

1099MO

Durvalumab plus tremelimumab influence on response to subsequent treatments in patients with neuroendocrine neoplasms (NENs) of gastroenteropancreatic and lung origins: Results from the phase II DUNE trial (GETNE 1601)

J. Hernando¹, J.L. Manzano², A. Teule³, C. López⁴, R. Garcia-Carbonero⁵, M. Benavent Viñuales⁶, A. Custodio⁷, A. Cubillo⁸, V. Alonso⁹, T. Alonso-Gordo¹⁰, A. Carmona-Bayonas¹¹, G. Crespo¹², M. Blanco¹³, P. Jimenez-Fonseca¹⁴, A. Viudez¹⁵, A. La Casta¹⁶, I. Sevilla¹⁷, M. Llanos¹⁸, Á. Segura¹⁹, J. Capdevila¹

¹ Medical Oncology Department, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain, ² Medical Oncology Department, Institut Català d'Oncologia (ICO) - Badalona, Hospital Germans Trias i Pujol, Badalona, Spain, ³ Medical Oncology Department, Institut Català d'Oncologia (ICO) - IDIBELL, Hospitalet de Llobregat, Spain, ⁴ Medical Oncology Department, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, ⁵ Medical Oncology Department, Hospital Universitario 12 de Octubre, Imas12, UCM, CNIO, Madrid, Spain, ⁶ Medical Oncology Department, University Hospital Virgen del Rocío, Instituto de Biomedicina de Sevilla (IBIS), Seville, Spain, ⁷ Medical Oncology Department, Hospital Universitario La Paz, Madrid, Spain, ⁸ Medical Oncology Department, Hospital Universitario HM Sanchinarro, Madrid, Spain, ⁹ Medical Oncology Department, Hospital Universitario Miguel Servet, Instituto de Investigación Sanitaria de Aragón (IISA), Zaragoza, Spain, ¹⁰ Medical Oncology, Hospital Universitario Ramón y Cajal, Madrid, Spain, ¹¹ Hematology and Medical Oncology Department, Hospital Universitario Morales Meseguer, UMU, IMIB, Murcia, Spain, ¹² Medical Oncology Department, Complejo Asistencial Universitario de Burgos, Burgos, Spain, ¹³ Medical Oncology Department, Hospital Universitario Gregorio Marañón, Madrid, Spain, ¹⁴ Medical Oncology Department, Hospital Universitario Central de Asturias, ISPA, Oviedo, Spain, ¹⁵ Medical Oncology Department, Complejo Hospitalario de Navarra, Pamplona, Spain, ¹⁶ Medical Oncology Department, Hospital Universitario Donostia, San Sebastián, Spain, ¹⁷ 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, Málaga, Spain, ¹⁸ Medical Oncology Department, Hospital Universitario de Canarias, San Cristobal de La Laguna, Spain ¹⁹ Medical Oncology Department, Hospital Universitario la Fe, Valencia, Spain

Background

Enhanced antitumoral activity of chemotherapy (CT) after progression on immune checkpoint blockade (ICB) has been suggested. Here we investigate the activity of systemic therapies after progression on ICB in the phase II DUNE study.

Methods

DUNE was a prospective open-label trial that recruited pts with NENs in four cohorts (C1-4): typical/atypical lung carcinoids (C1), G1/2 gastrointestinal (C2), G1/2 pancreatic (C3), and high grade (G3) NENs of gastroenteropancreatic (GEP) origin (C4). All pts were included after progression on standard therapies. Pts received 1500 mg durvalumab (D; up to 13 cycles) plus 75 mg tremelimumab (T; up to 4 cycles) every 4 weeks. The primary objective was 9 month (m) clinical benefit rate (CBR) for C1-3 and 9 m overall survival rate (OS) for C4. Secondary objectives included objective response rate (ORR) and progression-free survival (PFS) by iRECIST. Data from previous and subsequent treatments were analyzed post-hoc.

Results

The study enrolled 123 pts with a median PFS to previous treatment of 12.1 (95%CI: 6-18) / 16.5 (95%CI: 13-20) / 15.8 (95%CI: 9-23) / 6.1 (95%CI: 5-7) m for C1-4 respectively. After a median follow-up of 16.5 m, the median PFS to D+T for C1-4 was 5.6 (95%CI: 5-6) / 5.8 (95%CI: 3-9) / 5.5 (95%CI: 2-9) / 2.4 (95%CI: 2-3) m. Subsequent lines after progression on D+T were administered to 59 (48%) pts. For C1, CT (33%) and PRRT (33%) were the major subsequent strategies. Targeted therapy (50%) was the preferred option for C2 and CT for C3 (40%) and C4 (91%). Reported PFS to systemic therapies after progression on D+T (PFS2) were 6.5 (95%CI: 6-7) / 12.7 (95%CI: 0-26) / 7 (95%CI: 6-8) / 8.4 (95%CI: 0.7-16) m for C1-4 respectively. PFS2 was longer than PFS in all groups and superior to PFS of previous treatment in C4. ORR to subsequent treatment in C4 was 45%. Efficacy of subsequent lines was unrelated to PD-L1 status.

Conclusions

In the DUNE heavily pretreated population, sensitivity to systemic therapies after progression on D+T overcomes the expected PFS2, especially in high grade NENs. This finding opens a new potential study concept of sequential therapies, including immunotherapy, in advanced NENs.

Clinical trial identification

Editorial acknowledgement

We acknowledge to 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

AstraZeneca.

