A Phase 3 Study of Transarterial Chemoembolization Combined With Durvalumab Followed by Durvalumab ± Bevacizumab in Patients With Locoregional HCC: EMERALD-1

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Introduction
- Curative therapy is not always feasible for patients with intermediate-stage hepatocellular carcinoma (HCC) and a standard approach for treatment is locoregional therapy such as transarterial chemoembolization (TACE).
- TACE therapy achieves tumor responses, but progression is common and often occurs within 1 year.
- Checkpoint inhibitors have shown promising efficacy with durable response as treatment for advanced HCC when combined with TACE.
- Checkpoint inhibitors combined with VEGF inhibitors have also shown promise in advanced HCC.
- Combining durvalumab with VEGF inhibitors 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 monotherapy when given with either drug-eluting bead (DEB)-TACE or conventional TACE.
- 600 patients will be randomized 1:1:1 to Arm A, B, or C (Figure 1).
- Durvalumab (or its matched placebo) will be added to durvalumab (or its matched placebo) at least 14 days after the last TACE procedure.

Inclusion criteria
- Aged ≥18 years
- Confirmed HCC not amenable to curative therapy
- No prior TACE or systemic therapy for HCC
- Child-Pugh score class A to B
- ECOG PS 0 or 1 at enrolment

Exclusion criteria
- A history of nephrotic or nephritic syndrome
- Clinically significant cardiovascular disease
- Extravascular disease
- Evidence of main portal vein thrombosis (Vp3/Vp4)
- Prior or current evidence of bleeding diatheses, within 28 days following surgery, or GI perforation or active GI bleeding within 6 months of enrolment
- ECOG PS, Eastern Cooperative Oncology Group performance status; GI, gastrointestinal.

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

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References

Institutional review board and agency approvals
This study was conducted under an approved investigational new drug application. The study was submitted to relevant regulatory authorities and was conducted in accordance with the requirements stated in the approval.

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Figure 1: EMERALD-1 study design

Figure 2: EMERALD-1 study

Summary
- The EMERALD-1 study will expand the understanding of the efficacy and safety of durvalumab combined with TACE therapy followed by durvalumab with or without bevacizumab in patients with locoregional HCC who cannot undergo curative therapy.