Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

ASCO HIGHLIGHTS

31 MAYO - 4 JUNIO 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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Inmunoterapia en el tratamiento del CNMP estadío III

Dr. Javier Garde

Día 2

Con la colaboración de:

Bristol-Myers Squibb
illumina
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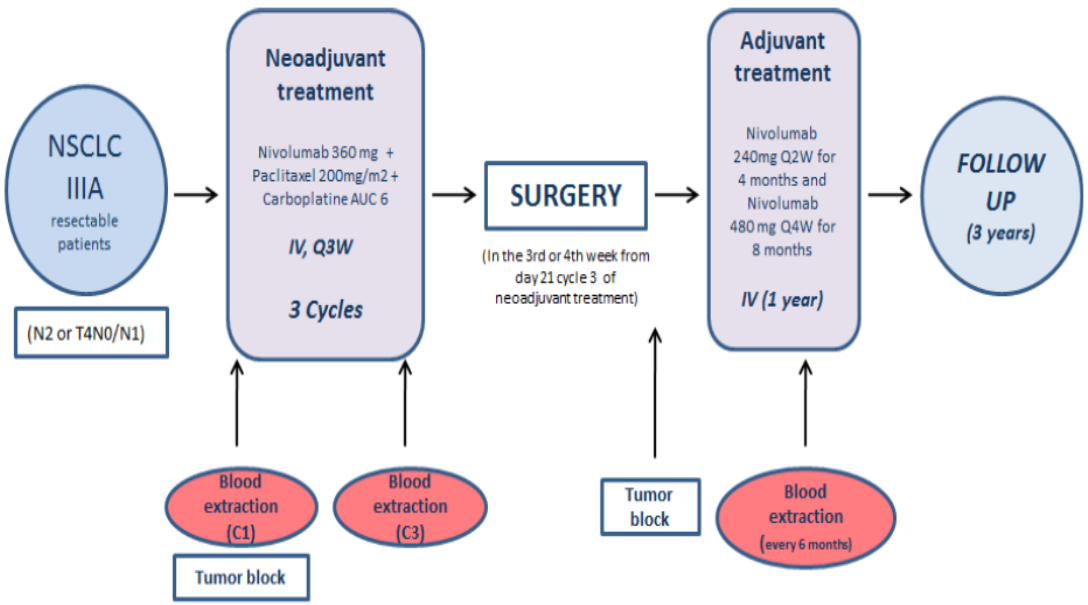


A Phase II, single-arm, open-label and multicenter study of resectable stage IIIA NSCLC patients with CT + IO as a neoadjuvant treatment (46 patients).

ELIGIBILITY CRITERIA:

Patients aged ≥ 18 years.

Stage IIIA NSCLC (7th edition) and resectable tumor.

ECOG Performance Status 0-1.

Forced expiratory volume (FEV1) ≥ 1.2 liters.

Adequate hepatic, hematological and renal functions.

EGFR and ALK mutated patients are ineligible.

Primary endpoint: Progression-Free Survival at 24 months.

Secondary endpoints::

Down-staging rate, complete resection rate and response rate (RR).

Toxicity profile.

Time to progression and 3-year overall survival.

Surgical outcome and operative and post-operative complications.

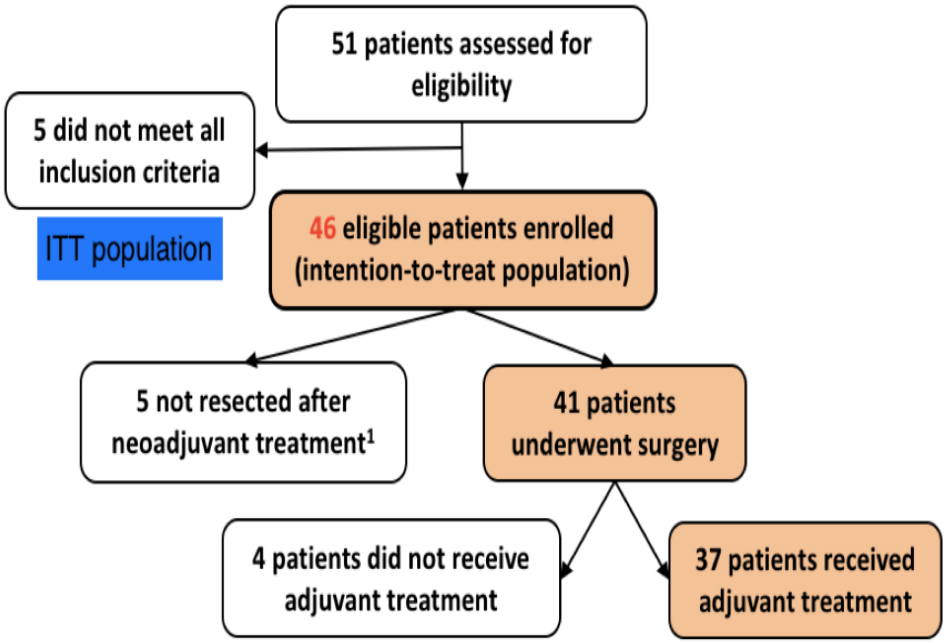
To explore the expression of other biomarkers.

