

# Overview of Current Clinical Trials for Early Stage Lung Cancer

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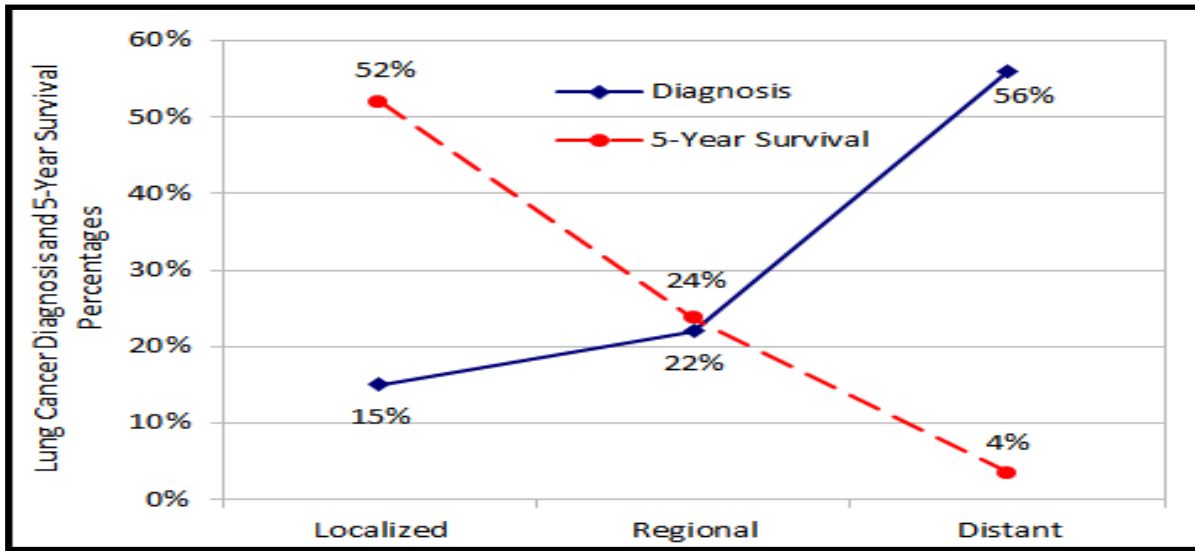
**Center for Thoracic Oncology**



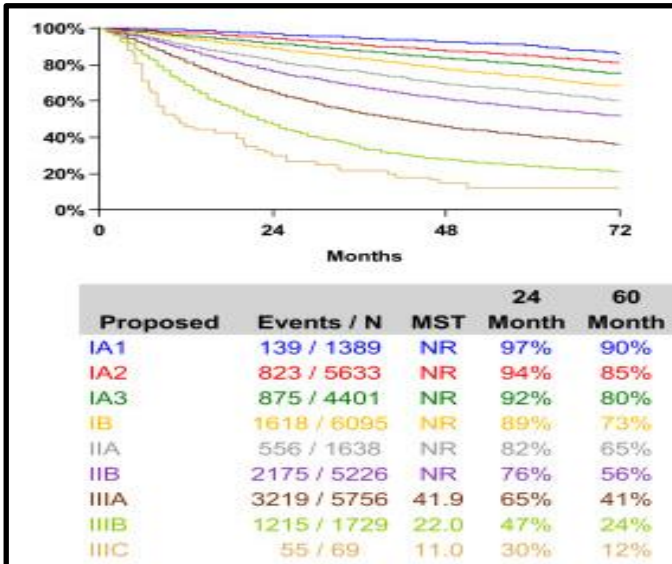
**Mount  
Sinai**

*The Tisch Cancer Institute*

# Lung Cancer Diagnosis and Survival by Stage

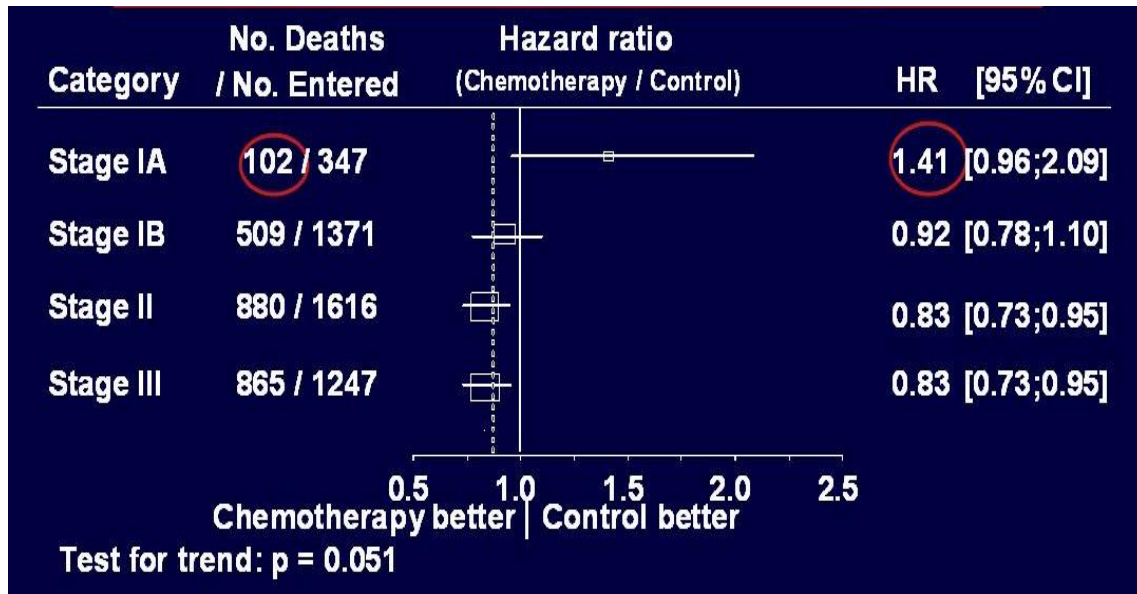


- ▶ **Early Stage (Resectable) approx 25-30% of NSCLC at Diagnosis**
- ▶ **Best chance for long-term survival and cure**
- ▶ **High rates of recurrence despite complete resection**
- ▶ **Reason for Recurrence**
  - **Occult micro-metastatic disease**
  - **Tumor seeding during surgery**
- ▶ **Majority of Recurrence is Distant**



