REUNIÓN **STREAMING**

Añade esta fecha
a tu calendario

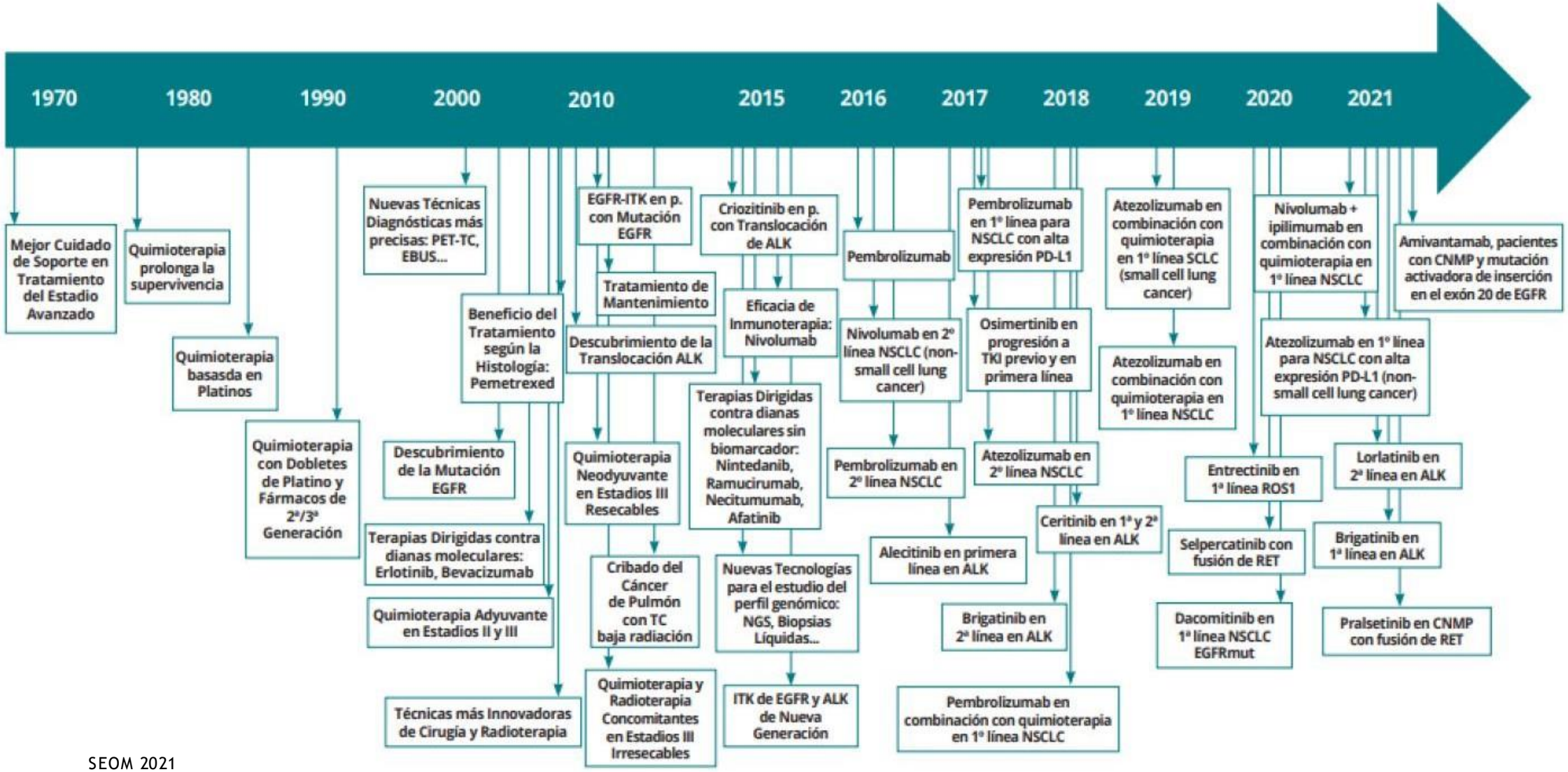
DICIEMBRE 15
De 16:00h a 18:00h

Novedades y Claves en Cáncer de Pulmón 2021

PROGRAMA **CIENTÍFICO**

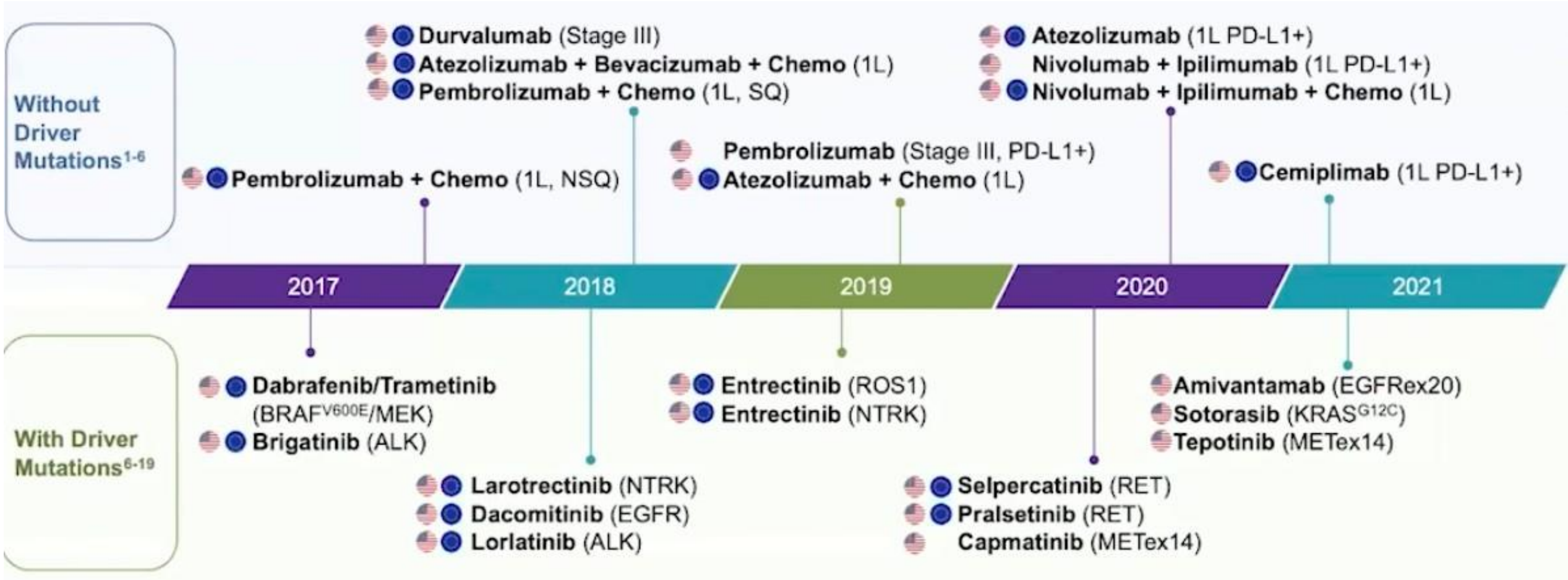
16:00 - 16:20	**Introducción**	Dr. Carlos Camps Hospital General Univ. de Valencia
16:20 - 16:40	**Biomarcadores pronósticos**	Dra. Paloma Martín Hospital Clínico Univ. de Valencia
16:40 - 17:00	**Estadios iniciales y enfermedad localmente avanzada**	Dr. José Miguel Sánchez Hospital Univ. de la Princesa, Madrid
17:00 - 17:20	**Enfermedad metastática (incluyendo inmunoterapia)**	Dra. Gretel Benítez Complejo Hospitalario Univ. Insular de las Palmas
17:20 - 17:40	**Cáncer de pulmón microcítico y otros tumores**	Dr. Joaquín Mosquera Hospital Univ. de A Coruña
17:40 - 18:00	**Conclusiones**	Dr. Joaquín Casal Complejo Hospitalario Univ. de Vigo

