16th CONGRESS Lung ON CANCER

BARCELONA 27 / 28 NOVEMBER 2025

GECP lung cancer research

SLCG studies: Advances stages NSCLC

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CONFLICTO DE INTERESES

The main author declare

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Support for attending meetings and/or travel: BMS, MSD, Takeda, Roche, Pfizer

Overview of the GECP Portfolio in Advanced NSCLC

Broad research program in immunotherapy, targeted therapies & translational biomarkers

Focus on unmet needs

– PD-L1–high disease without oncogenic divers

– Biomarker+ NSCLC in first-line setting

– NSCLC with brain metastasis

Integration of liquid biopsy, ctDNA dynamics, and CNS-specific endpoints

Key studies presented today:

ACTIVE	CLOSED
PALACE (GECP 22/01): ctDNA-guided adaptive immunotherapy	**CUBIK** (GECP 19/01): Translational characterization of brigatinib-treated ALK+ patients
	NIVIPI-Brain (GECP 21/02): Nivolumab + ipilimumab + platinum chemotherapy in patients with brain metastases

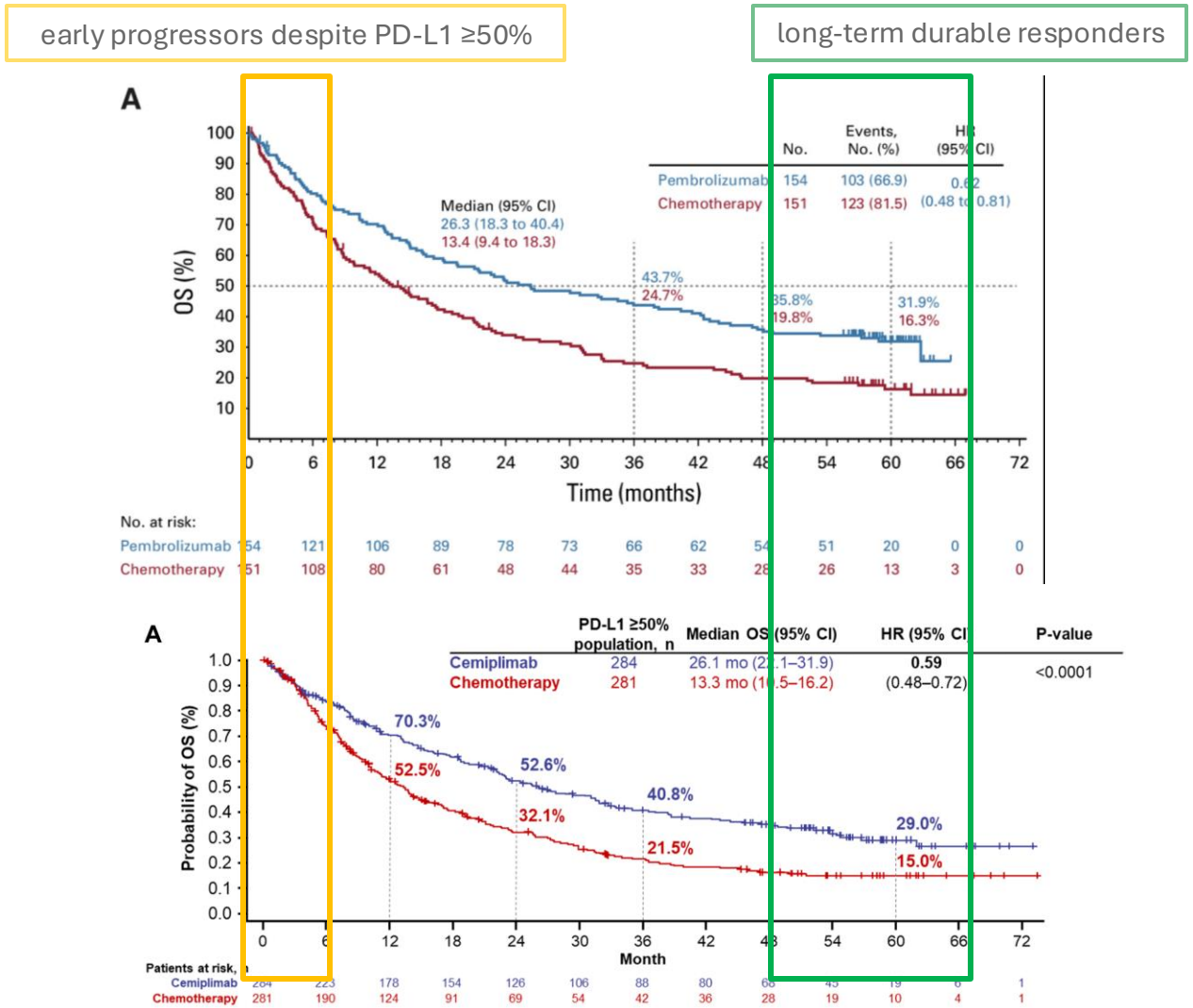
PALACE (GECP 22/01)

ACTIVE recruitment

Background

PD-L1 ≥50% NSCLC shows heterogeneous benefit with PD-(L)1 monotherapy

Some patients achieve deep and durable responses; others progress early despite high PD-L1



Reck et al., JCO 2021; Kilickap JTO 2025

PALACE (GECP 22/01)

ACTIVE recruitment

Background

PD-L1 ≥50% NSCLC shows heterogeneous benefit with PD-(L)1 monotherapy

Some patients achieve deep and durable responses; others progress early despite high PD-L1

ctDNA clearance after 1–2 cycles of immunotherapy correlates with:

– better ORR, longer PFS and OS

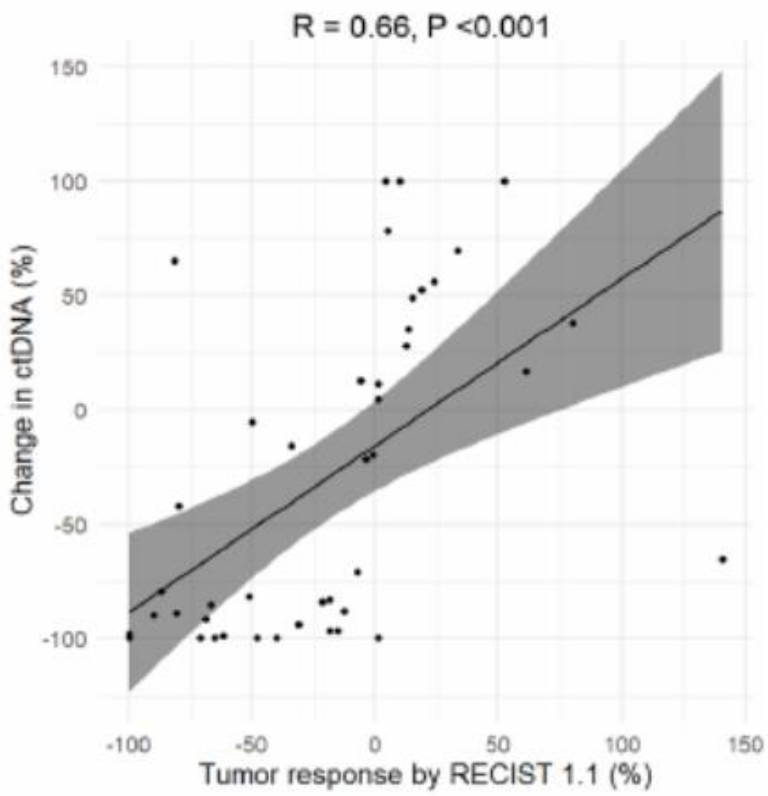
– early identification of primary resistance

