PROTOCOL SUMARY

1.0. Type of Study

Clinical Trial

1.1. Study Sponsor

Fundación GECP

Avda. Meridiana 358, 6a planta
08027 Barcelona

1.2. Tittle

"A Phase II open-label multicenter exploratory study to assess efficacy of Pembrolizumab re-challange as second or further line in patients with advanced non - small cell lung cancer"

REPLAY: Re-challenge Pembrolizumab study

1.3. Protocol Code

GECP 17/02

1.4. Principal Investigator and Coordinator

Principal Investigator: Dr. Luís Paz Ares, PH D
Coordinator: Dr. Santiago Ponce, Ph D

1.5. Participant Sites

19 sites in Spain

1.6. Drug: dose, type, administration

2 groups depending on when the progression disease is diagnosed but the treatment after progression will be the same: Pembrolizumab

Drug	Dose/Potency	Dose Frequency	Route of Administration	Regimen/Treatment Period	Use
Pembrolizumab	200 mg	Q3W	IV infusion	Day 1 of each 3 week cycle	Experimental
Chemotherapy will be at investigators choice.					

1.7. Type of Clinical trial

Phase II, Exploratory study, Open label

1.8. Principal and secondary objectives

Principal objective:

To evaluate the efficacy of Pembrolizumab re-challenge administered 200 mg iv every 21 days in second or further line for advanced NSCLC after progression to check point PD1 / PDL1 inhibitors measured by Overall Response Rate (ORR) per RECIST v1.1 and per modified RECIST (irRC).

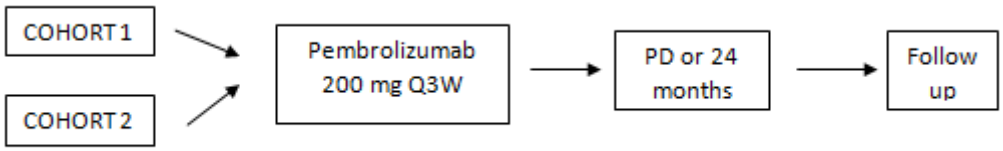
Hypothesis: Patients that have exhibit benefit to check point PD1 / PDL1 inhibitors may benefit from further Pembrolizumab therapy at the time of progression. The degree of benefit may depend on the initial response to previous check point PD1 /PDL1 inhibitors and its duration, and to the intercalation (or not) of any additional treatments such as chemotherapy among those patients without benefit to check point PD1/PDL1 inhibitors.