Avances en Cáncer de Pulmón

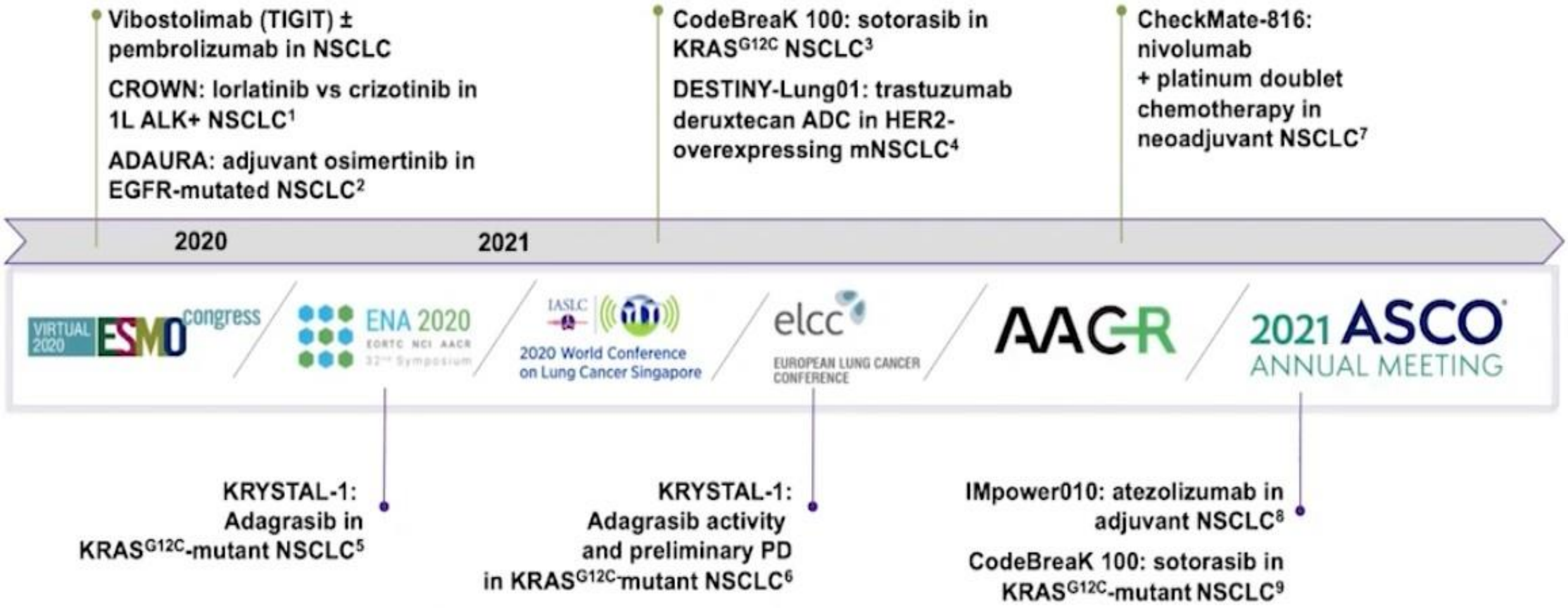


SEOM 2021

Avances en el cancer de pulmón en los últimos 5 años



Avances en el cancer de pulmón en el último año

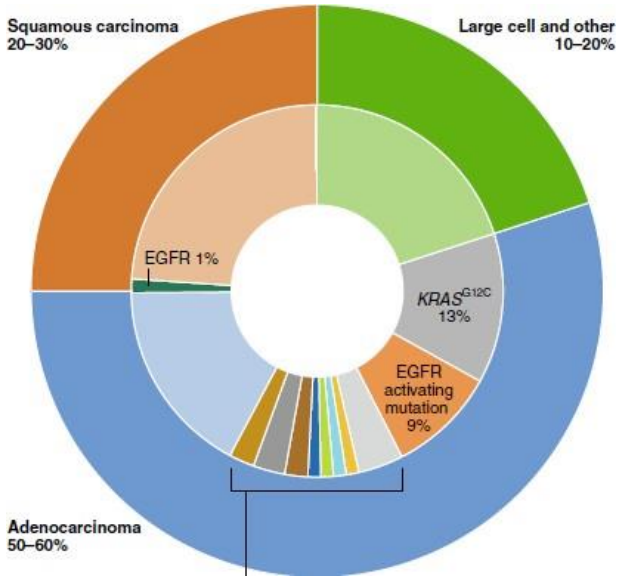


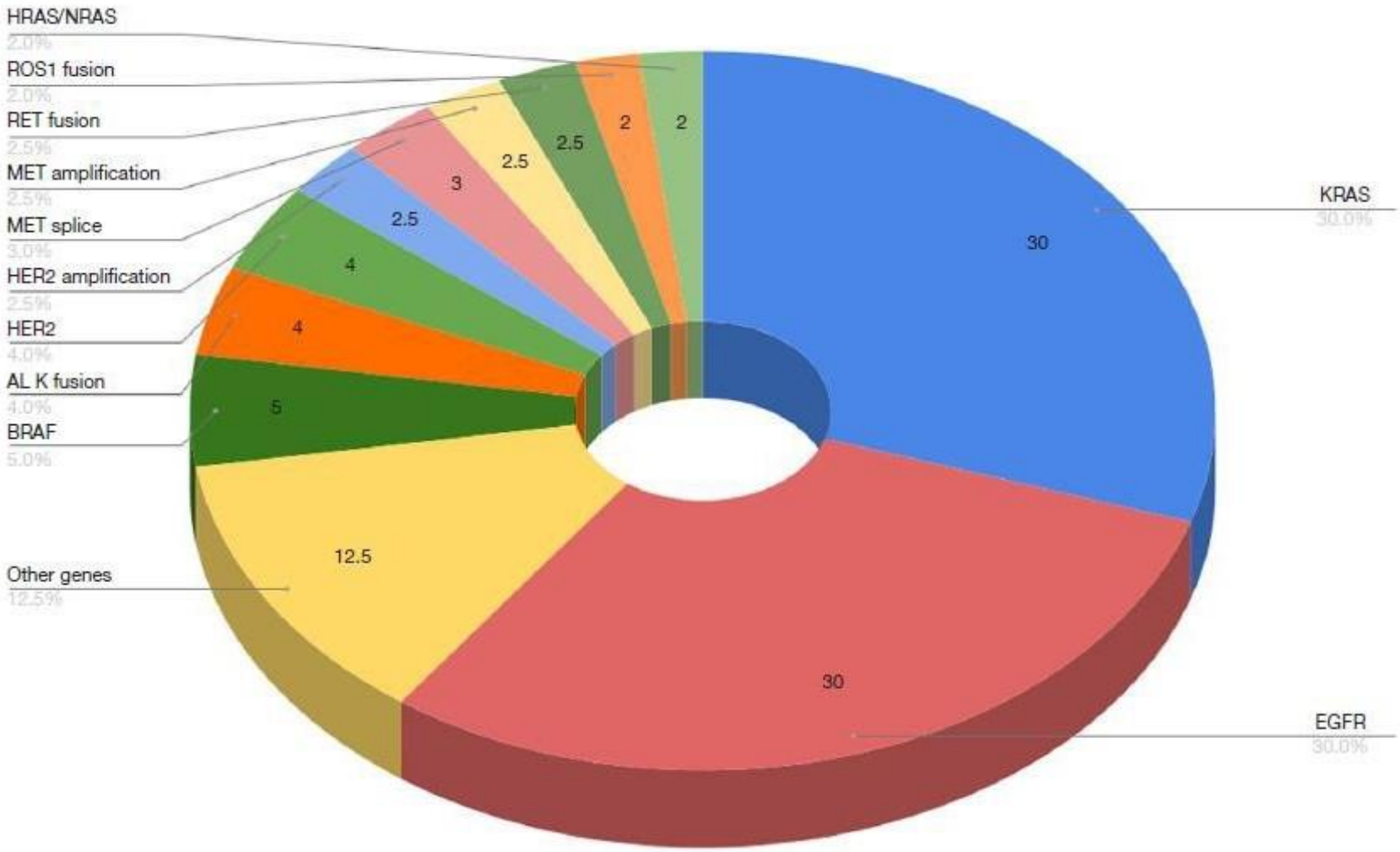
Avances para aumentar la supervivencia

TRATAMIENTO DEL CÁNCER DE PULMÓN NO MICROCÍTICO

- Tumores con mutación tratable
- Inmunoterapia

Cáncer de Pulmón con mutación driver





Wang M. Nature Med 2021

Overcoming EGFR TKI Resistance: A Focus of Many Ongoing Studies

Resistance mechanisms can be on- or off-target

On-target mechanisms affect the *EGFR* gene directly; off-target mechanisms, via alteration of another gene, eg, MET amplification, result in by-pass of the EGFR inhibitory activity of third-generation EGFR TKIs

Resistance mechanisms determine treatment approach

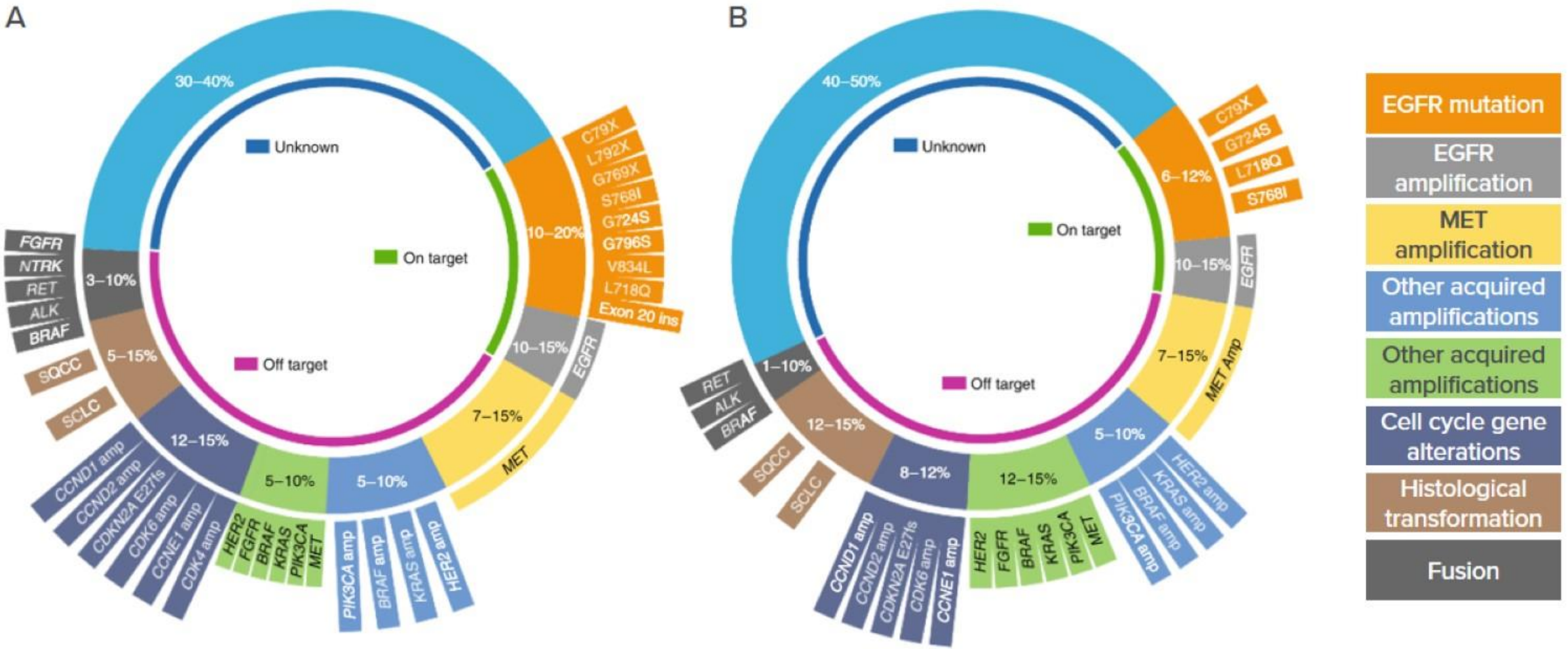
Different approaches to therapy selection and sequencing are being applied across different mechanisms of EGFR TKI resistance and evidence on efficacy is accumulating

Latest clinical data on overcoming resistance to EGFR TKIs have been presented at recent annual meetings

9 abstracts will be covered during this discussion

Biology of Resistance to Osimertinib

Resistance mechanisms arising after second-line (A) and first-line (B) osimertinib therapy