Adaptive strategies may:

– de-escalate unnecessary chemotherapy in early responders

– intensify therapy in non-clearers with poor prognosis

PALACE explores whether treatment intensification based on early ctDNA dynamics improves survival



Ricciuti B, et al. J Immunother Cancer 2021

PALACE (GECP 22/01 – SGZ-2021-13545)

Protocol overview

ECOG 0-1
Systemic therapy-naive
NO EGFR,ALK, ROS1

Stage IV and IIIB/C* NSCLC patients with PD-L1≥ 50%

TREATMENT
Cemiplimab 350 mg for 2 cycles Q3W

ctDNA persistent/non-clearers

1. If progression or ctDNA increase

CBDA - paclitaxel
Chemotherapy + Cemiplimab 350 mg, 4 cycles Q3W

Cemiplimab 350 mg monotherapy

Add chemo

2. If no progression or ctDNA stable/decreased

Cemiplimab 350 mg monotherapy Q3W

until disease progression, unacceptable toxicity

Continue

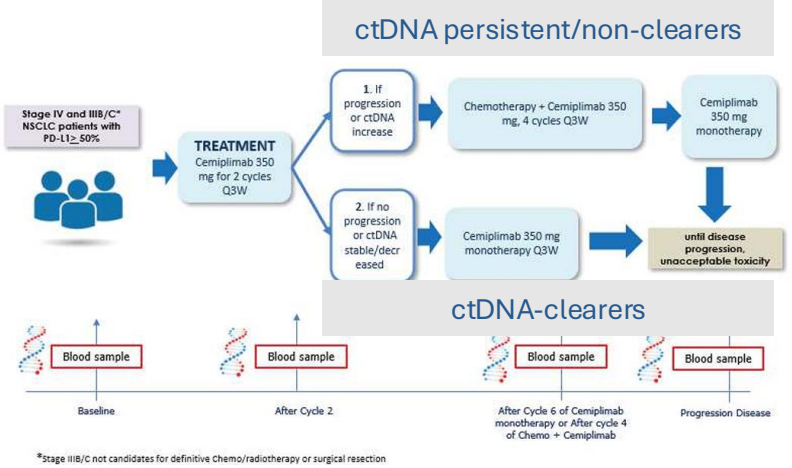
ctDNA-clearers

Blood sample — Baseline
Blood sample — After Cycle 2
Blood sample — After Cycle 6 of Cemiplimab monotherapy or After cycle 4 of Chemo + Cemiplimab
Blood sample — Progression Disease

*Stage IIIB/C not candidates for definitive Chemo/radiotherapy or surgical resection

PALACE (GECP 22/01 – SGZ-2021-13545)

Protocol overview



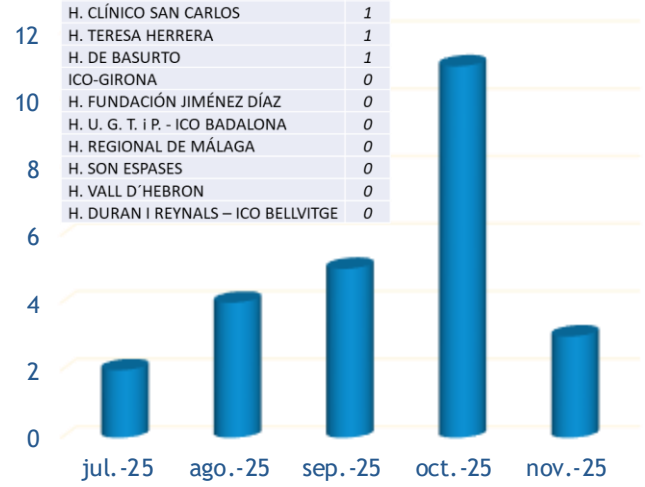
Primary Outcome Mesures
• Overall survival at 24 months using a ctDNA-guided adaptive treatment algorithm
Secondary Outcome Mesures
• PFS, ORR (RECIST 1.1), duration of response • ctDNA dynamics and correlation with radiologic response • Pattern of progression (CNS vs extracranial) • Safety of dynamic treatment intensification
Translational endpoints
• ctDNA clearance thresholds, molecular signatures of resistance

PALACE (GECP 22/01 – SGZ-2021-13545)

Recuitment and Challenges

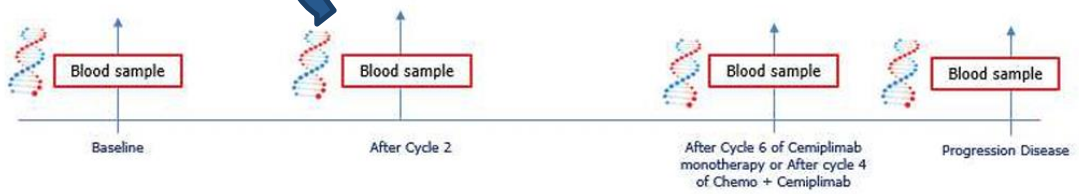
Sponsor: GECP
Planned number of patients: 63
First patient in (FPI): 29/07/2025
Included patients: 25 patients

HOSPITAL	Nº
H. PUERTA DE HIERRO	8
H. GENERAL DE ALICANTE	4
H. DE SALAMANCA	2
H. GENERAL DE VALENCIA	2
H. GENERAL DE ELCHE	2
H. SEVERO OCHOA	1
H. SANT PAU	1
H. SON LLÀTZER	1
H. U. DR NEGRÍN	1
H. CLÍNICO SAN CARLOS	1
H. TERESA HERRERA	1
H. DE BASURTO	1
ICO-GIRONA	0
H. FUNDACIÓN JIMÉNEZ DÍAZ	0
H. U. G. T. i P. - ICO BADALONA	0
H. REGIONAL DE MÁLAGA	0
H. SON ESPASES	0
H. VALL D´HEBRON	0
H. DURAN I REYNALS – ICO BELLVITGE	0



Recruitment reflects a biologically narrow window and logistic complexity around ctDNA sampling.