Disclosure

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. 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. C. López: Financial Interests, Personal, Other, Honoraria you have directly received for any speaker, consultancy or advisory role or similar activity: Ipsen; Financial Interests, Personal, Other, Honoraria you have directly received for any speaker, consultancy or advisory role or similar activity: Roche; Financial Interests, Personal, Other, Honoraria you have directly received for any speaker, consultancy or advisory role or similar activity: Eisai; Financial Interests, Personal, Other, Honoraria you have directly received for any speaker, consultancy or advisory role or similar activity: Novartis; Financial Interests, Personal, Other, Honoraria you have directly received for any speaker, consultancy or advisory role or similar activity: Pfizer; Financial Interests, Personal, Other, Honoraria you have directly received for any speaker, consultancy or advisory role or similar activity: AAA; Financial Interests, Personal, Other, Direct research funding paid directly to you as a project lead: Ipsen; Financial Interests, Personal, Other, Direct research funding paid directly to you as a project lead: Roche; Financial Interests, Personal, Other, Direct research funding paid directly to you as a project lead: Pfizer; Financial Interests, Personal, Other, Direct research funding paid directly to you as a project lead: Novartis. 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: Merk; 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 evaluating Axitinib in NETs, Nivolumab in NECs and Pembrolizumab-Olaparib in CRC: Pfizer; Financial Interests, Personal, Other, Financial support to investigator-initiated trials evaluating Axitinib in NETs, Nivolumab in NECs and Pembrolizumab-Olaparib in CRC: BMS; Financial Interests, Personal, Other, Financial support to investigator-initiated trials evaluating Axitinib in NETs, Nivolumab in NECs and Pembrolizumab-Olaparib in CRC: 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: Merck; 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, 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; Non-Financial Interests, Personal, Principal Investigator: BMS; Financial Interests, Principal Investigator: Pfizer. 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, Other, Speaker, consultancy or advisory role: Roche; Financial Interests, Personal, Other, Speaker, consultancy or advisory role: Sanofi; Financial Interests, Personal, Other, Speaker, consultancy or advisory role: Bayer; Financial Interests, Personal, Other, Speaker, consultancy or advisory role: Astellas; Financial Interests, Personal, Other, Speaker, consultancy or advisory role: Janssen-Cilag; Financial Interests, Personal, Other, Speaker, consultancy or 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: Ipsen; Non-Financial Interests, Personal, Project Lead: Pfizer; Non-Financial Interests, Personal, Project Lead: Roche; Non-Financial Interests, Personal, Member: Spanish Germ Cell Tumors Board; Non-Financial Interests, Personal, Advisory Board: SEOM. G. Crespo: Financial Interests, Personal, Other, Honoraria for speaker, consultancy or advisory role or similar: BMS; Financial Interests, Personal, Other, Honoraria for speaker, consultancy or advisory role or similar: Ipsen; Financial Interests, Personal, Other, Honoraria for speaker, consultancy or advisory role or similar: Roche; Financial Interests, Personal, Other, Honoraria for speaker, consultancy or advisory role or similar: Eisai; Financial Interests, Personal, Other, Honoraria for speaker, consultancy or advisory role or similar: Sanofi; Financial Interests, Personal, Other, Honoraria for speaker, consultancy or advisory role or similar: Janssen; Financial Interests, Personal, Other, Honoraria for speaker, consultancy or advisory role or similar: EUSA Pharma; Financial Interests, Personal, Other, Honoraria for speaker, consultancy or advisory role or similar: Pierre Fabre. M. Blanco: Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Invited Speaker: Lilly; Financial Interests, Personal, Other, travel and congress attendance grants: Lilly; Financial Interests, Personal, Other, travel and congress attendance grants: Roche; Financial Interests, Personal, Other, travel and congress attendance grants: Ipsen; Financial Interests, Personal, Principal Investigator: Astellas; Financial Interests, Personal, Principal Investigator: AAA; Financial Interests, Personal, Principal Investigator: BMS; Financial Interests, Personal, Principal Investigator: Merck; Financial Interests, Personal, Principal Investigator: Daichi-Saiko; Financial Interests, Personal, Principal Investigator: Beigene. 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. I. Sevilla: 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; Financial Interests, Personal, Invited Speaker: Ipsen. M. Llanos: Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Invited Speaker: Amgen; Financial Interests, Personal, Invited Speaker: Servier; Financial Interests, Personal, Invited Speaker: AAA; Financial Interests, Personal, Invited Speaker: Eisai; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Invited Speaker: Merck; Financial Interests, Personal, Invited Speaker: Lilly; Financial Interests, Personal, Invited Speaker: Bristol; Financial Interests, Personal, Invited Speaker: Sanofi; Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Advisory Role: Roche. 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: Merk; 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: Hutchinson Pharma; Financial Interests, Personal, Other, Scientific consultancy role, participation in Speaker's bureau: Exelixis; Financial Interests, Personal, Other, Receipt grants / research support: Eisai; Financial Interests, Personal, Other, Receipt grants / research support: AstraZeneca; Financial Interests, Personal, Other, Receipt grants / research support: AAA; Financial Interests, Personal, Other, Receipt grants / research support: Ipsen; Financial Interests, Personal, Other, Receipt grants / research support: Pfizer; Financial Interests, Personal, Other, Receipt grants / research support: Novartis; Non-Financial Interests, Personal, Leadership Role, Chair of GETNE: GETNE; Non-Financial Interests, Personal, Advisory Board: ENETS. All other authors have declared no conflicts of interest.

© *European Society for Medical Oncology*