

Supplementary Table 1. Phase 2 Trials of Targeted Chemotherapy for HCC

BCLC, Barcelona Clinic Liver Cancer classification; ECOG, Eastern Cooperative Oncology Group; PS, Performance Status. mAb, monoclonal antibody. VEGFR2 -Vascular endothelial growth factor receptor 2; CDK- cyclin-dependent kinase; EGFR- Epidermal growth factor receptor. TGF- Transforming growth factor.

TRIAL NAME, DRUG	CLINICAL TRIAL ID	MECHANISM OF ACTION	TITLE OF STUDY	LINE OF THERAPY	INCLUSION CRITERIA	STATUS	Date of Completion
CHR-2845, Tefinostat	NCT02759601	Histone deacetylase inhibitor	A Phase 1/2 Dose Escalation Trial of HDAC Inhibitor Tefinostat for Cancer Associated Inflammation in Hepatocellular Carcinoma	First/Second	Child pugh A, BCLC B-C, ECOG PS 0-2.	Recruiting	June 2018
Enzalutamide	NCT02528643	Androgen receptor blockade	A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Enzalutamide in Subjects With Advanced Hepatocellular Carcinoma	Second	Child Pugh A, BCLC B-C, ECOG PS 0-1. Failed Sorafenib	Recruiting	May 2019
Apatinib	NCT03046979	VEGFR2 inhibitor	Study of Apatinib in Advanced Hepatocellular Carcinoma(HCC)	Second	Child Pugh A, BCLC C, ECOG PS 0-1. Failed Sorafenib	Recruiting	December 2018
Milciclib	NCT03109886	CDK inhibitor	Phase 2A Exploratory Study of Oral Milciclib Maleate in Patients With Unresectable or Metastatic Hepatocellular Carcinoma	Second	Child Pugh A, BCLC C, ECOG PS 0-1. Failed Sorafenib	Recruiting	August 2019
CF102	NCT02128958	A3 adenosine receptor agonist	A Phase 2 Study in the Second-Line Treatment of Advanced Hepatocellular Carcinoma in Subjects With Child-Pugh Class B Cirrhosis	Second	Child Pugh A-B, BCLC B-C, ECOG PS 0-2. Failed Sorafenib	Recruiting	September 2018
INC280	NCT01737827	c-Met inhibitor	A Phase 2, Open Label, Single Arm, Multicenter Study of INC280 Administered Orally in Adults With Advanced Hepatocellular Carcinoma	First	Confirmed c-MET pathway dysregulation. Ahid pugh A. BCLC B-C. ECOG 0-2	Recruiting	July 2018
Anlotinib	NCT02809534	EGFR inhibitor	A Single Group, Open Label, Single-center Clinical Trial to Assess the Efficacy and Safety of Anlotinib in Patients With Hepatocellular Carcinoma	First/Second	Child pugh A, BCLC B-C, ECOG PS 0-2.	Recruiting	December 2017
LEE001	NCT02524119	CDK4/6 inhibitor	A Phase 2 Study of LEE011 and Chemoembolization In Patients With Advanced Hepatocellular Carcinoma	First	RB positive HCC, Locally advanced HCC, Child Pugh A-B, ECOG 0-2	Recruiting	September 2018
BTCRC-GI13-002, MLN0128	NCT02575339	mTOR inhibitor	An Open Label Randomized Phase I/2 Trial of MLN0128 Compared to Sorafenib in Patients With Advanced or Metastatic Hepatocellular Carcinoma: Big Ten Cancer Research Consortium	First	Child Pugh A, BCLC B-C, ECOG PS 0-1. No prior systemic therapy.	Recruiting	June 2020
TRC105	NCT02560779	Endoglin mAb+Multikinase inhibitor	An Open Label Phase 1B/2 Trial of TRC105 and Sorafenib in Patients With Hepatocellular Carcinoma (HCC)	First	Child Pugh A, BCLC B-C, ECOG PS 0-1. No prior systemic therapy.	Recruiting	September 2018
eFT508	NCT03318562	Mitogen-Activated Protein Kinase Interacting Kinase (MNK) 1 and 2 inhibitor	A PD Study of Oral eFT508 in Subjects With Advanced TNBC and HCC	First/Second	Child Pugh A, BCLC B-C, ECOG PS 0-1.	Recruiting	May 2018
Varlitinib	NCT03499626	EGFR and Her-2/neu inhibitor	Phase 1b of ASLAN001 (Varlitinib) in Patients With Advanced/ Metastatic Hepatocellular Carcinoma (HCC)	Second	Child Pugh A, BCLC B-C, ECOG PS 0-1. Failed Sorafenib/Lenvatinib	Recruiting	May 2021
Axinitib	NCT01334112	Tyrosine kinase inhibitor	A Phase 2 Trial of Axitinib (AG-013736) After Prior Antiangiogenic Therapy in Advanced Hepatocellular Carcinoma	Second	Child Pugh A, BCLC B-C, ECOG PS 0-1. Failed Sorafenib	Not Recruiting	March 2018
Enzalutamide	NCT02528643	Androgen receptor	A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Enzalutamide in Subjects With Advanced Hepatocellular Carcinoma	Second	Child Pugh A, BCLC B-C, ECOG PS 0-1. Failed Sorafenib	Not Recruiting	May 2019
LY2157299	NCT02178358	TGF b receptor inhibitor	A Randomized Phase 2 Study of LY2157299 Versus LY2157299 - Sorafenib Combination Versus Sorafenib in Patients With Advanced Hepatocellular Carcinoma	First	Child Pugh A, BCLC B-C, ECOG PS 0-1	Not Recruiting	December 2018
PD-0332991	NCT01356628	CDK inhibitor	A Phase 2 Study of PD-0332991 in Adult Patients With Advanced Hepatocellular Carcinoma	Second	RB positive HCC, Child Pugh A-B, BCLC B-C, ECOG 0-2. Failed Sorafenib	Not Recruiting	August 2019
ABC294640	NCT02939807	Sphingosine Kinase 2 inhibitor	A Phase 2 Study of ABC294640 in Patients With Advanced Hepatocellular Carcinoma Who Have Progressed on Sorafenib	Second	Child Pugh A, BCLC B-C, ECOG PS 0-1. Failed Sorafenib	Not Recruiting	May 2021
Tivozanib	NCT01835223	VEGF tyrosine kinase inhibitor	Multicenter Phase 1b/2 Study of Tivozanib in Patients With Advanced Inoperable Hepatocellular Carcinoma	First	Child Pugh A, BCLC B-C, ECOG PS 0-1	Not Recruiting	December 2019
BB1503	NCT02232633	Stemness kinase inhibitor	A Phase 2 Clinical Study of BB1503 in Adult Patients With Advanced Hepatobiliary Cancer	First	Child Pugh A, BCLC B-C, ECOG PS 0-1. HCC or Cholangiocarcinoma	Not Recruiting	December 2018
MSC2156119J	NCT01988493	c-Met inhibitor	A Multicenter, Randomized, Phase 1b/2 Trial to Evaluate the Efficacy, Safety, and Pharmacokinetics of MSC2156119J as Monotherapy Versus Sorafenib in Asian Subjects With MET+ Advanced Hepatocellular Carcinoma and Child-Pugh Class A Liver Function	First/Second	Asian patients with MET+tumors, Child Pugh A. BCLC B-C, ECOG PS 0-2	Not Recruiting	October 2018