Recruitment Challenges	Proposed Solutions
Narrow PD-L1 ≥50% / driver-negative window	Reflex PD-L1 + NGS at biopsy; pathology auto-flags candidates
Preference for chemo-IO first-line	emphasise IO→ctDNA→escalation safety
ctDNA workflow complexity	Dedicated kits, fixed shipments, guaranteed turnaround
Real-world fragility (ECOG, burden)	Pre-select clinically stable profiles suited for IO-first
Early activation variability	Patient-focused messaging: chance to avoid chemo if ctDNA clears



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Integration of liquid biopsy, ctDNA dynamics, and CNS-specific endpoints

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CUBIK (GECP 19/01)

CLOSED recruitment

Background

ALK+ NSCLC is highly sensitive to 2nd/3rd generation TKIs

Resistance inevitably occurs

Resistance patterns include:

– ALK mutations (e.g., G1202R)

– Off-target bypass pathways (MET, EGFR, KRAS, IGF1R)

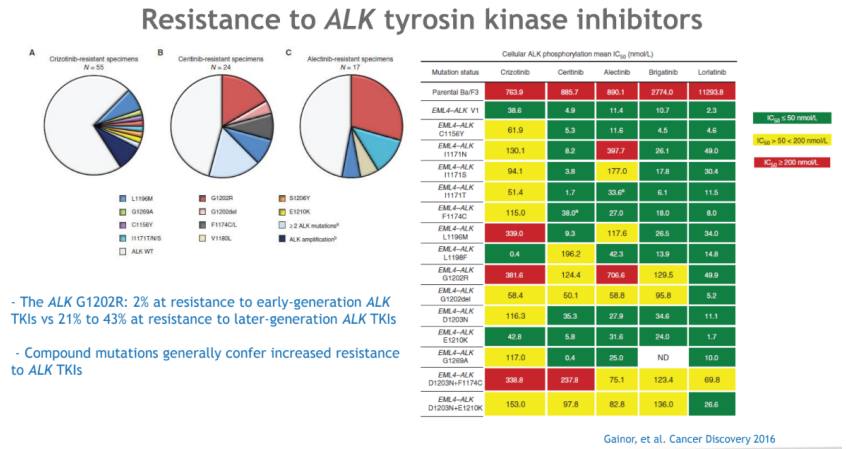
Liquid biopsy enables:

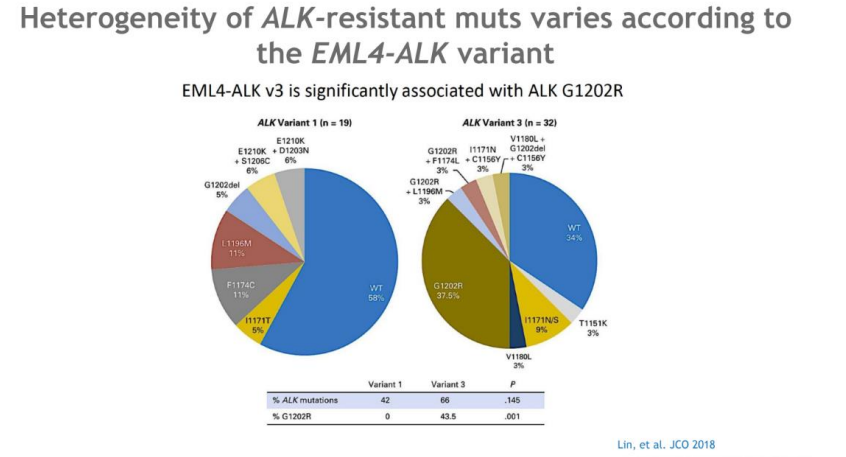
– real-time identification of emerging resistance

– tracking clonal evolution

– correlation between molecular progression and radiologic progression

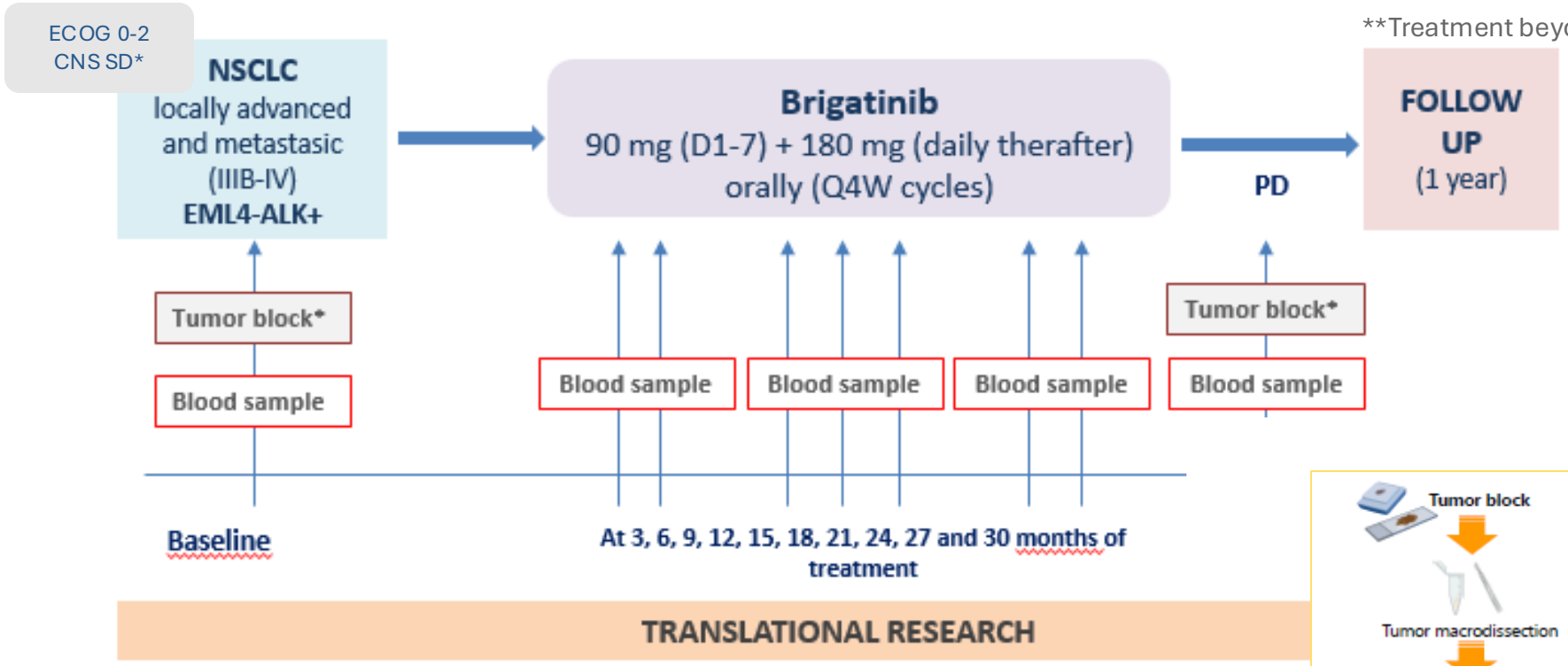
CUBIK is designed to deeply characterise brigatinib evolution in real-world GECP patients





CUBIK (GECP 19/01 – CCR-GECP-Brig)