To determine whether PD-L1 expression is a predictive biomarker for ORR.

To determine PFS in PD-L1+ (≥ 1%) population.

ABSTRACT 8509: Provencio M, et al. NEO-adjuvant chemo-immunotherapy for the treatment of STAGE IIIA resectable non-small-cell lung cáncer (NSCLC): A phase II multicentr exploratory study_ Final data of pateients who underwent surgical assessment.

QT-IT Neoadyuvante: Estudio NADIM



2 patients decided not to undergo resection, 3 did not fulfill surgical criteria for resectability

Clinical characteristics of patients (N=46)	
Gender	**N(%)**
Male / Female	34 (74) / 12 (26)
Race	
Caucasian	46 (100,0)
Age (median/range)	63 (41-77)
PS	
0 / 1	25 (54) / 21 (46)
Histology	
Adenocarcinoma	26 (56)
Squamous	16 (35,4)
NOS	4 (8,6)
Smoking status	
Former smoker vs Smoker	25 (55) / 21 (45)
Pack-year (median/range)	49 (20-114)
Comorbidities	
No / Yes	3 (6,5) / 43 (93,5)
Diabetes	10 (22)
COPD	9 (20)
Hypertension	15 (33)
Heart disease	8 (18)

Pathological response after Neoadjuvant treatment N=41		
	N (%)	**95% IC**
Major pathological response (MPR)	35 (86,4%)	71-95%
Complete pathological resp. (CPR)	25 (71,4%)	54-87%
Partial response	6 (15%)	-

Clínical response by RECIST criteria after Neoadjuvant treatment (ITT) N=46.	
Complete Response (CR)	3 (6,5%) (95%IC 0-16%)
Partial Response (PR)	33 (72%) (95%IC 56-85%)
Stable Disease (SD)	8 (17,5%)

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Toxicity										
GRADE	1		2		3		4		Total	
	N	%	N	%	N	%	N	%	N	%
Anemia	5	11.1	2	4.4	0	0.0	0	0.0	7	15.6
Febrile neutropenia	0	0.0	0	0.0	1	2.2	0	0.0	1	2.2
Neutropenia	0	0.0	1	2.2	2	4.4	1	2.2	4	8.9
Thrombocytopenia	2	4.4	1	2.2	0	0.0	0	0.0	3	6.7
Fatigue	12	26.7	6	13.3	1	2.2	0	0.0	19	42.2
Alopecia	2	4.4	11	26.7	0	0.0	0	0.0	14	31.1
Nausea	11	24.4	1	2.2	0	0.0	0	0.0	12	26.7
Arthralgia	8	17.8	1	2.2	0	0.0	0	0.0	9	20.0
Diarrhea	6	13.3	2	4.4	0	0.0	0	0.0	8	17.8
Decreased appetite	7	15.6	0	0.0	1	2.2	0	0.0	8	17.8
Vomiting	3	6.7	3	6.7	0	0.0	0	0.0	6	13.3
Myalgia	4	8.9	2	4.4	0	0.0	0	0.0	6	13.3
Constipation	3	6.7	2	4.4	0	0.0	0	0.0	5	11.1
Pruritus	4	8.9	1	2.2	0	0.0	0	0.0	5	11.1

Postsurgical Complications	N	%
Cardiac arrhythmia	1	14.3
Air leakage	1	14.3
Respiratory infection	3	42.9
Post-operative pain	1	14.3
Recurrent nerve paralysis	1	14.3
Thrombopenia	1	14.3
Post-surgery pneumonia	1	14.3
Cellulitis in left limb	1	14.3
Atrial fibrillation	1	14.3

