#IASLCUPDATES

Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

IASLC HIGHLIGHTS

7-10 DE SEPTIEMBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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BARCELONA

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Cáncer de pulmón no microcítico localizado y localmente avanzado. Neoadyuvancia

Dra. Anna Estival González

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

Early and Locally advanced NSCLC
NEOADJUVANT SETTING

- Surgical Outcomes in NEOSTAR

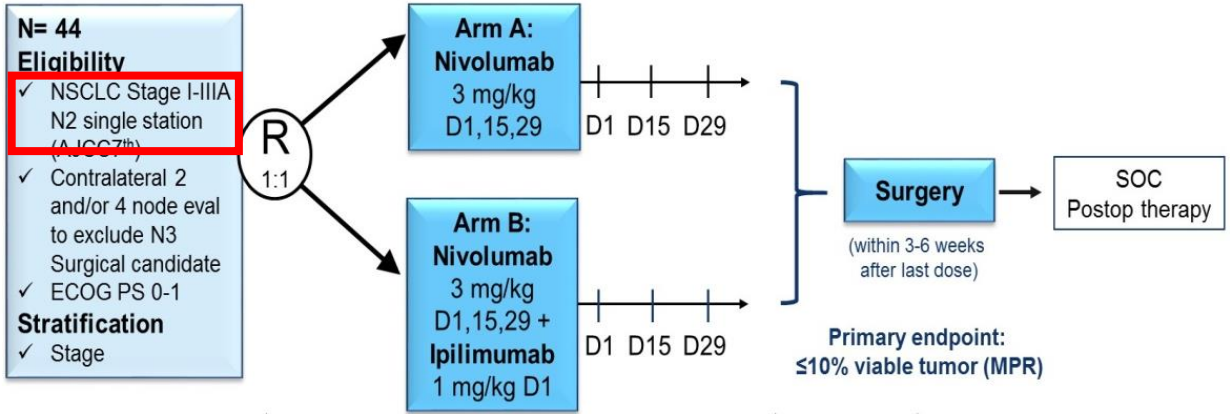
  NEOSTAR: phase II study of induction checkpoint blockade for untreated stage I-IIIA NSCLC amenable for surgical resection

- Immunophenotyping from LCMC3

  LCMC3. Neoadjuvant Atezolizumab in resectable NSCLC

- NADIM Study: NEO-ADJUVANT CHEMO/IMMUNOTHERAPY FOR THE TREATMENT OF RESECTABLE STAGE IIIA NON-SMALL-CELL LUNG CANCER (NSCLC): A PHASE II MULTICENTER EXPLORATORY STUDY. Updated Clinical Research and Outcomes

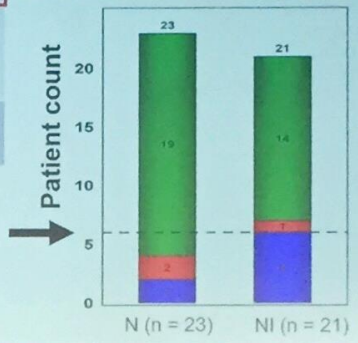
NEOSTAR: phase II study of induction checkpoint blockade for untreated stage I-IIIA NSCLC amenable for surgical resection. Surgical outcomes

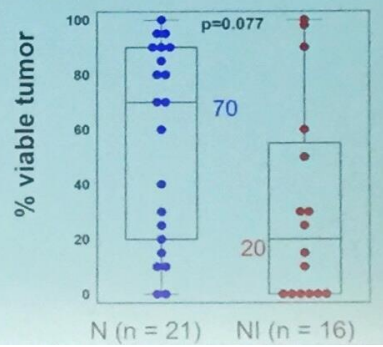


Overall ITT Resected + not resected*	Total n = 44	N n = 23	NI n = 21
MPR + pCR	11 (25%)	4 (17%)	7 (33%)
0% viable tumor (pCR)	8 (18%)	2 (9%)	6 (29%)
1-10% viable tumor	3 (7%)	2 (9%)	1 (5%)