Protocol overview

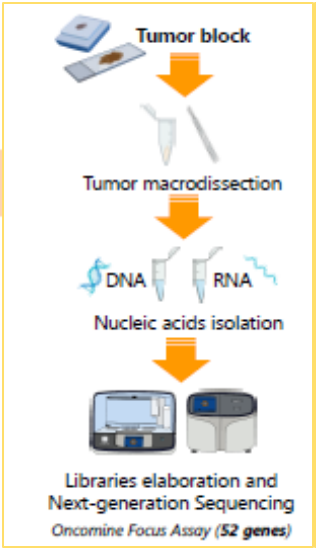


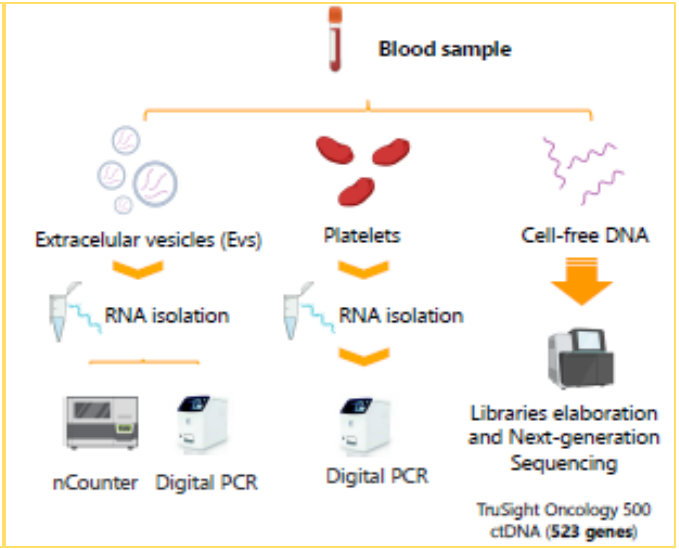
Primary Objective:

- Objective response rate (ORR)

Secondary Translational Objectives:

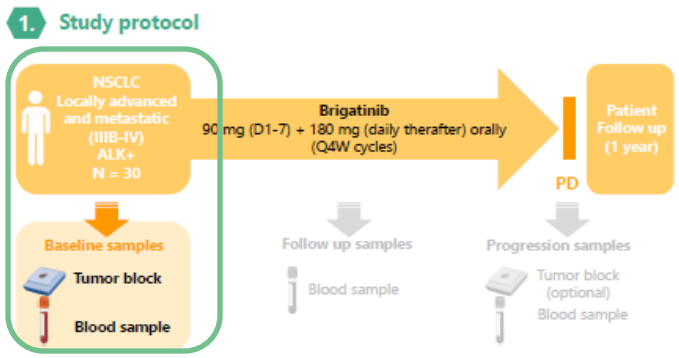
- Correlation of ctDNA findings with ORR and PFS
- Describe resistance mutations emerging during brigatinib treatment
- CNS control and intracranial progression-free survival
- Concordance between tumour genotyping and liquid biopsy
- Dynamics of variant allele fractions during treatment

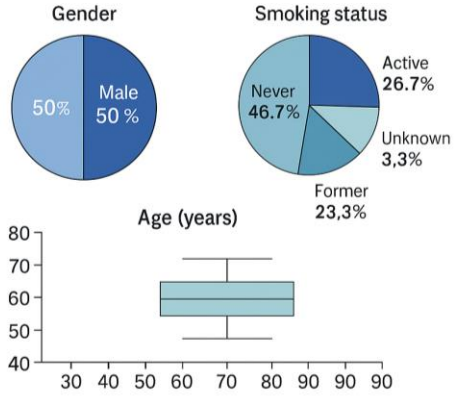




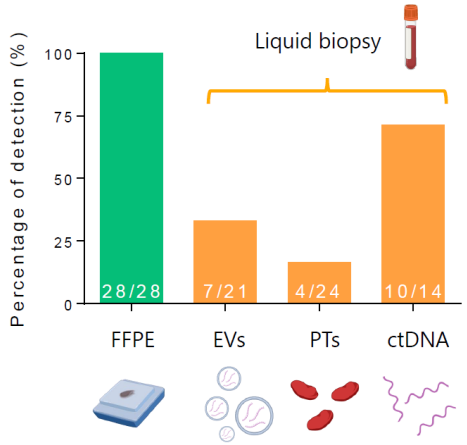
CNS SD*: CNS stable disease (treated/no)

CUBIK (GECP 19/01)



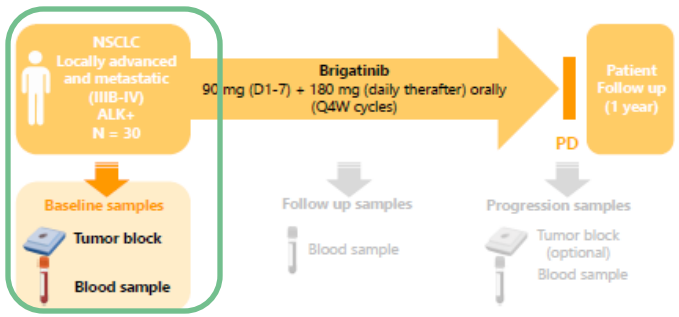


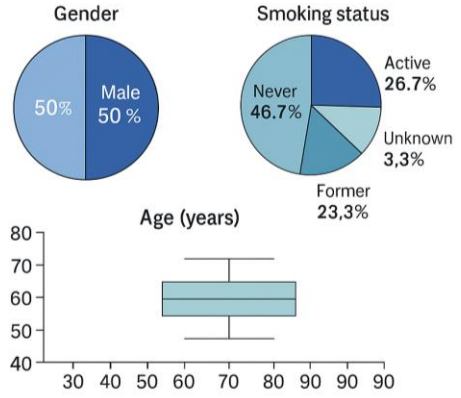
All patients had histologically confirmed adenocarcinoma (100%).



CUBIK (GECP 19/01)

1. Study protocol





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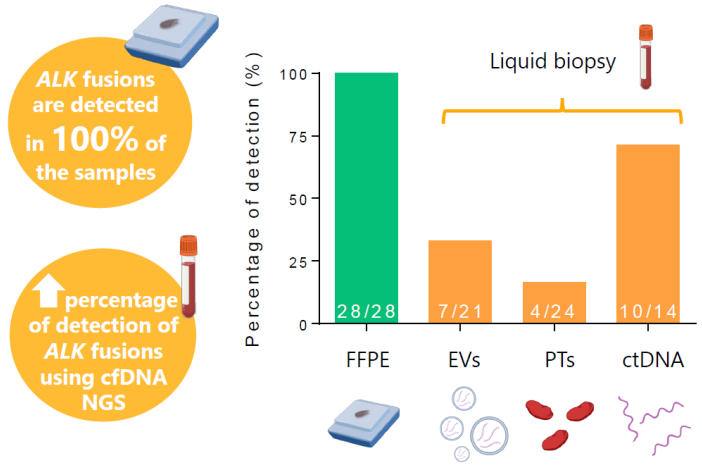
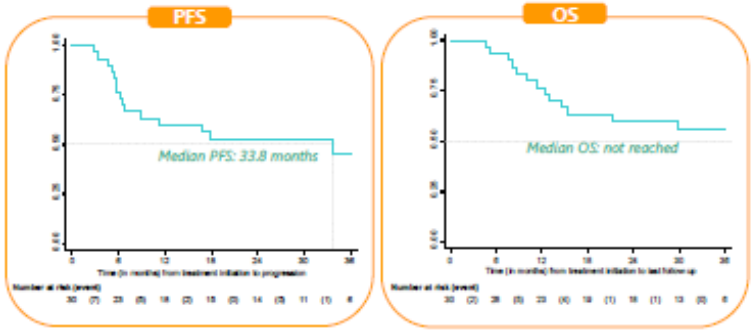


