中山醫學大學附設醫院

肝癌診療指引

本臨床指引參考AASLD、APASL、EASL與美國NCCN版本

再依據中山醫學大學附設醫院肝癌小組經驗作編修

肝癌多專科醫療團隊編修

2026/04/15	Version19.1
2025/11/26	Version19.0
2024/11/20	Version18.0
2023/11/15	Version17.0
2022/12/07	Version16.0
2021/11/17	Version15.0
2020/12/16	Version14.0
2019/11/20	Version13.0
2018/09/12	Version12.0
2017/11/22	Version11.0
2016/12/14	Version10.0
2015/11/25	Version9.0
2014/12/10	Version8.0
2013/12/25	Version7.0
2012/12/12	Version6.0
2011/12/14	Version5.1
2011/03/22	Version5.0
2010/02/11	Version4.0
2009/12/17	Version3.0
2008/11/14	Version2.0
2007/10/11	Version1.0

癌症委員會主任委員	癌症委員會執行長	癌症中心主任	抗癌藥物安全小組	團隊負責人

修訂內容

頁數	第 19 版	第 19.1 版
P1	**第二線用藥** **Regorafenib** Regorafenib(Stivarga) 40mg/tab po QD 40-160mg /day Bruix, J., Qin, S., Merle, P., Granito, A., Huang, Y.-H., Bodoky, G., Pracht, M., Yokosuka, O., Rosmorduc, O., Breder, V., Gerolami, R., Masi, G., Ross, P. J., Song, T., Bronowicki, J.-P., Ollivier-Hourmand, I., Kudo, M., Cheng, A. L., Llovet, J. M., … Han, G. (2017). Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): A randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet, 389(10064), 56-66. https://doi.org/10.1016/S0140-6736(16)32453-9 **Cabometyx** Cabometyx(Cabozantinib) 40mg/tab po QD 60mg /day Abou-Alfa, G. K., Meyer, T., Cheng, A.-L., Rimassa, L., Sen, S., Milwee, S.,El-Khoueiry, A. B. (2022). Safety and efficacy of cabozantinib for patients with advanced hepatocellular carcinoma who advanced to Child-Pugh B liver function at study week 8: A retrospective analysis of the CELESTIAL randomized controlled trial. BMC Cancer, 22, 377	**第一線用藥** **Ipilimumab + Nivolumab** Ipilimumab (Yervoy) 1-3mg/kg IV over 60 min every 3 weeks Nivolumab (OPDIVO)1- 3 mg/kg IV over 60 min every 3 weeks 備註: Ipilimumab (Yervoy) 每隔 3 週給藥一次，總共投予 4 劑。 Yau, T., Galle, P. R., Decaens, T., Sangro, B., Qin, S., da Fonseca, L. G., Karachiwala, H., Blanc, J.-F., Park, J.-W., Gane, E., Pinter, M., Peña, A. M., Ikeda, M., Tai, D., Santoro, A., Pizarro, G., Chiu, C.-F., Schenker, M., He, A., Chon, H. J., … Kudo, M. (2025). Nivolumab plus ipilimumab versus lenvatinib or sorafenib as first-linetreatment for unresectable hepatocellular carcinoma (CheckMate 9DW): An open-label, randomised, phase 3 trial. The Lancet. Advance online publication.

目錄

一、前言

1.根據衛生福利部113年死因統計年報：肝癌為國人主要癌症死因第二位，標準化死亡率為每十萬人口有32.1人。男性肝癌標準化死亡率為每十萬人口44.0人，女性肝癌標準化死亡率為每十萬人口20.5人。

2. 本院肝癌診斷流程的建立，係參考2010年AASLD，期以提高肝癌診斷證實率與準確性。

3. 本院肝癌分期採用美國TNM與歐洲BCLC二大癌症分期系統並行，後者除了考慮腫瘤大小因素外

4. 亦加入肝功能指標，以符合臨床科的需求。

5. 本院肝癌治療指引係多專科醫療團隊的整合，治療流程以實證醫學並參考國內外醫學中心治療指引，期以提高肝癌病人生活品質。

二、組織病理分期與分化

肝癌以肝細胞癌(hepatocellular carcinoma)為主，本指引對本院較為常見臨床肝癌加以論述。

癌的病理組織分化分為：

分化良好	(grade 1)
分化中度	(grade 2)
分化不良或未分化	(grade 3)
分化無法評估	(grade 4)

三、肝癌分期

(1)Barcelona Clinic Liver Cancer (BCLC)分期

Stage		PST	Tumor Status Tumor Stage	Liver Function Status
Stage 0： Very early	0	0-1	Single, ≦2cm	Serum bilirubin (WNL) or Child A
Stage A： Early	A	0-1	Single, ≦5cm 3 tumors and ＜3 cm	Serum bilirubin (WNL) or Child A~B
Stage B：Intermediate		0-1	Single, ≧5cmor multinodulars	Child-Pugh A~B
Stage C：Advanced		0-2	Vascular invasion or extrahepatic spread	Child-Pugh A~B
Stage D：End stage		3-4	Any	Child-Pugh C

Stage 0, A and B：all criteria should be fulfilled

Stage C and D：all least one criteria should be fulfilled

(2)Child-Pugh Score

points	1	2	3
Encephalopathy (grade)	None	1-2	3-4
Ascites	None	Moderate	Severe
Bilirubin-T (mg/dL)	＜2.0	2.0~3.0	＞3.0
Albumin(g/dL)	＞3.5	2.8~3.5	＜2.8
PT(sec) prolong INR	＜4.0 ＜1.7	4.0~6.0 1.7-2.3	＞6.0 ＞2.3

*Child-Phug Score is the sum of 5 items.

