



HCC case presentation

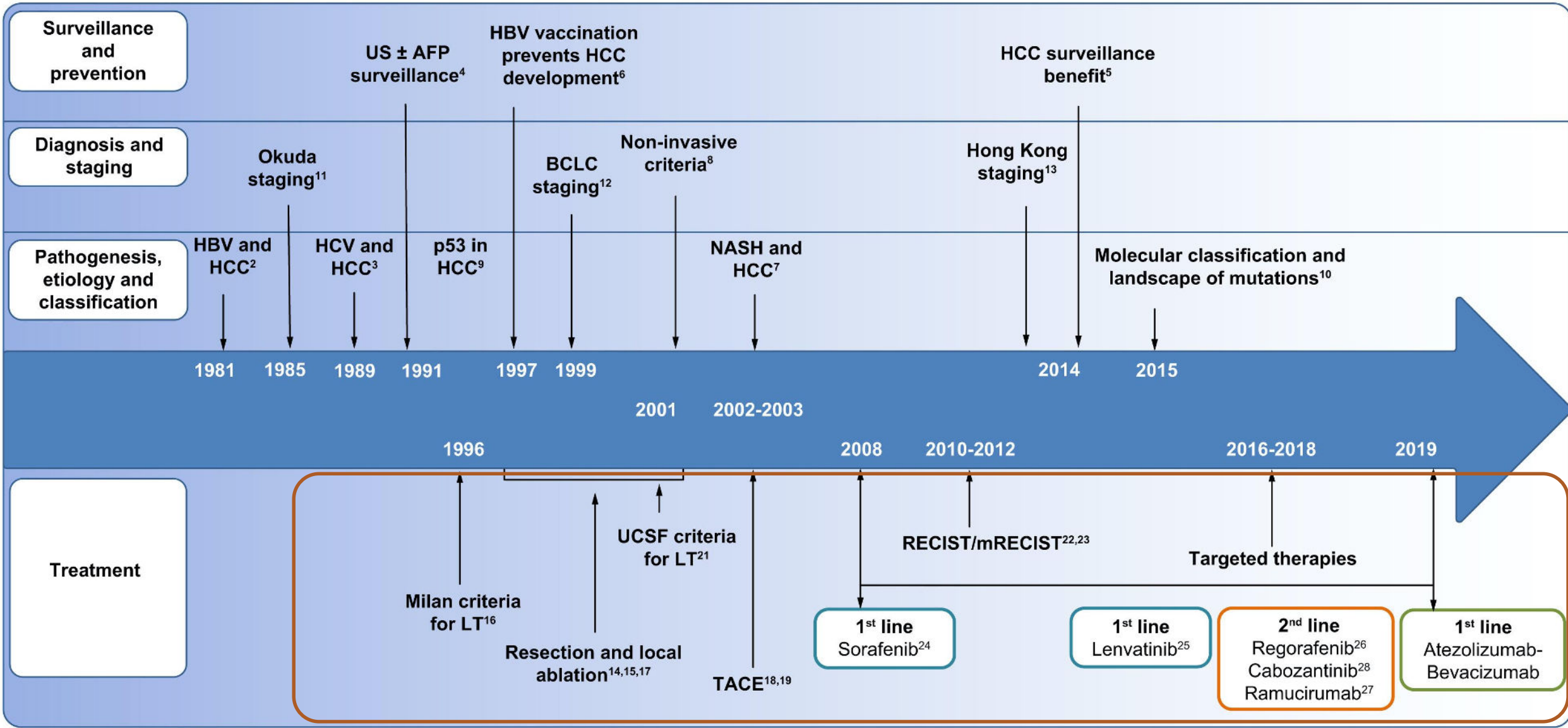
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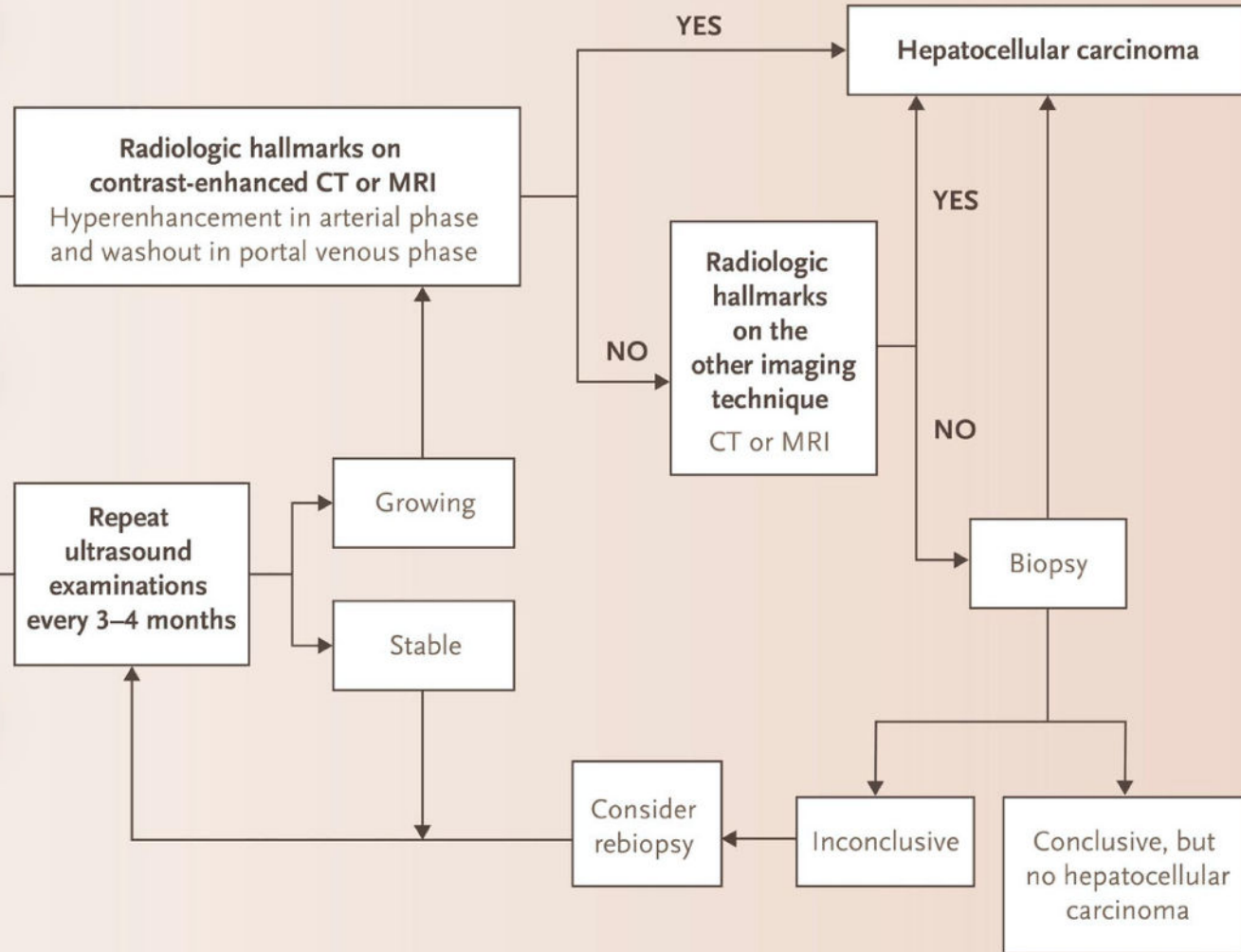
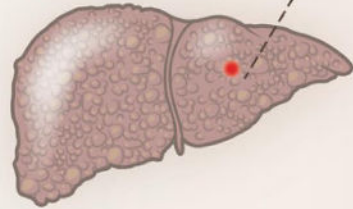
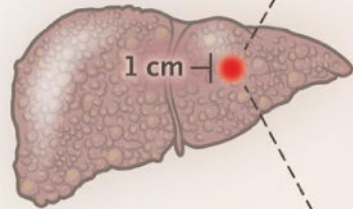
Transplant Hepatologist, Hospital Auxilio Mutuo