All patients

ORR 93,1%

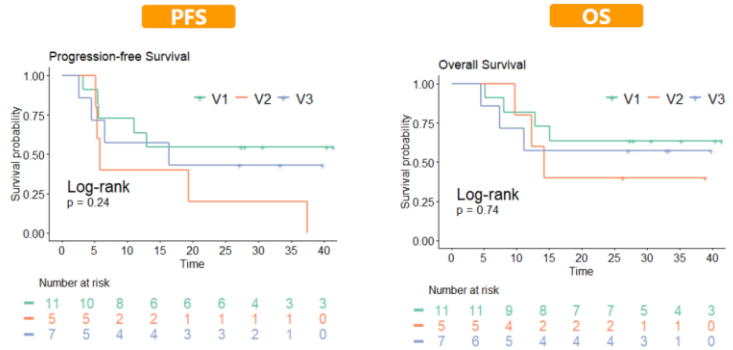
mDOR 14,7m



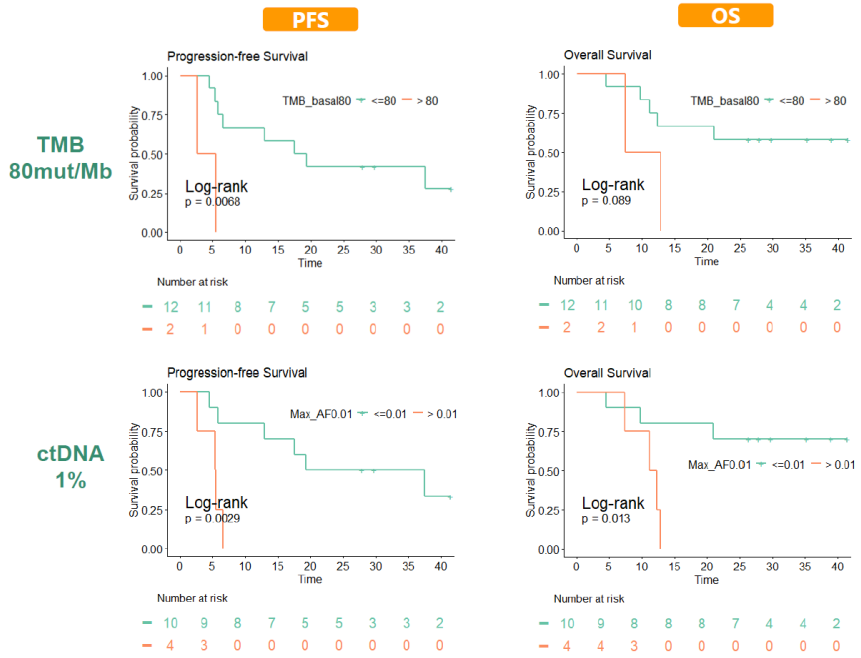
MEDIAN FOLLOW- UP: 33.6 months

Variant type

No significant differences in survival outcomes according to the type of variant



4. ctDNA and blood TMB prognostic value



CUBIK (GECP 19/01 – CCR-GECP-Brig)

Recuitment and future results

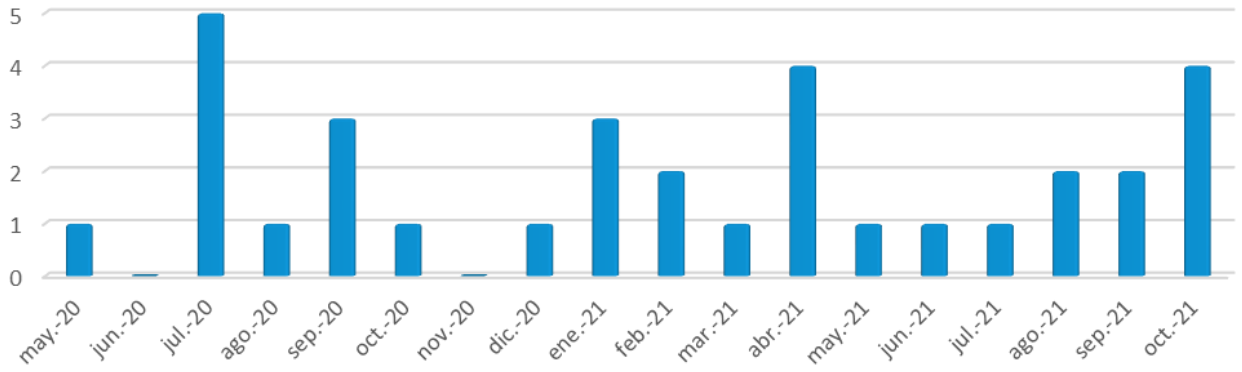
Sponsor: GECP

First patient in (FPI): 21/05/2020

Included patients: 33 patients

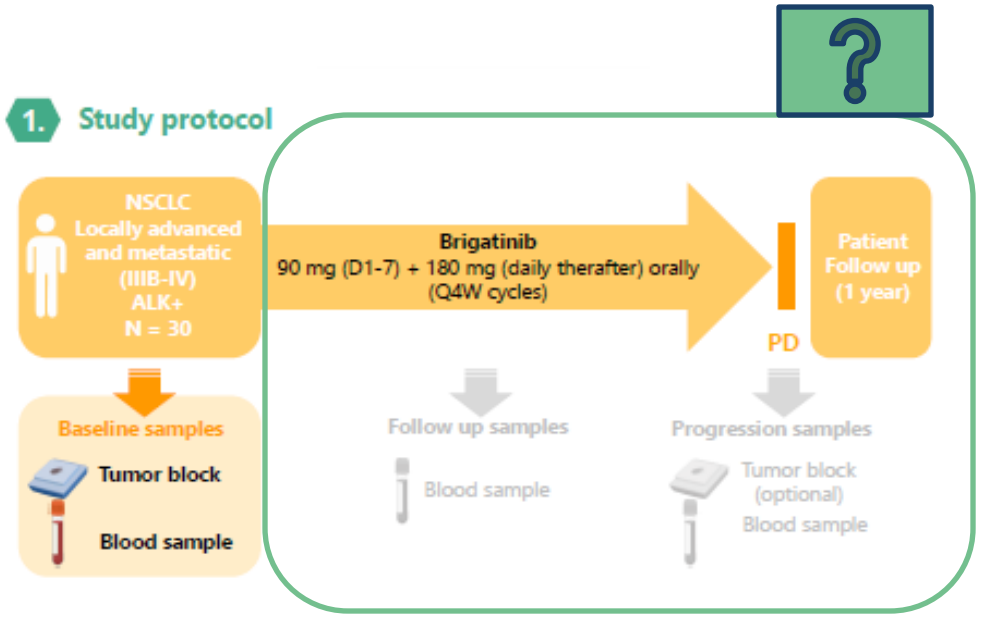
Last patient included: 27/10/2021

HOSPITAL	Nº
CH. LA CORUÑA	9
H. SON ESPASES	5
H. PUERTA DE HIERRO	4
H. REGIONAL DE MÁLAGA	4
H. DURAN I REYNALS – ICO BELLVITGE	3
H. INSULAR GRAN CANARIA	3
H. VALL D'HEBRON	2
H. FUNDACIÓN JIMÉNEZ DÍAZ	2
H. LA FE	1
H. SANT PAU	0
H. U. G. T. i P. - ICO BADALONA	0
H. DE CRUCES	0
H. CLÍNICO DE SALAMANCA	0
H. GENERAL DE ALICANTE	0
H. GENERAL DE VALENCIA	0
CH UNIVERSITÁRIO PORTO	0
CH UNIVERSITÁRIO COIMBRA	0
CH UNIVERSITÁRIO LISBOA	0



Serial molecular sampling is key

Treatment beyond progression allows correlation between molecular and clinical resistance timelines.