Summary of Neoadjuvant Immunotherapy Studies

	N resected	Stage	Drug(s)	Cycles	MPR	RECIST ORR
LCMC3	84	IB-IIIB	Atezo	2	18% (10-28)	7%
NEOSTAR						
Arm A	23	IA-IIIA	Nivo	3	17% (5-39)	22%
Arm B	21	IA-IIIA	Nivo/Ipi	3	33% (15-57)	19%
Forde et al[1]	20	IB-IIIA	Nivo	2	45% (23-68)	10%
Historical Control						
Chaft et al[2]	41	IB-IIIA	Cisplatin/Docetaxel/Bev	4	27% (15-43)	45%
Immunotherapy + chemotherapy						
NADIM[3]	30	IIIA	Nivo/Carbo/Paclitaxel	3	80% (61-92)	70%
Shu et al.[4]	11	IB-IIIA	Atezo/Carbo/Nab-Paclitaxel	2	64% (32-88)	73%

[1]Forde et al. *NEJM* 2018 [2]Chaft et al. *JTO* 2013 [3]Provencio et al. WCLC 2018 #OA01.05 [4]Shu et al. ASCO 2018 #8532

Pembrolizumab + QT/RTc

Abstract 8511 (270715)

Prospective phase I multi-institutional trial of PD-1 blockade with pembrolizumab during concurrent chemoradiation for locally advanced, unresectable non-small cell lung cancer

Authors: **Salma K. Jabbour**, Abigail T. Berman, Roy H. Decker, Yong Lin, Steven J. Feigenberg, Scott N. Gettinger, Charu Aggarwal, Corey J. Langer, Charles B. Simone II, Jeffrey D. Bradley, Joseph Aisner, Jyoti Malhotra

Results: Adverse Events

Event	Grade 2 (n)	Grade 3 (n)	Grade 4 (n)	Grade 5(n)
Pneumonitis	4 (Regimen 2 (1) and Dose Expansion (3))	1 (Regimen 2)		1 (Dose Expansion)
Nephritis	1 (Regimen 1)			
Thyroiditis	4 (Regimens 1,2,3,5)			
Transamanitis	1 (Regimen 2)			
Myositis	1 (Regimen 3)			
Hyperglycemia		1 (Regimen 5)		
Tracheoesophageal Fistula		1 (Regimen 5)		
Colovesical Fistula				1 (Regimen 1)

Subjects must have inoperable non-small cell lung cancer to be treated with definitive chemoradiation

→ N=approximately 24-30 subjects with inoperable non-small cell lung cancer

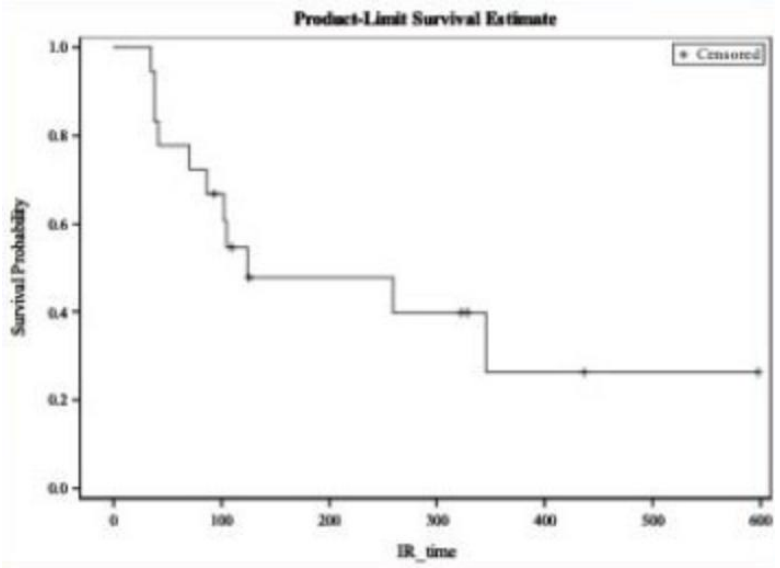
6 patient safety expansion cohort

→ Pembrolizumab beginning at 200 mg Q3W starting 2-6 weeks after CRT with subsequent dose escalation and advancing the timing to during chemoradiation