Surgical Stage	Recurrence	
	Local	Distant
1A	10%	15%
1B	10%	30%
2A	12%	40%
2B	12%	40%
3A	15%	60%

# Role of Adjuvant Chemotherapy to Reduce Risk of Recurrence

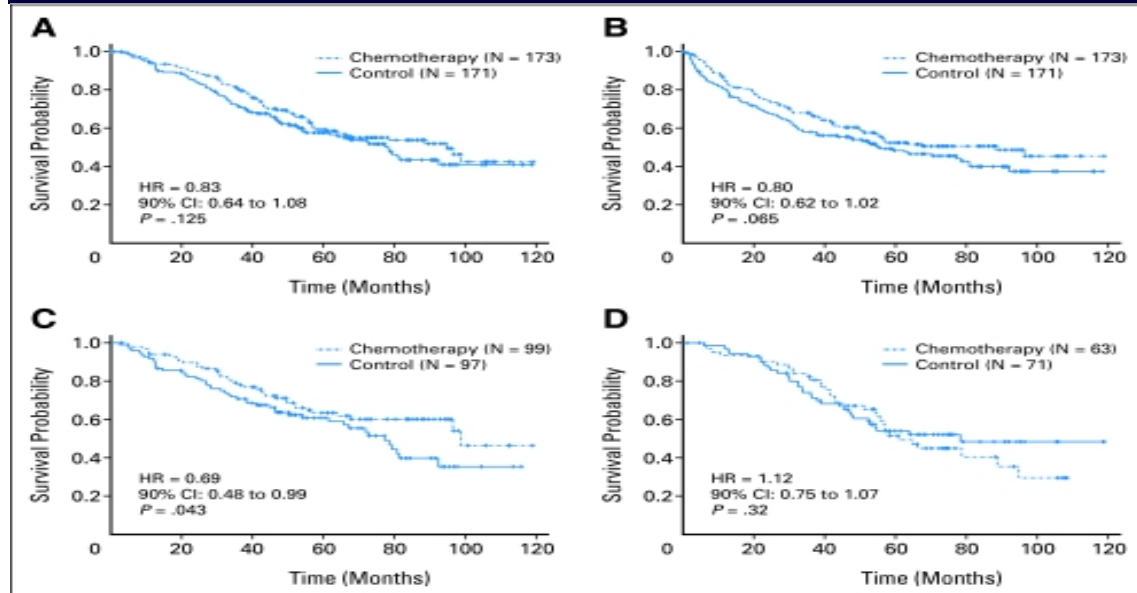


▶ **LACE Meta-analysis: 4584 patients from 5 RCTs**

▶ **5.4% absolute reduction of death at 5 years**

▶ **Stage 2 and 3 had most benefit**

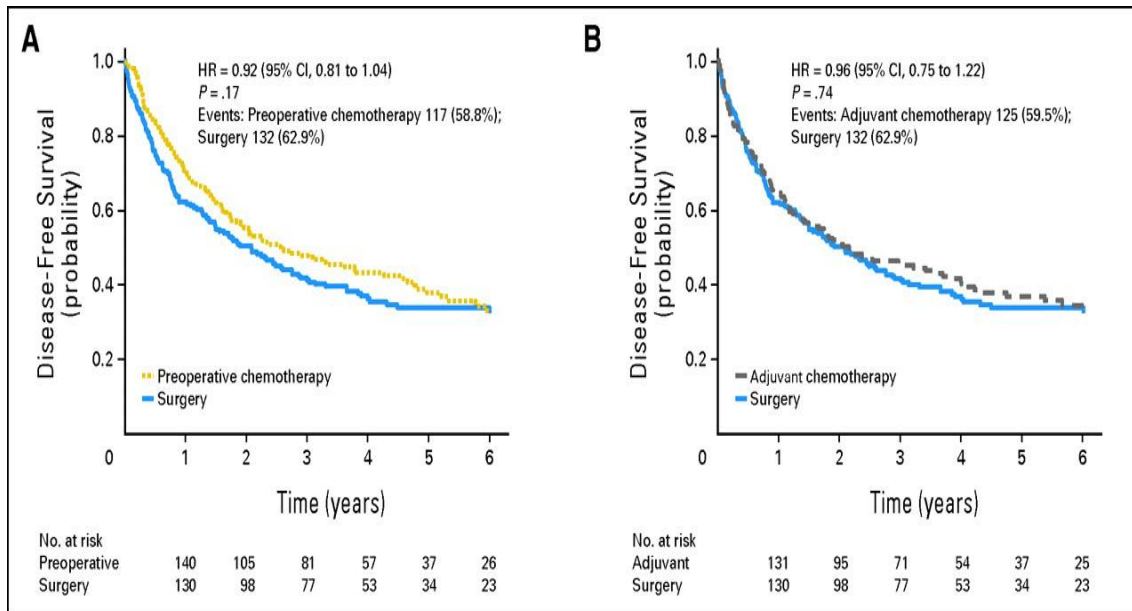
▶ **SOC:  $\geq 4$ cm tumors are considered for adjuvant platinum-based chemotherapy**



# Neo-adjuvant vs Adjuvant Treatment

## ▣ NATCH

- No difference in survival
- Neo-adj received more chemo without affecting surgery