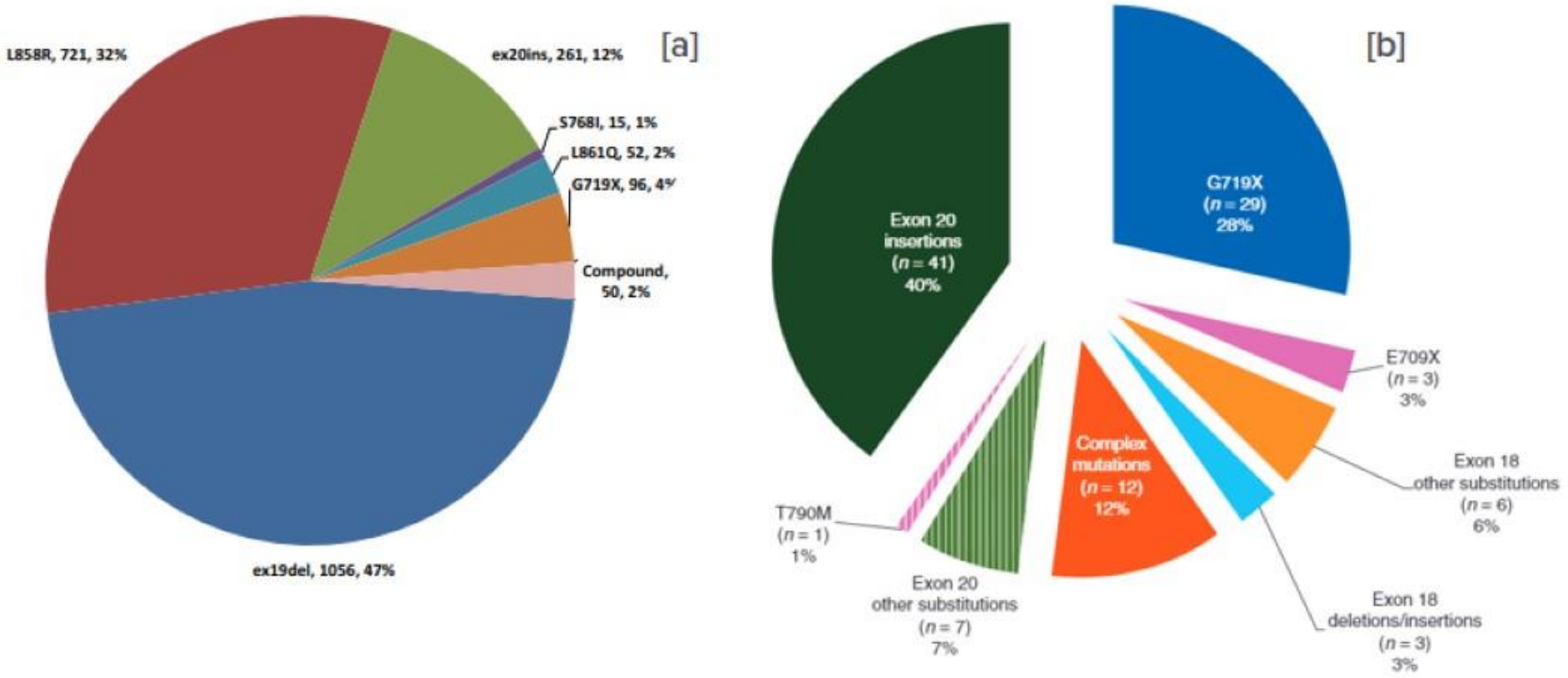
Passaro A, et al. *Nat Cancer*. 2021;2:377-391.

Acquired TKI Resistance: Presentations of Recent Data

EGFR/MET	HER3	MET	RET
▪ CHRYSALIS Phase 1, Amivantamab + Lazertinib[a]	▪ U31402-A-102 Phase 1, Patritumab deruxtecan (HER3-DXd)[c]	▪ INSIGHT 2 Phase 2, tepotinib + osimertinib[d]	▪ Case presentation, selpercatinib + osimertinib to overcome osimertinib resistance[e]
▪ CHRYSALIS-2 Phase 1/1b, Amivantamab + Lazertinib[b]			

a. Bauml J, et al. ASCO® 2021. Presentation 9006; b. Shu CA, et al. ASCO® 2021. Presentation TPS9132; c. Jänne PA, et al. ASCO® 2021. Presentation 9007; d. Zhu VW, et al. ASCO® 2021. Presentation TPS9136; e. Kim L, et al. ASCO® 2021. Presentation 3046.

EGFR Exon 20 Insertions Background



- *EGFR* exon 20 ins represent ~10% of *EGFR* mutation-positive NSCLC[a,c]
- Third most common *EGFR* mutation subtype, after exon 19 del and L858R (in exon 21)
- Most *EGFR* exon 20 ins are activating but not sensitizing to traditional EGFR TKIs
- Conventional chemotherapy is a first-line option; more recently amivantamab specifically approved by FDA for this indication[d]

a. Riess JW, et al. *J Thorac Oncol*. 2018;13:1560-1568; b. Beau-Faller M, et al. *Ann Oncol*. 2014;25:126-131.
c. Vyse S, et al. *Signal Transduct Target Ther*. 2019;4:5; d. Rybrevant (amivantamab) [PI]. 2021.

Exon 20 TKI Resistance: Presentations of Recent Data

Amivantamab

- CHRYSALIS Amivantamab in *EGFR* exon 20 ins population vs Real-World treatments[a]

Mobocertinib

- Phase1/2, EXCLAIM and platinum-pretreated population cohorts[b]

Poziotinib

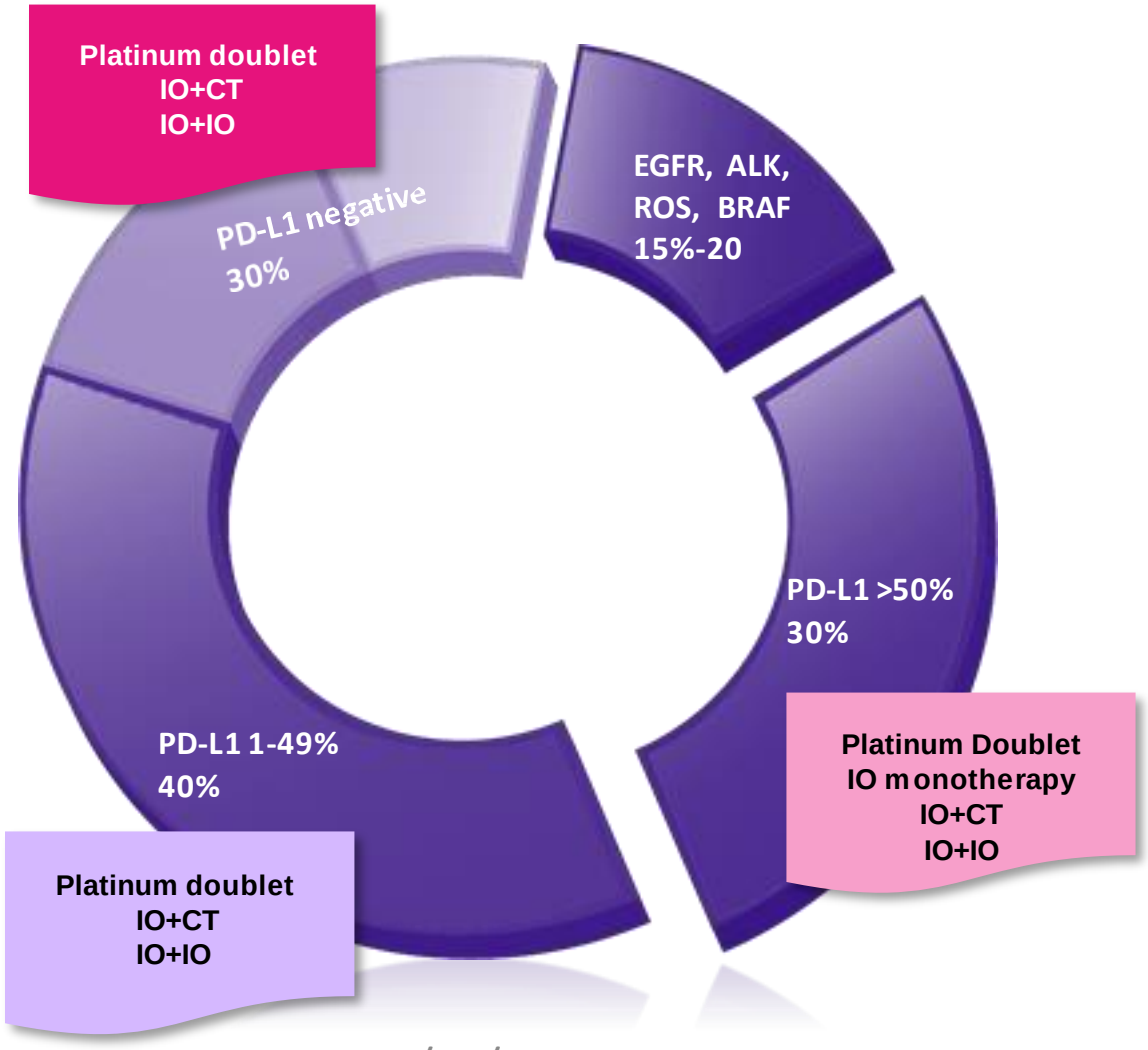
- ZENITH20 Phase 2, CNS activity of poziotinib[c]

DZD9008

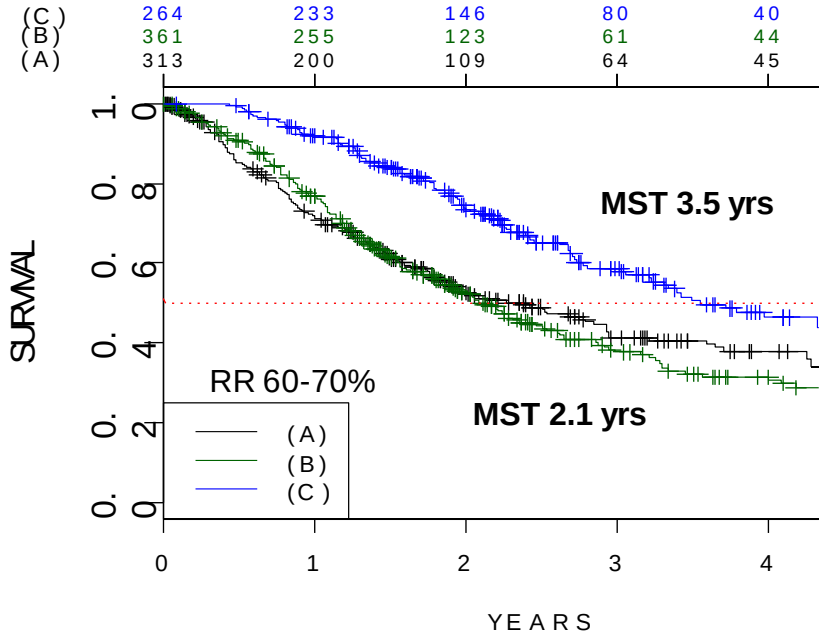
- WU-KONG1 and WU-KONG2 Phase 1, preliminary efficacy and safety results[d]

a. Minchom AR, et al. ASCO® 2021. Poster presentation 9052; b. Ramalingham SS, et al. ASCO® 2021. Poster Discussion presentation 9014; c. Le X, et al. ASCO® 2021. Poster abstract 9093; d. Yang JCH, et al. ASCO® 2021. Oral presentation 9008.