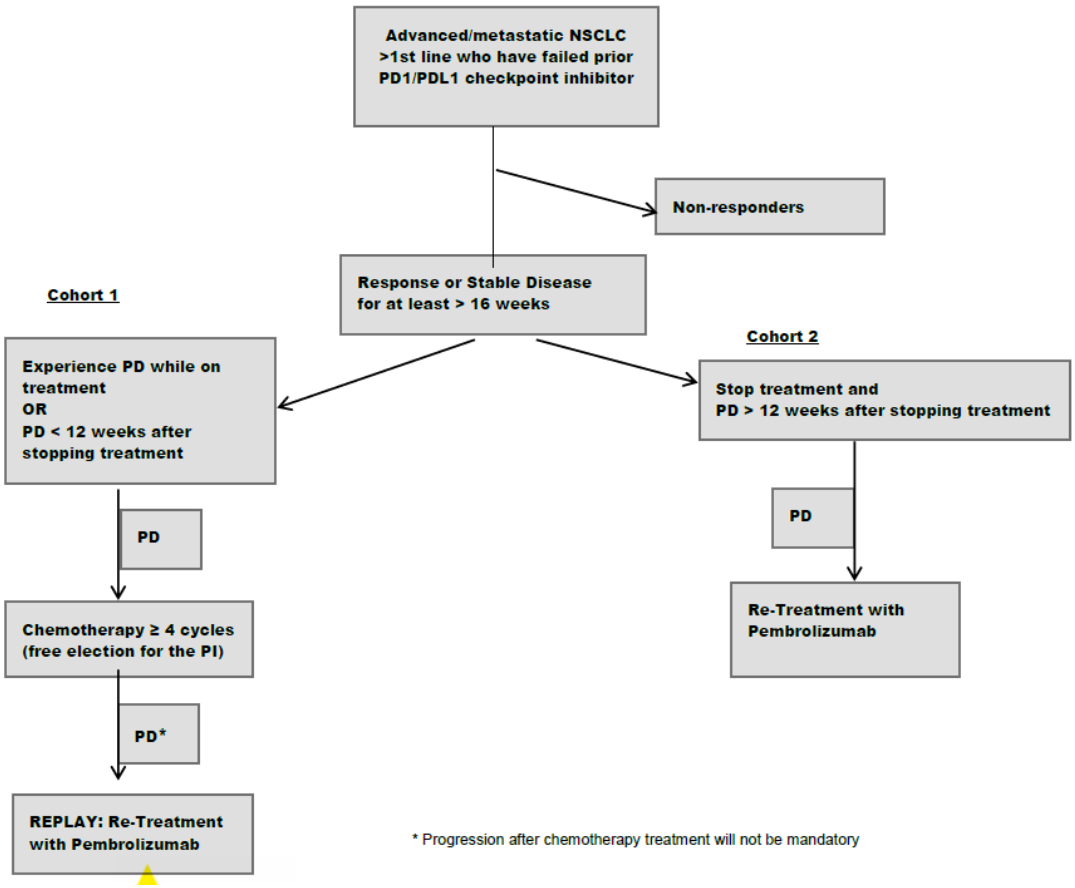
Secondary objectives:

- To evaluate the efficacy of Pembrolizumab re-challenge administered 200 mg iv every 21 days in second or further line for advanced NSCLC after progression to check point PD1 / PDL1 inhibitors measured by Progression Free Survival (PFS) per RECIST v1.1 and per modified RECIST. and Overall Survival (OS).

- To evaluate the safety and tolerability profile of Pembrolizumab re-challange administered 200 mg iv every 21 days in second or further line for advanced NSCLC after progression to check point PD1 / PDL1 inhibitors measured by Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 (U.S. Department of Health and Human Services - National Cancer Institute - National Institutes of Health)

1.9. Trial design and patient selection diagram





1.10 Disease

Advanced/metastatic NSCLC ≥1st or further line, who have failed prior PD1/PDL1 checkpoint inhibitor

1.11. Exploratory Objective

To evaluate predictive and prognostic exploratory biomarkers in archival or fresh tumor tissue and blood and their association with disease status and/or response to treatment.

1.12 Study population and simple size

2 groups depending on when the progression disease is diagnosed but the treatment after progression will be the same: Pembrolizumab

Cohort 1: Documented prior benefit (Stable Disease, Partial Response, Complete Response) to check point PD1/PDL1 inhibitor (Nivolumab, Pembrolizumab, Darvolumab, Atezolizumab, Avelumab or others) for at least 16 weeks (Stable Disease, Partial Response, Complete Response) and progression while on treatment (or <12 weeks after stopping) with the same PD-1/PD-L1 inhibitors. These patients should have received subsequent treatment with Chemotherapy for at least 4 courses

Cohort 2: Documented prior benefit (Stable Disease, Partial Response, Complete Response) to check point PD1/PDL1 inhibitor (Nivolumab, Pembrolizumab, Darvolumab, Atezolizumab, Avelumab or others) for at least 16 weeks (Stable Disease, Partial Response, Complete Response) and progression >12 weeks after stopping treatment. No subsequent treatment before rechallenge is allowed in this cohort

Sample size: 110 patients, 55 in each cohort

1.13. Study duration

The sponsor estimates that the trial will require approximately 4 years (2 years of inclusion period + 1 year to achieve (FPLV) + 1 year of follow up

Each subject will participate in the trial from the time the subject signs the Informed Consent Form (ICF) through the final protocol-specified contact. Estimated period of time of two years per patient.