IFCT-1701 DICIPLE: a randomized phase 3 trial comparing continuation Nivolumab-Ipilimumab doublet immunotherapy until progression versus observation in patients with PDL1-positive stage IV Non-Small Cell Lung Cancer (NSCLC) after Nivolumab-Ipilimumab induction treatment

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G. Zalcman, A.C. Toffart, A.-C. Madroszyk Flandin, O. Molinier, C. Dayen, T. Egenod, A. Dixmier, E. Giroux Leprieur, P. Masson, N. Cloarec, L. Thibonnier, L. Favier, D. Debieuvre, J. Mazieres, S. Van Hulst, E. Pichon, E. Amour, F. Morin, P.-J. Souquet

Sponsored by the French Cooperative Thoracic Intergroup (IFCT) – 75009 PARIS (France)

BACKGROUND

We raise the hypothesis that a 'stop and go' strategy with induction by double immunotherapy Nivolumab + Ipilimumab combination during 6 months, followed by observation in patients with disease control (DC) at 6 months, would not be inferior to immunotherapy combination continuation until progression or unacceptable toxicity, in terms of progression-free survival, allowing lower toxicities cumulative rates, better quality of life and lower costs. Such strategy should not penalize overall survival, provided resuming immunotherapy at disease progression before second-line platinum-based chemotherapy.

OBJECTIVES

- **Primary objective**
  According to a non-inferiority design, the primary objective will be to observe not significantly different median 1st Progression-Free Survival (PFS) from the date of randomization (thus in disease controlled patients) for the 'stop and go' arm B, as compared to the standard arm A with immunotherapy until progression or unacceptable toxicity, followed by cisplatin-based chemotherapy at progression.
- **Secondary objectives**
  Quality of life
  Overall survival
  Safety and Tolerance

ELIGIBILITY CRITERIA

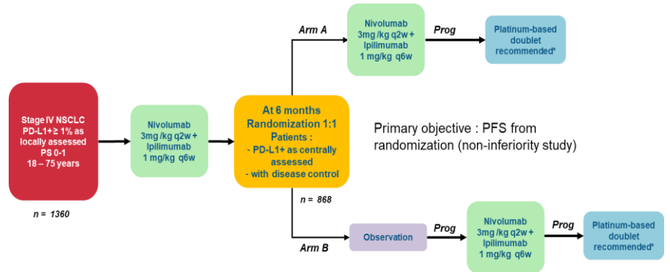
Inclusion Criteria

- Histologically-proven NSCLC (squamous or non-squamous)
- Stage IV (M1, including M1a pleural involvement) disease (8th classification TNM, UICC 2015)
- ECOG PS < 1
- Measurable tumor disease by CT or MRI per RECIST 1.1 criteria
- Available tumor samples for centralized PD-L1 immunohistochemistry analysis
- PD-L1 tumor content ≥ 1% and < 50% tumor cells as assessed locally by the investigator center

Exclusion Criteria

- Known EGFR activating tumor mutation (deletion LREA in exon 19, L858R or L861X mutations in exon 21, G719A/S mutation in exon 18) or HER exon 20 insertion (either tissue or plasma cfDNA mutation).
- Known ALK or ROS1 gene rearrangement as assessed by IHC, FISH or NGS sequencing

TRIAL DESIGN



* following the French National Cancer Institute (INCa) guidelines of March 2015 for stage IV, chemo-naive NSCLC, platinum-based doublet for at least 4 cycles, followed by maintenance single chemotherapy until progression or unacceptable toxicity.

On-study tumor assessments will begin at Week 6 post inclusion (± 7 days) and be performed every 6 weeks (± 7 days) until Week 24. After Week 24, tumour assessments will be performed every 8 weeks (± 7 days) until progression.

TREATMENTS

- **INDUCTION** : Patients are treated by nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 6 weeks during 24 weeks.
- **ARM A** : Patients are treated by nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 6 weeks until progression or unacceptable toxicity.
- **ARM B** : Patients are observed until progression then are treated by nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 6 weeks until progression or unacceptable toxicity

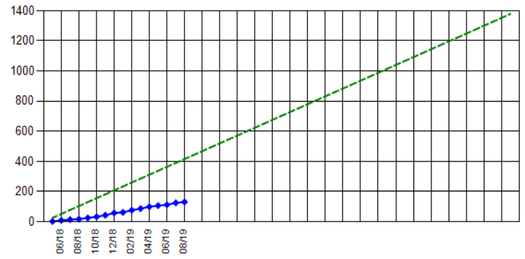
STATISTICAL METHODS

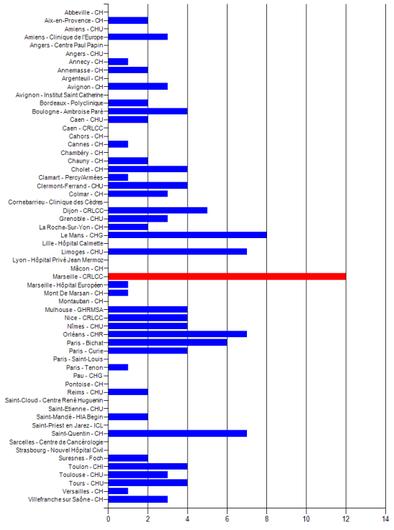
Randomized Phase III study (Fleming two-stage method), with a 2.5% unilateral alpha risk, and a power of 80%

Assuming an estimated median PFS duration of 20 months from randomization, and a pre-specified non-inferiority limit for the hazard ratio (HR) of 1.25 to be excluded, it was estimated that a total of 868 patients (651 events needed) would be needed to be randomized (1:1). Non-inferiority will be concluded if the upper limit of the 95% confidence interval (CI) of the HR will be ≤ 1.25

ACCRUAL (02-SEPT-2019)

131 enrolled patients from 37 French centres – 19 patients randomized





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Poster online
www.ifct.fr

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