Class Ａ：5~6 points, good operative risk

Class B：7~9 points, moderate operative risk

Class Ｃ：10~15 points, poor operative risk

(3) Okuda staging system

Stage	肝臟被腫瘤取代的比率		腹水		血清白蛋白		血清總膽紅素	
	+ (>50%)	- (<50%)	+	-	+ (<3g/dL)	- (>3g/dL)	+ (>3mg/dL)	- (<3mg/dL)
I	四項都沒有出現							
II	四項中出現1~2項							
III	四項中出現3~4項							

(4) 8th AJCC T-N-M 分期

Primary Tumor(T)	
TX	Primary tumor cancer be assessed
T0	No evidence of primary tumor
T1	Solitary tumor ≦2cm，or >2cm without vascular invasion
T1a	Solitary tumor ≦2cm
T1b	Solitary tumor ＞2cm without vascular invasion
T2	Solitary tumor ＞2cm with vascular invasion，or multiple tumors，none>5cm
T3	Multiple tumors，at least one of which is ＞5cm
T4	Single tumor or multiple tumors of any size involving a major branch of the portal vein or hepatic vein，or tumor(s) with direct invasion of adjacent organs other than the gallbladder or with perforation of visceral peritonem
Regional Lymph Nodes(N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph nodes metastasis

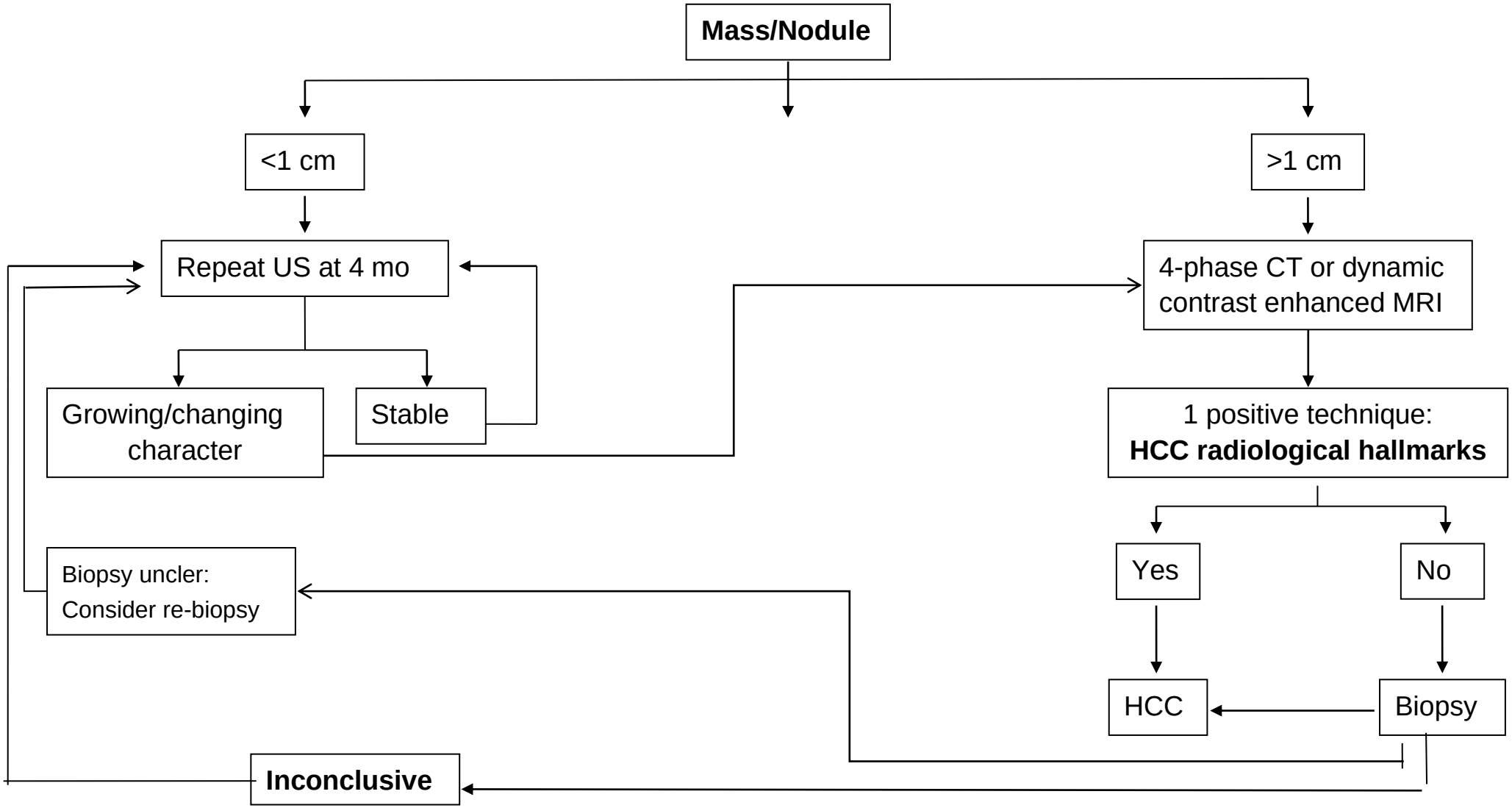
Distant Metastasis(M)	
M0	No distant metastasis
M1	Distant metastasis

T-N-M Stage Grouping			
IA	T1a	N0	M0
IB	T1b	N0	M0
II	T2	N0	M0
IIIA	T3	N0	M0
IIIB	T4	N0	M0
IVA	Any T	N1	M0
IVB	Any T	Any N	M1

Fibrosis Score(F)	
F0	Fibrosis score 0-4 (no to moderate fibrosis)
F1	Fibrosis score 5-6 (severe fibrosis or cirrhosis)

Histologic Grade(G)	
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

四、肝癌診斷 EASL 2025 年 Diagnosis Guide



五、肝癌治療

1. Liver transplantation.

(1)親屬捐肝之活體肝臟移植條件:成年人或十八歲以上之未成年人已結婚者，得捐贈部分肝臟予其五親等以內之親屬；十八歲以上之未成年人，經其法定代理人之書面同意，得捐贈部分肝臟予其五親等以內之血親。

(2)五等親範圍:1.配偶(應與捐贈者生有子女或結婚二年以上) 2.直系血親卑親屬。3.父母。4.兄弟姊妹。5.祖父母。6.曾祖父母或三親等旁系血親。7. 一親等直系姻親。