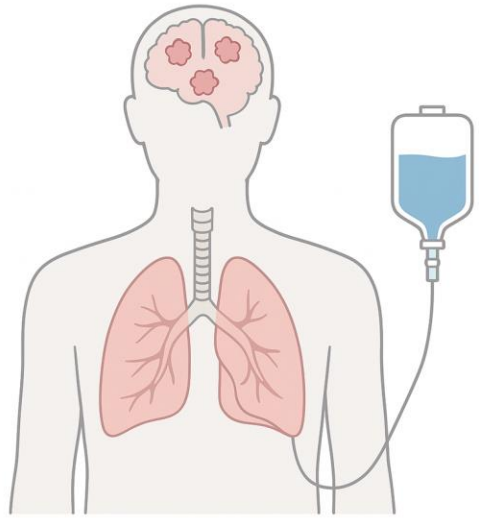


NIVIPI-Brain (GECP 21/02)

CLOSED recruitment

Background

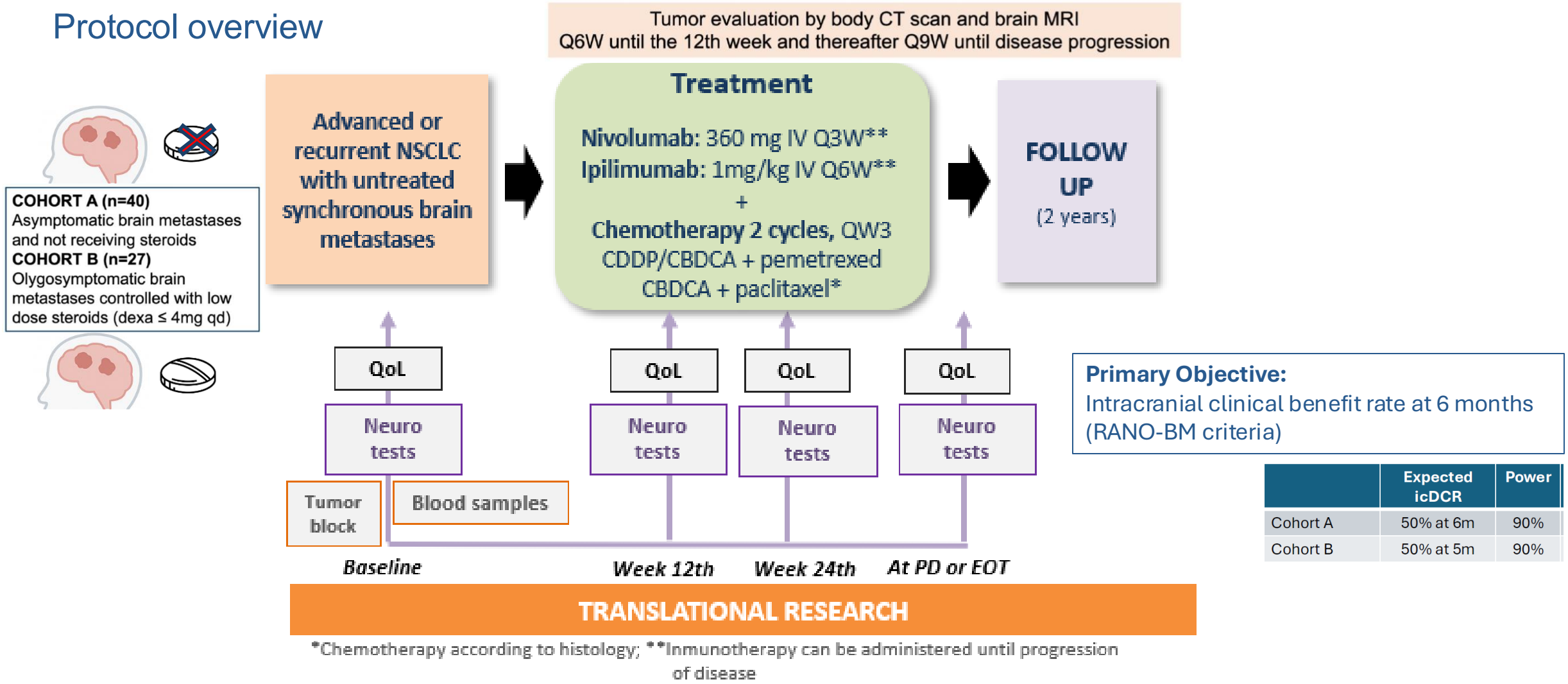
- Chemo-IO or IO monotherapy is the standard of care systemic treatment in patients with advanced non-oncogene addicted NSCLC with brain metastases
- Dual blockade of PD-1 an CTLA-4 has demonstrated significant intracranial efficacy in patients with advanced melanoma and NSCLC with brain metastases
- In selected cases, upfront chemo-IO with deferral of brain radiotherapy may be acceptable when endorsed by a multidisciplinary team
- In the NIVIPI-Brain trial (GECP 21/02), we investigated the efficacy and safety of the combination of nivolumab plus ipilimumab combined with a short course of chemotherapy in patients with NSCLC who had untreated brain metastases



Le Rhun et al. Ann Oncol 2021; Tawbi et al. New Engl J Med 2018; Long et al. Lancet Oncol 2018; Paz-Ares et al. J Thorac Oncol 2023

NIVIPI-Brain (GECP 21/02 - CA209-6E4)

Protocol overview



Primary Objective:
Intracranial clinical benefit rate at 6 months (RANO-BM criteria)

	Expected icDCR	Power
Cohort A	50% at 6m	90%
Cohort B	50% at 5m	90%

Secondary Objectives:
• Intracranial ORR, PFS and OS, Time to brain radiotherapy, Steroid tapering feasibility, Safety of nivo+ipi+chemotherapy in BM patients, Translational analyses: immune profiles associated with CNS response

NIVIPI-Brain (GECP 21/02 - CA209-6E4)