## Neo-Adjuvant

### Advantages

### Disadvantages

Improved treatment delivery/better compliance

Treatment-related toxicities can delay surgery

Prevention or early treatment of micro-metastatic disease

Treatment-related changes may complicate the surgery

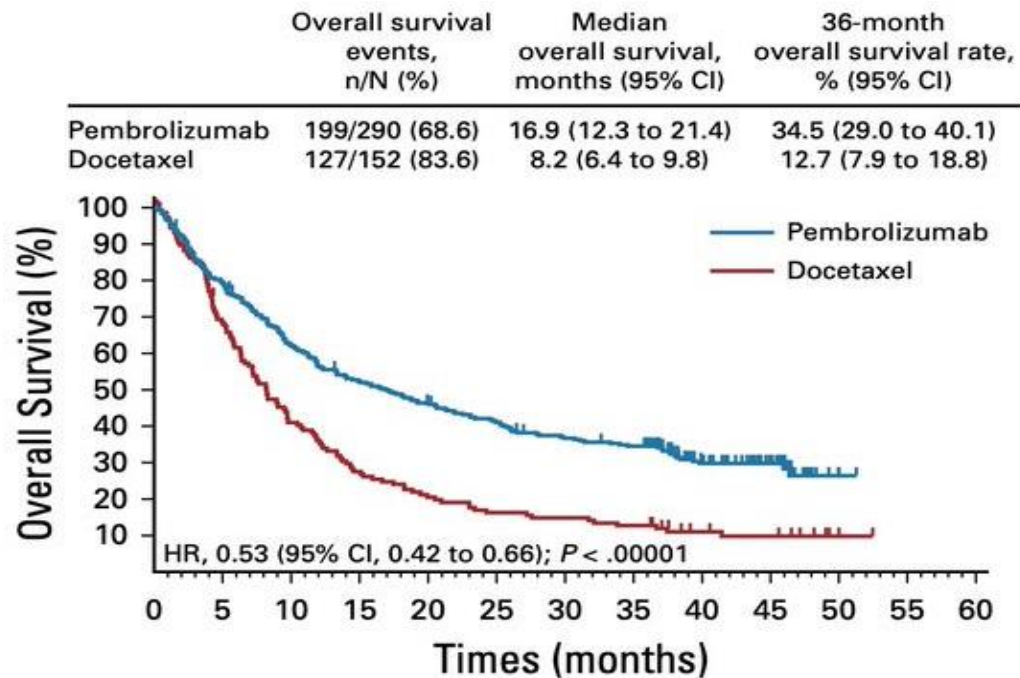
Tumor down-staging

Disease progression through treatment

In vivo assessment of treatment sensitivity

Patient anxiety

## Immunotherapy

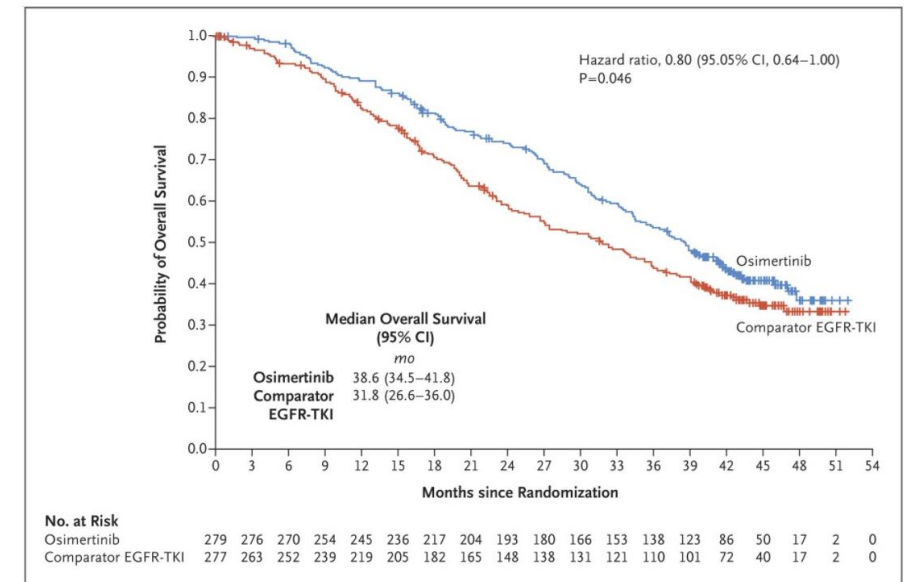


No. at risk:

Pembrolizumab	290	229	178	149	131	115	101	94	50	26	1	0	0
Docetaxel	152	97	58	39	29	23	21	18	10	8	1	0	0

## Targeted

### FLAURA: Osimertinib v Gefitinib/Erlotinib in First-line EGFRm Advanced NSCLC



# Neoadjuvant PD-1 blockade ± chemo



## Neoadjuvant PD-1 Blockade in Resectable Lung Cancer

M. Forde, J.E. Chaft, K.N. Smith, V. Anagnostou, T.R. Cottrell, M.D. Hellmann, M. Zahurak, S.C. Yang, D.R. Jones, S. Broderick, R.J. Battafarano, M.J. Velez, N. Rekhtman, Z. Olah, J. Naidoo, K.A. Marrone, F. Verde, H. Guo, J. Zhang, J.X. Caushi, H.Y. Chan, J.-W. Sidhom, R.B. Scharpf, J. White, E. Gabrielson, H. Wang, G.L. Rosner, V. Rusch, J.D. Wolchok, T. Merghoub, J.M. Taube, V.E. Velculescu, S.L. Topalian, J.R. Brahmer, and D.M. Pardoll



