Durvalumab plus tremelimumab in patients with grade 3 neuroendocrine neoplasms of gastroenteropancreatic origin: updated results from the multicenter phase II DUNE trial (GETNE 1601)

Jaume Capdevila1, Stefania Landolfi, Jordi Hernández, Alexandre Teule, Rocío García-Carbonero, Ana Custodio, Antonio Cibillo, Teresa Alonso-Gordoa, Alberto Carmona-Bayonas, Guillermo Crespo, Montserrat Blasco, Antonio Víudez, Adelaida La Casta, Isabel Sevilla, Ángel Segura, Carlos López, Marta Benavent-Villaluens, Paola Nuciforo, Jose Luis Manzano.

BACKGROUND

The rationale to use immune checkpoint blockade in neuroendocrine neoplasms (NENs) has been scarce, due to the low tumor mutational burden, PD-L1 expression, and infiltration of these tumors. To date, PD-1 inhibitors in monotherapy have demonstrated a limited activity. 1-3 Combination of anti-PD-1 and anti-CTLA-4 recently suggested promising activity in high-grade NENs with an ORR of 20% vs no improvement in low-grade NENs. In line with these treatments, with durvalumab (D) plus tremelimumab (T) showed limited activity in patients (pts) with well differentiated neuroendocrine tumors (NETs) but surpassed the primary endpoint in grade 3 (G3) neuroendocrine neoplasms (NENs) suggesting a promising overall survival (OS) rate in a heavily pretreated population. 4 Here we update the results of the G3 NENs cohort with central pathological review.

OBJECTIVES

The aim of this trial is to assess the efficacy of durvalumab and tremelimumab in gastroenteropancreatic neuroendocrine neoplasms of different origins.

1. The primary objective for C1-3 is the efficacy of D by means of clinical benefit rate (CBR). Primary objective for C4 was the 9 months (m) OS, expected to be over 23%.
2. Secondary objectives included efficacy by means of objective response rate (ORR), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and a translational molecular endpoint to explore prognostic role of tumor and blood biomarkers within the trial population.

METHODS

DUNE was a prospective open-label trial that recruited pts with advanced NENs after progression to standard therapies in four cohorts (C1-4): typical/atypical lung carcinoids (C1), G1/G2 gastrointestinal (C2), G1/2 pancreatic (C3), and G3 NENs of gastroenteropancreatic origin (C4) after progression to first-line platinum-based chemotherapy (C4) (Fig. 1). Pts received 1500 mg durvalumab (up to 13 cycles) plus 75 mg tremelimumab (up to 4 cycles) once every 4 weeks.

RESULTS

Table 1. Baseline characteristics for C4 by stratified survival status at 32 m (N=123) overall survival; no long-term survivors harvested from the start of treatment (Table 2) revealed a strong correlation of molecular characteristics from the full dataset of DUNE trial.

Table 2. Stratified analysis of survival.

REFERENCES

4. Capdevila J, Lopes J, Capdevila A, et al. A multicenter phase II trial of durvalumab plus tremelimumab for treatment of patients with advanced neuroendocrine neoplasms (NENs) of gastroenteropancreatic or long-term follow up (up to 13 cycles) were administered to each patient. Disease progression was defined as ≤ 50% reduction in any measurable or non-measurable lesion.

CONCLUSIONS

1. PFS and OS did not improve significantly from benchmark studies.
2. One third of G3 NENs pts experienced a prolonged OS over one year regardless of tumor differentiation, Ki67 level or PD-L1 expression, confirmed by central pathological review.
3. Immunotherapy deserves further evaluation in G3 NENs.