VIRTUAL ESMO congress 2020

LBA67

TRAMUNE, a phase Ib study combining trabectedin and durvalumab, results of the expansion cohort in patients with advanced pretreated soft tissue sarcomas

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Background

Trabectedin (T) activity is partly mediated by targeting tumor associated macrophages. We report results of a multicenter phase Ib study assessing safety and preliminary efficacy of T combined with the PDL1 inhibitor durvalumab (D) in patients (pts) with unresectable or metastatic STS and relapsed OC, focusing on the STS expansion cohort.

Methods

This trial followed a conventional 3+3 design and included two dose-expansion cohorts (STS and OC). Pts aged >18, with unresectable or metastatic pretreated STS or relapsed OC were eligible. Primary objective was to assess safety, dose limiting toxicities (DLT), maximum tolerated dose (MTD) and recommended phase II dose of T given on day 1 as 3-hour infusion combined with D at fixed dose of 1120 mg on day 2, every 3 weeks. Three dose levels were investigated: 1 mg/m2, 1.2 mg/m2 and 1.5 mg/m2. Secondary objectives comprised antitumor activity of the combination in terms of objective response (OR) rate, 6-month progression-free rate (PFR), progression-free survival (as per RECIST v.1.1) and overall survival (OS), and to explore immune biomarkers of T+D activity on serial tumor biopsies and metabolomics on plasma samples. At least one OR was needed to consider the combination active.

Results

Between October 2017 and November 2019, 40 pts were included: nine in the dose escalation phase (3 at 1.0 mg/m2 and 6 at 1.2 mg/m2), 15 in the OC cohort and 16 in the STS cohort. With one DLT (grade 4 ALT increase), 1.2 mg/m2 was considered the MTD of T combined with 1120mg/m2 of D. In the STS expansion cohort, median follow-up was 10.7 months (IC95%: 3.1-13.5). Overall, 16 patients were assessable for safety and 14 for efficacy. Most frequent related AE were grade 1-2 nausea (15.1%), grade 1-2 fatigue (11.3%) Eight patients (50%) had drug-related grade 3/4 adverse events (AEs), mostly being neutrophil count decreased (35.7%), and there were 2 grade 5 AE (multi-organ failure and febrile aplasia). Six patients (42.9%) experienced tumor shrinkage, resulting in one partial response (ORR = 7.1%; CI95%: 0.2 - 33.9).The 6-month PFR was 28.6% (CI95%: 8.4 - 58.1).

Conclusions

Combination of T+D has activity in STS. Updated efficacy and biomarker analyses will be presented at the meeting.

Clinical trial identification

NCT03085225.

Legal entity responsible for the study

Institut Bergonie.

Funding

PharmaMar, AstraZeneca.

Disclosure

M. Toulmonde: Travel/Accommodation/Expenses: PharmaMar. A. Bessede: Officer/Board of Directors: Immusmol. J-Y. Blay: Advisory/Consultancy, Research grant/Funding (institution): PharmaMar. All other authors have declared no conflicts of interest.