Memorial Sloan Kettering Cancer Center

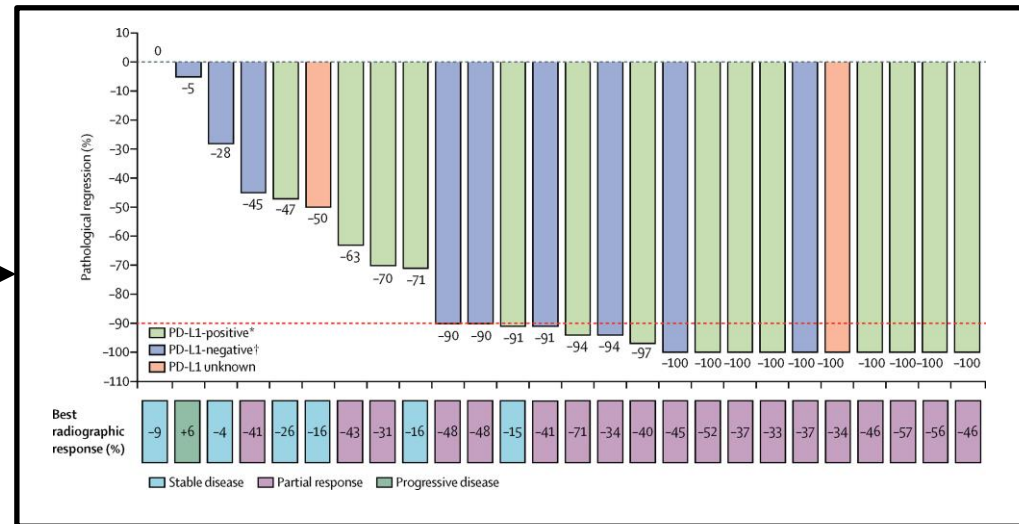
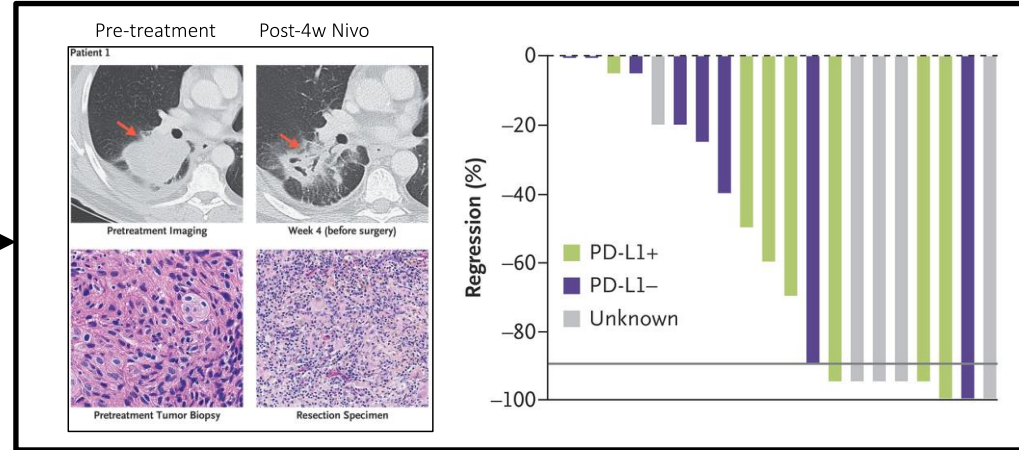


