

## LBA41

### **Nivolumab (nivo) ± ipilimumab (ipi) in pre-treated patients with advanced, refractory pulmonary or gastroenteropancreatic poorly differentiated neuroendocrine tumors (NECs) (GCO-001 NIPINEC)**

N. Girard<sup>1</sup>, J. Mazieres<sup>2</sup>, J. Otto<sup>3</sup>, H. Lena<sup>4</sup>, C. Lepage<sup>5</sup>, T. Egenod<sup>6</sup>, D. Smith<sup>7</sup>, J. Madelaine<sup>8</sup>, L. Gérinière<sup>9</sup>, F. El Hajbi<sup>10</sup>, A. Ferru<sup>11</sup>, C. Clément-Duchêne<sup>12</sup>, A. Madroszyk<sup>13</sup>, J. Desrame<sup>14</sup>, F. Morin<sup>15</sup>, A. Langlais<sup>15</sup>, P. Michel<sup>16</sup>, C. Louvet<sup>17</sup>, V. Westeel<sup>18</sup>, T. Walter<sup>19</sup>

<sup>1</sup> Thorax Institute, Institut Curie, Paris, France, <sup>2</sup> Thoracic Oncology Department, Centre Hospitalier Universitaire de Toulouse - Hôpital Larrey, Toulouse, France, <sup>3</sup> Oncology, Centre Antoine Lacassagne, Nice, France, <sup>4</sup> Pneumology, Hôpital Pontchaillou, Rennes, France, <sup>5</sup> Hepato Gastroenterology and Digestive Oncology, CHU Dijon, Dijon, France, <sup>6</sup> Thoracic Oncology Department, CHU Limoges - Hôpital Dupuytren, Limoges, France, <sup>7</sup> Hepato Gastroenterology and Digestive Oncology, Hôpital Haut Leveque, Pessac, France, <sup>8</sup> Pneumology Department, CHU de Caen - Hôpital Cote de Nacre, Caen, France, <sup>9</sup> Pneumology, HCL - Centre Hospitalier Lyon Sud, Pierre-benite, France, <sup>10</sup> Oncology, Centre Oscar Lambret, Lille, France, <sup>11</sup> Oncology, CHU Poitiers, Jean Bernard Hôpital, Poitiers, France, <sup>12</sup> Oncology, Institut de Cancérologie de Lorraine, Vandœuvre-lès-Nancy, France, <sup>13</sup> Medical Oncology, Institute Paoli Calmettes, Marseille, France, <sup>14</sup> Oncology, Hôpital privé Jean Mermoz, Lyon, France, <sup>15</sup> Clinical Research Unit, French Cooperative Thoracic Intergroup, Paris, France, <sup>16</sup> Hepato-Gastroenterology, Rouen University Hospital, Rouen, France, <sup>17</sup> Oncology, Institute Mutualiste Montsouris, Paris, France, <sup>18</sup> Pneumology, CHRU Besançon - Hôpital Jean Minjoz, Besançon, France <sup>19</sup> Gastroenterology and Digestive Oncology, HCL - Hôpital Edouard Herriot, Lyon, France

## **Background**

Neuroendocrine Carcinomas (NECs) are a distinct family of poorly differentiated morphology, sharing molecular, clinical and outcome characteristics. No standard-of-care exists after the failure of first-line platinum-based chemotherapy (CT) regimens. Nivo±ipi has been reported to provide survival benefit versus standard CT in metastatic solid cancers.

## **Methods**

GCO-001 NIPINEC is a multicenter, non-comparative, randomized (1:1) phase 2 trial with a two-step design (early stopping for futility after 50% of accrual). Main inclusion criteria were histologically proven NEC (large- and small-cell for gastroenteropancreatic (GEP) NECs, and large-cell for lung NECs), in 2<sup>nd</sup> or 3<sup>rd</sup> line refractory to platinum-based CT, and PS 0-2. Patients received nivo 3 mg/kg q2w ± ipi 1 mg/kg q6w, for 2 years or until progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) at 8 weeks assessed by investigators (power of 90%, alpha risk at 5% two-sided). Other endpoints included progression-free survival (PFS), overall survival (OS) and safety. NCT number: NCT03591731.

## **Results**

From Dec 2018 to Mar 2021, 185 patients (93 GEP and 92 lung) were enrolled in 50 centers. Median age was 64.4 years (range 26.4–87.1), 71% males, 70% smokers, 91% with ECOG PS 0 or 1, 24% with asymptomatic brain metastases. 170 (92%) patients were evaluable for the primary endpoint. ORR at 8 weeks was 7.2% (95%CI [2.7-15.1]) with nivo and 14.9% (95%CI [8.2-24.2]) with nivo+ipi. Median PFS was 1.8 months (95%CI [1.7-2.0]) with nivo and 1.9 months (95%CI [1.6-2.1]) with nivo+ipi. Median OS was 7.2 months (95%CI [3.7-14.1]) with nivo and 5.8 months (95%CI [3.3-7.6]) with nivo+ipi. 3 patients (3.5%) and 7 patients (8.9%) experienced treatment discontinuation because of toxicity with nivo and nivo+ipi respectively. 2 treatment-related deaths were observed with nivo (meningoencephalitis and pneumonitis). Most frequent grade ≥ 3 AEs were asthenia (7.3%), anaemia (6.3%) and alkaline phosphatase increased (5.8%).