Pre-specified trial efficacy boundary: ≥ 6 MPRs

Evaluable* Resected on trial	Total n = 37	N n = 21	NI n = 16
MPR + pCR	11 (30%)	4 (19%)	7 (44%)
0% viable tumor (pCR)	8 (22%)	2 (10%)	6 (38%)
1-10% viable tumor	3 (8%)	2 (10%)	1 (6%)





30% Total
44% Nivo-Ipi

Cascone T, J Clin Oncol 37, 2019 (suppl; abst 8504)

NEOSTAR: phase II study of induction checkpoint blockade for untreated stage I-IIIA NSCLC amenable for surgical resection. Surgical outcomes

Rate and Completeness of Resection

Total rate of resection
89% (39/44)

Resection ON trial
85% (37/44)

100% R0 resection rate

2 patients resected OFF trial

1 **Nivolumab:** disease progression vs *NIF (cT2N2)→ chemotherapy → surgery

1 **Nivolumab Ipilimumab:** colitis, steroids **SAE 3 (cT2N0) → chemotherapy → surgery

*NIF: nodal immune flare
** Treatment related adverse event

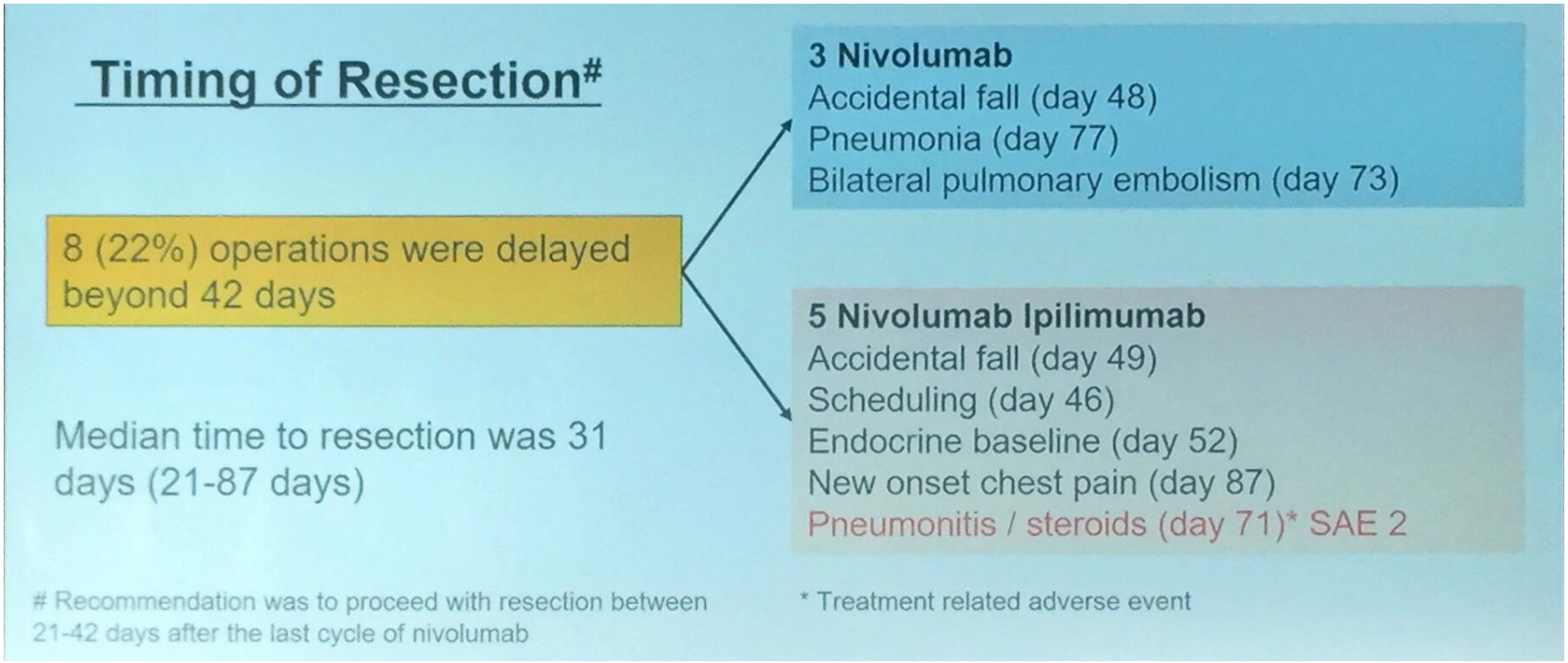
5 patients NOT resected

1 **Nivolumab:** hypoxia/large pleural effusion **SAE 3 (cT3N0)