JOHNS HOPKINS

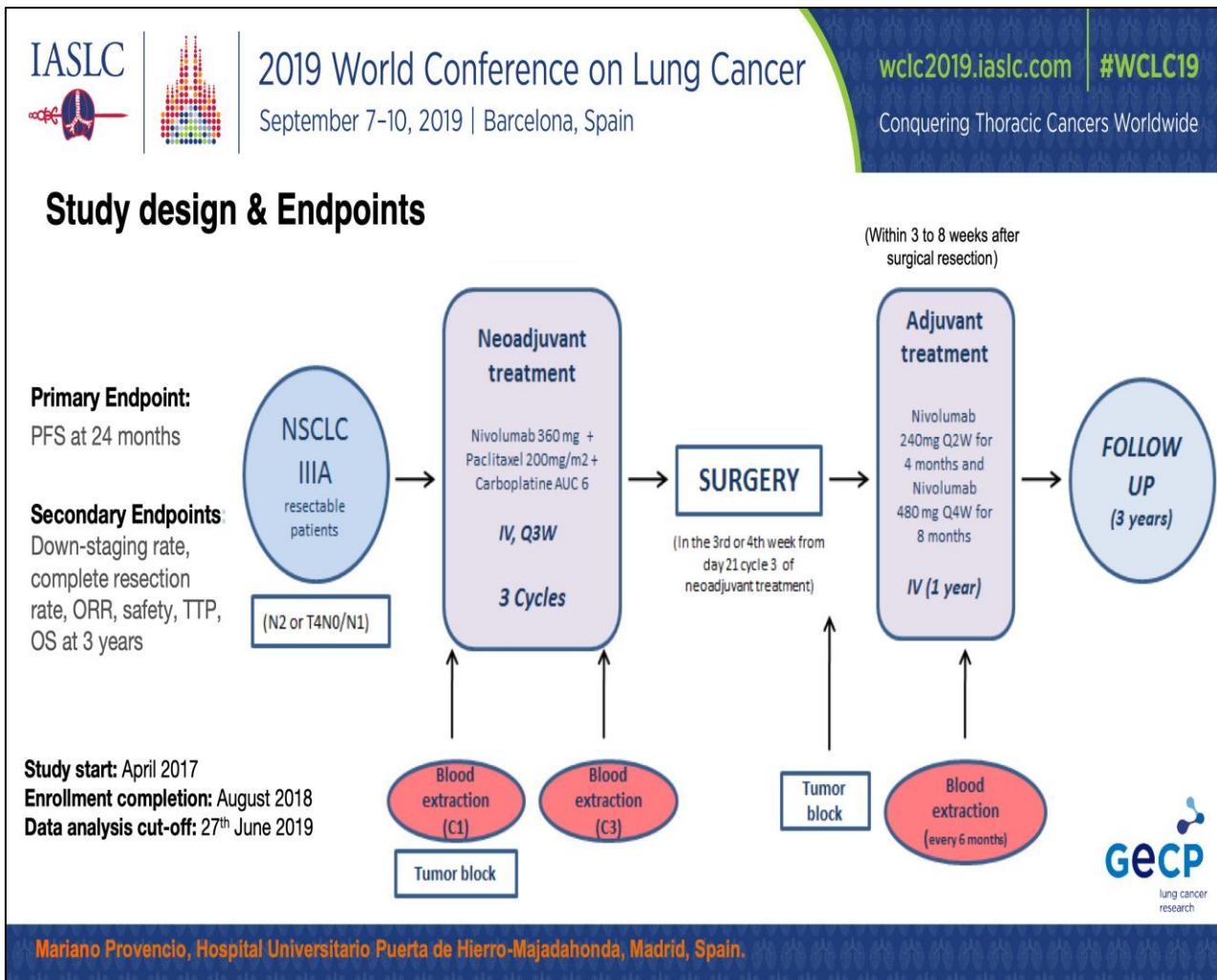
THE LANCET Oncology

## Neoadjuvant atezolizumab and chemotherapy in patients with resectable non-small-cell lung cancer: an open-label, multicentre, single-arm, phase 2 trial

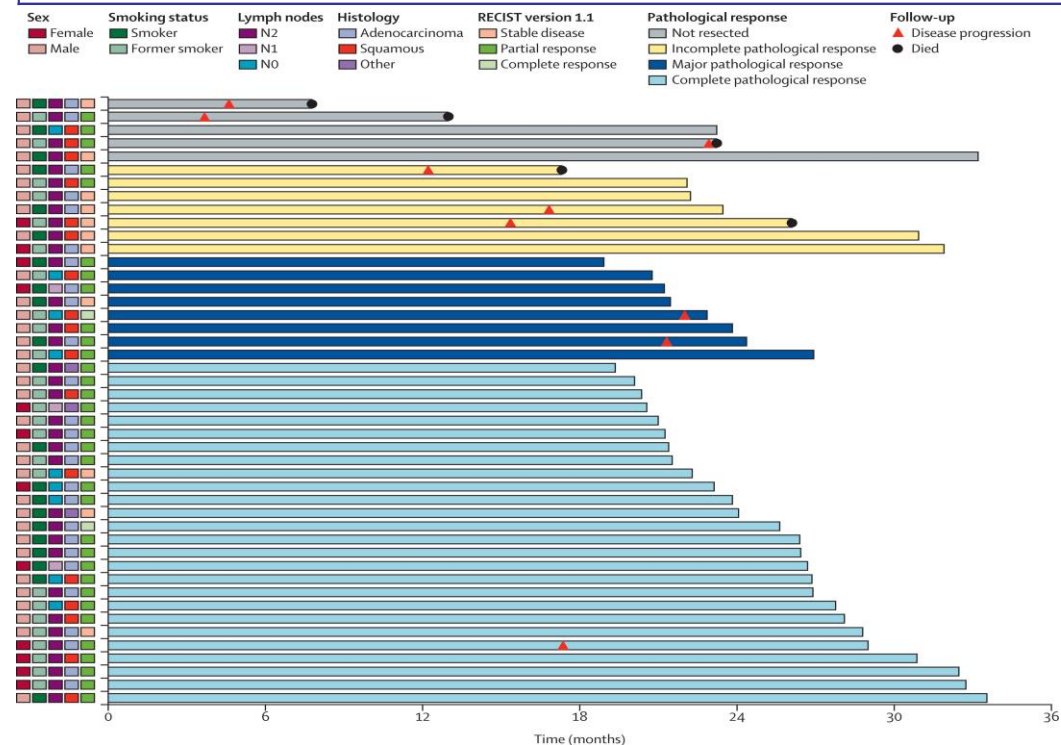
Catherine A Shu, Justin F Gainor, Mark M Awad, Codruta Chiuzan, Claud M Grigg, Aliyah Pabani, Robert F Garofano, Mark B Stoopler, Simon K Cheng, Abby White, Michael Lanuti, Frank D'Ovidio, Matthew Bacchetta, Joshua R Sonett, Anjali Saqi, Naiyer A Rizvi



# Neoadjuvant PD-1 blockade + chemo: 83% Major Pathological Response



Pathologic response	N=41	% (CI 95%)
Major Pathological Response (MPR)	34/41	83 (68-93)
Complete Response (CR)	24/41	59 (42-74)
> 10% residual viable tumor	7/41	17 (7-32)