(3)若要接受屍體捐肝則條件從嚴(單一腫瘤小於或等於 5 公分，或多發生性腫瘤小於或等於 3 顆，且每一顆大小小於或等於3公分)

(4)活肝移植：單一腫瘤≦6.5cm；或多發腫瘤≦3個，最大直徑≦4.5cm，全部腫瘤直徑和≦8cm。

2. 外科手術治療

(1)None or controlled ascites

(2)Bilirubin小於2

(3)Child A與ICG≤15%可行大範圍的肝切除，Child B與ICG＞15%時應視病人整體情況，病人與手術醫師討論之後決定

3. Local therapy(PEIT or RFA)，relative contraindication：

(1)Tumor numbers：多於3個

(2) Tumor size：> 5 cm；（≦3 cm，則可考慮取代Surgery）

(3)Ascites(massive or uncontrollable)

(4)Bleeding tendency (platelet＜80000 or prolonged PT＞5 seconds)

(5)PEIT > 2 cm，則不建議,除非RFA無法執行.

4.Contraindication to TACE

(1)Thrombus in the main portal vein (severe)

(2)Encephalopathy .

(3)Biliary obstruction .

(4)Child-Pugh C cirrhosis：lobar or main portal vein thrombus poor candidates for TACE.

5.Relative contraindication to TACE :

(1)Serum bilirubin > 3mg/dL.

(2)Lactate dehydrogenase >425 units/L.

(3)Aspartate aminotransferase >100 units/L .

(4)Tumor burden involving >50 percent of the liver .

(5)Cardiac or renal insufficiency.

(6)Ascites, recent variceal bleed, or significant thrombocytopenia.

6.依病人performance status and liver reserve，由醫師針對實際狀況考量與病患討論後決定，不建議作為常規之治療方式：

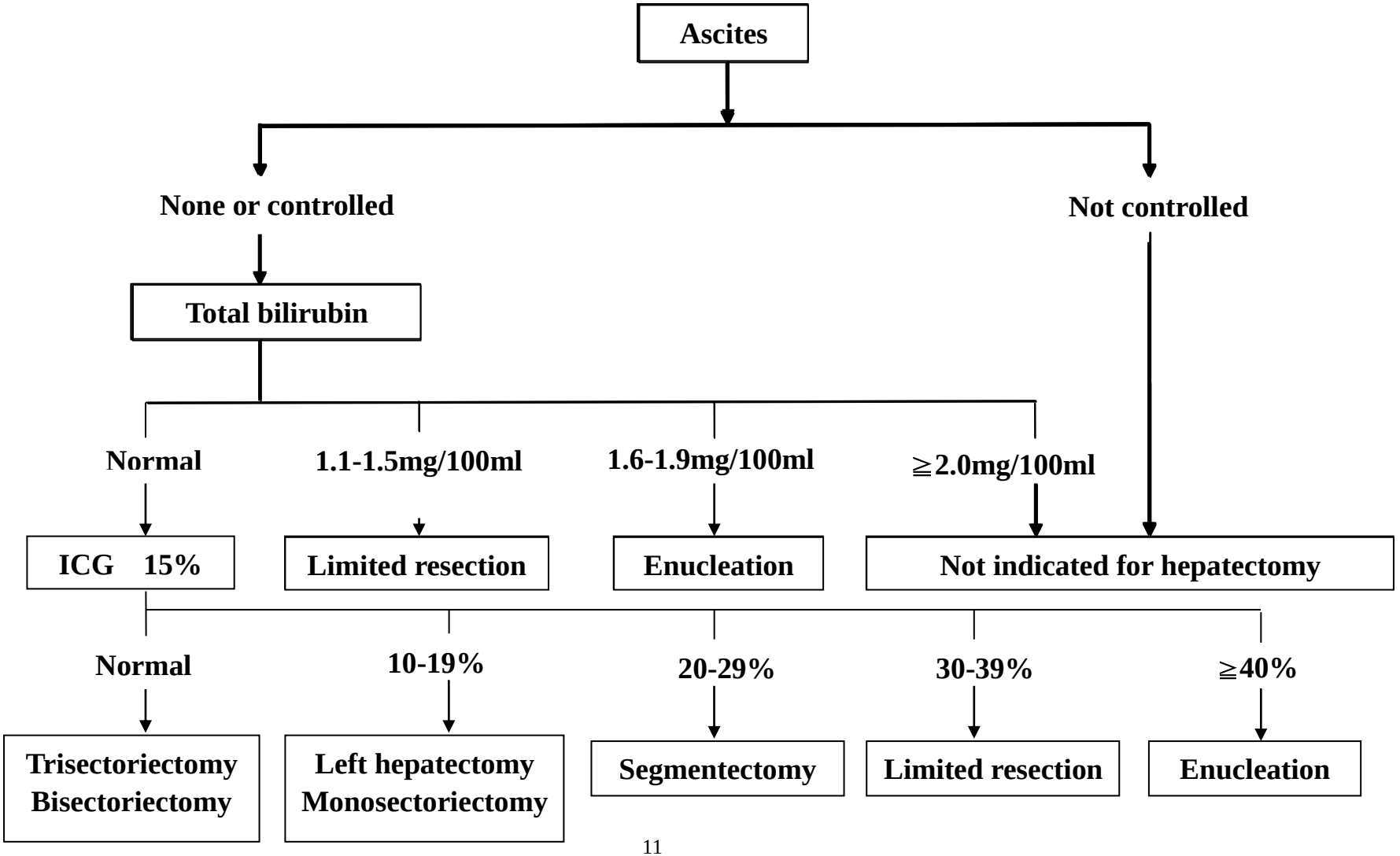
(1)Chemotherapy agents such as doxorubicin(Epirubicin, Mitoxantrone), 5-FU,cisplatin,Etoposide,Gemcitabine(自費)等