4 **Nivolumab Ipilimumab:**
nodal progression (cT1N2)
local tumor progression (unresectable) (cT3N1)
smoking and high surgical risk (cT2N0)
refused surgery *NIF (cT2N1)

*NIF: nodal immune flare
** Treatment related adverse event

NEOSTAR: phase II study of induction checkpoint blockade for untreated stage I-IIIA NSCLC amenable for surgical resection. Surgical outcomes



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Neoadjuvant Atezolizumab in Resectable NSCLC Patients: Clinical and Immunophenotyping Results From the Interim Analysis of the Multicenter Trial LCMC3

Filiz Oezkan,[1] Kai He,[1] Dwight H. Owen,[1] Maciej Pietrzak,[1] Ju Hwan Cho,[1] Rhonda Kitzler,[1] Rebecca Pearson,[1] Valerie W. Rusch,[2] Jamie E. Chaft,[2] Robert Suh,[3] Justin D. Blasberg,[4] Karen L. Reckamp,[5] Dan J. Raz,[5] Peter J. Kneuertz,[1] Lauren Fiorillo,[1] Edward Garon,[3] Alan Nicholas,[6] Ann Johnson,[6] Katja Schulze,[6] Jessica Grindheim,[6] Romain Banchereau,[6] See Phan,[6] Paul A. Bunn Jr,[7] David J. Kwiatkowski,[8] Bruce E. Johnson,[9] Mark G. Kris,[2] Ignacio I. Wistuba,[10] Jay M. Lee,[3] Gerard Lozanski,[1] David P. Carbone[1]

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Con la colaboración de:

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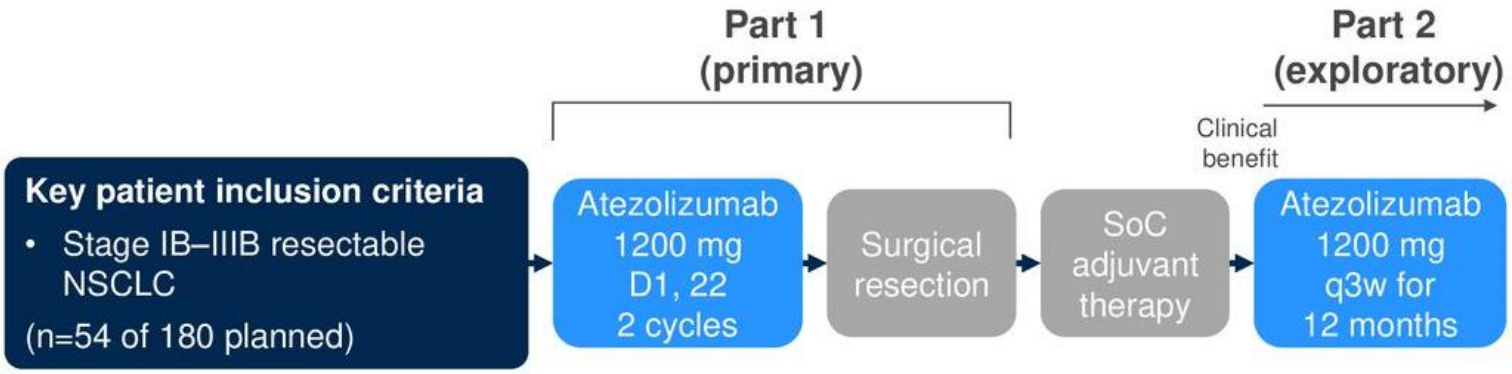
LCMC3. Neoadjuvant Atezolizumab in resectable NSCLC. Immunophenotyping.