Where are we today…

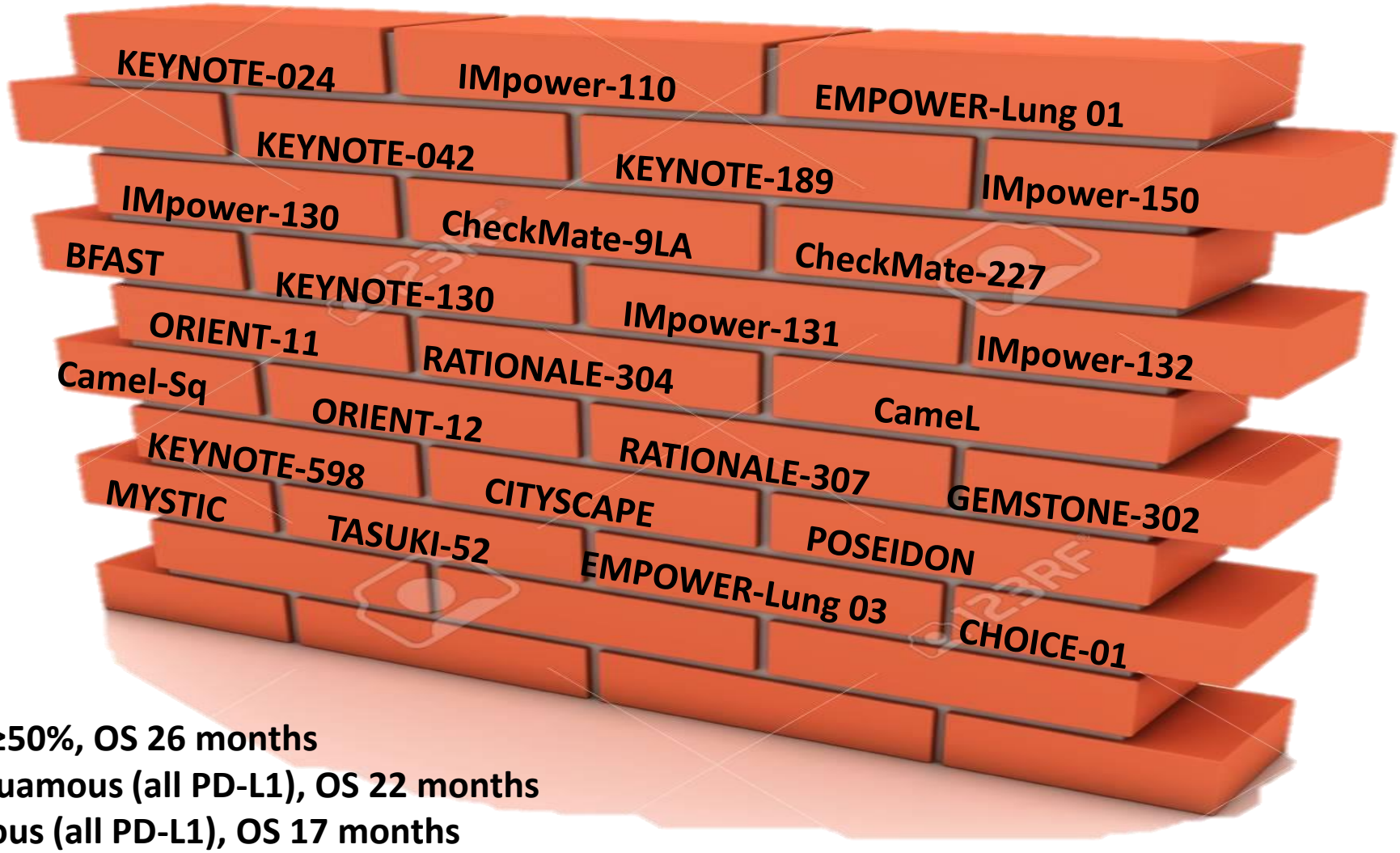


Personalized approach



Kris M, et al. JAMA 2014

A solid wall, but It is not easy to decide…..



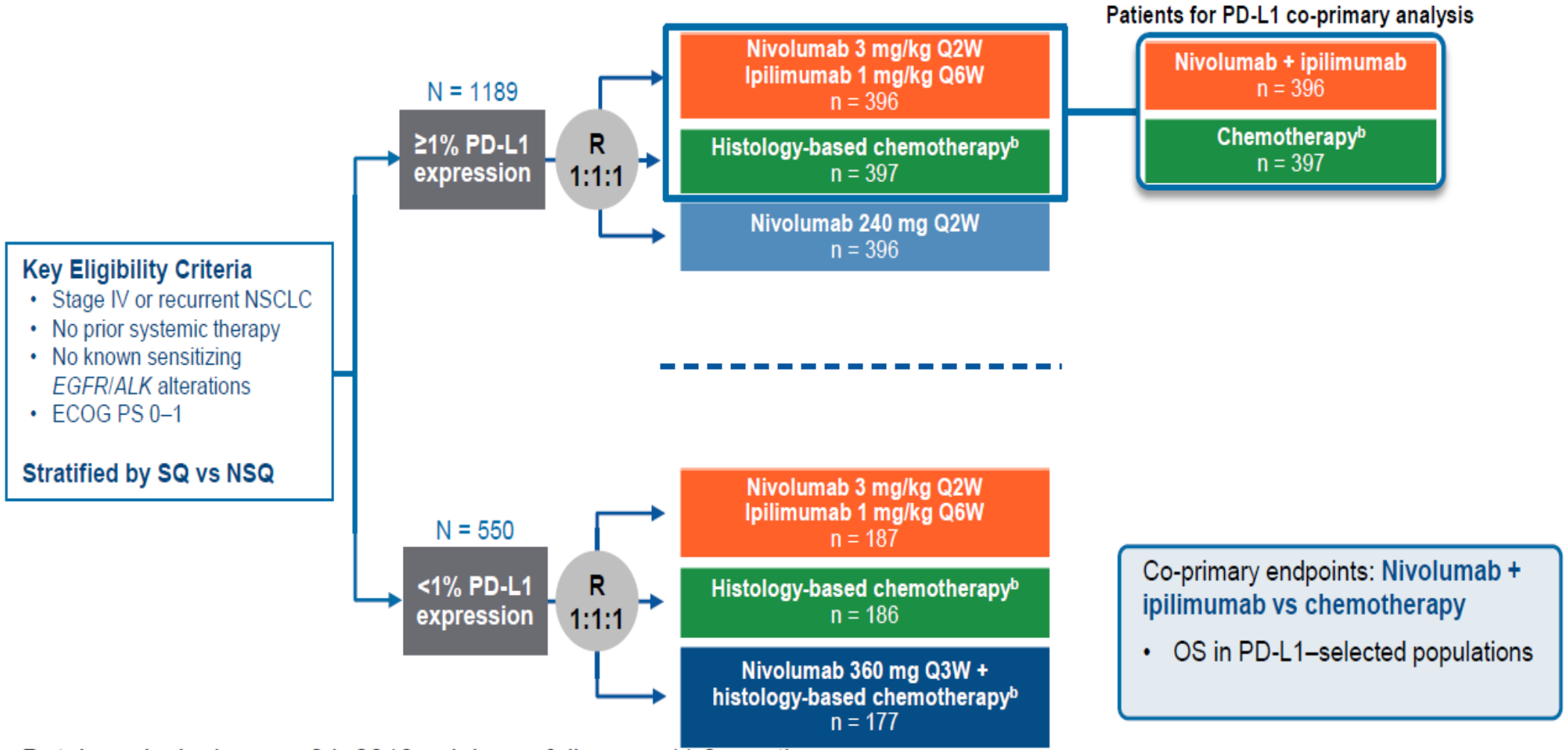
TODAY

PD-L1 ≥50%, OS 26 months

Non-Squamous (all PD-L1), OS 22 months

Squamous (all PD-L1), OS 17 months

CheckMate 227 Part 1 Study Design[a]



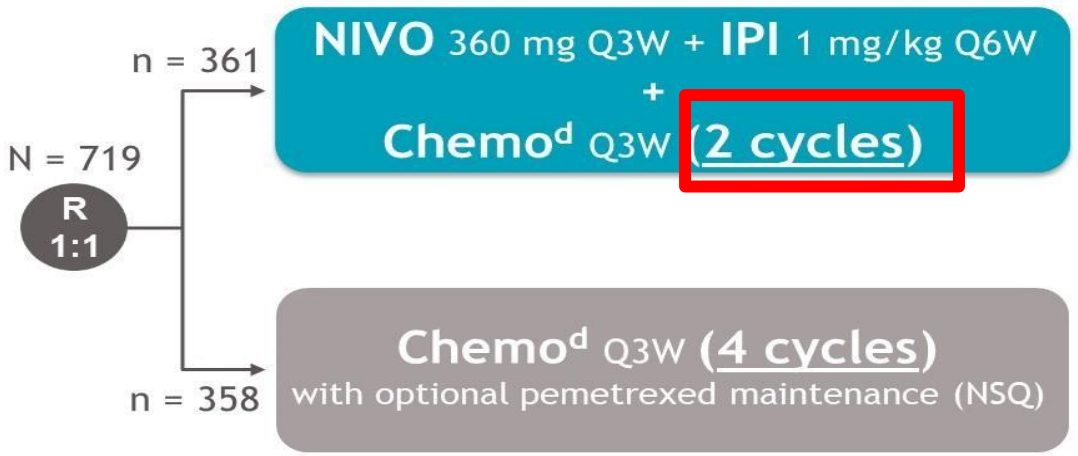
Database lock: January 24, 2018; minimum follow-up: 11.2 months

