2021 ESMO congress

1098O

Nivolumab plus platinum-doublet chemotherapy as first-line therapy in unresectable, locally advanced or metastatic G3 neuroendocrine Neoplasms (NENs) of the gastroenteropancreatic (GEP) tract or unknown (UK) origin: Preliminary results from the phase II NICE-NEC trial (GETNE T1913)

M.C. Riesco-Martinez[1], J. Capdevila[2], V. Alonso[3], P. Jimenez-Fonseca[4], A. Teule[5], E. Grande[6], I. Sevilla[7], M. Benavent Viñuales[8], T. Alonso-Gordoa[9], A. Custodio[10], J. Hernando[2], E. Polo[3], O.A. Castillo Trujillo[4], R. Garcia-Carbonero[1]

[1] Medical Oncology Department, Hospital Universitario 12 de Octubre, Imas12, UCM, Madrid, Spain, [2] Medical Oncology Department, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, [3] Medical Oncology Department, Instituto Aragones de Investigacion Sanitaria, Hospital Universitario Miguel Servet, Zaragoza, Spain, [4] Medical Oncology Department, Hospital Universitario Central de Asturias, ISPA, Oviedo, Spain, [5] Medical Oncology Department, Institut Català d´Oncologia (ICO) - IDIBELL, L'Hospitalet de Llobregat, Spain, [6] Medical Oncology Department, MD Anderson Cancer Center Madrid, Madrid, Spain, [7] Medical Oncology Department, Investigación Clínica y Traslacional en Cáncer / Instituto de Investigaciones Biomédicas de Málaga (IBIMA) / Hospitales Universitarios Regional y Virgen de la Victoria de Málaga, Malaga, Spain, [8] Medical Oncology Department, University Hospital Virgen del Rocío, Instituto de Biomedicina de Sevilla (IBIS), Seville, Spain, [9] Medical Oncology, Hospital Universitario Ramón y Cajal, Madrid, Spain[10] Medical Oncology Department, Hospital Universitario La Paz, Madrid, Spain

Background

Grade 3 (G3) NENs encompass a heterogeneous group of tumors with aggressive behaviour and poor survival. Standard front-line platinum-based chemotherapy (CT) has limited efficacy, with an ORR of 31%, a median PFS of 4-5 m and a median OS of 11 m. G3 NENs are associated with a high mutational burden and PD-L1 expression that might lead to a favorable response to immunotherapy (IT). The aim of this study is to assess the safety and potential synergy of the combination of CT plus IT in patients with advanced CT-naïve G3 NENs.

Methods

NICE-NEC is a non-randomized, open-label, phase II trial that recruited patients (pts) with histologically confirmed metastatic or unresectable G3 NENs of GEP/UK origin, treatment-naïve and ECOG 0-2 across 12 centers belonging to the Spanish Taskforce of Neuroendocrine Tumors (GETNE). Pts received Nivolumab 360 mg iv d1/ Carboplatin AUC 5 iv d1/ Etoposide 100 mg/m2 d1-3 every 3 weeks (up to 6 cycles) followed by Nivolumab 480 mg every 4 weeks (up to 24 m) as maintenance tx. Primary endpoint was 12mOS rate. Secondary endpoints include ORR by RECIST 1.1, PFS and safety.

Results

From 2019-2021, 38 pts were enrolled. Median age was 61y, 68% male, 29% ECOG 0, 53% poorly differentiated and 66% Ki67 >55%. 81.6% were GEP; pancreas 37%, stomach 16% and colorectum 16% were the most common sites. 74% had ≥2 metastatic organs involved. With a median follow up of 6 m, disease control rate (DCR) was 84% including an ORR of 50% (47% PR; 3% CR). Median and 6m-PFS rate were 5.7 m (95%CI: 5.1-7.8) and 39% (95%CI: 25-62), respectively. ≥G3 AEs were reported in 61% pts. Most frequent toxicities were hematological: neutropenia (53%), febrile neutropenia (10%) and anemia (11%).

Conclusions

Preliminary results show promising activity of adding Nivolumab to CT as first-line therapy for G3 NENs, with DCR of 84% and greater ORR than benchmark studies. Nivolumab did not significantly increase the toxicity profile of standard CT. Final survival results require further follow-up and translational studies are ongoing.