- **Study objective**
  - To examine major pathologic response rate (MPR) and biomarkers in patients with resectable stage 1B–IIIB NSCLC receiving neoadjuvant atezolizumab (interim analysis of 54 patients from Part 1 of the study)



Primary endpoint

- MPR

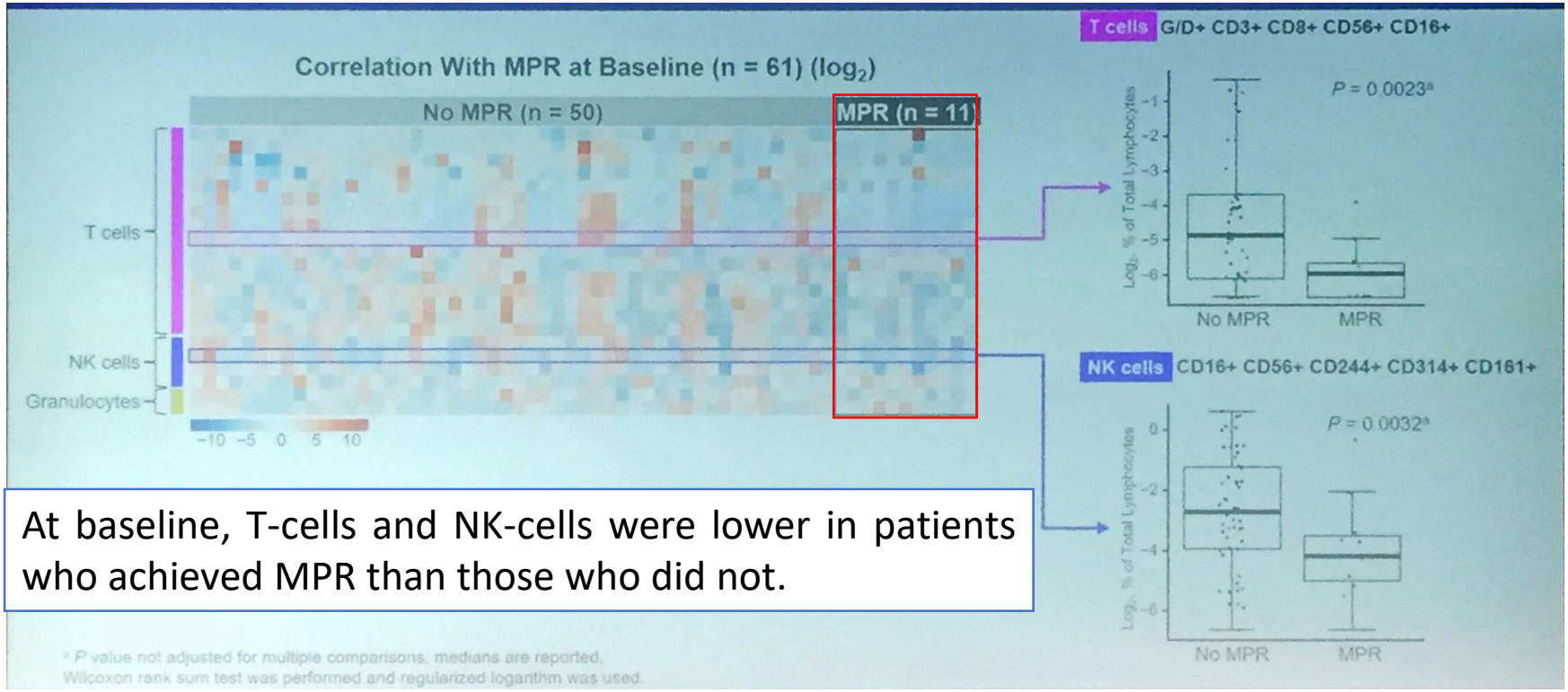
Secondary endpoints

- Safety, response by PD-L1, OS, DFS

Rusch VW et al. J Thorac Oncol 2018;13(suppl):Abstr MA04.09

LCMC3. Neoadjuvant Atezolizumab in resectable NSCLC. Immunophenotyping.