[a]NCT02477826 [b]**NSQ:** pemetrexed + cisplatin or carboplatin, Q3W for ≤4 cycles, with optional pemetrexed maintenance following chemotherapy or nivolumab + pemetrexed maintenance following nivolumab + chemotherapy; **SQ:** gemcitabine + cisplatin, or gemcitabine + carboplatin, Q3W for ≤4 cycles; [c]The TMB co-primary analysis was conducted in the subset of patients randomized to nivolumab + ipilimumab or chemotherapy who had evaluable TMB ≥10 mut/Mb

CheckMate 9LA study design[a]

Key eligibility criteria
- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No sensitizing *EGFR* mutations or known *ALK* alterations
- ECOG PS 0-1

Stratified by PD-L1[b] (< 1%[c] vs ≥ 1%), sex, and histology (SQ vs NSQ)



Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

Primary endpoint
- OS

Secondary endpoints
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

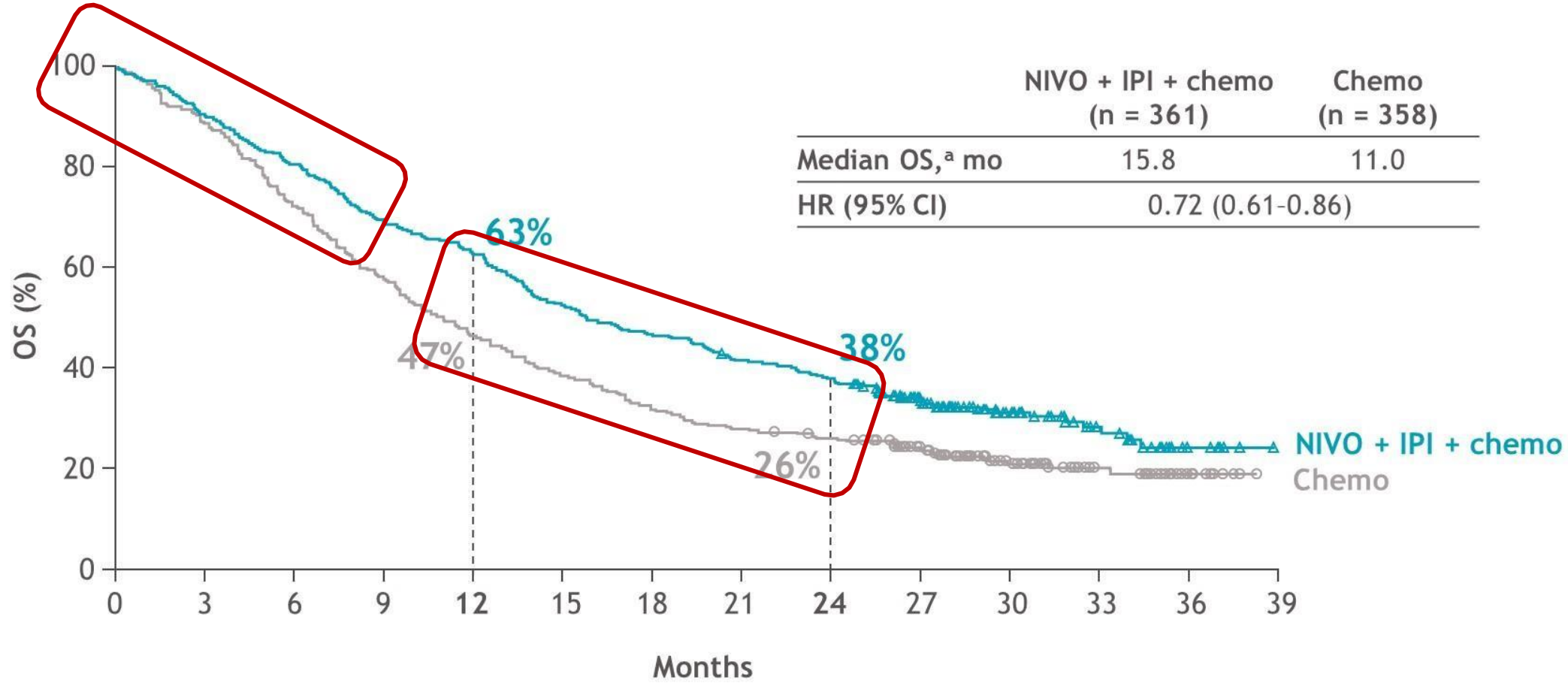
Exploratory endpoints
- Safety

DBL: February 18, 2021; minimum / median follow-up for OS: 24.4 months / 30.7 months.

[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

2-Year update: OS in all randomized patients

	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
Median OS,[a] mo	15.8	11.0
HR (95% CI)	0.72 (0.61-0.86)	

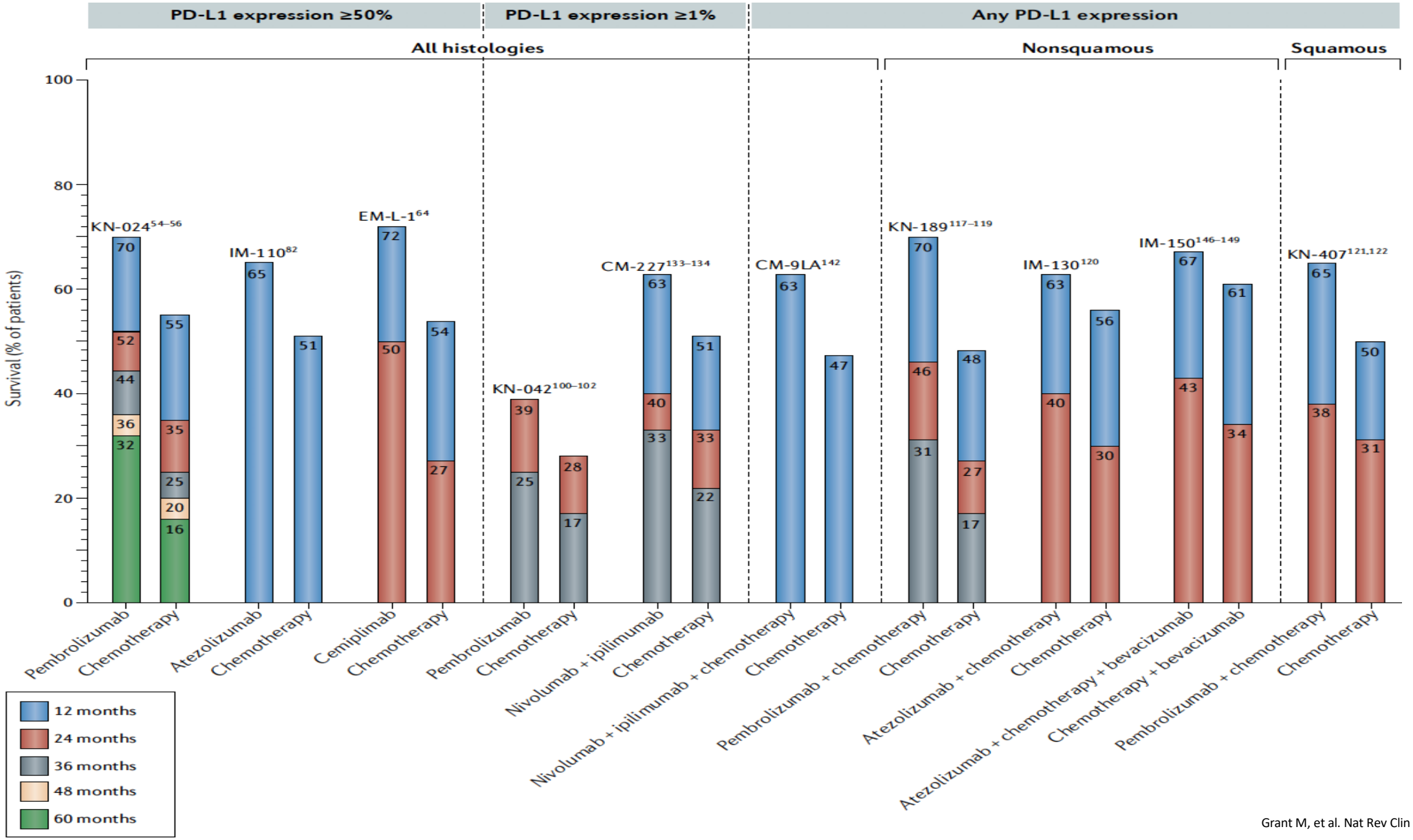


No. at risk														
NIVO + IPI + chemo	361	326	292	250	227	191	170	150	137	95	50	23	7	0
Chemo	358	319	260	208	168	139	115	102	93	69	40	18	8	0

Minimum follow-up: 24.4 months.
[a]95% CI = 13.9-19.7 (NIVO + IPI + chemo) and 9.5-12.7 (chemo).

Reck M, et al. ASCO 2021

WHAT WILL BE THE NEXT IMMUNOTHERAPY COMBINATION?

