SYNOPSIS

TITLE	**BLaDE** **B**RAF V600-mutated **L**ung carcinoma treated with the combination of **D**abrafenib- trametinib: a retrospective **E**valuation
SCIENTIFIC COMMITTEE	Jean-Bernard Auliac (CHI, Créteil) Aurélie Swalduz (Centre Léon Bérard, Lyon) Pierre-Jean Souquet (Hospices Civils de Lyon)
PHASE	Not applicable
TYPE OF STUDY	Retrospective observational study (cohort) / secondary use of existing data
PRODUCT EVALUATED	**D**abrafenib- trametinib
METHOD	**The primary objective** is to evaluate overall survival (OS) at 12 months in non-small cell lung cancer (NSCLC) *BRAF V600E*-mutated patients receiving the combination of dabrafenib-trametinib as second line or more treatment **Secondary objectives are:** To determine: ○ OS at 18 and 24 months and median OS in NSCLC *BRAF V600E*-mutated patients receiving the combination of dabrafenib-trametinib as second line or more treatment ○ OS at 12, 18 and 24 months and median OS in NSCLC *BRAF V600E*-mutated patients receiving the combination of dabrafenib-trametinib as first-line treatment ○ OS at 12, 18 and 24 months and median OS in NSCLC *BRAF V600E*-mutated patients regardless of the treatment received ○ OS at 12, 18 and 24 months and median OS in NSCLC *BRAF V600E*-mutated patients not treated by the combination of dabrafenib-trametinib, according to the treatment and the line received ○ OS at 12 months and median OS in NSCLC *BRAF V600 non E*-mutated patients according to the treatment and the line received ○ Real-world progression-free survival (PFS) ▪ in NSCLC *BRAF V600E*-mutated patients receiving the combination of dabrafenib-trametinib as first-line treatment ▪ in NSCLC *BRAF V600E*-mutated patients receiving the combination of dabrafenib-trametinib as second-line treatment or more ▪ in NSCLC *BRAF V600E*-mutated patients not treated by the combination of dabrafenib-trametinib, according to the treatment and the line received ▪ in NSCLC *BRAF V600 non E*-mutated patients according to the treatment and the line received ○ Best response ▪ in NSCLC *BRAF V600E*-mutated patients receiving the combination of dabrafenib-trametinib as first-line treatment ▪ in NSCLC *BRAF V600E*-mutated patients receiving the combination of dabrafenib-trametinib as second-line treatment or more

	○ Reason of treatment discontinuation and suspension (including toxicity, in particular thrombosis and QTc prolongation) ○ Duration of treatment ○ Duration of treatment beyond progression ○ Duration Response Rate ○ Efficacy of subsequent therapies ○ Reason of subsequent therapies discontinuation ○ NSCLC *BRAF V600 (E or non E)* patients'characteristics ○ Description and impact of co-mutations on efficacy of dabrafenib-trametinib combination ○ Eligible but not included patients'characteristics (size, reasons of no inclusion, description of type of center, investigator's specialty) **Population included** All patients with histologically or cytologically confirmed extensive stage NSCLC with *BRAF V600* (E or non E) mutation diagnosed on tumor sample and/or on liquid biopsy (co mutations allowed) between 01/01/2016 and 31/12/2019 **<u>Study endpoints:</u>** ○ <u>The primary endpoint</u> will be the OS for NSCLC BRAF V600E-mutated patients receiving dabrafenib-trametinib as second-line treatment or more and will be determined as the time from the first dose of treatment with dabrafenib-trametinib to death from any cause. OS rate will be measured at 12 months. **<u>Secondary endpoints:</u>** ○ OS will be determined as the time from the date of first dose of treatment or the diagnosis to the date of death due to any cause. OS rate at 12, 18, 24 months and median OS will be measured ○ *Real-world* PFS will be defined as the time from first dose of treatment (with dabrafenib-trametinib combination or other treatment) to first occurrence of disease progression (defined by the treating physician) or death from any cause during the study. PFS rate at 12 months and median PFS will be measured. ○ Duration of treatment will be defined as time from first dose of dabrafenib-trametinib combination to discontinuation (interruption of more than 2 months) ○ Duration of treatment with dabrafenib-trametinib combination beyond progression will be defined as time between first occurrence of disease progression and treatment discontinuation ○ Duration Response Rate will be defined as the time from the date of the first documented response (complete or partial) to the earliest date of disease progression ○ Best response: best response recorded from the start of treatment with dabrafenib-trametinib combination until disease progression or start of further anti-cancer treatment ○ Reason of dabrafenib-trametinib discontinuation and suspension will be collected, including toxicity in particular thrombosis and QTc prolongation)

<table>
<tr><td></td><td>

Efficacy of subsequent therapies will be evaluated using PFS and best response
Baseline characteristics: these will be collected in the study at NSCLC diagnosis and initiation of dabrafenib-trametinib treatment combination

Sample size
The expected precision according to the sample size of this analysis is based on the results of the pivotal study (57 patients treated with dabrafenib-trametinib combination): 66 % OS at 12months (11).
With the above information, the inclusion of 200 patients will allow for a precision of less than 7% in the 12 months overall survival. The BLaDE study will thus aim to collect the data of 200 BRAF V600E patients for the primary objective.

Data will be collected at the care sites from the source medical records by IFCT research study assistants entering the full-compliant 21FRpart11/GPRD E-IFCT database (MARVIN, XCLINICAL).
</td></tr>
<tr><td>TIMELINES</td><td>
<table>
<tr><th>Study scheduled</th><th>Dates</th></tr>
<tr><td>Selection period</td><td>1st January 2016 – 31st December 2019</td></tr>
<tr><td>Centers recruitment and administrative procedures with participating centers</td><td>October 2020-December 2020</td></tr>
<tr><td>Main data collection period</td><td>1st January 2021 – 30th Mars 2021</td></tr>
<tr><td>Data management and Statistical analysis</td><td>1st April 2021 – 31st June 2021</td></tr>
<tr><td>Final data management and statistical analysis</td><td>1st September 2021</td></tr>
<tr><td>Final clinical study Report completion</td><td>Q4 2021</td></tr>
</table>
</td></tr>
<tr><td>SPONSOR</td><td>IFCT (Intergroupe Francophone de Cancérologie Thoracique)</td></tr>
</table>