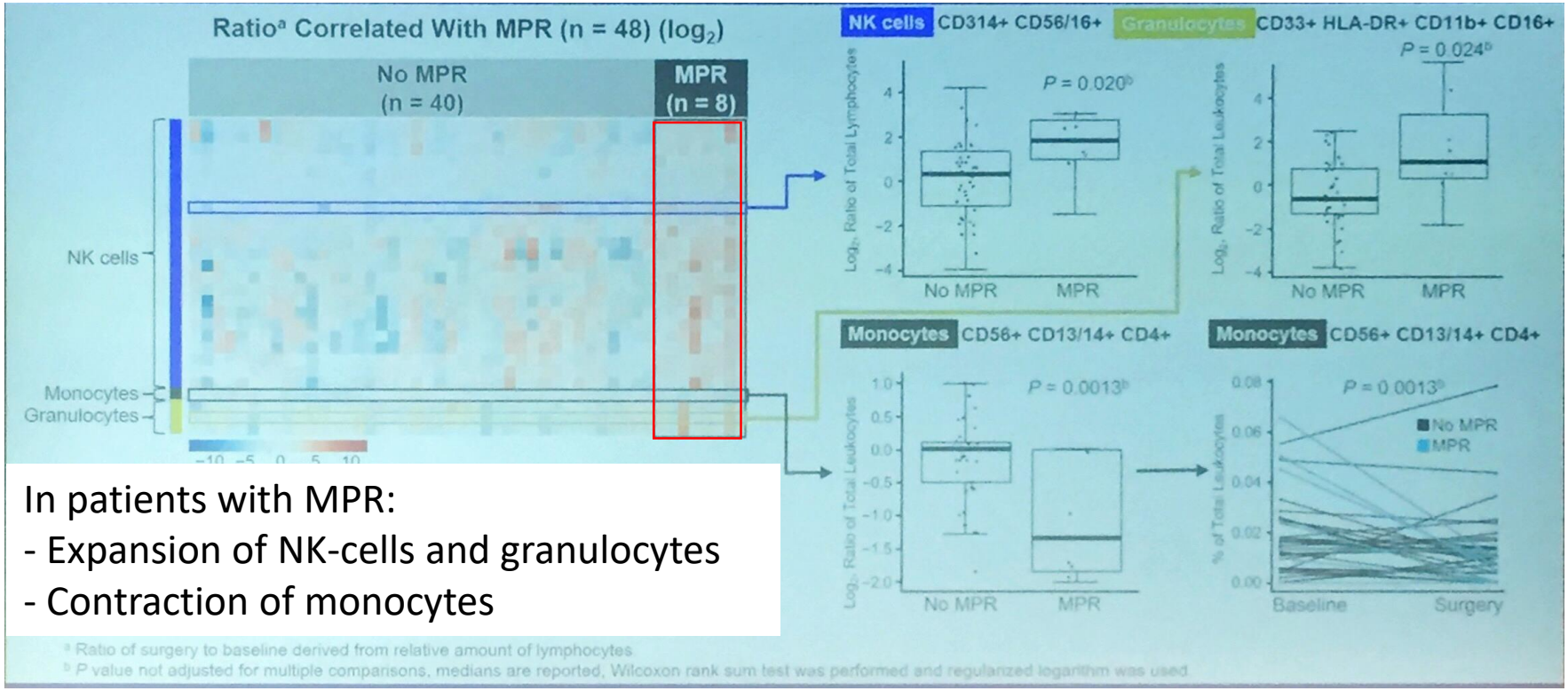
Peripheral blood immunophenotyping: Baseline by MPR



At baseline, T-cells and NK-cells were lower in patients who achieved MPR than those who did not.

LCMC3. Neoadjuvant Atezolizumab in resectable NSCLC. Immunophenotyping.