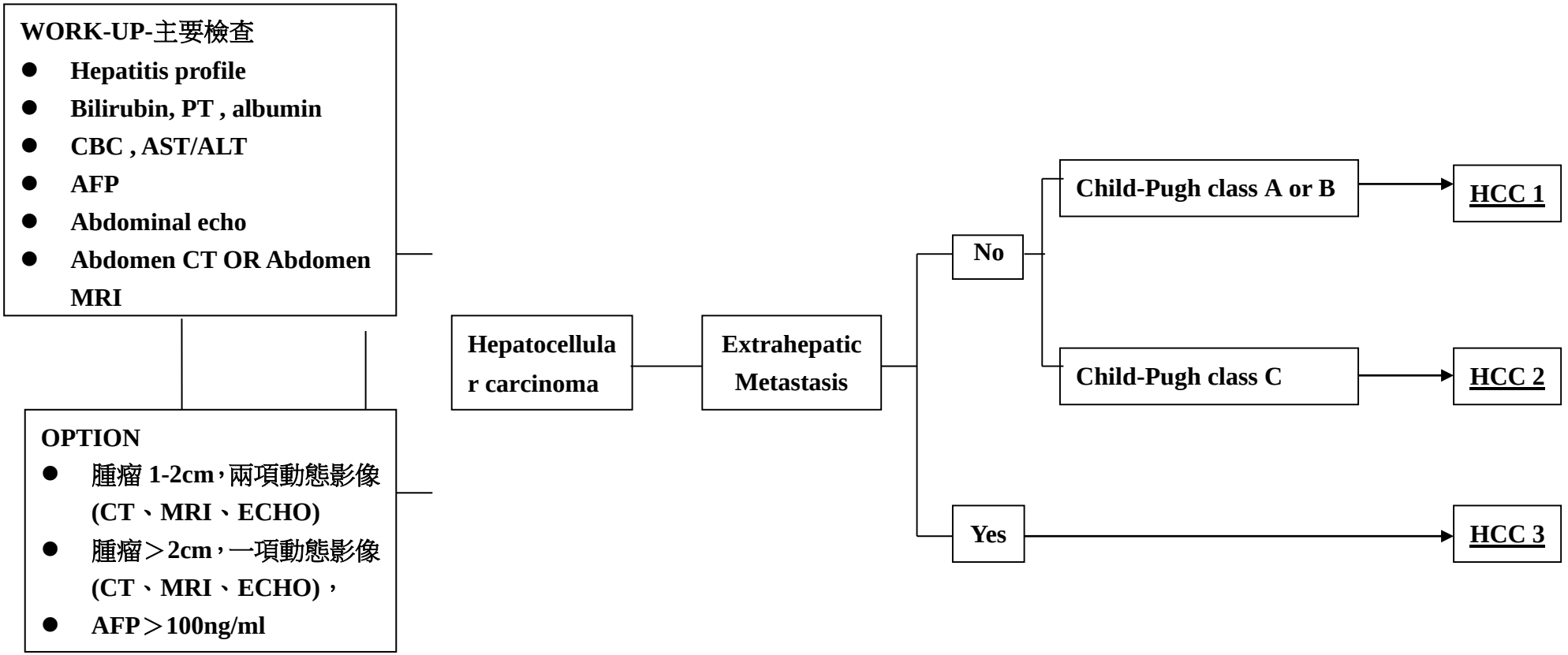
(2)Oral Agents(自費) such as Thalidomide, UFT....

7.Enrolled onto clinical trial as indication and patients' preference：Targeted agents, immune therapy(Nivolumab), gene therapy.

