Clinical trial identification: NCT03867084.

Editorial acknowledgement: Medical writing and/or editorial assistance was provided by Matthew Graywack, PhD, of the ApotheCom pmbmblltub team (Yardley, PA, USA) and funded by Merck & Sharp & Dohme Corp.

Legal entity responsible for the study: Merck & Sharp & Dohme Corp.

Funding: Merck Sharp & Dohme Corp.

Disclosure: A. Vogel: Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution); Novartis. A.L. Cheng: Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer. A. El-Khoueiry: Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution); Eisai. A. Siegel: Advisory/Consultancy: BMS; Research grant/Funding (institution): Merck & Co., Inc.; Shareholder/Stockholder/Stock options: M.D. Anderson Cancer Center. T. Yau: Honoraria (self), Advisory/Consultancy, Research grant/Funding (institution): Bayer; Research grant/Funding (institution): Novartis. Z. Ren: Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer. A.B. El-Khoueiry: Honoraria (self), Advisory/Consultancy, Travel/Accommodation/Expenses: Pfizer. All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1132

KEYNOTE-937 trial in progress: adjuvant pembrolizumab in patients with hepatocellular carcinoma (HCC) and complete radiologic response after surgical resection or local ablation


1Gastroenterology, Hannover Medical School, Hannover, Germany; 2Medical Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA; 3Department of Medical Oncology, National Taiwan University Hospital Cancer Center, Taipei City, Taiwan; 4Medical Oncology, University of Hong Kong, Queen Mary Hospital, Hong Kong, China; 5Hepatobiliary Surgery, Zhongshan Hospital, Fudan University, Shanghai, China; 6Medical Oncology, Merck & Co., Inc., Kenilworth, NJ, USA; 7Department of Gastroenterology and Hepatology, Kindai University School of Medicine, Osaka, Japan

Background: For patients with HCC undergoing potentially curative surgical resection or local ablation, 5-year recurrence rates are between 50% and 80%; there is currently no standard of care for adjuvant treatment. Pembrolizumab, a programmed death 1 inhibitor, is approved for the treatment of patients with HCC who have previously received sorafenib. There is currently no direct evidence of benefit with pembrolizumab in the HCC adjuvant setting, but a favorable benefit/risk profile is anticipated based on data from other indications. KEYNOTE-937 (NCT03867084) is a randomized, double-blind, phase III trial designed to evaluate the safety and efficacy of adjuvant pembrolizumab versus placebo in patients with HCC who have had a complete radiologic response after surgical resection or local ablation.

Trial design: Eligible patients are aged ≥18 yrs with confirmed HCC, complete radiologic response after complete resection or local ablation, 5-year recurrence rates are between 50% and 80%; there is currently no standard of care for adjuvant treatment. Pembrolizumab, a programmed death-1 inhibitor, is approved for the treatment of patients with HCC who have previously received sorafenib. There is currently no direct evidence of benefit with pembrolizumab in the HCC adjuvant setting, but a favorable benefit/risk profile is anticipated based on data from other indications. KEYNOTE-937 (NCT03867084) is a randomized, double-blind, phase III trial designed to evaluate the safety and efficacy of adjuvant pembrolizumab versus placebo in patients with HCC who have had a complete radiologic response after surgical resection or local ablation.

ALT-H-004: A phase II study of anlotinib combined with TACE as adjuvant therapy in hepatocellular carcinoma patients at high risk of post-surgery recurrence

W. Wu 1, Z. Wang 2, X. Du 3, L. Zhang 4

1Department of Hepatobiliary Surgery, The First Affiliated Hospital of Xi’an Jiaotong University, Xi’an, China; 2Department of General Surgery, The Second Affiliated Hospital of Air Force Medical University/Tangdu Hospital, Xi’an, China; 3Department of General Surgery, The First Hospital of Lanzhou University/The First School of Clinical Medicine, Lanzhou, China

Background: HCC is one of the most common malignant tumors with high incidence and mortality worldwide. It is acceptable that adjuvant therapy is an efficient treatment for reducing recurrence in patients with hepatocarcinoma, especially in those with high recurrence factors. Regional therapies and tyrosine kinase inhibitors (TKIs), which were recommended as standard treatments for unresectable and advanced HCC pts, had limited and minimal disease-free survival as adjuvant therapy, respectively. Anlotinib, a novel multi-target TKI, mainly targeting VEGFR1-3, showed durable anti-tumor activity and manageable toxicity as first or second-line treatment of advanced HCC pts in an open-label phase II trial (NCT02809534). Consistent with these, we conducted a multicenter open-label, phase II study to evaluate anti-tumor efficacy and safety for anlotinib plus TACE in HCC pts with high recurrence risks after surgery.

Trial design: This was a single arm, multicenter phase II trial. A total number of 48 pts with histologically confirmed HCC would be enrolled. The eligibility criteria included: previously not receive any tumor-related treatment except hepatectomy and met any of the following high-risk criteria: 1) ≥5cm and/or tumor diameter ≥3cm, 2) tumor microvascular invasion grade M1 or M2, portal vein carcinoma thrombus resection (Cheng’s classification); 18-75 years old; 3) Child-Pugh score B or C; 4) radiologic response after complete resection or local ablation confirmed by CT/MRI within 3 months. In the following three months, patients would be stratified according to the 9055 patients were randomized assigned 1:1:1 to pembrolizumab 200 mg or placebo IV every 3 weeks. Treatment would continue for up to 17 cycles (≤1 year) or until disease recurrence, unacceptable toxicity, or withdrawal. Primary endpoints are recurrence-free survival and overall survival. The secondary endpoints are safety and tolerability and health-related quality of life. Exploratory endpoints include distant metastasis-free survival, overall survival, disease-specific survival, progression-free survival and health-related quality of life. Tumor imaging will be performed every 12 weeks during recurrence or Week 28 (=year 4), whichever occurs first. Adverse events, graded per National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0, will be recorded up to 30 days after last dose (90 days for serious AEs). Recruitment for this study began in May 2019.