Clinical trial identification

EudraCT 2019-001546-18; NCT03980925.

Editorial acknowledgement

We acknowledge MFAR Clinical Research staff for their assistance in the development of this abstract.

Legal entity responsible for the study

Grupo Español de Tumores Neuroendocrinos y Endocrinos (GETNE).

Funding

Bristol Myers Squibb (BMS).

Disclosure

M.C. Riesco-Martinez: Financial Interests, Personal, Invited Speaker: Servier; Financial Interests, Personal, Invited Speaker: Merk; Financial Interests, Personal, Advisory Role: AAA; Financial Interests, Institutional, Research Grant, Grant for investigator-initiated study.: BMS; Financial Interests, Institutional, Research Grant, Grant for investigator-initiated study.: MSD. J. Capdevila: Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Amgen; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Bayer; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Eisai; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: AAA; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Ipsen; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Pfizer; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Merck; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Sanofi; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Novartis; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Lilly; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: ITM; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Hudchinson Pharma; Financial Interests, Personal, Other, Scientific consultancy role - Participation in speaker´s bureau: Exelixis; Financial Interests, Personal, Other, Receipt of grants / research supports: Eisai; Financial Interests, Personal, Other, Receipt of grants / research supports: AstraZeneca; Financial Interests, Personal, Other, Receipt of grants / research supports: AAA; Financial Interests, Personal, Other, Receipt of grants / research supports: Ipsen; Financial Interests, Personal, Other, Receipt of grants / research supports: Pfizer; Financial Interests, Personal, Other, Receipt of grants / research supports: Novartis; Non-Financial Interests, Personal, Member, Chair of GETNE: GETNE; Non-Financial Interests, Personal, Member, Advisory member: ENETS. P. Jimenez-Fonseca: Financial Interests, Personal, Advisory Role: Bristol; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: MSD; Financial Interests, Personal, Advisory Role: Mylan; Financial Interests, Personal, Advisory Role: Baxter; Financial Interests, Personal, Invited Speaker: HRA Pharma; Financial Interests, Personal, Invited Speaker: LeoPharma; Financial Interests, Personal, Invited Speaker: Rovi; Financial Interests, Personal, Invited Speaker: Sanofi. A. Teule: Financial Interests, Personal, Other, Speaking, writing, public presentations, advisory service, travel grants: Novartis; Financial Interests, Personal, Other, Speaking, writing, public presentations, advisory service, travel grants: IPSEN; Financial Interests, Personal, Other, Speaking, writing, public presentations, advisory service, travel grants: AAA; Financial Interests, Personal, Other, Speaking, writing, public presentations, advisory service, travel grants: Pfizer; Financial Interests, Personal, Other, Speaking, writing, public presentations, advisory service, travel grants: AstraZeneca. E. Grande: Financial Interests, Personal, Invited Speaker: Adacap; Financial Interests, Personal, Advisory Board: Astellas; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb; Financial Interests, Institutional, Advisory Board: Caris Life Sciences; Financial Interests, Personal, Invited Speaker: Eisai; Financial Interests, Personal, Invited Speaker: Eusa Pharma; Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Invited Speaker: Janssen; Financial Interests, Personal, Invited Speaker: Lilly; Financial Interests, Personal, Invited Speaker: Merk kGa; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Novartis; Financial Interests, Institutional, Advisory Board: ONCODNA (Biosequence); Financial Interests, Personal, Invited Speaker: Pfizer; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Advisory Board: Sanofi-Genzyme; Non-Financial Interests, Institutional, Research Grant: Astellas; Non-Financial Interests, Institutional, Research Grant: AstraZeneca; Non-Financial Interests, Institutional, Other, Coordinating PI: Ipsen; Non-Financial Interests, Institutional, Research Grant: Lexicon; Non-Financial Interests, Institutional, Research Grant: MTEM/Threshold; Non-Financial Interests, Institutional, Research Grant: Nanostring technologies; Non-Financial Interests, Institutional, Research Grant: Pfizer; Non-Financial Interests, Institutional, Research Grant: Roche; Non-Financial Interests, Personal, Advisory Board: ENETS. I. Sevilla: Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Advisory Role: Ipsen; Financial Interests, Personal, Invited Speaker: Novartis; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: Syrtex; Financial Interests, Personal, Invited Speaker: PharmaMar; Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Invited Speaker: Bayer; Financial Interests, Personal, Invited Speaker: AAA. M. Benavent Viñuales: Financial Interests, Personal, Invited Speaker: Pfizer; Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Invited Speaker: Novartis. T. Alonso-Gordoa: Financial Interests, Personal, Other, Speaker, consultancy or advisory role: Ipsen; Financial Interests, Personal, Other, Speaker, consultancy or advisory role: Pfizer; Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Advisory Role: Sanofi; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: Astellas; Financial Interests, Personal, Advisory Role: Janssen-Cilag; Financial Interests, Personal, Advisory Role: MSD; Financial Interests, Personal, Other, Speaker, consultancy or advisory role: BMS; Financial Interests, Personal, Other, Speaker, consultancy or advisory role: Eisai; Financial Interests, Institutional, Other, Clinical Trial: Roche; Financial Interests, Institutional, Other, Clinical Trial: AstraZeneca; Financial Interests, Institutional, Other, Clinical Trial: BMS; Financial Interests, Institutional, Other, Clinical Trial: MSD; Financial Interests, Institutional, Other, Clinical Trial: Eisai; Financial Interests, Institutional, Other, Clinical Trial: Pfizer; Financial Interests, Institutional, Other, Clinical Trial: Ipsen; Financial Interests, Institutional, Other, Clinical Trial: GSK-Novartis; Financial Interests, Institutional, Other, Clinical Trial: Clovis; Financial Interests, Institutional, Other, Clinical Trial: Nektar Therapeutics; Financial Interests, Institutional, Other, Clinical Trial: Janssen-Cilag; Financial Interests, Institutional, Other, Clinical Trial: Astellas; Financial Interests, Institutional,