Peripheral blood immunophenotyping: Ratio Surgery / Baseline by MPR



In patients with MPR:
- Expansion of NK-cells and granulocytes
- Contraction of monocytes

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NADIM study: neo-adjuvant chemo/immunotherapy for the treatment of resectable stage IIIA non-small-cell lung cancer (NSCLC): a phase II multicenter exploratory study. Updated clinical research and outcomes

M. Provencio[1], E. Nadal[2], A. Insa[3], R. Garcia Campelo[4], J. Casal[5], M. Domine[6], M. Majem[7], D. Rodriguez-Abreu[8], A. Martinez-Marti[9], J. De Castro[10], M. Cobo[11], G. López-Vivanco[12], E. Del Barco[13], R. Bernabe[14], N. Viñolas[15], I. Barneto[16], S. Viteri[17], P. Martin Martorell[3], M. Jove[2], V. Calvo[1], B. Massuti[18]

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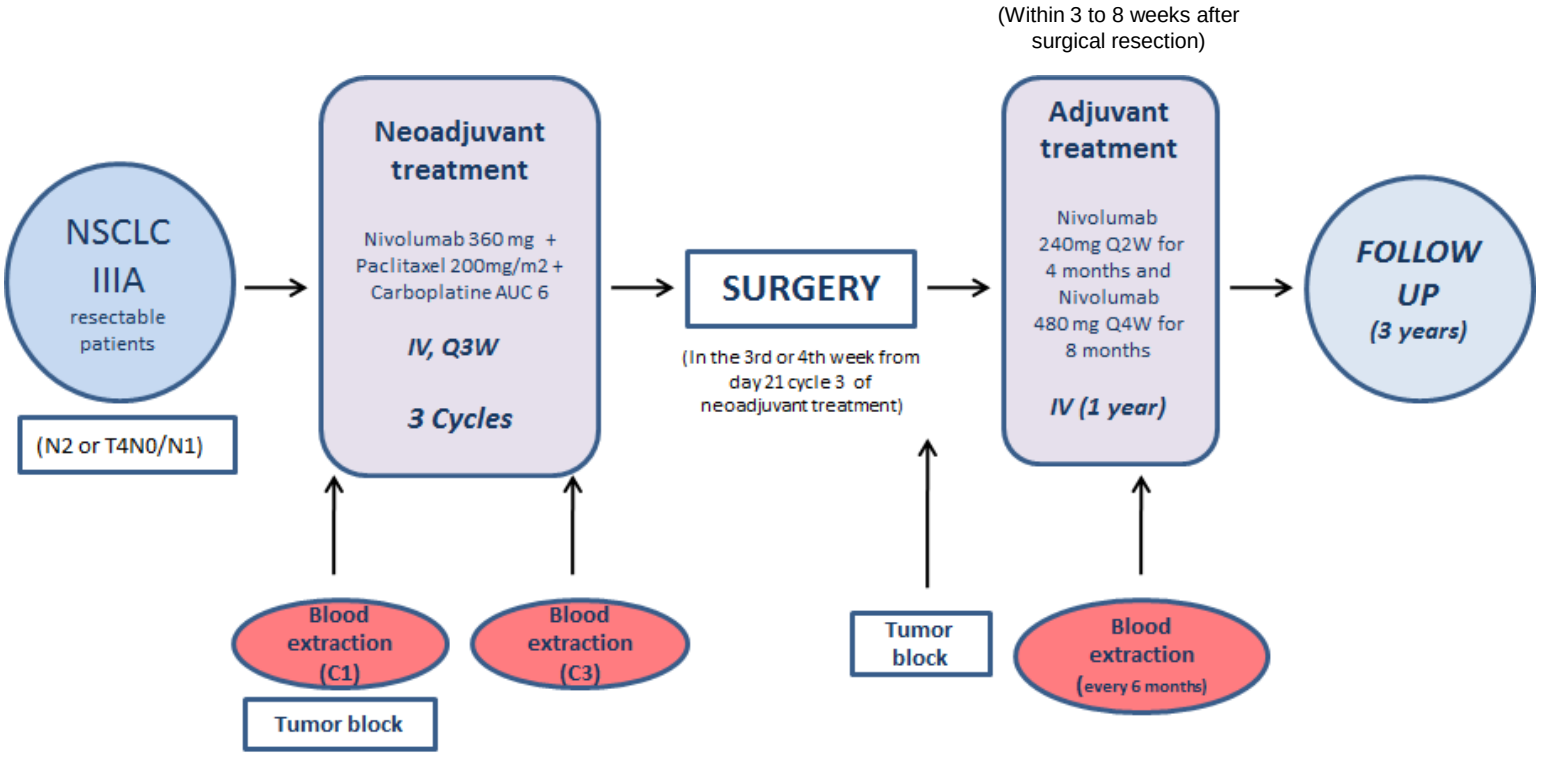
NADIM study: neo-adjuvant chemo/immunotherapy for the treatment of resectable stage IIIA non-small-cell lung cancer (NSCLC): a phase II multicenter exploratory study. Updated clinical research and outcomes

