LEAP-012

Combining systemic & locoregional therapy in unresectable HCC:
A quick reference on key findings and clinical impact

PUBLICATION SNAPSHOT

TACE combined with lenvatinib plus pembrolizumab versus dual placebo for unresectable, non-metastatic HCC (LEAP-012):
A multicentre, randomised, double-blind, Phase 3 study[1]

Key eligibility criteria

- Confirmed HCC not amenable to curative treatment
- ≥1 measurable HCC lesion per RECIST v1.1
- All lesions treatable with TACE (maximum of 2 treatments per tumour)
- No portal vein invasion or extrahepatic disease
- Child–Pugh liver class A
- ECOG PS 0 or 1

R 1:1

- **Lenvatinib + pembrolizumab + TACE**
- **Placebo + placebo + TACE**

Endpoints

Primary: PFS (RECIST v1.1) and OS

Secondary: ORR, DoR, TTP, PFS (mRECIST), and safety

LEAP-012 met its primary endpoint in PFS

Lenvatinib + pembrolizumab + TACE showed a statistically significant and clinically meaningful **improvement in PFS** versus **double placebo + TACE**

Early trend toward **improvement in OS** versus placebo + TACE

- OS will be retested in future analysis

MEDIAN PFS

14.6 mo vs **10.0 mo**

p=0.0002

No new safety signals were identified

The **safety profile** was consistent with known safety profiles of lenvatinib, pembrolizumab, and TACE

Placing LEAP-012 in clinical context

LEAP-012 is a positive study

Builds on the approach of combining IO-based therapy with locoregional therapy

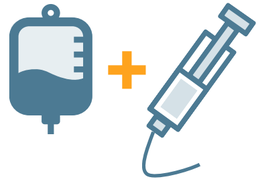
EMERALD-1, evaluating durvalumab +/- bevacizumab with TACE, also supports the approach[2]

MORE DATA NEEDED

- **Overall survival**
- **Quality of life**
- **TARE (Y90)**
  TARE is increasingly used and its role in multimodal therapy should be clarified

Key clinical takeaways

LEAP-012 further **supports** the approach of combining locoregional therapies with IO-based therapies



Future directions include additional data on **OS** and **QoL**, to further define the **long-term benefits** and **clinical applicability**

Locoregional therapies combined with **IO-based therapies** should be more frequently considered in clinical practice, particularly for patients **with intermediate HCC as a potential strategy** to **downstage** or **downsize** the disease

1. Kudo M, et al. Lancet. 2025;405:203-215; 2. Sangro B, et al. Lancet. 2025;405:216-232

DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy); mRECIST, modified Response Evaluation Criteria in Solid Tumours; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QoL, quality of life; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; TACE, transarterial chemoembolisation; TARE, transarterial radioembolisation; TTP, time to progression; Y90, yttrium-90;

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