Other, Clinical Trial: Bayer; Non-Financial Interests, Personal, Project Lead: Pfizer; Non-Financial Interests, Personal, Project Lead: Roche; Non-Financial Interests, Personal, Project Lead: Ipsen; Non-Financial Interests, Personal, Member: Spanish Germ Cell Tumors Board; Non-Financial Interests, Personal, Advisory Role: SEOM. J. Hernando: Financial Interests, Personal, Invited Speaker: Eisai; Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Invited Speaker: Novartis; Financial Interests, Personal, Invited Speaker: AAA; Financial Interests, Personal, Invited Speaker: Angelini. R. Garcia-Carbonero: Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: AAA; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Advanz Pharma; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Bayer; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: BMS; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: HMP; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Ipsen; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Merck; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Midatech Pharma; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: MSD; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Novartis; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: PharmaMar; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Pfizer; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Pierre Fabre; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Roche; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Sanofi; Financial Interests, Personal, Other, Scientific Advice, Speakers Bureau, Honoraria: Servier; Financial Interests, Personal, Other, Financial support to investigator-initiated trials: Pfizer; Financial Interests, Personal, Other, Financial support to investigator-initiated trials: BMS; Financial Interests, Personal, Other, Financial support to investigator-initiated trials: MSD; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: ARMO Biosciences; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: AstraZeneca; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Pfizer; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Novartis; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Ipsen; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Roche; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Pharmacyclics; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Boston Biomedicals; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Merk; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: MSD; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Amgen; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Sanofi; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Bayer; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Bristol-Myers-Squibb; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Boehringer; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Sysmex; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Gilead Sciences; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Servier; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Adacap; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: VCN; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: Lilly; Financial Interests, Institutional, Other, Institutional support for the conduct of clinical trials or for molecular diagnostic platforms: PharmaMar; Non-Financial Interests, Personal, Member, Member of the Executive Committee: GETNE; Non-Financial Interests, Personal, Member, Member of the Executive Committee: ENETS; Non-Financial Interests, Personal, Principal Investigator: Pfizer; Non-Financial Interests, Personal, Principal Investigator: BMS; Non-Financial Interests, Personal, Member: EORTC; Non-Financial Interests, Personal, Member: ASCO; Non-Financial Interests, Personal, Member: ESMO; Non-Financial Interests, Personal, Member: SEOM; Non-Financial Interests, Personal, Member: TTD; Non-Financial Interests, Personal, Member: GEMCAD. All other authors have declared no conflicts of interest.