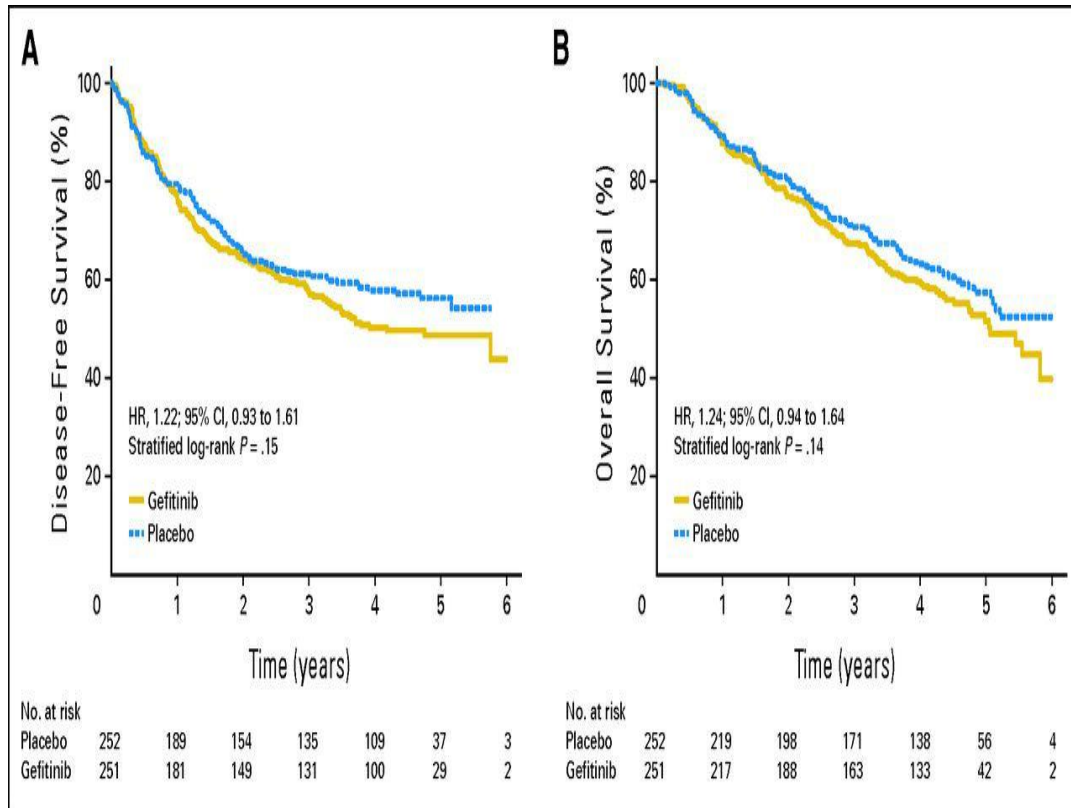
# Adjuvant Immunotherapy Trials in NSCLC

Study Name	Drug	Sample Size	Results	Identifier
MAGRIT	MAGE vaccine	2312	HR: 1.02 (95% CI: 0.89-1.18)	NCT00480025
PEARLS	Pembrolizumab	1080 (Estimated)	Ongoing	NCT02504372
BR31	Durvalumab	1360 (Estimated)	Ongoing	NCT02273375
IMpower010	Atezolizumab	1280 (Estimated)	Ongoing	NCT02486718
ANVIL	Nivolumab	903 (Estimated)	Ongoing	NCT02595944