Study design & Endpoints



Primary Endpoint:
PFS at 24 months

Secondary Endpoints:
Down-staging rate, complete resection rate, ORR, safety, TTP, OS at 3 years

Study start: April 2017
Enrollment completion: August 2018
Data analysis cut-off: 27th June 2019

NADIM study: neo-adjuvant chemo/immunotherapy for the treatment of resectable stage IIIA non-small-cell lung cancer (NSCLC): a phase II multicenter exploratory study. Updated clinical research and outcomes

RESULTS

Objective Response Rate (RECIST v1.1)

	N	%
Complete response (CR)	2	4.3
Partial Response (PR)	32	69.6
Stable disease (SD)	12	26.1

All patients received 3 neoadjuvant cycles except for one who only received two cycles[3]

[3] One patient decided to withdraw from the study and only received 2 cycles

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)

Chemotherapy only…
- Major pathological responses are rare (<20%)
- Radiological complete responses are exceptional 0-4%

Down-staging rate (ITT): 90.2% (37/41 patients)

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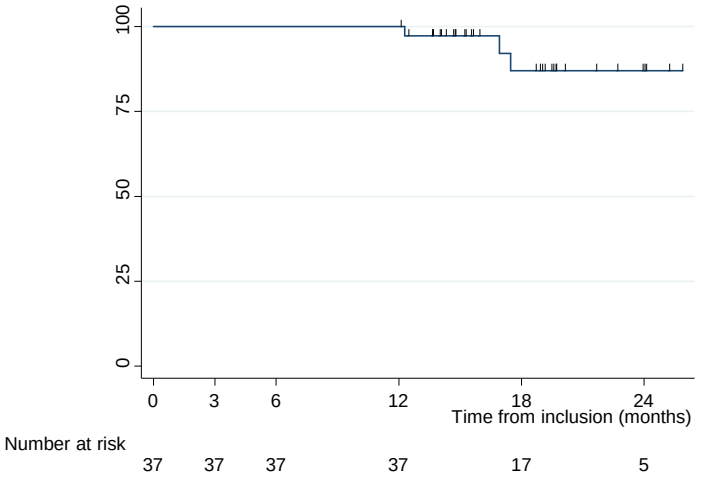
RESULTS

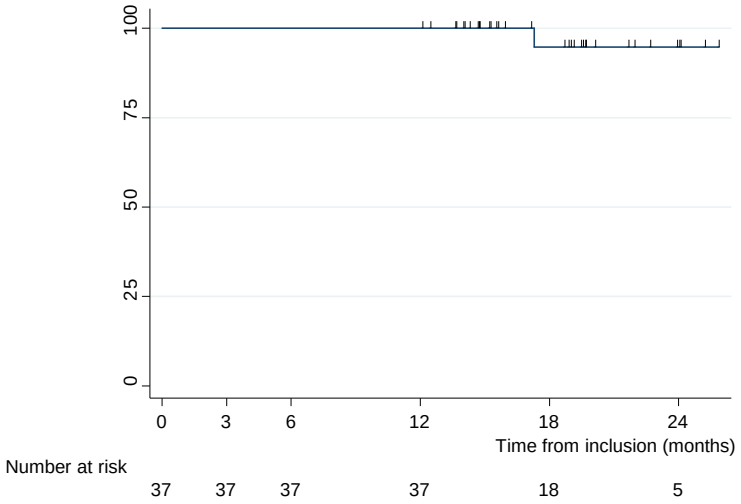
PROGRESSION FREE SURVIVAL (PP)



PFS at 12 months: 100%

PFS at 18 months: 87% (95% CI: 64; 96)