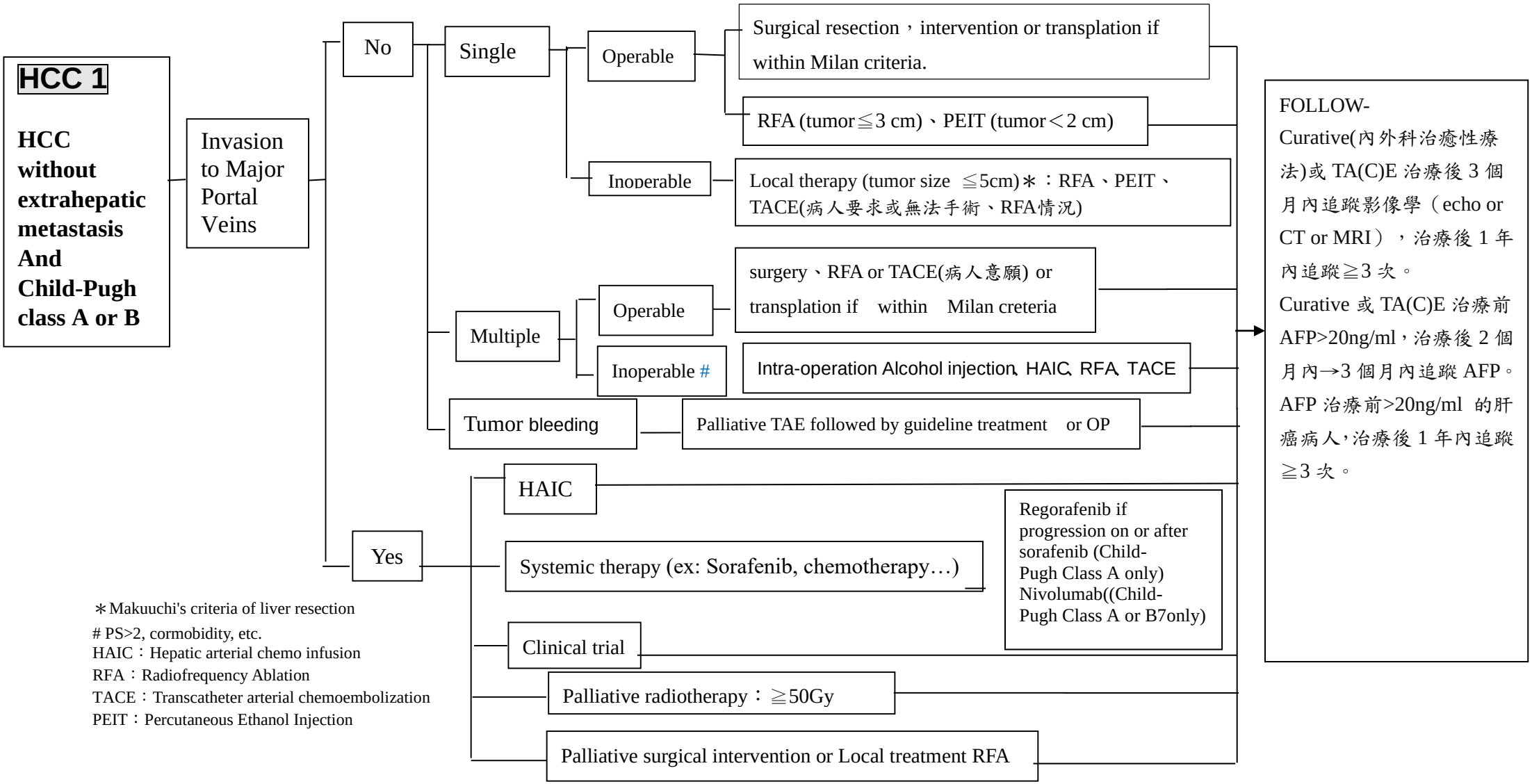
8.Makuuchi’s criteria

9. Y90-SIRT:不適合手術切除肝臟,體能狀態為 0 - 1，腫瘤主要位於單一器官，沒有明顯感染，肝臟功能正常，沒有腹水或肝臟衰竭的其它症狀。

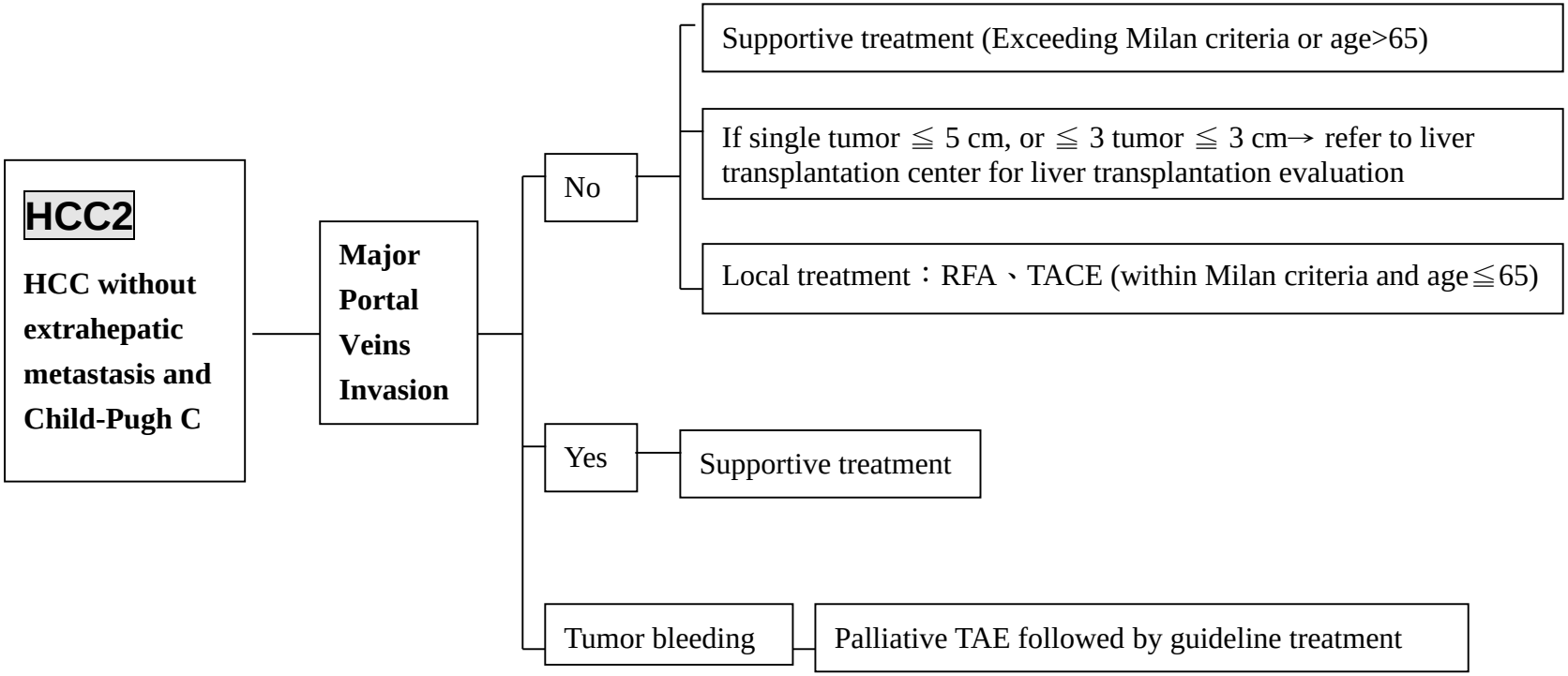

Ascites
None or controlled
Not controlled
Total bilirubin
Normal
1.1-1.5mg/100ml
1.6-1.9mg/100ml
≧2.0mg/100ml
ICG 15%
Limited resection
Enucleation
Not indicated for hepatectomy
Normal
10-19%
20-29%
30-39%
≧40%
Trisectoriectomy
Bisectoriectomy
Left hepatectomy
Monosectoriectomy
Segmentectomy
Limited resection
Enucleation