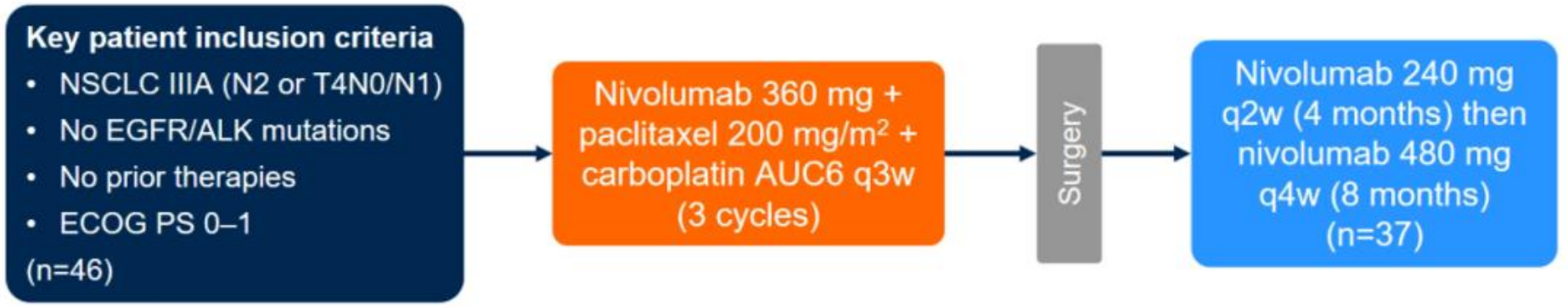


Grant M, et al. Nat Rev Clin Oncol 2021

CÁNCER DE PULMÓN NO METASTÁSICO

OA20.01: Long Term Survival in Operable Stage IIIa NSCLC Patients Treated With Neoadjuvant Nivolumab Plus Chemotherapy - NADIM Study – Provencio M, et al
OA20.02: Pre-Treatment Levels of ctDNA for Long-term Survival Prediction in Stage IIIA NSCLC Treated With Neoadjuvant Chemo-Immunotherapy – Romero A, et al

- **Study objective**
  - To evaluate the efficacy and safety of neoadjuvant nivolumab + chemotherapy in patients with resectable stage IIIA NSCLC along with the prognostic value of pre-treatment levels of ctDNA in the phase 2 NADIM study



Primary endpoint
- PFS

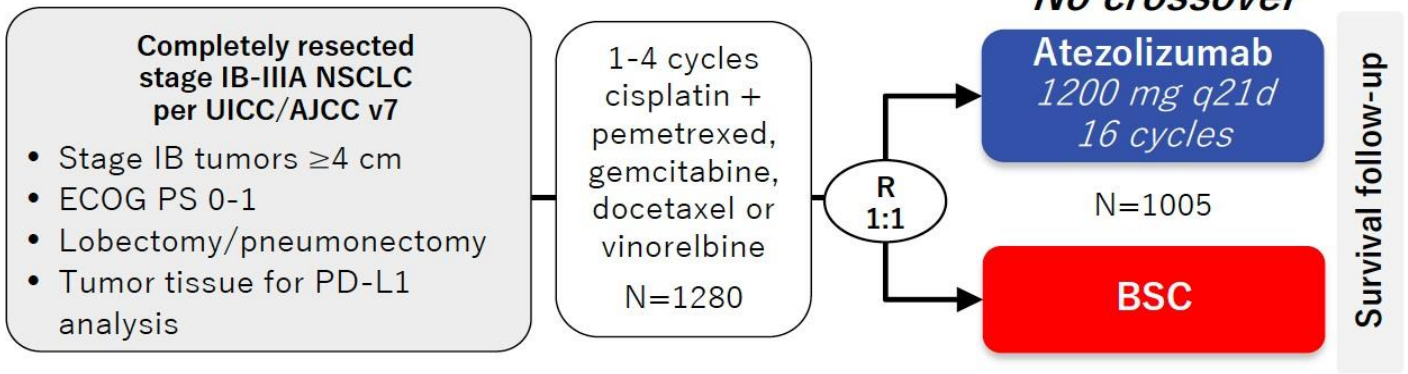
Secondary endpoints
- OS, ORR, cPR, MPR, downstaging rate, complete resection, safety

Exploratory endpoints
- Translational biomarkers, PD-L1, TMB, TILs, ctDNA

Provencio M, et al. J Thorac Oncol 2021;16(suppl):Abstr OA20.01
Romero A, et al. J Thorac Oncol 2021;16(suppl):Abstr OA20.02

IMpower010: Characterization of Stage IB-IIIA NSCLC Patients by Type and Extent of Therapy Prior to Adjuvant

IMpower010 study design

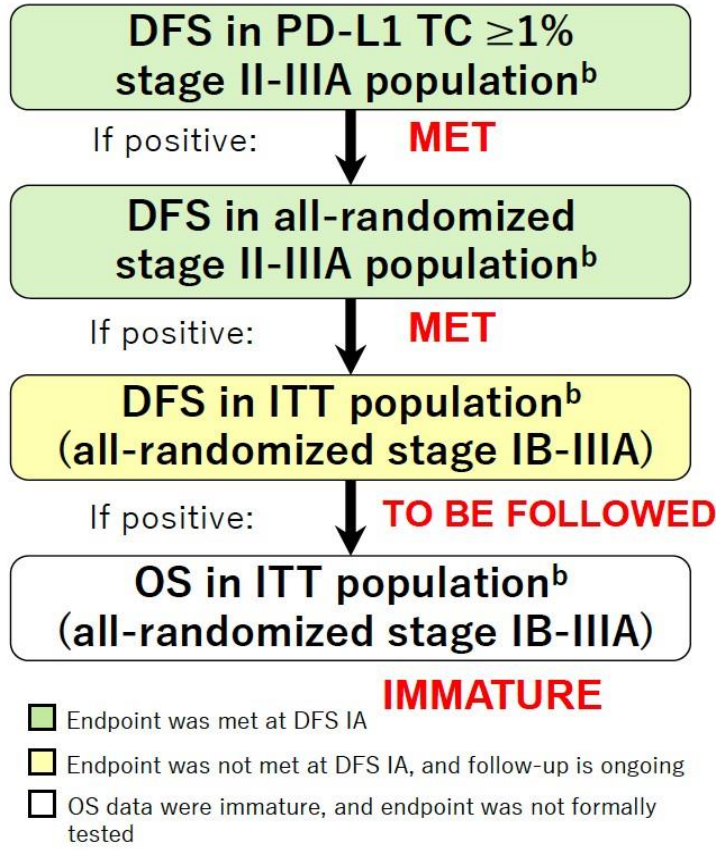


Stratification factors
- Male vs female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  1. PD-L1 TC ≥1% (SP263) stage II-IIIA population
  2. All-randomized stage II-IIIA population
  3. ITT (all-randomized stage IB-IIIA) population

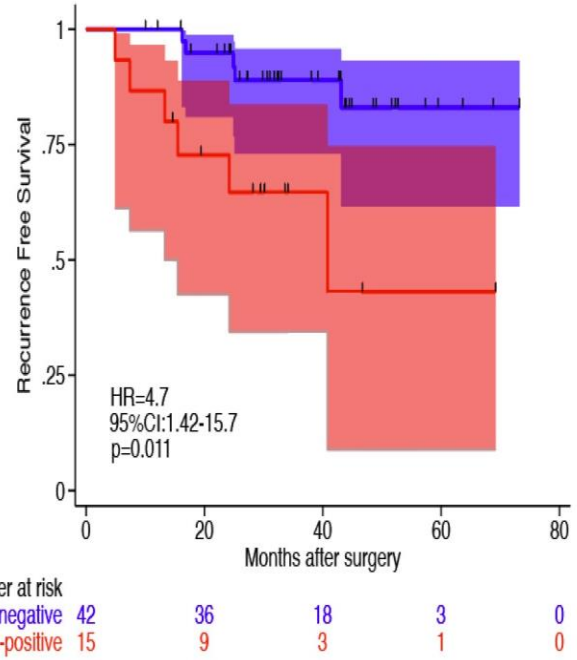
Both arms included observation and regular scans for disease recurrence on the same schedule.
IC, tumor-infiltrating immune cells. [a] Per SP142 assay. [b] Two-sided α=0.05.

Hierarchical statistical testing



Altorki N, et al. PL 02.05

ctDNA detection pre-surgery associated with shorter RFS



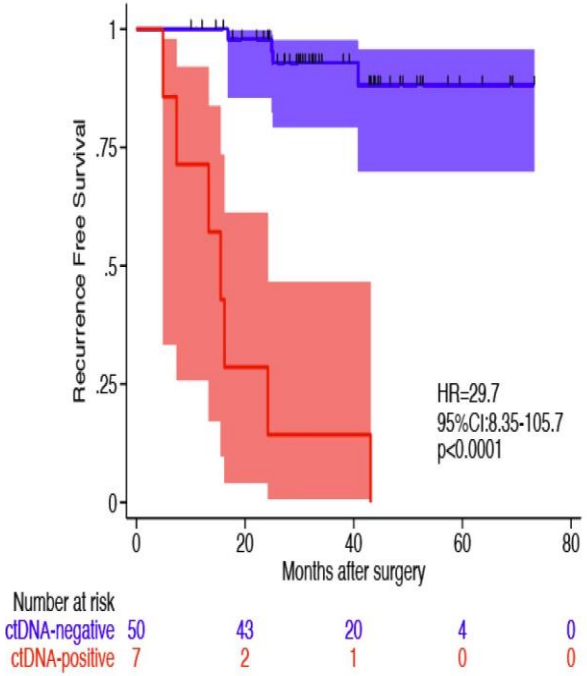
ctDNA status prior to surgery

ctDNA positivity pre-surgery also correlated with

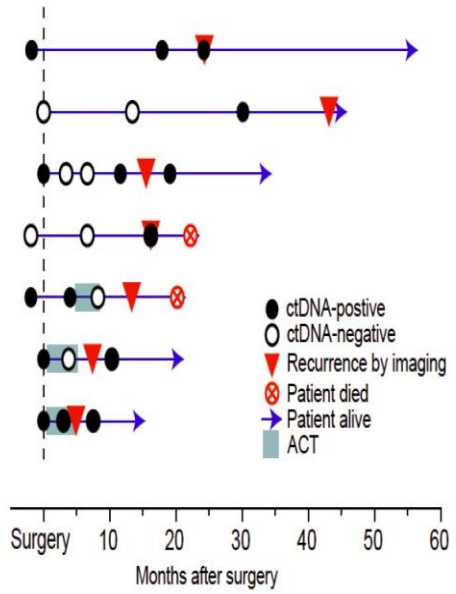
- Higher stage (p<0.0001)
- Lymph node positivity (p<0.0001)

Pre-surgery ctDNA+ (N=15)	N (%)
Stage	
I	7 (47)
II	2 (13)
III	6 (40)
Relapsed	7 (47)
No adjuvant therapy	3 out of 7

Longitudinal ctDNA+ preceded radiological recurrence



Longitudinal ctDNA monitoring



- Median lead time: 3.9 mths
- Longitudinal ctDNA negativity associated with favourable outcomes with NPV of 94% (45/49)

ctDNApositivity (baseline & longitudinal) was associated with relapse in early-stage NSCLC

Molecular recurrence (ctDNA) preceded radiological findings by a median of 3.9 months