Ethic Committee approval: 22/09/2021

AEMPS approval: 08/10/2021

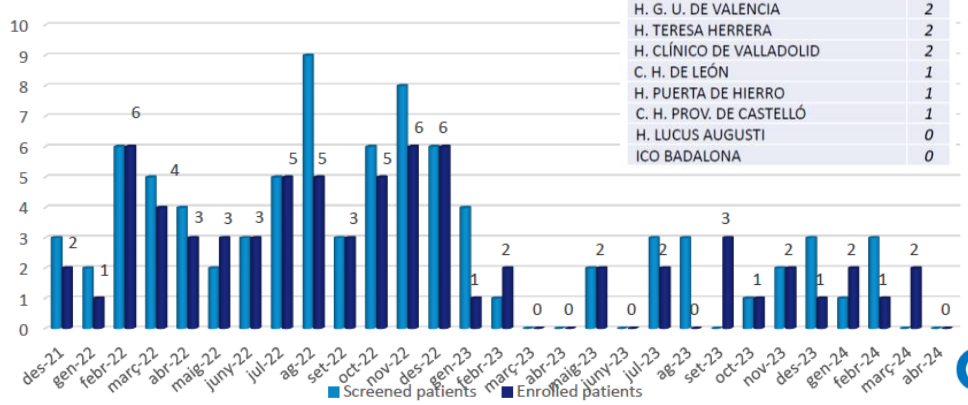
First site opened: 18/11/2021

First patient in (FPI): 02/12/2021

Included patients: 71 patients (44 cohort A & 27 cohort B)

Last patient included: 15/03/2024

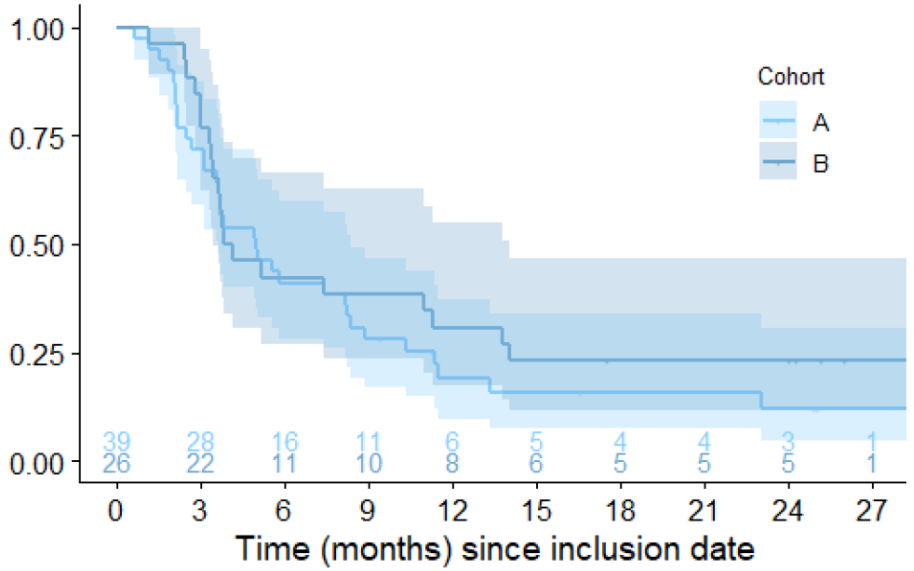
HOSPITAL	Nº
H. REGIONAL DE MÁLAGA	14
H. U. 12 DE OCTUBRE	8
ICO BELLVITGE	7
C. H. DE JAÉN	7
H. SANT PAU	6
H. VALL D'HEBRON	5
H. SON LLÀTZER	3
H. FUNDACIÓN JIMÉNEZ DÍAZ	3
H. INSULAR GRAN CANARIA	2
H. U. Y POLITÉCNICO LA FE	2
H. G. U. DE VALENCIA	2
H. TERESA HERRERA	2
H. CLÍNICO DE VALLADOLID	2
C. H. DE LEÓN	1
H. PUERTA DE HIERRO	1
C. H. PROV. DE CASTELLÓ	1
H. LUCUS AUGUSTI	0
ICO BADALONA	0



NIVIPI-Brain (GECP 21/02)

CLOSED recruitment

Primary Endpoint: Intracranial DCR (by RANO-BM)



Cohort	Intracranial DCR
A	At 6 months 41% (95% CI 28-60)
B	At 5 months 46% (95% 31-79)

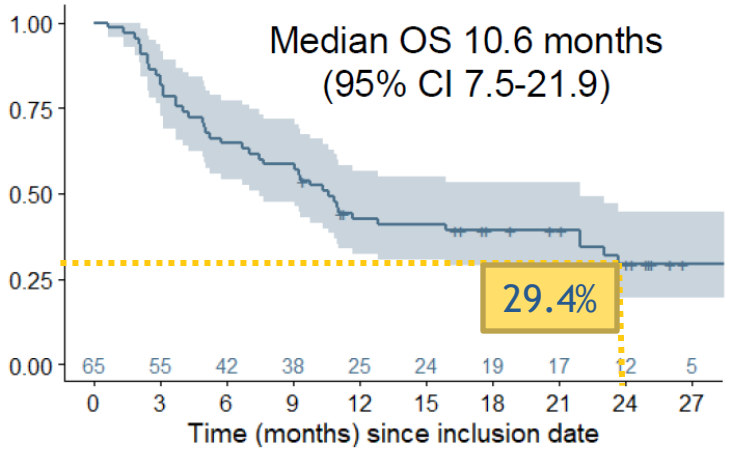
As the intracranial DCR is below 50%, the study did not achieve the expected efficacy

Reasons for treatment discontinuation:
- Progression: 36 (55.4%)
- Toxicity: 13 (20%)
- Patient decision: 1 (1.5%)
- Physician decision: 3 (3.5%)
- Death: 3 (4.6%)

"did not meet the primary endpoint in patients with advanced NSCLC with untreated brain metastases since the intracranial DCR rate was below the pre-specified threshold"

Overall Survival Analysis

All patients



2y OS rate = 29.4% (95% CI 19.4-44.7)
Median FUP 24.9 months

"No major differences in terms of overall survival were observed between cohort A and B (oligosymptomatic or corticosteroids treatment)"

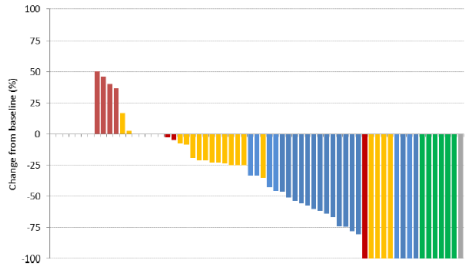
NIVIPI-Brain (GECP 21/02)

CLOSED recruitment

Best Overall Response Rate (ORR) in all patients

CNS Best ORR (by RANO-BM)

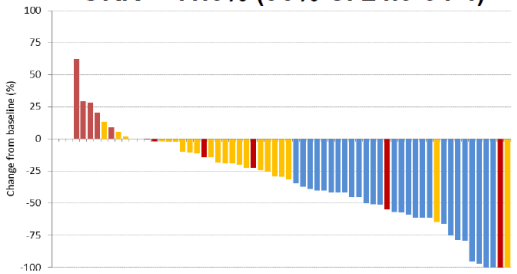
ORR = 41.5% (95% CI 24.9-54-4)