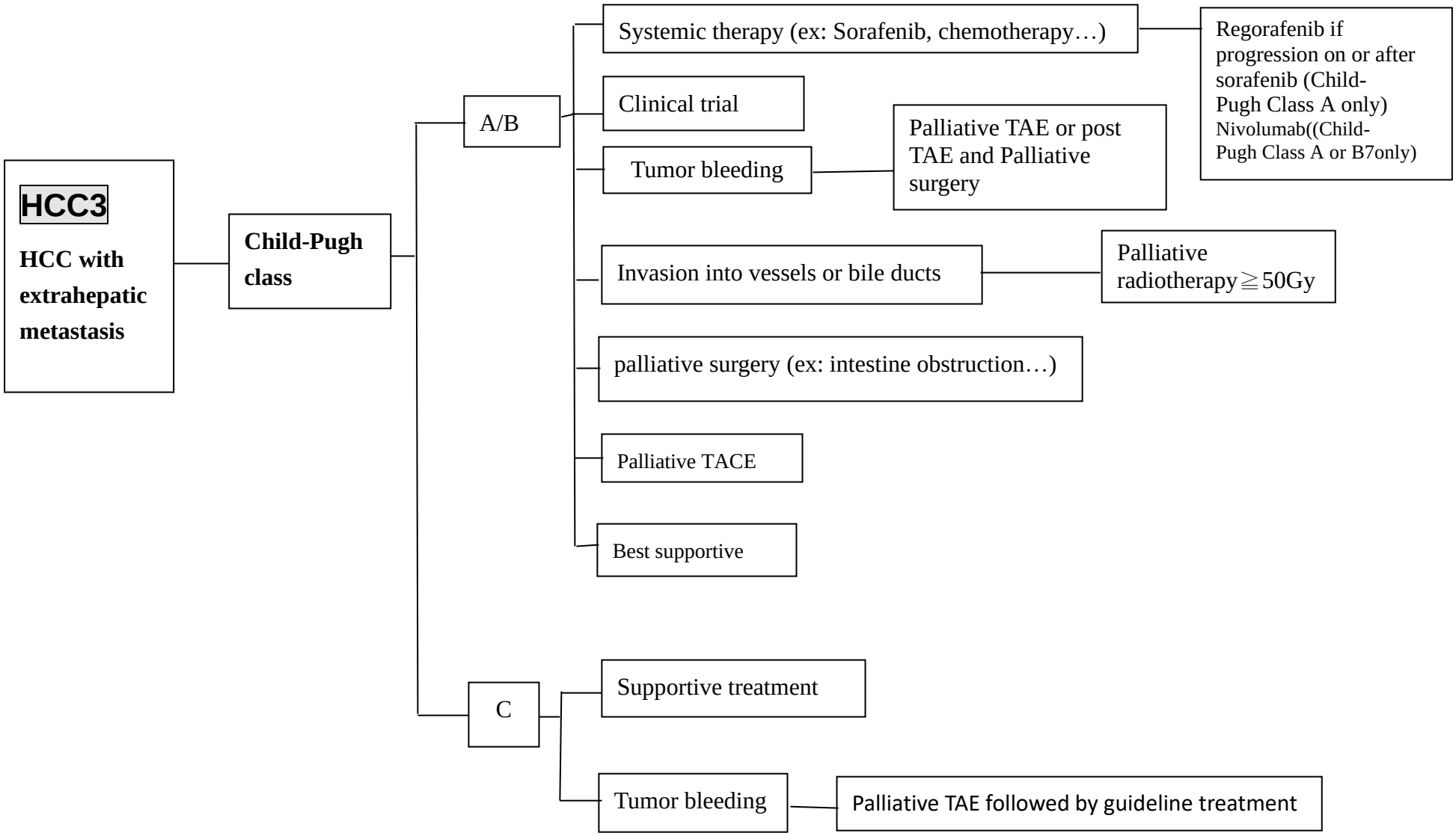


¡Positive AFP >100 ng/mL: (Waidely E, Al-Yuobi AR, Bashammakh AS, et al. Serum protein biomarkers relevant to hepatocellular carcinoma and their detectionAnalyst 2016;141:36-44), or if AFP increases by ≥7 ng/mL/month on at least 3 determinations (Arrieta O, Cacho B, Morales-Espinosa D, et al. The progressive elevation of alpha fetoprotein for the diagnosis of hepatocellular carcinoma in patients with liver cirrhosis. BMC Cancer 2007;7:28). Positive AFP should prompt CTor MRI regardless of US results.

