2021 ESMO congress

LBA37

IMMUTACE: A biomarker-orientated, multi center phase II AIO study of transarterial chemoembolization (TACE) in combination with nivolumab performed for intermediate stage hepatocellular carcinoma (HCC)

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Background

Immunotherapy based combinations recently revolutionized the treatment of patients (pts) with advanced HCC, but its significance in earlier stages remains to be determined. TACE is commonly used as first line treatment in intermediate HCC, but outcome of pts treated with TACE in real-life cohorts is still poor with a median overall survival (OS) below 20 months. The release of neoantigens following local treatments is projected to trigger synergistic effects with anti-PD-1 antibodies, thus providing a rational for the combination of immunotherapy with TACE. The aim of this study was to determine the safety and efficacy of TACE with nivolumab.

Methods

This is a phase II trial, that recruited 59 pts at 10 sites in Germany between 06/2018 and 06/2020. Pts received up to 2 TACE treatments followed by nivolumab (240 mg/ Q2W), initiated on day 2-3 after the first TACE session and continued until progression for a maximum treatment duration of two years. One additional local treatment was allowed upon first progression. Primary endpoint (EP) was ORR (mRECIST; with an ORR exceeding 55% as promising for further investigations). Secondary EPs include PFS, TTFS, OS, QoL, and safety/tolerability. Tumor tissue was obtained at baseline and blood samples were collected longitudinally and subjected to an extensive biomarker analysis.

Results

49 pts (14.3% HCV and 8.2% HBV) were enrolled and received at least one dose of nivolumab. Median tumor size was 3 cm (0.6 – 14.7 cm) and median no. 3 (1 – 12). ORR was 71%. At a median follow-up of 14.6 months, mPFS was 6.14 mo (95% CI; 5.16 – 7.56; 41 events). Provisional mOS was 28.32 mo (95% CI; 20.60 – not estimable; 18 events). Grade ≥3 treatment-related adverse events occurred in 34.7% of pts. Correlative analysis of efficacy with genetic alterations, gene expression signatures and immune cell populations is ongoing.

Conclusions

The study met its primary EP and provides evidence for the efficacy of TACE in combination with nivolumab without new safety signals in pts with intermediate HCC and no prior systemic therapy. Our findings support further evaluation of nivolumab-based combinations for the treatment of intermediate HCC.

Clinical trial identification

NCT03572582; AIO-HEP-0217.

Legal entity responsible for the study

AIO-Studien-gGmbH.

Funding

BMS.

Disclosure

A. Vogel: Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Invited Speaker: Sanofi; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Advisory Board: BMS; Financial Interests, Personal, Invited Speaker: MSD; Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Invited Speaker: Novartis; Financial Interests, Personal, Invited Speaker: Eisai; Financial Interests, Personal, Advisory Board: Eisai; Financial Interests, Personal, Invited Speaker: Ipsen; Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Personal, Invited Speaker: Incyte; Financial Interests, Personal, Advisory Board: Incyte; Financial Interests, Personal, Invited Speaker: PierreFabre; Financial Interests, Personal, Advisory Board: PierreFabre; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Invited Speaker: Lilly; Financial Interests, Personal, Advisory Board: Lilly; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Invited Speaker: Roche; Financial Interests, Personal, Invited Speaker: MSD; Financial Interests, Personal, Invited Speaker: Beigene; Financial Interests, Personal, Invited Speaker: Jiangsu Hengrui Medicines. 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