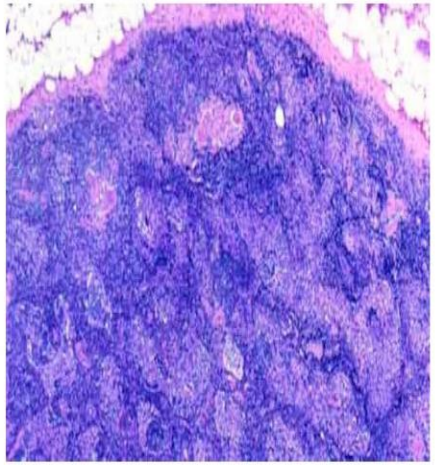
INMUNE CELL PROFILES AS PREDICTORS OF SURVIVAL IN SURGICALLY TREATED NSCLC

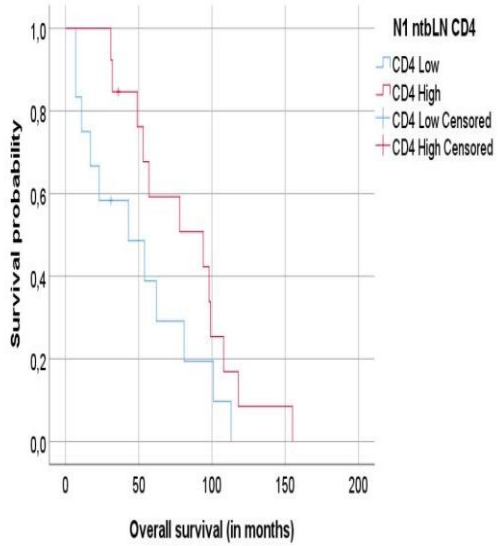
Methods & Outcomes

- Tissues collected:
  - Tumor
  - Affected lymph nodes
  - Unaffected N1 lymph nodes
  - Unaffected N2 lymph nodes
- Investigation of morphology and gene expression analysis
- Outcomes: OS and/or PFS

Source: https://www.minimed.at/medizinische-themen/krebs/lungenkrebs/

Results



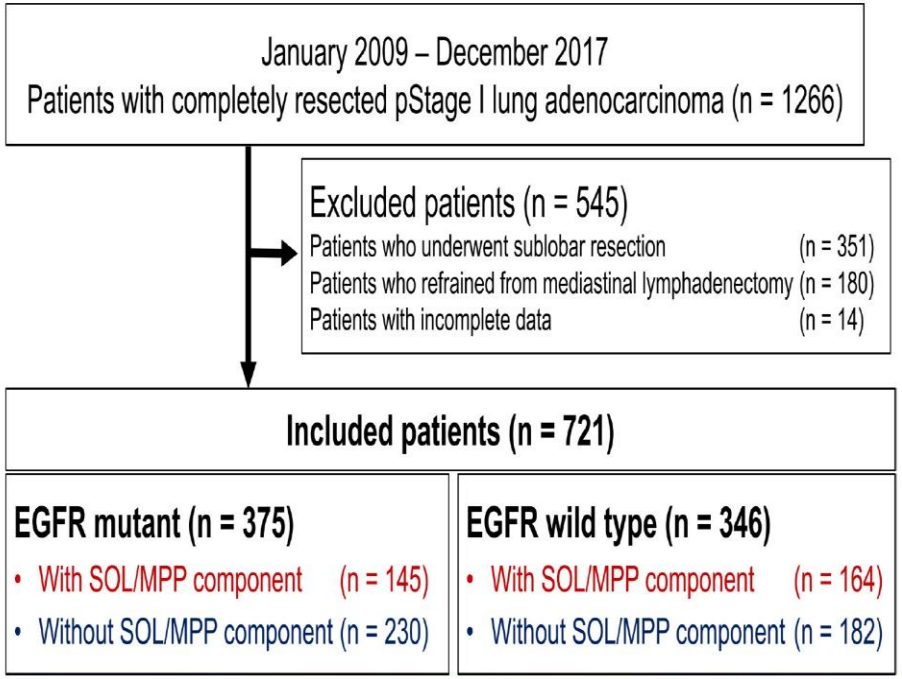


- Sinus histiocytosis and TiL density are associated with PFS and OS, respectively
- CD4 expression in N1 and N2 lymph nodes is associated with PFS and OS, respectively

Sellmer L, et al. MA 08.06

Presence of High-Grade Subtype Predicts Recurrence of Stage I Lung Adenocarcinoma Only in EGFR-Mutated Patients

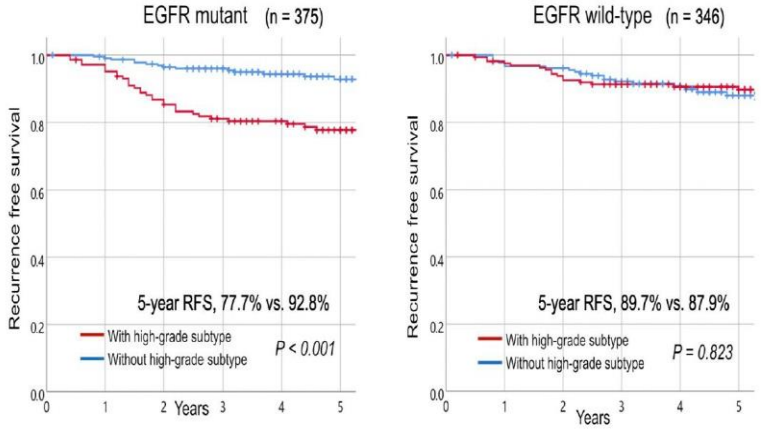
- The OS and RFS of 721 patients with pStage I lung Ad were compared according to EGFR mutation status and presence of > 5% high-grade subtype (solid or micropapillary) component.



'High-grade' subtype associated with worse RFS in pathological stage I, but only in *EGFR*-mutated subgroup

>5% SOL/MPP N=721	*EGFR*-Mt N=375 (52%)	*EGFR*-Wt N=346 (48%)
+	N=145 (39%)	N=164 (47%)
-	N=230 (61%)	N=182 (53%)

Median follow-up 5.2 years

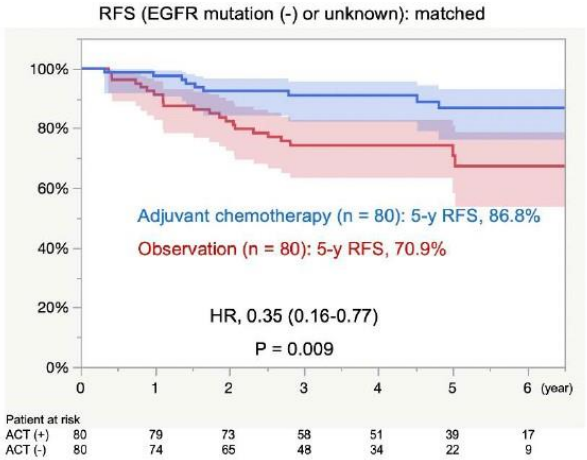


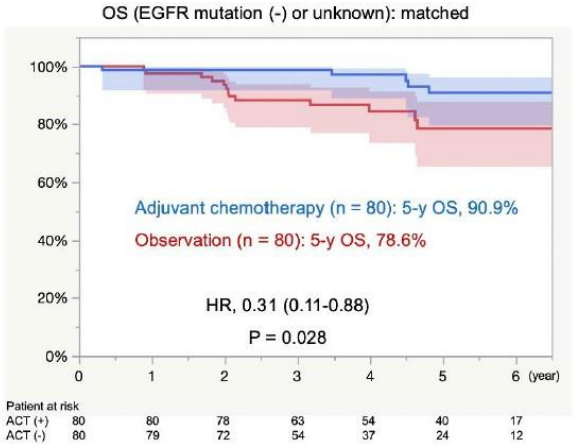
There were no significant differences in OS

- The combination of EGFR mutation and the presence of high-grade subtype predicted recurrence in stage I lung adenocarcinoma.
- Histological subtypes, should be considered when evaluating the risk of recurrence in patients with EGFR-mutated lung adenocarcinoma.