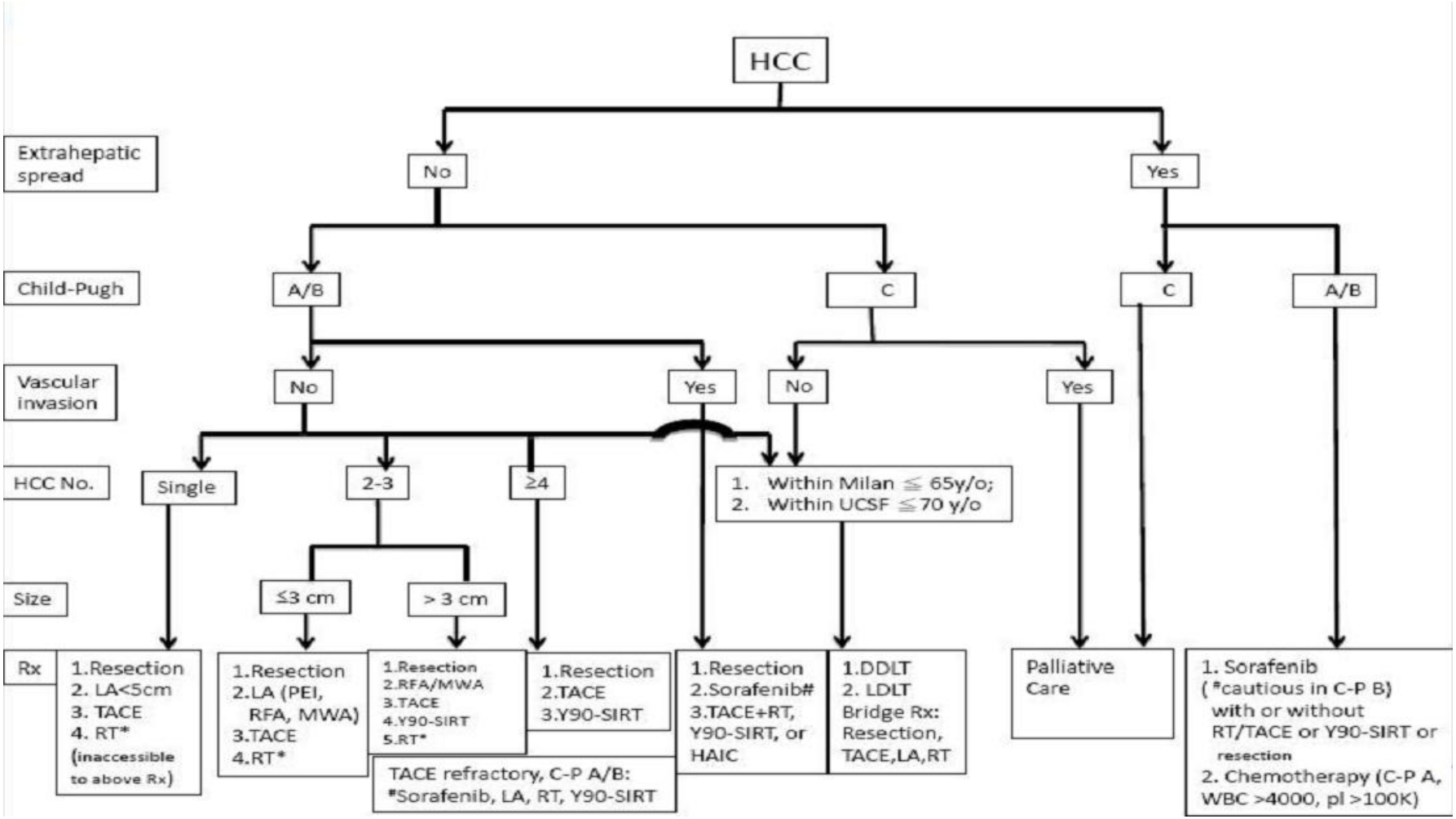


＊Makuuchi's criteria of liver resection
PS>2, cormobidity, etc.
HAIC：Hepatic arterial chemo infusion
RFA：Radiofrequency Ablation
TACE：Transcatheter arterial chemoembolization
PEIT：Percutaneous Ethanol Injection


HCC2
HCC without extrahepatic metastasis and Child-Pugh C
Major Portal Veins Invasion
No
Supportive treatment (Exceeding Milan criteria or age>65)
If single tumor ≦ 5 cm, or ≦ 3 tumor ≦ 3 cm→ refer to liver transplantation center for liver transplantation evaluation
Local treatment：RFA、TACE (within Milan criteria and age≦65)
Yes
Supportive treatment
Tumor bleeding
Palliative TAE followed by guideline treatment


HCC3
HCC with extrahepatic metastasis
Child-Pugh class
A/B
Systemic therapy (ex: Sorafenib, chemotherapy…)
Regorafenib if progression on or after sorafenib (Child-Pugh Class A only)
Nivolumab((Child-Pugh Class A or B7only)
Clinical trial
Tumor bleeding
Palliative TAE or post TAE and Palliative surgery
Invasion into vessels or bile ducts
Palliative radiotherapy≧50Gy
palliative surgery (ex: intestine obstruction…)
Palliative TACE
Best supportive
C
Supportive treatment
Tumor bleeding
Palliative TAE followed by guideline treatment

TLCA HCC treatment guideline 2023



六、放射線治療

1. 放射線治療適應症包括:

   A 不能開刀、不適合 RFA 或血管栓塞或者以上治療後失敗、復發的病人。

   B 肝門靜脈阻塞或其他如轉移性腫瘤、tumor bleeding 等緩和性治療 。

   C 肝癌引致各處轉移，放射治療可緩解症狀或控制疾病。

2. 治療方式包-CRT, IMRT, Arc therapy, TomoTherapy, Rdixact 以及 SBRT（ 建議搭配呼息調控技術或 4D-CT simulation 或 tumor tracking 等）

3. 肝癌患者做放射線治療前應評估 Child-Pugh score 及 ECOG status

4. 劑量建議

Regimen	Dose	Notes
**SBRT	40–60 Gy in 3–5 fractions	Preferred if dose constraints met
Hypofractionation	37.5–72 Gy in 10–15 fractions	Acceptable alternative
Conventional fractionation	50–66 Gy in 25–33 fractions	For patients unsuitable for SBRT

**SBRT 健保給付條件（ 需事先送審):

1. 原發性肝膽單一病灶（可為原發性肝癌或肝內膽道癌，同時無肝外淋巴侵犯和遠端轉移），肝功能為 Child-Pugh A 至 B 級，ECOG status≦2（或 Karnofsky Performance Scale/KPS≧70），病灶最大徑≦5 公分。且經評估無法進行下列之一的治療或下列之一的治療失敗者（依病歷紀錄）：A. 手術切除，B. 血管栓塞治療，C. 電燒灼治療。
2. 需經外科醫師會診，麻醉科醫師評估不適合接受治癒性術式切除者(附病歷紀錄）或多專科團隊討論會之結論認為不適合接受治癒性術式切除者(附會議記錄)。

Constraints for organ at risk Normal organ dose responses from the QUANTEC project.

Reference:

NCCN Clinical Practice Guidelines in Oncology, 2025
Perez and Brady's Principles and Practice of Radiation Oncology, 7th ed, 2018
Eric K. Hansen, Handbook of Evidence-Based Radiation Oncology

七、Advanced/Metastastic regimens

第一線用藥

Sorafenib

Sorafenib(Nexavar) 200mg/tab	po	QD	400- 800mg /day

Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. N Engl J Med 2008;359:378-390.
Cheng AL, Kang YK, Chen Z, et al. Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: a phase III randomised, double-blind, placebo-controlled trial. Lancet Oncol 2009;10:25-34.

Lenvatinib

Lenvatinib(Lenvima) 4 mg/cap	po	QD	8-12mg/day

備註:依病患腎功能調整劑量

Kudo, M., Finn, R. S., Qin, S., Han, K. H., Ikeda, K., Piscaglia, F., et al. (2018). Lenvatinib versus sorafenib in first-line treatment of unresectable hepatocellular carcinoma: A randomised phase 3 non-inferiority trial. The Lancet, 391(10126), 1163–1173.