OVERALL SURVIVAL (PP)



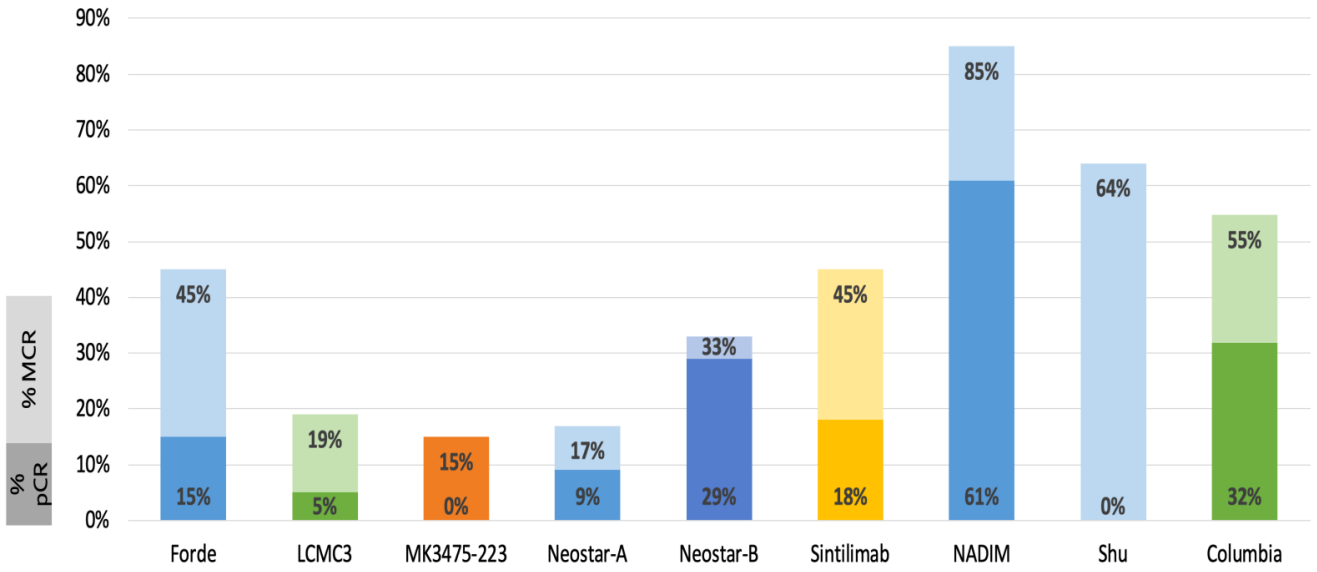
Overall Survival at 12 months: 100%

Overall Survival at 18 months: 95% (95% CI:68; 99)

NADIM study: neo-adjuvant chemo/immunotherapy for the treatment of resectable stage IIIA non-small-cell lung cancer (NSCLC): a phase II multicenter exploratory study. Updated clinical research and outcomes

Complete pathologic response rate higher than ever previously seen

Complete pathologic response rate MORE MUCH higher than ever previously seen



Neoadjuvant treatment	Nivolumab x2	Atezolizumab x2	Pembrolizumab x2	Nivolumab x3	Nivo + Ipilimumab x3	Sintilimab x2	Carbo – Pacli – Nivo x3	Carbo – Nab pacli – Nivo x2	Atezolizumab – Carbo – Nab pacli X4
Stage	IB - IIIA	I - IIIB	I - II	I - IIIA	I - IIIA	IB - IIIA	IIIA	IB - IIIA	IB - IIIA
Patient #	20	77	15	23	21	22	46	11	19
% surgery unattended	0%	11%	13%	11%	-	0%	11%	-	0%

Complete pathologic response rate MORE MUCH higher than ever previously seen

The 18 m PFS >80% is also promising and may translate into increased overall survival (>90% at 18 m)

A new randomized phase II clinical trial (**NADIM-2**) is currently ongoing (same neo-adjuvant Nivolumab + CT schema followed by a shorter adjuvant **Nivolumab** monotherapy of **6 months** vs. standard CT)

Congratulations to all investigators and to the Spanish Lung Cancer Group