

Press release

Encouraging results observed with nivolumab alone or in combination with ipilimumab in refractory or relapsing Malignant Pleural Mesothelioma patients: Updated data from IFCT-1501 MAPS-2 trial

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The French Cooperative Thoracic Intergroup (IFCT) announced today updated data from the IFCT-1501 MAPS-2 trial evaluating the safety and efficacy of nivolumab or nivolumab combined with ipilimumab for previously treated unresectable malignant pleural mesothelioma (MPM) patients. The study, also presented at ASCO 2017, in which the thoracic oncology department of Bichat – Claude-Bernard hospital AP-HP (Pr Gérard Zalcman) participated, was sponsored by the IFCT. Bristol-Myers Squibb supplied nivolumab and ipilimumab, and a research grant to the IFCT.

The 12-week disease control rate, the primary endpoint of the study, was 44.4% [95% CI: 31.2-57.7%] with nivolumab, and 50% [36.7-63.3%] with nivolumab plus ipilimumab, as assessed by an independent panel of expert thoracic radiologists. The objective response rate was 18.5% [8.2%-28.9%] with nivolumab, and 27.8% [15.8%-39.7%] with nivolumab plus ipilimumab. With a median follow-up of 15 months (July, 31th 2017), the median progression-free survival was 4.0 months for monotherapy and 5.6 months for the combined-treatment group. The median overall survival was 13.6 months with nivolumab and not reached for the combined-treatment group. Grade 3/4 toxicities were slightly increased in the combined treatment group (nivolumab: 12.7%/0% versus nivolumab plus ipilimumab: 22.9%/3.3%) with 3 treatment-related deaths in the combined treatment group.

PD-L1 immunohistochemistry (IHC) was performed on 99/125 available and assessable tissue blocks obtained from the diagnosis biopsies: only 41 (41,4%) had 1% or more PD-L1 positive tumor cells (with only 3 with 50% or more, and 7 with 25% or more). Positive PD-L1 IHC did not predict longer progression-free survival or overall survival, either in the whole population or in each treatment group separately.

These updated data will be featured today, September 10, during the Annual Meeting of the European Society for Medical Oncology (ESMO) press briefing and presented during an oral session from 9:15-10:45 AM (Abstract LBA58_PR).

Gérard Zalcman, Co-Principal investigator of this study, Head of the Thoracic Oncology Department of Bichat – Claude-Bernard Hospital AP-HP, stated : *“Both nivolumab or nivolumab plus ipilimumab” reached their endpoint in 2nd /3rd line mesothelioma patients without any unexpected toxicity, leading to meaningful progression-free and overall survivals. These updated results support the efficacy of checkpoints inhibitors in mesothelioma patients, deserving future phase 3 trials in this orphan disease with no standard treatment after first-line pemetrexed-based treatment”.*

About IFCT-1501 MAPS-2

IFCT-1501 MAPS-2 is a Phase 2 multi-center randomized, non-comparative study evaluating nivolumab monotherapy and nivolumab plus ipilimumab combination therapy in patients with previously treated recurrent malignant pleural mesothelioma (MPM).

From March to August 2016, 125 patients were enrolled in 21 centers in France. Eligible patients, previously treated by 1 or 2 systemic chemotherapy lines, were randomized into two treatment groups: Patients received nivolumab (3 mg/kg every 2 weeks) or nivolumab (3 mg/kg every 2 weeks) combined with ipilimumab (1 mg/kg every 6 weeks) until progression or unacceptable toxicity. The primary endpoint is disease control rate (DCR). Secondary endpoints include number of participants with treatment-related adverse events, progression-free survival, overall survival, quality of life, evaluation of predictive value of tumor PD-L1 score and prognostic value of biomarkers.

Rationale for immunotherapy in mesothelioma

MPM is a highly aggressive tumour. Occupational asbestos exposure is the main factor involved in pathogenesis, which can explain the rise in incidence of mesothelioma patients since the 1960s (Bertazzi 2005, Goldberg 2006). Although mesothelioma is rare in the general population (prevalence in the non-exposed population <1 case/million individuals per year), around 100 cases per million per year in exposed individuals leads to an incidence between 900 and 1000 cases per year in France (Le Stang 2010, Cherié-Chaline 2012). Mesothelioma is a disease in which immune and inflammatory host response is thought to play a major role. The encouraging results of the previous IFCT trial, reported at the ASCO 2015 annual meeting, showed that when bevacizumab was used with the current standard-of-care combination of pemetrexed and cisplatin, it improved survival in patients with mesothelioma. Unfortunately, all patients in that study experienced disease progression. Early data indicate that the combination of PD-1 and CTLA-4 receptor blockade may improve antitumor activity, and suggest further study to evaluate anti-PD-1 plus anti-CTLA-4 combination in MPM patients.

About the French Cooperative Thoracic Intergroup (IFCT)

The IFCT is an independent, non-profit academic research intergroup specializing in thoracic oncology. Its objective is to improve survival and quality of life for thoracic cancer patients. Established in 1999, the IFCT has its own operational infrastructure and is equipped to design, promote, and carry out clinical studies in France and internationally, and to communicate the findings thus obtained. The IFCT's activity regularly results in the introduction of new drugs or strategies that improve the efficacy, safety, and/or economic impact of anti-cancer therapies. This, in turn, leads to better patient management. All IFCT projects are coordinated by a Clinical Research Unit accredited by the National Cancer Institute (INCa) and the National League Against Cancer.

About AP-HP

AP-HP (Greater Paris University Hospitals) is a European world-renowned university hospital. Its 39 hospitals treat 8 million people every year: in consultation, emergency, during scheduled or home hospitalizations. The AP-HP provides a public health service for everyone, 24 hours a day.

The mission is a duty as well as a great source of pride. AP-HP is the leading employer in the Greater Paris area: 100,000 staff members – doctors, researchers, paramedical staff, administrative personnel and workers – work there.

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