ILCA 2020
11-13 SEPTEMBER
INTERNATIONAL LIVER CANCER ASSOCIATION
VIRTUAL CONFERENCE

A Randomized, Placebo-Controlled Study of Transarterial Chemoembolization Combined With Concurrent Durvalumab Followed by Durvalumab or Durvalumab Plus Bevacizumab Therapy in Patients With Locoregional Hepatocellular Carcinoma (HCC): EMERALD-1

P-05

Bruno Sangro,[1] Masatoshi Kudo,[2] Shukui Qin,[3] Zhenggang Ren,[4] Stephen Chan,[5] Joseph Erinjeri,[6] Yasuaki Arai,[7] Philip He,[8] Shethah Morgan,[8] Gordon Cohen,[9] Riccardo Lencioni[10]

[1]Liver Unit, Clínica Universidad de Navarra and CIBEREHD, Pamplona, Spain; [2]Kindai University, Osaka, Japan; [3]Department of Medical Oncology, PLA Cancer Center & Bayi Clinical Trial Institute, Nanjing, China; [4]Zhongshan Hospital, Fudan University, Shanghai, China; [5]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong; [6]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [7]National Cancer Center, Tokyo, Japan; [8]AstraZeneca, Cambridge, United Kingdom; [9]AstraZeneca, Gaithersburg, MD, USA; [10]University of Pisa School of Medicine, Pisa, Italy

Summary

- The EMERALD-1 study will expand our understanding of the potential clinical benefits of adding durvalumab or durvalumab with bevacizumab to TACE for patients with locoregional HCC who are not candidates for curative therapy.

Introduction

- Curative therapy is not always an option for patients with intermediate-stage HCC and a **standard approach for treatment is locoregional therapy such as TACE**.
- TACE therapy achieves tumor responses, **but progression and recurrence are common and often occur within 1 year**.[1]
- **Immune checkpoint inhibitors have shown promising efficacy with durable response as treatment for advanced HCC when combined with TACE**.[2,3]
- The immune checkpoint inhibitor atezolizumab combined with the VEGF inhibitor bevacizumab have been approved in HCC.[4,5]
- **Combining durvalumab with the VEGF inhibitor bevacizumab and TACE therapies warrants evaluation in patients with locoregional HCC**.

Methods

- **EMERALD-1 (NCT03778957)** is a randomized, double-blind, placebo-controlled, multicenter Phase 3 study assessing efficacy and safety for durvalumab when given concurrently with either DEB-TACE or conventional TACE followed by durvalumab ± bevacizumab in patients with locoregional HCC not amenable to curative therapy.
- 600 patients will be randomized 1:1:1 to Arms A, B, or C (**Figure 1**).
- Durvalumab (or its matched placebo) will begin at least 7 days following the initial TACE procedure.
- Bevacizumab (or its matched placebo) will be added to durvalumab (or its matched placebo) at least 14 days after the last TACE procedure.

Figure 1. EMERALD-1 study design

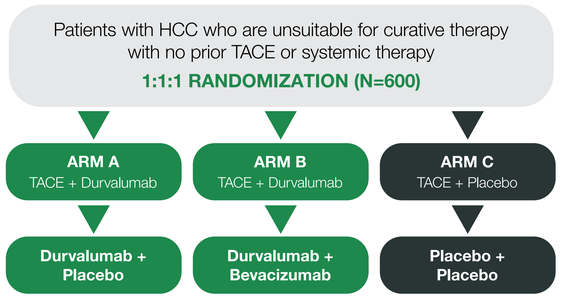
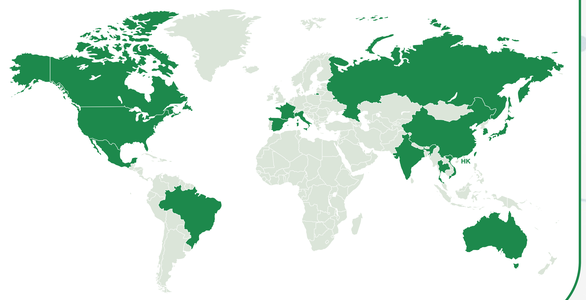


Figure 2. EMERALD-1 participating regions



Study Endpoints

1
- Assess PFS (by BICR using RECIST v 1:1)

2
- Evaluate PFS for all arms using modified RECIST (by BICR)
- Evaluate overall survival for all arms
- Investigate the relationship between baseline PD-L1 expression and efficacy outcomes
- Measure time to progression for all arms
- Evaluate objective response, duration of response, and disease control rate
- Assess disease-related symptoms, impacts, and HRQoL for all arms
- Evaluate safety and tolerability profile of all arms

Key exploratory objectives
- Investigate the association of candidate biomarkers with efficacy measures using blood and tissue samples
- Explore the impact of treatment and disease state on health care utility and resources

Key Inclusion Criteria

- Aged ≥18 years
- Histologically or radiologically confirmed HCC not amenable to curative therapy
- No prior TACE or systemic therapy for HCC
- Child-Pugh Score A to B7
- ECOG PS of 0 or 1 at enrollment

- Patients with HBV or HCV alone may be enrolled, but patients who are HBV+ must have adequately controlled viral suppression prior to enrollment and HBV/HCV replication will be monitored during the study and treated if appropriate.
- Patients are required to have an upper endoscopy performed to evaluate varices and risk of bleeding within 6 months of randomization.

Key Exclusion Criteria

- A history of nephrotic or nephritic syndrome
- Clinically significant cardiovascular disease
- Extrahepatic disease
- Evidence of main portal vein thrombosis (Vp3/Vp4)
- Prior or current evidence of bleeding diathesis, within 28 days following surgery, or GI perforation or active GI bleeding within 6 months of enrollment

- A tumor tissue sample is mandatory and may either be taken during the first TACE procedure or taken ≤3 months prior to randomization.
- There are currently 17 countries and regions participating in the EMERALD-1 study (**Figure 2**).

References

1. Lencioni R, et al. *Hepatology.* 2016;64(1):106-116.
2. Kelley RK, et al. *J Clin Oncol.* 2017;35(abstr 4073).
3. Duffy AG, et al. *J Hepatol*. 2017;66(3):545-551.
4. Finn RS, et al. *N Engl J Med*. 2020;382:1894-1905.
5. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-atezolizumab-plus-bevacizumab-unresectable-hepatocellular-carcinoma.

Abbreviations

BICR, blinded independent central review; DEB, drug-eluting bead; ECOG PS, Eastern Cooperative Oncology Group performance status; GI, gastrointestinal; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HRQoL, health-related quality of life; PD-L1, programmed death ligand-1; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumors; TACE, transarterial chemoembolization; VEGF, vascular endothelial growth factor.

Acknowledgments

This study was funded by AstraZeneca. The authors would like to thank the patients, their families and caregivers, and all investigators involved in this study. Medical writing support, which was in accordance with Good Publication Practice (GPP3) guidelines, was provided by Jubilee Stewart, PhD, of Parexel (Hackensack, NJ, USA) and Anne-Marie Manwaring of Parexel (Littlehampton, UK) and was funded by AstraZeneca.

Contact Information

Shethah.Morgan@astrazeneca.com