr Yang, MD, PhD,[p] Yasushi Yatabe, MD, PhD[q]



*if adenocarcinoma component is present

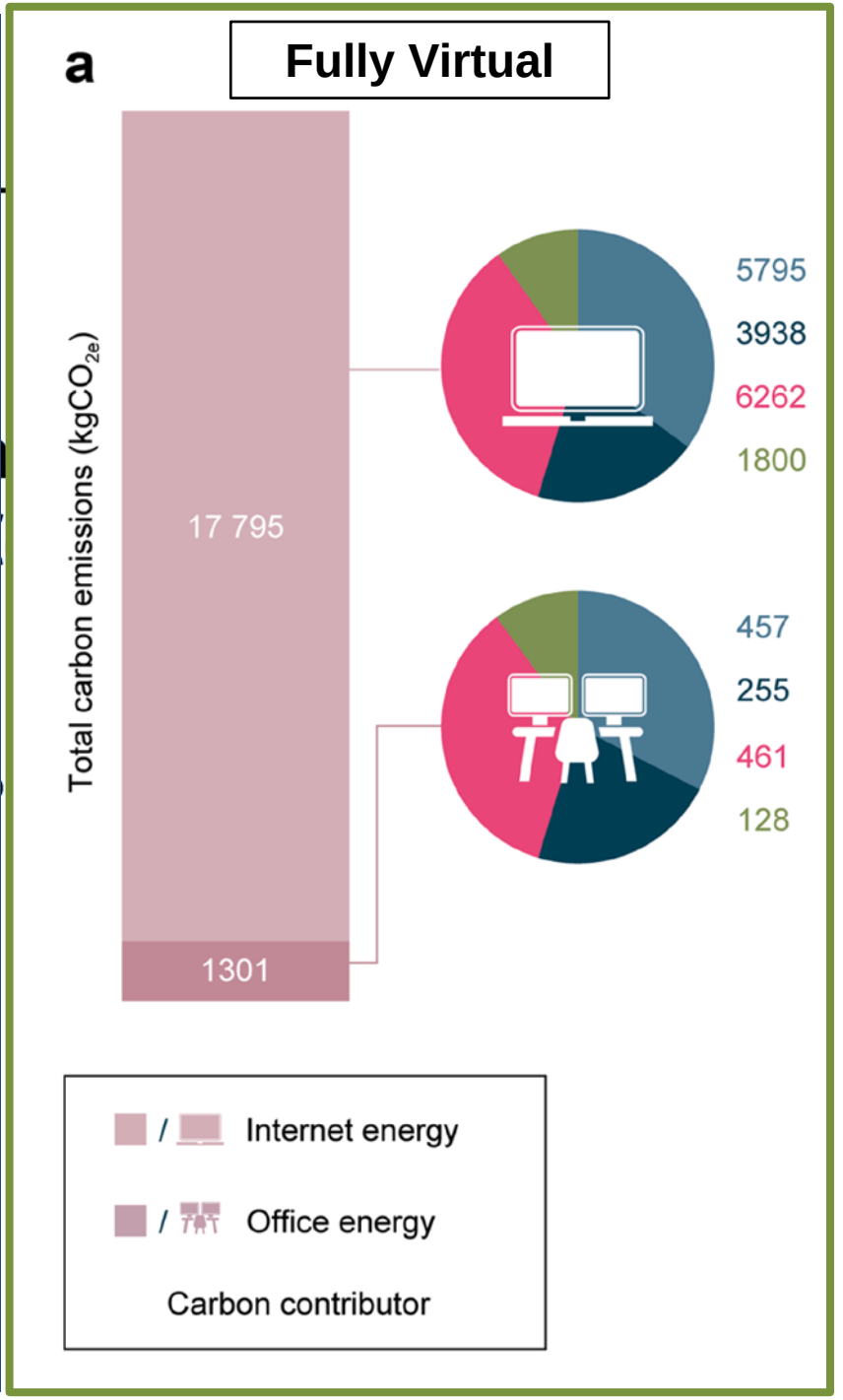
**According to the local protocols, treatment and clinical trials if available

Before We Stop



Can we move to hybrid mode as default for the sake of the planet?

For ourselves, our children & future generations?




Climate change is the
greatest threat of our time.
Gina McCarthy
quotefancy


Climate change is real. It is happening right now. It is the most urgent threat facing our entire species, and we need to work collectively together and stop procrastinating.
Leonardo DiCaprio
quotefancy

‘Earthshot’

Image credit: WallpaperCave