SYNOPSIS

CODE	IFCT-2102 Lung KG12Ci
COORDINATING INVESTIGATORS	Marie WISLEZ - APHP Hôpital Cochin Paris Celine MASCAUX - CHU Strasbourg Florian GUISIER – CHU Rouen
SPONSOR	IFCT (Intergroupe Francophone de Cancérologie Thoracique)
TITLE	Assessment and follow-up of patients with KRAS G12C-mutated metastatic Non-Small Cell Lung Cancer who received sotorasib as part of the French Early Access Program (ATU)
SCIENTIFIC COMMITTEE	Marie Wislez (CHU Paris Hopital Cochin) Celine Mascaux (CHU Strasbourg) Florian Guisier (CHU Rouen) Michele Beau Faller (CHU Strasbourg) Benoit Roch (CHU Montpellier) Pascale Missy (IFCT) Franck Morin (IFCT)
TYPE OF STUDY	Retrospective observational study (cohort)
PRODUCT EVALUATED	Sotorasib
SELECTION CRITERIA	INCLUSION CRITERIA • Patients with Stage IV NSCLC at time of initiation of treatment with sotorasib • Presence of KRAS G12C mutation diagnosed on tumor sample and/or on liquid biopsy (co mutations allowed) • Patients who received at least one dose of the treatment with sotorasib as part of the French Early Access Program (ATU program) • Patients who were informed about the study and do not object for their data to be collected • Age > 18 years EXCLUSION CRITERIA • Patients enrolled in a sotorasib clinical trial • Patients with a psychiatric history that hinders the comprehension of the information leaflet • Patients under curatorship or guardianship • Unable to obtain data collection
FOLLOW-UP	The follow-up period is defined as the period from the date of sotorasib initiation (as part of the French Early Access Program (ATU)) until the date of death or end of study whichever occur first.
POPULATIONS	The 2 groups of patients (those who started sotorasib under a “nominative” cohort and those who started sotorasib under “cohort” ATU) will be analysed separately.
SCIENTIFIC OBJECTIVES	The primary objective is to evaluate real-world progression-free survival (rwPFS) Secondary objectives are: • Description of patients’ clinical and biological characteristics • Estimation of overall survival (OS) • Estimation of duration of treatment with sotorasib • Best response (complete response, partial response, stable disease, progression) • Duration of response • Reason of treatment discontinuation and suspension (including toxicity) • Duration of treatment with sotorasib beyond 1st progression • Site of disease progression • Doses adaptations

	• Treatments received before sotorasib, efficacy, duration and reason of discontinuation • Subsequent therapies, efficacy, duration and reason of discontinuation • Description and impact of co-mutations (with highlighting technique) on sotorasib treatment efficacy (OS and rwPFS) • Impact of PDL1 expression (<1, 1-49, >=50) on sotorasib treatment efficacy (OS and rwPFS) • Variant allele frequency (VAF) of KRAS G12C if available (optional) Study endpoints: The primary endpoint: rwPFS will be defined as the date of the first dose of sotorasib to the date of first occurrence of disease progression (defined by the treating physician) or death from any cause during the study Secondary endpoints: • Patients' clinical and biological characteristics will be collected in the study at NSCLC diagnosis and initiation of sotorasib • OS will be determined as the time from the date of first dose of sotorasib to the date of death due to any cause during the study • Duration of treatment is defined as the time from the date of first dose of sotorasib to the date of discontinuation of treatment with sotorasib or death from any cause during the study • Pattern of tumor progression: sites of disease progression after treatment with sotorasib • Best response will be defined as the best response recorded from the start of treatment with sotorasib until disease progression or start of further anti-cancer treatment • Duration of response will be defined as the time from the date of the first documented response (complete or partial) to the earliest date of disease progression • Reason of sotorasib discontinuation and suspension will be collected, including toxicity • Duration of treatment with sotorasib beyond progression will be defined as time between first occurrence of disease progression and treatment discontinuation • Description of treatments received before and after sotorasib treatment by line of therapy and by type of treatment • Description of treatments received before and after sotorasib treatment • Efficacy of treatments received before and after sotorasib will be evaluated using rwPFS and best response by line of therapy • Reason of discontinuation of treatments received before and after sotorasib treatment will be collected • Co-mutations and PDL-1 status (with highlighting technique) on sotorasib treatment efficacy (OS and rwPFS) • VAF of KRAS G12C if available (optional)
STATISTICAL ANALYSIS	General Information The quantitative variables will be described by the number of values entered, the number of missing data, the mean, the standard deviation, the median, the 1st and the 3rd quartile, the minimal and maximal values. The categorical variables will be described by the number of values entered, the number of missing values, the frequency and the percentage per category. If relevant, the 95% Wald confidence intervals can be calculated. For time to event endpoints, Kaplan-Meier (KM) curves and KM proportions at selected time points, the number of subjects with event and the number of subjects censored will be used to summarize the data.

