

Is There Still a Place for Tyrosine Kinase Inhibitors for the Treatment of Hepatocellular Carcinoma at the Time of Immunotherapies? A Focus on Lenvatinib

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Table S1. Clinical trials of lenvatinib for HCC.

A: Phase III clinical trials.					
Protocol	Identifier	Study Title	Interventions	Number Enrolled	Primary Completion
Lenvatinib as Adjuvant (Stage A)	NCT04227808	Lenvatinib as adjuvant therapy for patients who underwent radical resection of HCC with a high risk of recurrence.	Drug: lenvatinib Procedure: Surgery	50	Dec 2022
	NCT03838796	Lenvatinib combined with TACE for preventing recurrence in high-risk patients	Drug: lenvatinib Procedure: TACE	482	Dec 2021
	NCT04053972	The impact on recurrence risk of adjuvant lenvatinib for patients with HCC and microvascular invasion (MVI) after hepatectomy.	Drug: lenvatinib Procedure: Surgery	377	Dec 2022
Lenvatinib and Locoregional treatment (Stage B or C)	NCT03838796	Lenvatinib combined with TACE for preventing recurrence in high-risk patients	Drug: lenvatinib Procedure: TACE	482	Dec 2021
	NCT04246177	Lenvatinib (E7080/MK-7902) with pembrolizumab (MK-3475) in combination with TACE vs. TACE in participants with incurable/non-metastatic HCC (LEAP-012).	Drug: lenvatinib Drug: pembrolizumab Drug: oral placebo Drug: IV placebo Procedure: TACE	950	Apr 2025
	NCT03775395	Sorafenib combined with hepatic arterial infusion chemotherapy (HAIC) compared with lenvatinib combined with HAIC in patients with advanced HCC.	Drug: lenvatinib Drug: sorafenib Procedure: Hepatic arterial infusion chemotherapy	250	Dec 2021
	NCT03905967	Lenvatinib plus TACE vs. lenvatinib alone for advanced HCC patients.	Procedure: TACE Drug: lenvatinib	336	Apr 2023

Lenvatinib and systemic treatment (Stage C) First-line	NCT04687163	Lenvatinib plus hepatic artery infusion of 130 mg/m ² oxaliplatin, leucovorin, and fluorouracil vs. sorafenib or lenvatinib plus hepatic artery infusion of 85 mg/m ² oxaliplatin, leucovorin, and 1200 mg/m ² fluorouracil for unresectable advanced HCC: a randomised phase 3 trial.	Drug: HAIC of oxaliplatin, and 5-FU hepatic arterial infusion of oxaliplatin, leucovorin and 5-FU Drug: lenvatinib or sorafenib	400	Dec 2022
	NCT04053985	Transarterial chemoinfusion (TAI) combined with lenvatinib in advanced HCC.	Drug: lenvatinib Procedure: TAI	206	Dec 2022
	NCT04194775	CS1003 in combination with lenvatinib compared to placebo in combination with lenvatinib as first-line therapy in subjects with advanced HCC.	Drug: CS1003+ lenvatinib Drug: CS1003 placebo+ lenvatinib	525	Jun 2023
	NCT04039607	Nivolumab plus ipilimumab vs. standard of care (sorafenib or lenvatinib) in all randomised participants with advanced HCC who have not received prior systemic therapy.	Drug: nivolumab Drug: ipilimumab Drug: sorafenib Drug: lenvatinib	650	Mar 2023
	NCT04523493	Toripalimab combined with lenvatinib vs. placebo combined with lenvatinib as 1st-line therapy for advanced HCC.	Combination drug: toripalimab combined with lenvatinib		May 2024

B: Phase II clinical trials.

Protocol	Identifier	Study Title	Interventions	Number Enrolled	Primary Completion
Lenvatinib as Neo-adjuvant (Stage A)	NCT04241523	Lenvatinib as a preoperative conversion therapy in patients with potentially resectable HCC.	Drug: lenvatinib 4 mg oral	50	Oct 2021
	NCT04273100	PD-1 mAb combined with lenvatinib and TACE in the treatment of BCLC B/C HCC: single arm, single centre, non-	Combination product: PD-1 mAb combined with TACE and lenvatinib	56	Dec 2020

		randomised, open label study.			
Lenvatinib + locoregional treatment (Stage B or C)	NCT04531228	TACE-HAIC plus lenvatinib for patients with unresectable HCC.	Procedure: TACE-HAIC plus lenvatinib	60	Apr 2021
	NCT04368078	A phase IIB clinical study. Lenvatinib plus toripalimab in patients with advanced HCC and to analyse potential biomarkers of therapeutic response.	Drug: lenvatinib Drug: toripalimab	76	April 2022
	NCT04444167	An open-label multi-centre phase Ib/II study. Anti-PD-1/CTLA-4 bispecific antibody AK104 plus lenvatinib as first-line therapy for patients with advanced HCC.	Biological: AK104 Drug: lenvatinib	30	Jan 2022
Lenvatinib and systemic treatment (Stage C) First-line	NCT03841201	Immunotherapy with nivolumab in combination with lenvatinib for patients with multinodular, advanced stage HCC in first-line therapy.	Drug: lenvatinib Drug: nivolumab	50	Jul 2021
	NCT04401800	Tislelizumab in combination with lenvatinib in unresectable locally advanced or metastatic HCC.	Drug: lenvatinib Drug: tislelizumab	66	Sep 2022
	NCT04443309	Lenvatinib in combination with camrelizumab as first-line therapy in patients with advanced HCC.	Drug: camrelizumab Drug: lenvatinib	53	Aug 2022
	NCT04170179	Systemic chemotherapy of oxaliplatin, 5-fluorouracil, and leucovorin plus lenvatinib and toripalimab in	Procedure: Systemic chemotherapy Drug: lenvatinib Drug: toripalimab	25	Nov 2020

		patients with HCC with extrahepatic metastases.			
	NCT03899428	Immune check-point therapy vs. target therapy in reducing serum HBsAg levels in patients with HBeAg-positive advanced HCC (VICI-5).	Drug: durvalumab Drug: sorafenib Drug: lenvatinib Drug: regorafenib Drug: cabozantinib	30	Dec 2021
C: Phase I clinical trials.					
Protocol	Identifier	Study Title	Interventions	Number Enrolled	Primary Completion
Lenvatinib and systemic treatment (Stage C)	NCT04008797	Phase 2 dose (RP2D) of E7386 in combination with lenvatinib.	Drug: E7386 Drug: lenvatinib	42	Mar 2022