Ichinose J, et al. MA 08.01

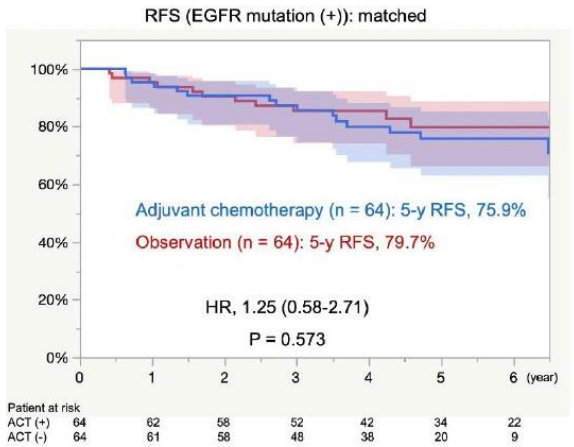
***EGFR* wildtype/?**

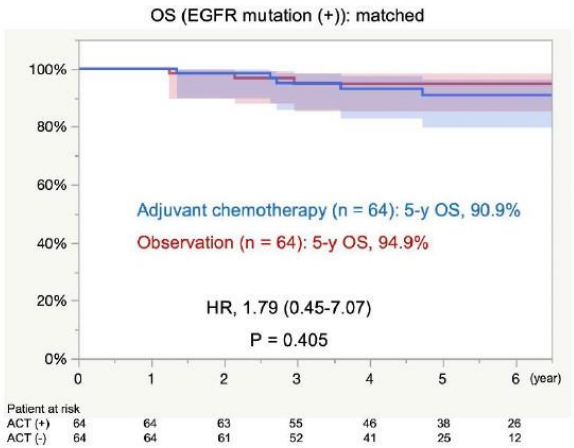




RFS and OS superior with adjuvant chemotherapy

***EGFR* mutant**



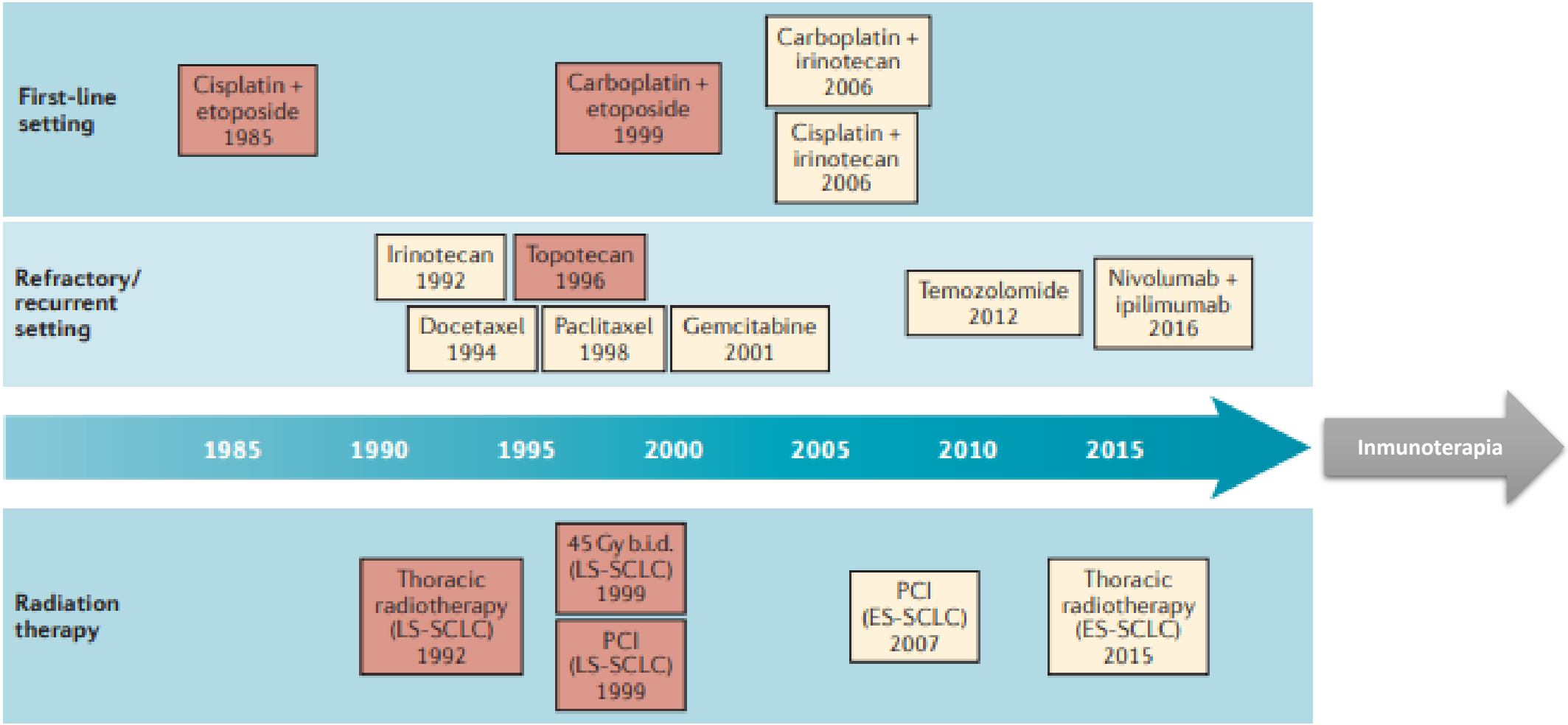


RFS and OS not different with or without adjuvant chemotherapy

- The role of adjuvant chemotherapy for high-risk stage I lung adenocarcinoma was different by the EGFR mutation status.
- EGFR mutation status should be tested in patients with high-risk stage I lung adenocarcinoma to decide the application of adjuvant chemotherapy.

Tsutani Y, et al. MA 08.03

SCLC ….. Pocos avances…

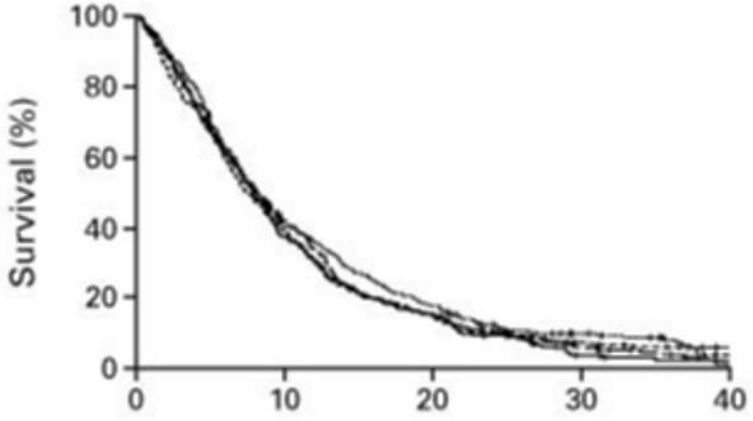


Sabari JK, *et al. Nat Rev Clin Oncol* 2017.

La inmunoterapia ha permitido (junto a la terapia dirigida) mejorar la supervivencia en el NSCLC avanzado

2002 **2010s** **2020s**

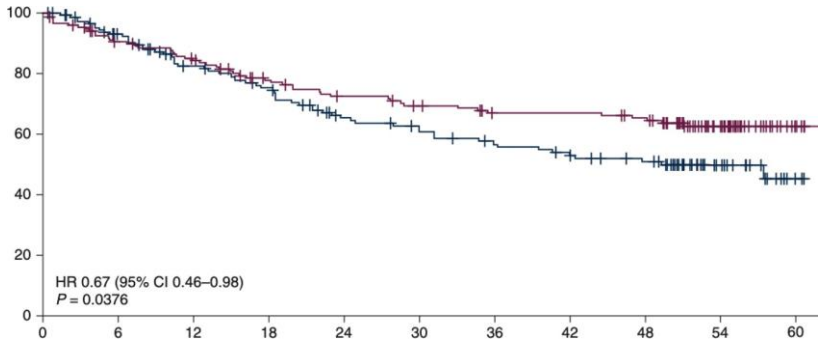
QUIMIOTERAPIA



mOS 16.9m
SG a 5 años <10%

Schiller NEJM 2002

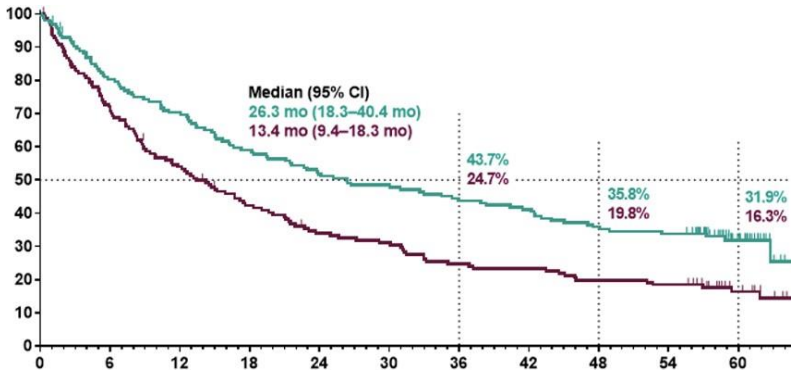
TERAPIA DIRIGIDA



Alectinib
SG a 5 años 62.5%

Mok Ann Oncol 2020

INMUNOTERAPIA



KEYNOTE-024
SG a 5 años 32%

Reck JCO 2020

¿Estamos doblando la curva?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Effect of Advances in Lung-Cancer Treatment on Population Mortality

Nadia Howlader, Ph.D., Gonçalo Forjaz, D.V.M., Meghan J. Mooradian, M.D.,

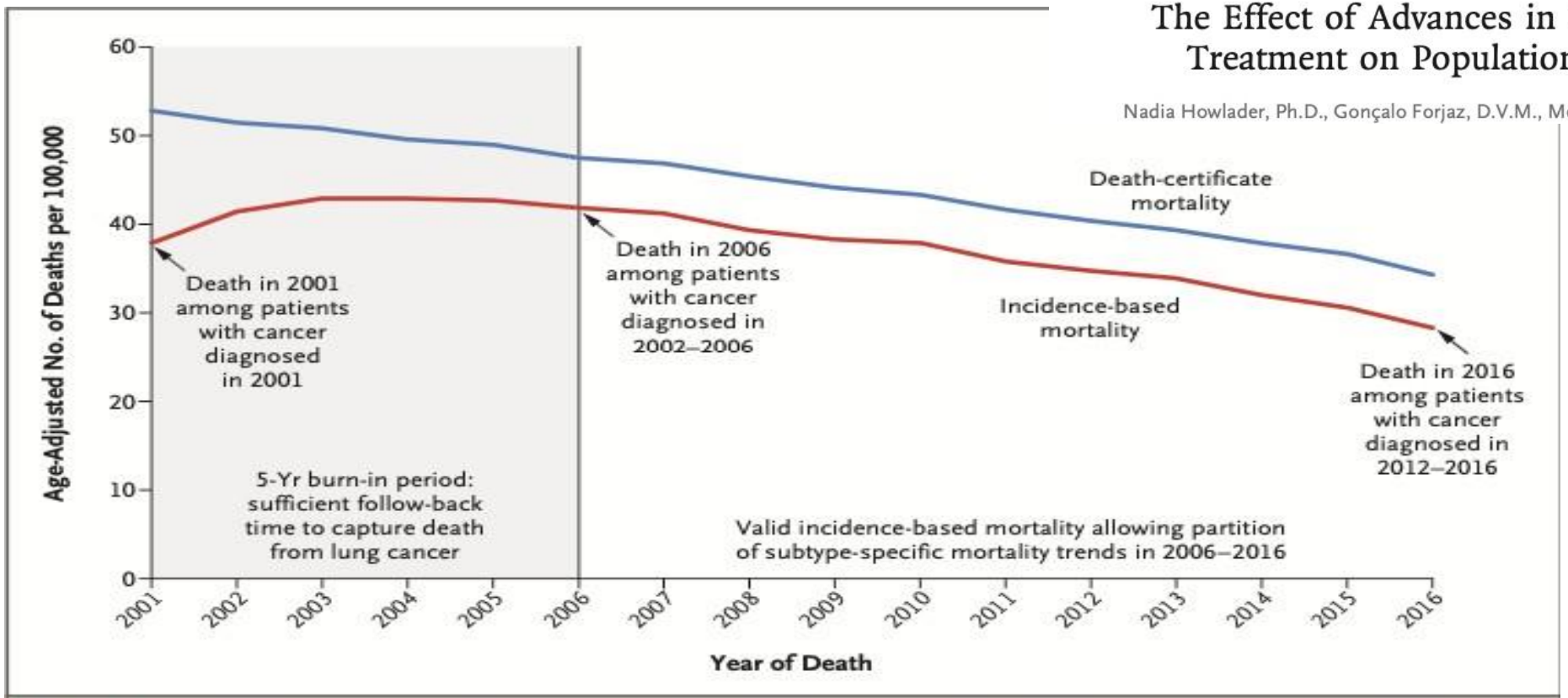


Figure 1. Mortality Estimates Based on Data from Death Certificates and on Incidence among Patients with Lung or Bronchus Cancer.

N Engl J Med 383;7 August 13, 2020