→ Monitor for safety

Start of Pembrolizumab	Pembrolizumab Dose	Regimen
2-6 Weeks After CRT (Day 56-84)	100 mg Q3Weeks	-1
2-6 Weeks After CRT (Day 56-84)	200 mg Q3Weeks	1 *
2 Weeks Before End Of CRT (Day 28)	100 mg Q3Weeks	2
2 Weeks Before End Of CRT (Day 28)	200 mg Q3Weeks	3
At start of CRT (Day 0)	100 mg Q3Weeks	4
At start of CRT (Day 0)	200 mg Q3Weeks	5

*starting dose level

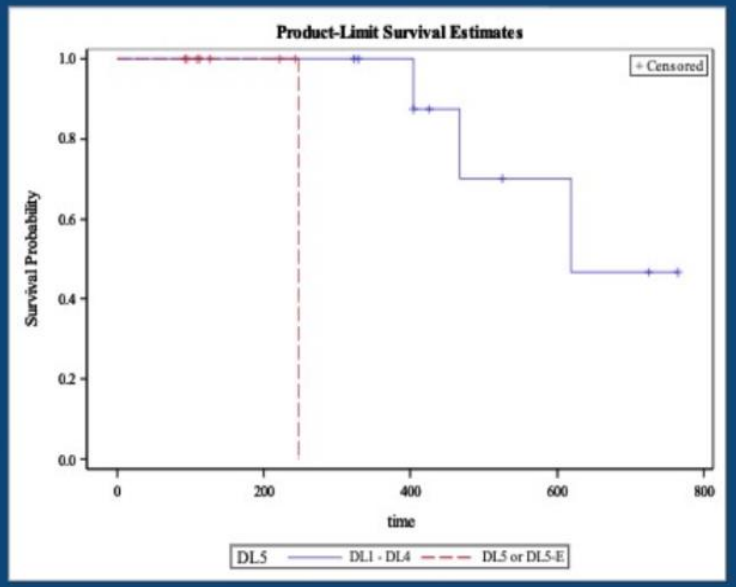


Salma K, et al. Prospective phase I multi-institutional trial of PD-1 blockade with Pembrolizumab duriing concurrent chemorradiation for locally advanced unresectabgle non-small cell Lung cancer

Pembrolizumab + QT/RTc

Results

- 23 subjects enrolled from 8/2016-11/2018
- Median age: 69 years (range 53-85), 52% women
- Stage IIIA: 22%, Stage IIIB: 78%
- No DLT upon completion of Regimen 5
- Grade ≥3 immune-related adverse events (irAE) occurred in 4 patients (18%)
- 2 subjects expired before receiving pembrolizumab



Kaplan-Meier Curve for PFS
Median PFS as for subjects with ≥ 2 cycles of pembrolizumab: 20.3 months (as of 2/2019)

Salma K, et al. Prospective phase I multi-institutional trial of PD-1 blockade with Pembrolizumab duriing concurrent chemorradiation for locally advanced unresectabgle non-small cell Lung cancer

Atezolizumab + QT/RTc

Abstract 8512 (270735)

Phase II trial combining atezolizumab concurrently with chemoradiation therapy in locally advanced non-small cell lung cancer

Authors: **Steven H. Lin**, Yan Lin, Isabel Mok, Jenean A. Young, See Phan, Alan Sandler, Vassiliki Papadimitrakopoulou, John Heymach, Anne S. Tsao

Stage 1 (n=10)

Concurrent ChemoRadiation* → Consolidation Chemo** + **MPDL3280A** IV Q3weeks x 2 cycles → **MPDL3280A** IV Q3weeks for 1 year

If no concerning toxicities

Stage 2 (n=30)

Concurrent ChemoRadiation* + **MPDL3280A** IV Q3weeks → Consolidation Chemo** + **MPDL3280A** IV Q3weeks x 2 cycles → **MPDL3280A** IV Q3weeks for 1 year

*weekly carboplatin AUC 2 and paclitaxel 50 mg/m2 administered concurrent with thoracic radiation
**carboplatin AUC 6 and paclitaxel 200 mg/m2 IV Q 3 weeks for 2 cycles.

Steven H et, al Phase II trial combining Atezolizumab concurrently with chenorradiation therapy in locally advanced non-small lung cancer.