Atezolizumab+Bevacizumab

Atezolizumab(Tecentriq) 1200 mg	IV over 60 min every 3 weeks
Bevacizumab(Avastin) 15mg/kg	IV over 60 min every 3 weeks

Llovet, J. M., Ricci, S., Mazzaferro, V., Hilgard, P., Gane, E., Blanc, J.-F., et al. (2008). Sorafenib in advanced hepatocellular carcinoma. *The New England Journal of Medicine*, 359(4), 378–390.

Tremelimumab+ Imfinzi

Tremelimumab 300mg	IV over 60 min(僅第一次療程)
Imfinzi 1500 mg	IV over 60 min every 4 weeks

Llovet, J. M., et al. (2021). Hepatocellular carcinoma. *Nature Reviews Disease Primers*, 7, 6.
IMJUDO (tremelimumab-actl) [Prescribing information]. (2022). U.S. Food and Drug Administration.
IMFINZI (durvalumab) [Prescribing information]. (2022). U.S. Food and Drug Administration.

Ipilimumab + Nivolumab

Ipilimumab (Yervoy) 1-3mg/kg	IV over 60 min every 3 weeks
Nivolumab (OPDIVO)1- 3 mg/kg	IV over 60 min every 3 weeks

備註: Ipilimumab (Yervoy) 每隔 3 週給藥一次，總共投予 4 劑。

Yau, T., Galle, P. R., Decaens, T., Sangro, B., Qin, S., da Fonseca, L. G., Karachiwala, H., Blanc, J.-F., Park, J.-W., Gane, E., Pinter, M., Peña, A. M., Ikeda, M., Tai, D., Santoro, A., Pizarro, G., Chiu, C.-F., Schenker, M., He, A., Chon, H. J., … Kudo, M. (2025). Nivolumab plus ipilimumab versus lenvatinib or sorafenib as first-linetreatment for unresectable hepatocellular carcinoma (CheckMate 9DW): An open-label, randomised, phase 3 trial. The Lancet. Advance online publication.

第二線用藥

Regorafenib

Regorafenib(Stivarga) 40mg/tab	po	QD	40-160mg /day

Bruix, J., Qin, S., Merle, P., Granito, A., Huang, Y.-H., Bodoky, G., Pracht, M., Yokosuka, O., Rosmorduc, O., Breder, V., Gerolami, R., Masi, G., Ross, P. J., Song, T., Bronowicki, J.-P., Ollivier-Hourmand, I., Kudo, M., Cheng, A. L., Llovet, J. M., … Han, G. (2017). Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): A randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet, 389(10064), 56–66. https://doi.org/10.1016/S0140-6736(16)32453-9

Cabometyx

Cabometyx(Cabozantinib) 40mg/tab	po	QD	60mg /day

Abou-Alfa, G. K., Meyer, T., Cheng, A.-L., Rimassa, L., Sen, S., Milwee, S.,El-Khoueiry, A. B. (2022). Safety and efficacy of cabozantinib for patients with advanced hepatocellular carcinoma who advanced to Child-Pugh B liver function at study week 8: A retrospective analysis of the CELESTIAL randomized controlled trial. BMC Cancer, 22, 377

Nivolumab

Nivolumab (OPDIVO)1- 3 mg/kg	IV over 60 min every	2weeks

Yau, T., Galle, P. R., Decaens, T., Sangro, B., Qin, S., da Fonseca, L. G., Karachiwala, H., Blanc, J.-F., Park, J.-W., Gane, E., Pinter, M., Peña, A. M., Ikeda, M., Tai, D., Santoro, A., Pizarro, G., Chiu, C.-F., Schenker, M., He, A., Chon, H. J., … Kudo, M. (2025). Nivolumab plus ipilimumab versus lenvatinib or sorafenib as first-linetreatment for unresectable hepatocellular carcinoma (CheckMate 9DW): An open-label, randomised, phase 3 trial. The Lancet. Advance online publication.

Ramucirumab

Ramucirumab(Cyramza) 8 mg/kg	IV over 30 min every 3weeks

Zhu, A. X., Kang, Y. K., Yen, C. J., Finn, R. S., Galle, P. R., Llovet, J. M., et al. (2019). Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased alpha-fetoprotein concentrations (REACH-2): A randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet Oncology, 20(2), 282–296.

Pembrolizumab

Pembrolizumab(Keytruda) 2 mg/kg	IV over 60 min every 3weeks

Zhu AX, et al.Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224). Lancet Oncology. 2018;19(7):940–952.

八、安寧緩和照護原則

若預期疾病難以治癒時，病人存活期小於 6 個月便適合安寧療護(Pomeranz & Brustman, 2005；Waldrop & Rinfrette, 2009）。若藉由症狀、檢驗數據、及確切的腫瘤診斷，證實臨床上該惡性腫瘤已經廣泛侵犯、或進展快速；功能分數（Palliative Performance Scale）低於 70%；拒絕進一步腫瘤治癒性治療，或者在治療之下仍持續惡化者，即可轉介緩和醫療團隊（彭等，2006）。

九、完治率定義

癌別	分期	治療方式	完治率定義
肝癌	第 I 期	OP、RFA、TACE	後續追蹤腹部電腦斷層，報告顯示無轉移或復發，即可算首次治療完成
	第 II 期	TACE	
	第 III 期	Palliative TAE、OP (Tumor bleeding)	治療後完成，即可算首次完成治療
		口服標靶	療程滿 3 個月就可算完成治療(治療中轉安寧，算完成治療)
		口服標靶 R/T	口服標靶服用滿 3 個月及 R/T 療程結束，即可算首次治療完成
		免疫治療	療程滿 3 個月就可算完成治療(治療中轉安寧，算完成治療)
	第 IV 期	TACE 1 次	即可算首次完成治療
		口服標靶+免疫治療	療程滿 3 個月就可算完成治療(治療中轉安寧，算完成治療)
		口服標靶	
		免疫治療	

備註:

肝內膽管癌:

(1)第 I 期:手術後，後續追蹤腹部電腦斷層，報告顯示無轉移或復發，即可算首次治療完成。

(2)第 II、III 期:接受手術及化療療程滿 3 個月就可算完成治療。

(3)第 IV 期:palliative C/T 療程滿 3 個月就可算完成治療。

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