Clinical Benefit Rate (CBR) = 73.8%
6 CR, 21 RP and 21 SD

Systemic Best ORR (by RECIST)

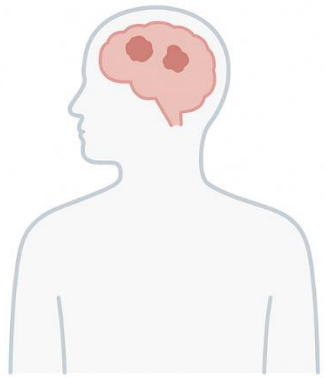
ORR = 41.5% (95% CI 24.9-54-4)



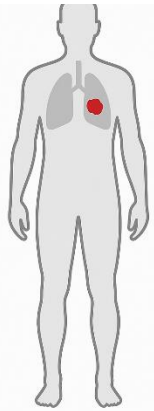
Clinical Benefit Rate (CBR) = 78.4%
27 RP and 24 SD

Most responses were concordant between both compartments, but 4 patients with clinical benefit by RECIST (CR, PR or SD) had intracranial PD, while only 1 patient with CNS clinical benefit had PD by RECIST

Intracranial

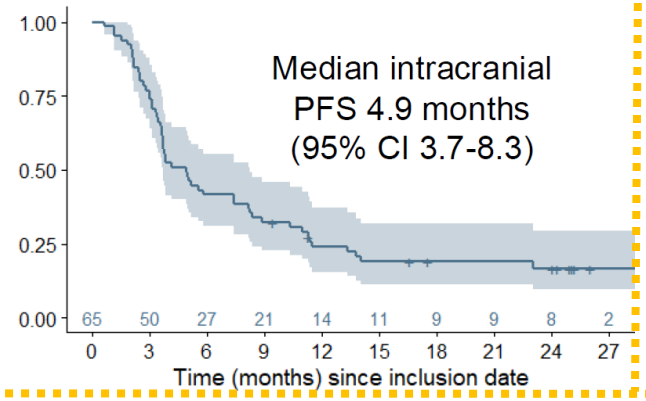


Systemic

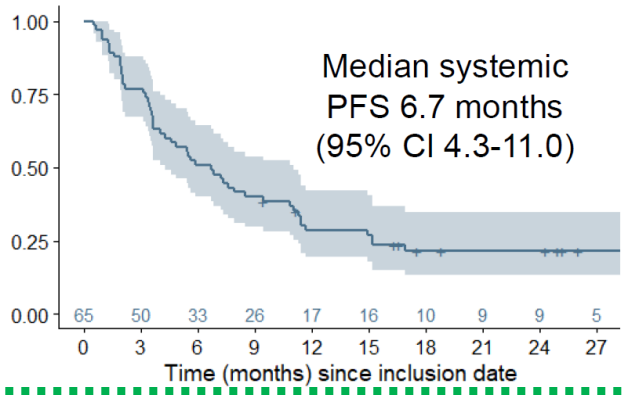


Intracranial and Systemic PFS in both cohorts

CNS PFS (by RANO-BM)



Systemic PFS (by RECIST)



NIVIPI-Brain (GECP 21/02)

CLOSED recruitment

Safety results

Median number of cycles (range)	
Nivolumab	7 (1-33)
Ipilimumab	4 (1-17)
G3-4 Treatment-related AEs	
Nivolumab	19 (29.2%)
Ipilimumab	20 (30.7%)
Chemotherapy	27 (41.5%)
Severe Adverse Events	
All	31 (63.1%)
G3-G4	29 (44.6%)
G5	0 (0%)

Neurological adverse events in all patients regardless of their relationship and their frequency (n=65)

	n	%	G1	G2	G3	G4	G5
Headache	11	16.90%	10	0	1	0	0
Other	10	15.40%	5	1	4 (*)	0	0
Seizure	3	4.60%	1	0	1	1	0
Cognitive disturbance	1	1.50%	0	0	1	0	0
Paresthesia	6	9.20%	6	0	0	0	0
Dizziness	5	7.70%	3	2	0	0	0
Somnolence	3	4.60%	3	0	0	0	0
Dysgeusia	2	3.10%	1	1	0	0	0
Syncope	2	3.10%	2	0	0	0	0
Insomnia	2	3.10%	2	0	0	0	0
Muscle weakness	2	3.10%	1	0	0	0	0
Neuralgia	1	1.50%	1	0	0	0	0
Peripheral sensory neuropathy	1	1.50%	1	0	0	0	0
Tremor	1	1.50%	1	0	0	0	0
Depression	1	1.50%	1	0	0	0	0

(*) stroke (n=2) desorientation (n=1), weakness in lower limbs (n=1)

To Conclude

Integrating the SLCG-Trials into the NSCLC Landscape

These trials address three distinct biological niches — PD-L1–high, ALK+, and CNS-metastatic disease — while sharing a strong translational identity

Clinic and translational bridge: extensive translational programs that will inform future personalised strategies

Represent complementary strategies the SLCG is exploring to personalise therapy in advanced NSCLC

- ctDNA-guided adaptive immunotherapy
- targeted therapy evolution analysis: real-time resistance genomics in ALK+ patients
- CNS-focused immunotherapy: dedicated strategy for patients with brain mets

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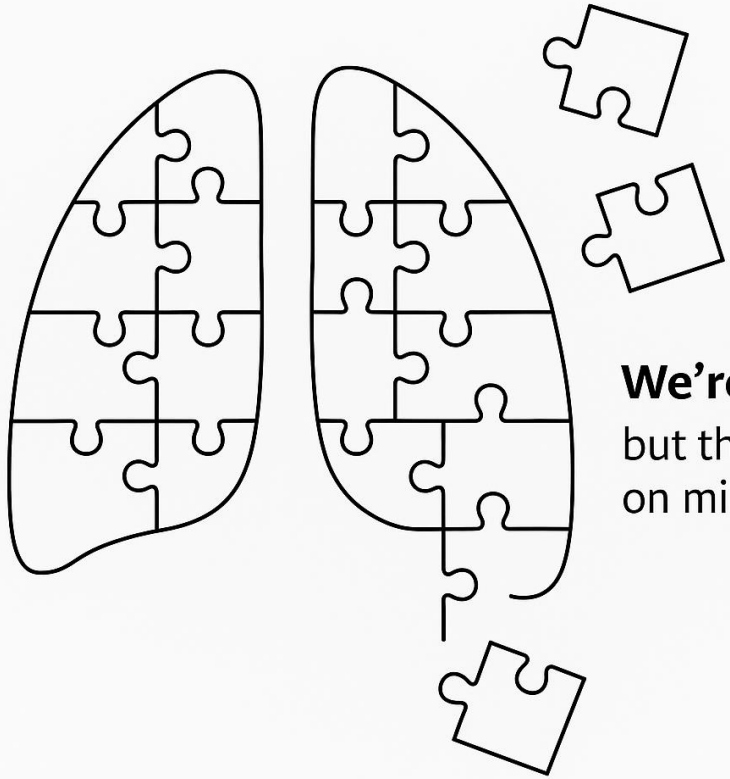

We're getting closer...
but the puzzle still insists on missing a few pieces.

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GECP lung cancer research