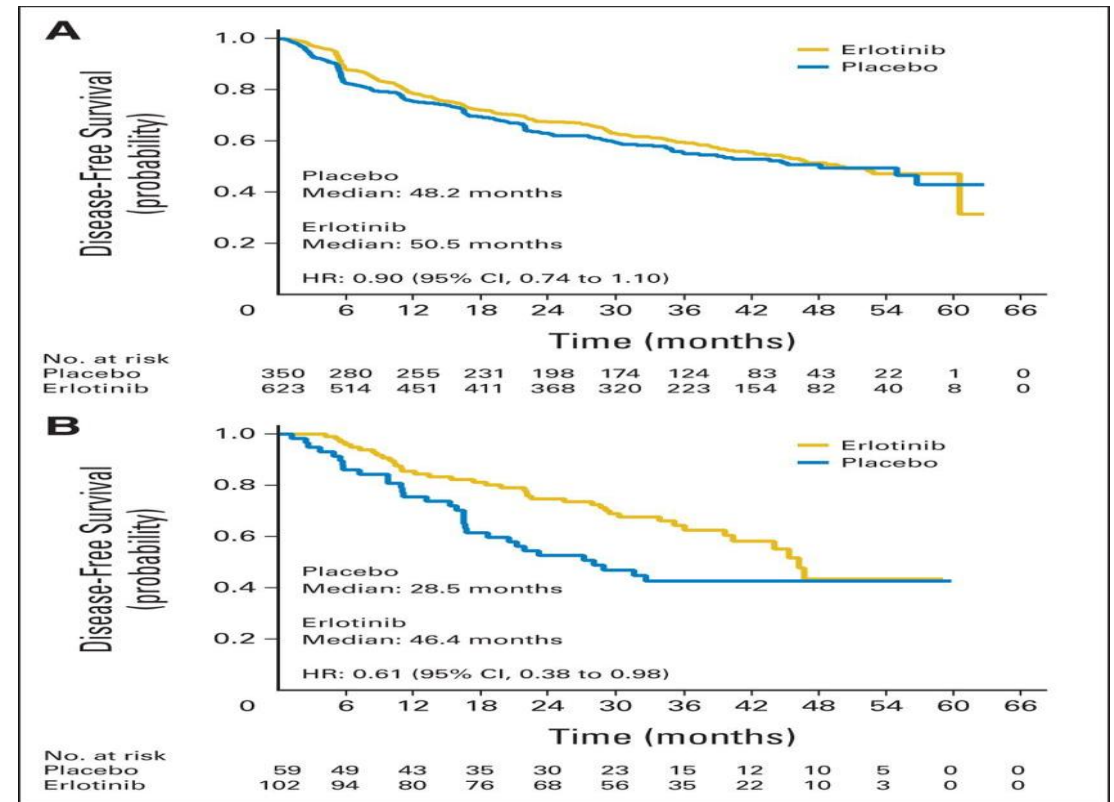


# Molecular Targeted Trials: EGFR TKIs

## BR19 Trial: Adjuvant Gefitinib vs Placebo with no survival benefit in unselected patients

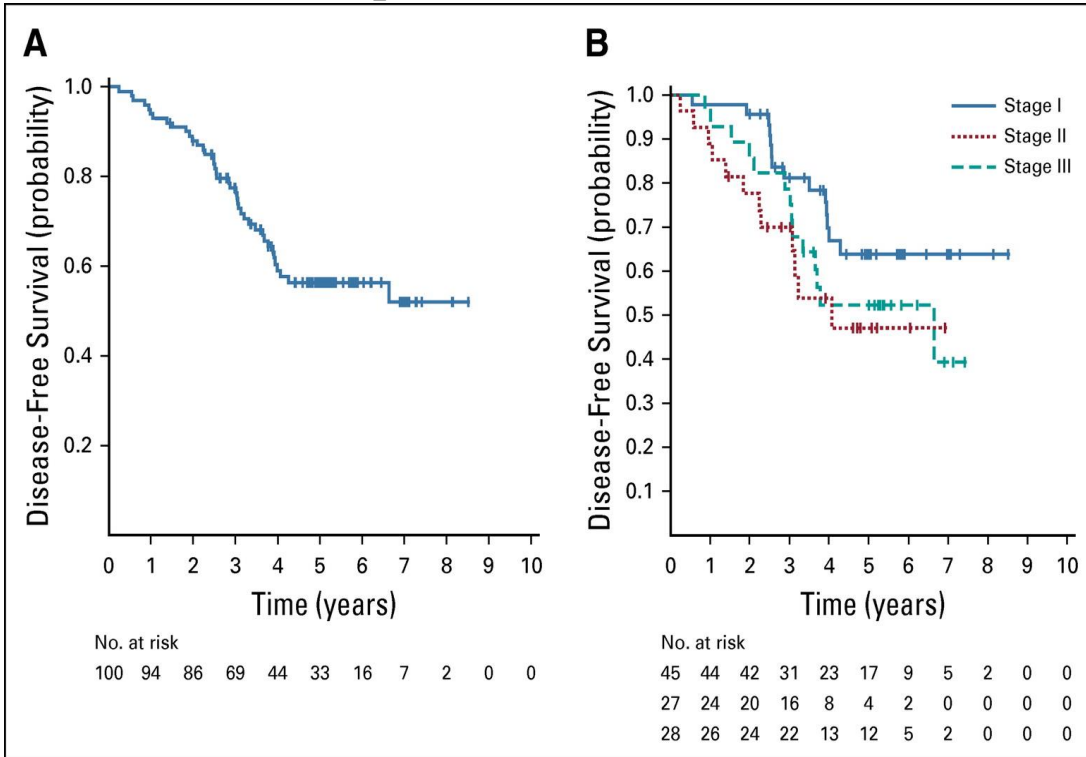


## RADIANT Trial: Adjuvant Erlotinib no DFS benefit in EGFR protein expressing NSCLC or EGFRm NSCLC



# Molecular Targeted Trials: EGFR TKIs

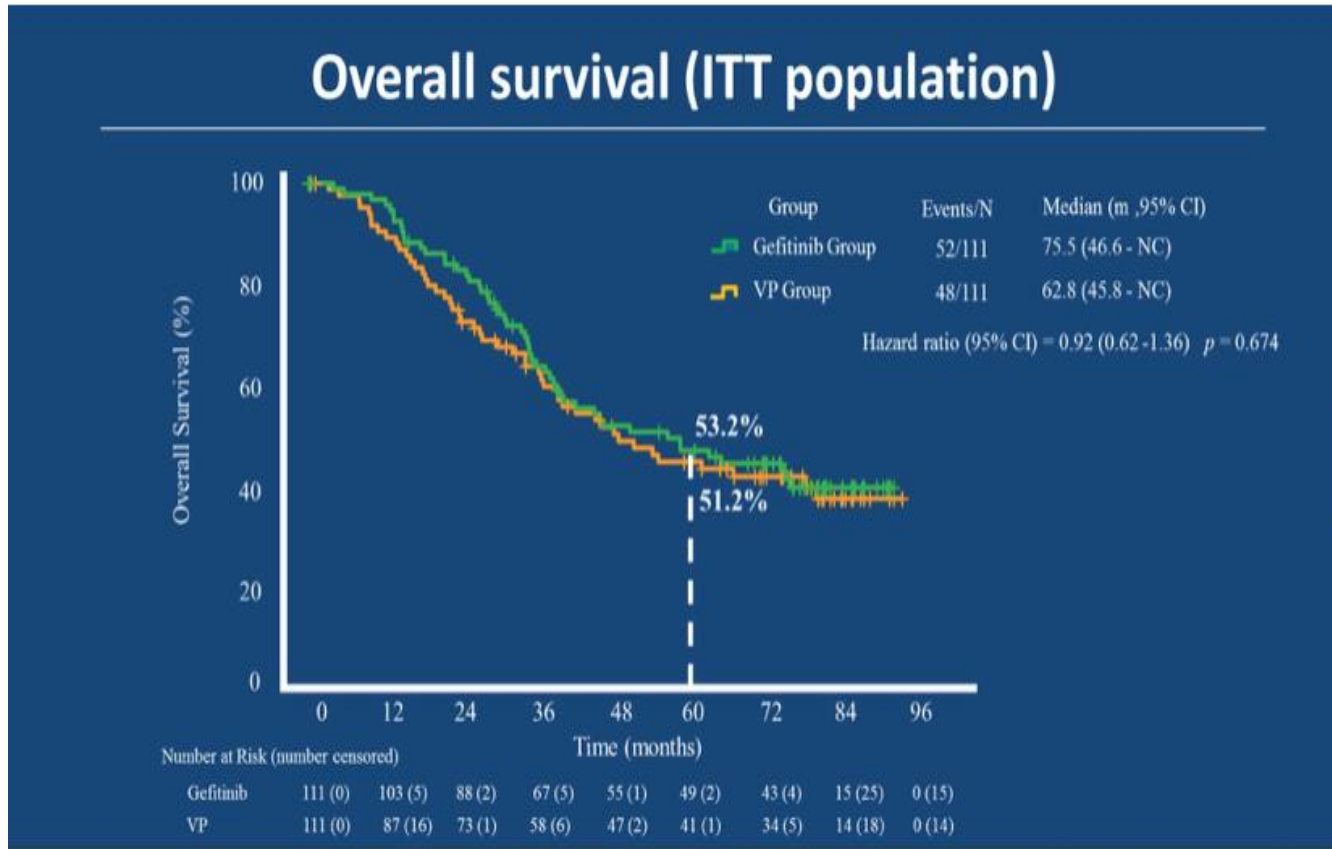
## SELECT Trial: Adjuvant Erlotinib with DFS benefit in EGFR mutated patients