Toxicity Summary

N=10	Part 1
All AEs	201
All Grade 3+ AEs	16
% pts developed any Grade 3+	6 of 10 (60%)
AEs leading to withdraw from tx	3 of 10 (30%)
% pts with immune-related Grade 3+ AEs	3 of 10 (30%)

Grade 2 AEs of special interest	Frequency
Dyspnea	4 of 10 (40%)
Pneumonitis	1 of 10 (10%)
Arthralgia	1 of 10 (10%)

Patients with Grade 3+ AEs	Frequency
Dyspnea (Grade 3)	1 of 10 (10%)
Arthralgia (Grade 3)	1 of 10 (10%)
Lung infection (Grade 5); Tracheoesophageal fistula (Grade 5)	1 of 10 (10%)

N=30	Part 2
All AEs	451
All Grade 3+ AEs	41
% pts developed any Grade 3+	20 of 30 (67%)
AEs leading to withdraw from tx	5 of 30 (17%)
% pts with immune-related Grade 3+ AEs	6 of 30 (20%)

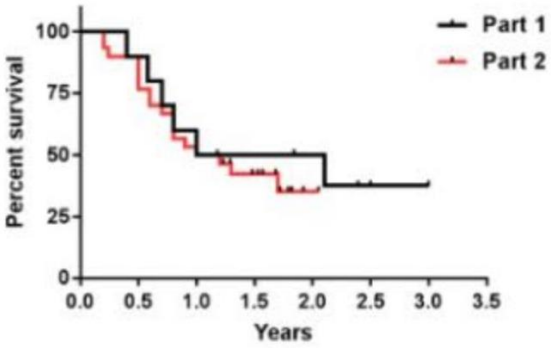
Grade 2 AEs of special interest	Frequency
Nephritis	1 of 30 (3%)
Arthalgia	2 of 30 (7%)
Diarrhea	1 of 30 (3%)
Dyspnea	1 of 30 (3%)
Fatigue	1 of 30 (3%)
Hypothyroidism	1 of 30 (3%)
Pneumonitis	4 of 30 (13%)
Rash	5 of 30 (17%)

Patients with Grade 3+ AEs	Frequency
Diarrhea (Grade 3), Radiation pneumonitis (Grade 3)	1 of 30 (3%)
Nephritis (Grade 3), Fatigue (Grade 3)	1 of 30 (3%)
Fatigue (Grade 3)	2 of 30 (7%)
Heart failure (Grade 3)	1 of 30 (3%)
Respiratory failure NOS (Grade 4)	1 of 30 (3%)

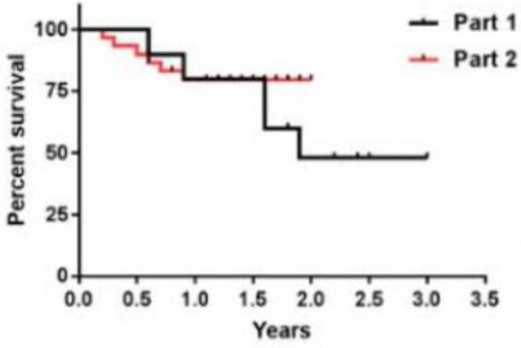
Preliminary Efficacy analysis

- Median F/U time
  - **Part 1**: 1.85 years; in all survivors: 2.39 years
  - **Part 2**: 1.26 years; in all survivors: 1.42 years
- Median Survival
  - **PFS: Part 1:** 1.55 years; **Part 2:** 1.1 years
  - **OS: Part 1:** 1.9 years; **Part 2:** Not reached

Progression Free Survival

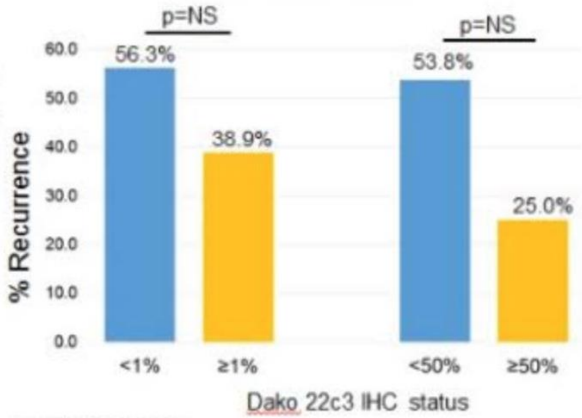


Overall Survival



Patients with any recurrence and Baseline PD-L1 status by 1% and 50% cut-off

N=34 evaluable



NS=Not significant