## **Conclusions**

Nivo+ipi only reached the primary endpoint in 2nd/3rd line NECs pts with acceptable toxicity.

## **Clinical trial identification**

EudraCT 2017-003863-37.

## **Legal entity responsible for the study**

Intergroupe Francophone de Cancérologie Thoracique.

## Funding

BMS.

## Disclosure

N. Girard: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Boehringer; Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Personal, Advisory Board: Lilly; Financial Interests, Personal, Advisory Board: Teva; Financial Interests, Personal, Advisory Board: Seagen; Financial Interests, Personal, Advisory Board: Takeda; Financial Interests, Personal, Advisory Board: Grunenthal; Financial Interests, Personal, Advisory Board: GSK; Financial Interests, Personal, Advisory Board: Lilly; Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: AbbVie; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Advisory Board: Sanofi; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Principal Investigator: Roche; Financial Interests, Personal, Principal Investigator: Boehringer; Financial Interests, Personal, Principal Investigator: AstraZeneca; Financial Interests, Personal, Principal Investigator: MSD; Financial Interests, Personal, Principal Investigator: BMS; Financial Interests, Personal, Principal Investigator: Seagen; Financial Interests, Personal, Principal Investigator: Janssen; Financial Interests, Personal, Principal Investigator: Lilly; Financial Interests, Personal, Writing Engagements: Edimark; Financial Interests, Personal, Writing Engagements: Fréquence médicale; Other, Personal, Other: AstraZeneca. J. Mazieres: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Daiichi; Financial Interests, Personal, Advisory Board: Pierre Fabre; Financial Interests, Personal, Advisory Board: Amgen; Financial Interests, Institutional, Research Grant: Pierre Fabre. H. Lena: Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Takeda; Non-Financial Interests, Institutional, Principal Investigator: BMS; Non-Financial Interests, Institutional, Principal Investigator: AstraZeneca; Non-Financial Interests, Institutional, Principal Investigator: Roche; Non-Financial Interests, Institutional, Principal Investigator: AbbVie; Non-Financial Interests, Institutional, Principal Investigator: GSK; Financial Interests, Personal, Advisory Board: Lilly; Non-Financial Interests, Institutional, Principal Investigator: Lilly; Non-Financial Interests, Institutional, Principal Investigator: Celgene; Non-Financial Interests, Institutional, Principal Investigator: Novartis; Financial Interests, Personal, Advisory Board: Pfizer; Non-Financial Interests, Institutional, Principal Investigator: Pfizer; Financial Interests, Personal, Advisory Board: Amgen; Non-Financial Interests, Institutional, Principal Investigator: Amgen; Non-Financial Interests, Institutional, Principal Investigator: Regeneron. C. Lepage: Financial Interests, Personal, Training: Bayer; Financial Interests, Personal, Training: Amgen; Financial Interests, Personal, Training: Ipsen; Financial Interests, Personal, Training: Pierre Fabre; Financial Interests, Personal, Other, Congress invitation: Novartis; Financial Interests, Personal, Other, Congress invitation: Merck; Financial Interests, Personal, Other, Congress invitation: Ipsen; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Personal, Advisory Board: ADVANCED ACCELERATOR APPLICATIONS (AAA). A. Madroszyk: Financial Interests, Personal, Other, Accommodation, lunch, transportation: BMS. P. Michel: Financial Interests, Personal, Advisory Board: Servier; Financial Interests, Personal, Advisory Board: BAYER; Financial Interests, Personal, Invited Speaker: MERCK. C. Louvet: Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Servier; Financial Interests, Personal, Advisory Board: Amgen. V. Westeel: Financial Interests, Personal, Other, Honoraria: AstraZeneca; Financial Interests, Personal, Other, Honoraria: BMS; Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Takeda; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Invited Speaker: MSD; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Institutional, Sponsor/Funding: Boehringer Ingelheim; Financial Interests, Institutional, Sponsor/Funding: MSD; Financial Interests, Personal, Other, Travel, accommodations, expenses: AstraZeneca; Financial Interests, Personal, Other, Travel, accommodations, expenses: BMS; Financial Interests, Personal, Other, Travel, accommodations, expenses: Pfizer; Financial Interests, Personal, Other, Travel, accommodations, expenses: Roche. T. Walter: Financial Interests, Personal, Advisory Board: Novartis - AAA; Non-Financial Interests, Personal, Funding: Ipsen; Non-Financial Interests, Institutional, Project Lead: Roche. All other authors have declared no conflicts of interest.