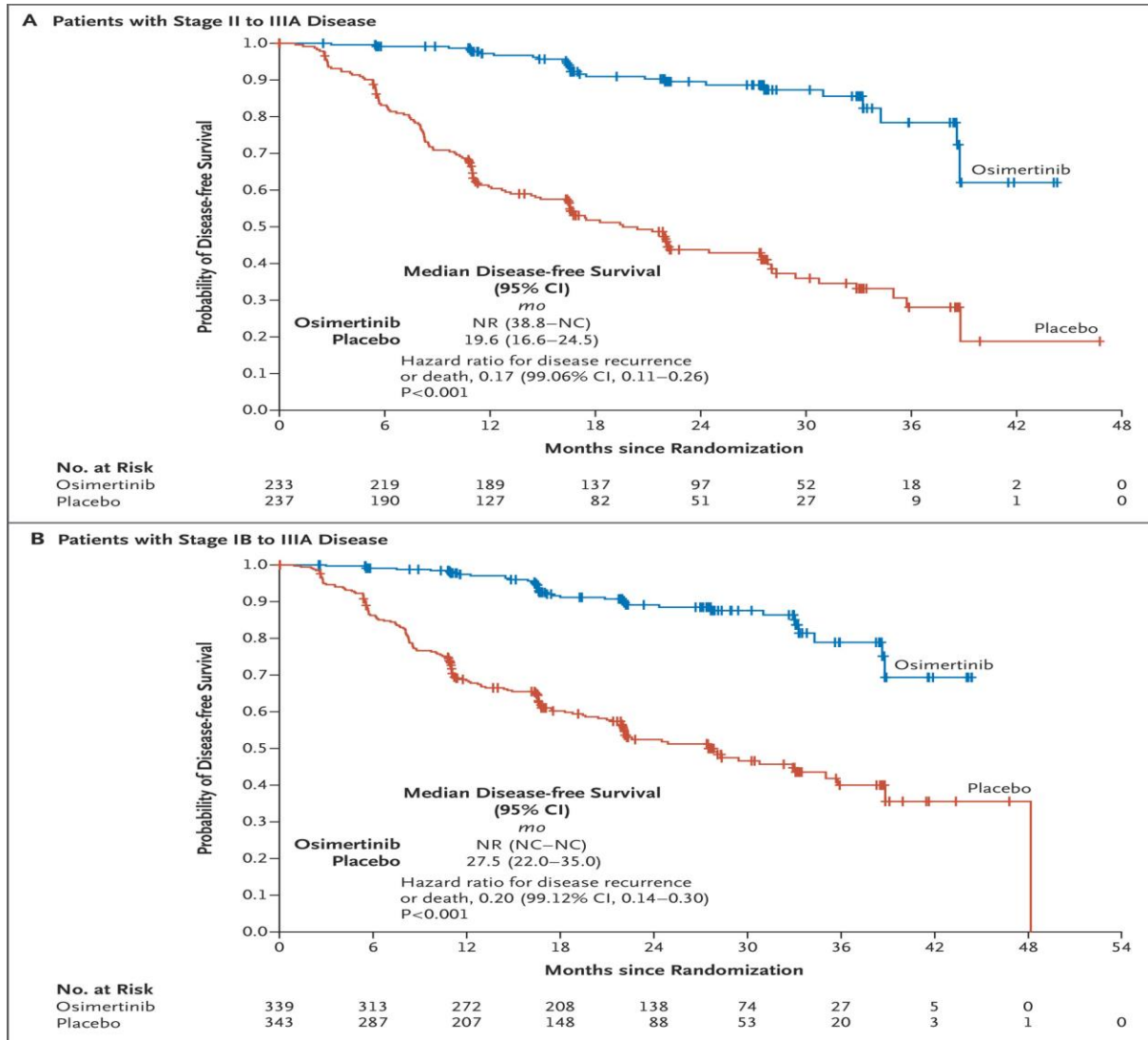
## CTOG 1104 Trial: Adjuvant Gefetinib vs. VP with DFS benefit in EGFR mutated patients



# Molecular Targeted Trials: Updated CTOG – No OS Benefit



# Molecular Targeted Trials: ADAURA



## ▶ Key Inclusion Criteria

- Completed resected stage IB-IIIa NSCLC with or without adjuvant chemotherapy
- EGFR+ (exon 19 and 21 mutations)

## ▶ DFS: HR 0.21 (95% CI 0.16-0.28)

- Consistent across all subgroups

## ▶ Stage 2 and 3 had most benefit

## ▶ ?Overall Survival Benefit

# CONCLUSIONS

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- ▶ **Early Stage Resectable Lung Cancer Still Represents the Best Opportunity for Long-Term Survival and Cure**
- ▶ **Neo-adjuvant and Adjuvant Treatments Improve Surgical Outcomes in Selected Patients**
- ▶ **Must Balance the Advantages and Disadvantages of Neo-adjuvant Approaches**
- ▶ **Validation of Endpoints for Clinical Trials (Major Pathological Response; Disease Free Survival)**
- ▶ **Chemotherapy has a Role in Surgical Management of High-Risk NSCLC**
- ▶ **Novel Biomarkers Needed to Predict Disease Recurrence Post-Surgery**