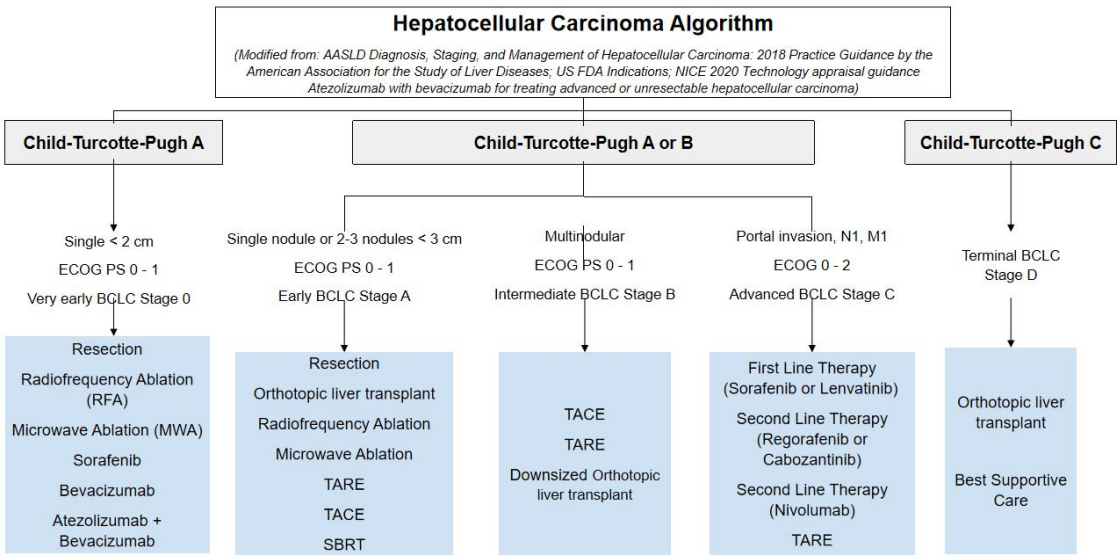
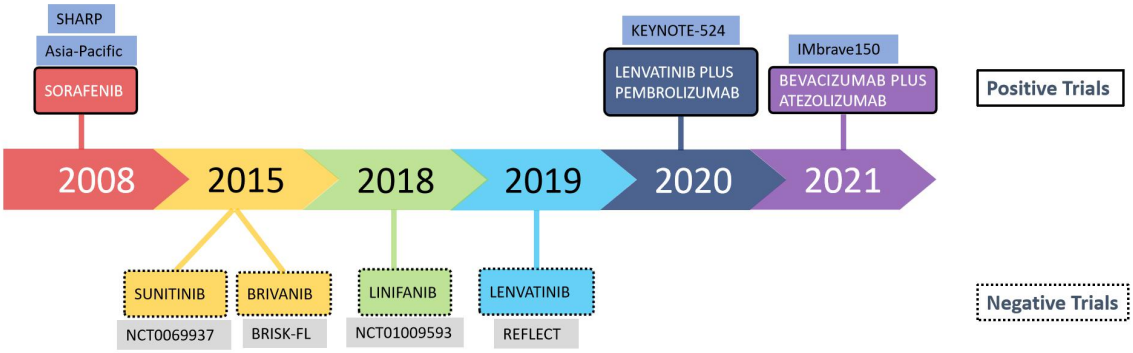


N, nodal metastasis; M, extrahepatic metastasis.

Supplementary Figure 1 Hepatocellular carcinoma treatment algorithm.



Supplementary Figure 2 Development of first-line treatment for hepatocellular carcinoma.

Supplementary Table 1 Response evaluation criteria in solid tumors criteria

Criteria	RECIST 1.0	RECIST 1.1	Comment
Minimum target lesion diameter by CT or MRI at baseline	≥ 20 mm	≥ 10 mm	Entry was restricted to those with measurable disease
Measurable lesions	Up to five *per* organ and ten lesions in total, representative of all involved organs	Up to two *per* organ and maximum of five lesions in total, representative of all involved organs	
Prior treatment	Tumor lesions that are situated in a previously irradiated area not considered measurable	Tumor lesions situated in a previously irradiated area, or in an area subjected to other local-regional therapy, are usually not considered measurable unless there has been demonstrated progression in the lesion	
Non- target lesions	All other lesions (or sites of disease) were identified as non-target lesions and recorded at baseline	Multiple non-target lesions involving the same organ were assessed as a single item on the case record form (*e.g.*, "multiple enlarged pelvic lymph nodes" or "multiple liver metastasis)	
Criteria for response (according to sum of target lesions diameters)			Confirmation of CR or PR after at least 28 d required for RECIST 1.0 only and for RECIST 1.1 if

			primary endpoint
CR	Disappearance of lesions	Disappearance of lesions	Primary endpoint
PR	≥ 30% decrease	≥ 30% decrease	Both target and non-target lesions in the liver were assessed at follow-up
SD	< 30% decrease or < 20% increase	< 30% decrease or < 20% increase	Note: Appearance of new lesion as indicator of progression is only relevant for overall response evaluation
PD	Any increase	≥ 20% or ≥ 5 mm increase	
PET	No specific recommendations	FDG-PET may be considered to complement CT scanning in assessment of progression and the confirmation of CR	Results from PET were not considered in this study

RECIST: Response evaluation criteria in solid tumors; FDG-PET: Fluorodeoxyglucose-positron emission tomography; MRI: Magnetic resonance imaging.

Supplementary Table 2 Child-Turcotte-Pugh scoring tool

	Points		
	1	**2**	**3**
Encephalopathy	None	Grade 1-2 (or precipitant induced)	Grade 3-4 (or chronic)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2 to 3	> 3
Albumin (g/dL)	> 3.5	2.8 to 3.5	< 2.8
International normalized ratio	< 1.7	1.7 to 2.3	> 2.3
Child-Turcotte-Pugh classifications			
Class A	**Class B**		**Class C**
Mild, least severe liver disease. Well-preserved liver function	Moderately severe liver disease. Moderate liver dysfunction. Significant functional compromise		Most severe liver disease. Decompensated function
< 6 points	7 to 9 points		10 to 15 points

Supplementary Table 3 Barcelona clinic liver cancer staging classification

Variables		Tumor Status		
Stage	**PST**	**Tumor stage**	**Okuda stage**	**Liver functional status**
Stage A: Early HCC				
A1	0	Single	I	No portal hypertension and normal bilirubin
A2	0	Single	I	Portal hypertension and normal bilirubin
A3	0	Single	I	Portal hypertension and abnormal bilirubin
A4	0	3 tumors < 3 cm	I-II	Child Pugh A-B
Stage B: Intermediate HCC	0	Large multinodular	I-II	Child Pugh A-B
Stage C: Advanced HCC	1-2	Vascular invasion or extrahepatic spread	I-II	Child Pugh A-B
Stage D: End-stage HCC	3-4	Any	III	Child Pugh C

Stage A and B: All criteria should be fulfilled; Stage C: At least one criteria; PST 1-2 or vascular invasion/extrahepatic spread; Stage D: At least one criteria; PST 3-4 or Okuda stage III/Child-Pugh C. Modified from Lovett *et al*, (1999). HCC: Hepatocellular carcinoma.