<table>
<tr><td></td><td>All analysis will be descriptive and no hypotheses will be tested.

ANALYSIS OF OUTCOMES MEASURES
The following criteria will be analyzed:
Patients' characteristics (demographic, clinical, biological and tumoral characteristics, treatment history, mutations profile) will be described as defined in the general information section.
OS: non-deceased patients at the end of follow-up will be censored as of the date of the latest news. OS will be estimated using the Kaplan-Meier method. Median survival will be described along with Kaplan-Meier estimates at 3, 6, 12 and 18 months with associated 95% confidence intervals.
rwPFS: patients who have not progressed by the end of the follow-up will be censored on the date of their last news or on the D1 of subsequent treatment, if applicable rwPFS will be estimated using the Kaplan-Meier method. Median rwPFS will be described as well as Kaplan-Meier estimates at 3, 6, 12 and 18 months with associated 95% confidence intervals.
Additional exploratory analyses can be discussed with the Scientific Committee.
Duration of treatment: patients still ongoing treatment at the end of follow-up will be censored as of the date of the latest news. The median will be estimated using the Kaplan-Meier method.
Duration of response: patients who have not progressed by the end of the follow-up will be censored as of the date of the latest news. The median will be estimated using the Kaplan-Meier method
The prognostic factors of patient survival will be sought from the initial characteristics of patients using a Cox regression model. Each parameter will be tested in a model univariate. A multivariate model will be tested with all variables of model univariate and a backward selection will be used.</td></tr>
<tr><td>Sample size</td><td>300 to 400 patients expected for IFCT-2102 Lung KG12Ci. We aim to include all the patients who meet the inclusion criteria from the start to the end of the French Expanded Access Program for sotorasib</td></tr>
<tr><td>TIMELINES</td><td>
<table>
<tr><th>Study scheduled</th><th>Dates</th></tr>
<tr><td>Centers recruitment and administrative procedures with participating centers</td><td>October 2021 April 2022
(expected date of ATUc end)</td></tr>
<tr><td>Main data collection period</td><td>October 2021– November 2023</td></tr>
<tr><td>First Clinical Study Report (patients clinical and biological characteristics)</td><td>June 2022</td></tr>
<tr><td>2nd Clinical Study Report (all patients clinical and biological characteristics)</td><td>December 2022</td></tr>
<tr><td>3rd Clinical Study Report (Follow-up at 3 months)</td><td>February 2023</td></tr>
<tr><td>4th Clinical Study Report (Follow-up at 6 months)</td><td>May 2023</td></tr>
<tr><td>Final clinical study Report completion (follow-up at 18 months)</td><td>May 2024</td></tr>
<tr><td>Data management and Statistical analysis</td><td>November 2021 – May 2022, June 2022, December 2022, February 2023, May 2023, May 2024</td></tr>
</table>
</td></tr>
</table>