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Submitted by:
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NCCN Guidelines Panel: Hepatobiliary Cancers

Dear NCCN Guidelines Panel:

On behalf of Genentech, Inc., please find updated data from the Phase 1b GO30140 study enclosed for your review.[1-2]

Request:

Consider the inclusion of Tecentriq® (atezolizumab) and Avastin® (bevacizumab) as an initial first-line treatment for patients with previously untreated, unresectable hepatocellular carcinoma (HCC).

Rationale:

Data reported from the GO30140 study continue to demonstrate the activity of Tecentriq and Avastin in patients with previously untreated, unresectable HCC.[1-2]

Arm A:[1]
- In 104 patients with unresectable HCC and Child-Pugh score of up to B7, treatment with Tecentriq and Avastin resulted in an ORR of 36%, CR of 12%, and DCR of 71%. Responses were observed in all assessed patient subgroups, including patients with high-risk disease. At baseline, 88% of patients had extrahepatic spread and/or macroscopic vascular invasion.
- Median PFS was 7.3 months (95% CI 5.4–9.9). Responses were durable with 54% of patients showing responses ≥ 9 months and 30% ≥ 12 months. 76% of patients had an ongoing response at time of analysis.
- The primary endpoint for Arm A was ORR per IRF-assessed RECIST 1.1 with a median duration of follow up of 12.4 months.

Arm F: [2]
- A total of 119 patients were randomized to receive either Tecentriq and Avastin combination or Tecentriq monotherapy.
- Data from Arm F demonstrate the superiority of the combination of Tecentriq and Avastin over Tecentriq monotherapy with a median PFS of 5.6 months vs 3.4 months [HR of 0.55 (80% CI 0.40–0.74), p=0.0108].
- The primary endpoint for Arm F was PFS per IRF RECIST 1.1 with a median duration of follow up of 6.6 months.

In both arms, the combination of Tecentriq and Avastin was generally well tolerated and toxicities were manageable.[1-2]

- The safety profile of Tecentriq and Avastin was consistent with previously reported safety risks of the individual medicines.[1-2]
- Arm A: Grade 3-4 treatment related adverse events were noted in 39% of the study population. Ten percent of AEs lead to study withdrawal.[1]

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- Arm F: Grade 3-4 treatment related adverse events were noted in 20% of patients treated with Tecentriq and Avastin and 5% of patients treated with Tecentriq monotherapy. Three percent of AEs lead to study withdrawal in patients treated with Tecentriq and Avastin and 2% in patients treated with Tecentriq monotherapy.[2]

FDA Clearance:

The U.S. Food and Drug Administration granted Breakthrough Therapy Designation for Tecentriq in combination with Avastin as first-line treatment for patients with advanced or metastatic HCC.[3]

- Tecentriq and Avastin are not FDA-approved for the treatment of HCC. Please refer to the product prescribing information for the full FDA-approved indications and safety information of Tecentriq and Avastin, available at:
    - https://www.gene.com/medical-professionals/medicines/tecentriq
    - https://www.gene.com/medical-professionals/medicines/avastin

Thank you for your consideration. If you have any questions, please contact us at the phone number and email provided above.

Respectfully submitted,
Patrice Esser, PharmD, MPH

References:

1. Kyung-Hun Lee, Baek-Yeol Ryoo, Chih-Hung Hsu, et al. Phase Ib Study Results: Subgroup Efficacy Analysis of Atezolizumab+ Bevacizumab in Patients With Previously Untreated, Unresectable Hepatocellular Carcinoma. Presented at the International Liver Cancer Association Conference in Chicago, USA; September 20-22, 2019. ILCA Oral Presentation 0-32.
2. Michael S Lee, Baek-Yeol Ryoo, Chih-Hung Hsu, et al. Randomised Efficacy and Safety Results for Atezolizumab + Bevacizumab in Patients With Previously Untreated, Unresectable Hepatocellular Carcinoma. Presented at the European Society for Medical Oncology (ESMO) Conference in Barcelona, Spain; September 27–October 1, 2019. ESMO Presentation #LBA39.
3. Genentech, Inc. (2018, July 17). *FDA Grants Breakthrough Therapy Designation for Genentech's TECENTRIQ in Combination With Avastin as First-Line Treatment for Advanced or Metastatic Hepatocellular Carcinoma (HCC)* [Press release]. Retrieved from https://www.gene.com/media/press-releases/14736/2018-07-17/fda-grants-breakthrough-therapy-designat