HCC case 1

- 69 years-old man with alcohol and HCV related cirrhosis, naïve to therapy, referred to liver transplant clinic for evaluation of liver mass identified on surveillance by primary provider
- Biopsy with histology consistent with HCC
- Former IVDA and smoker
- No previous complications of portal hypertension
- AFP was 138.6, Bilirubin 3.3, MELD Na 10



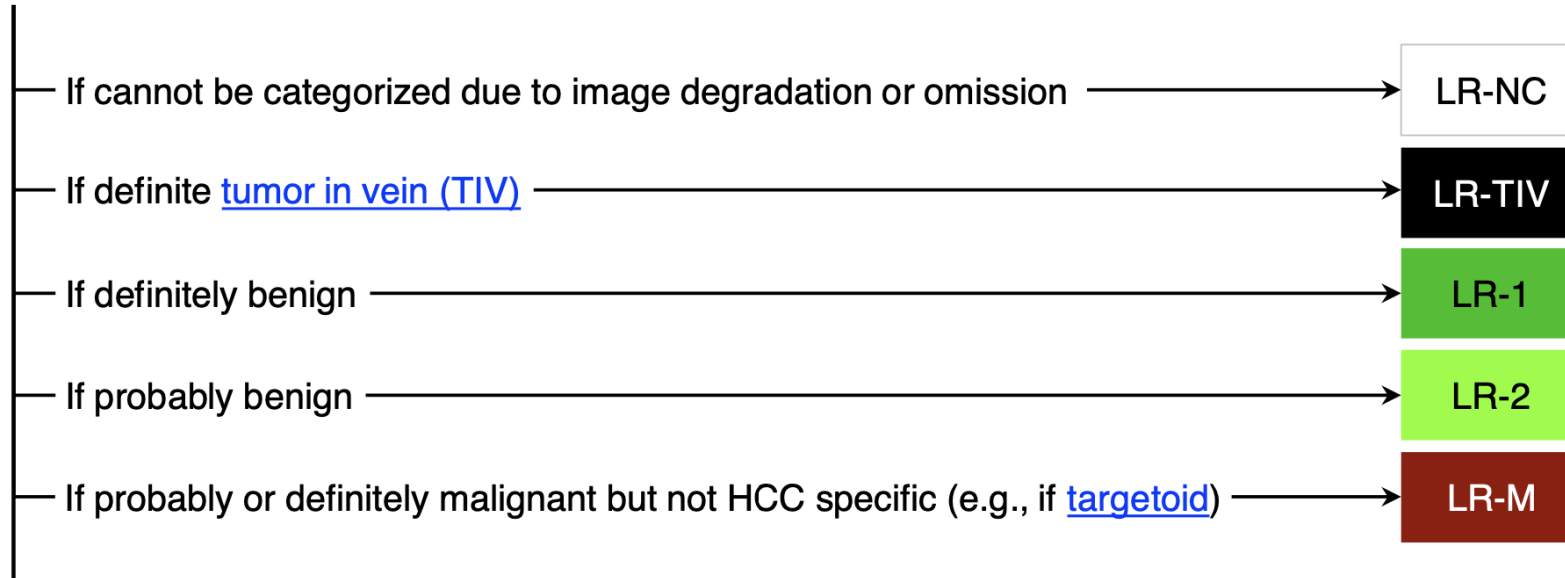
Liver nodule in cirrhosis
detected on ultrasonography



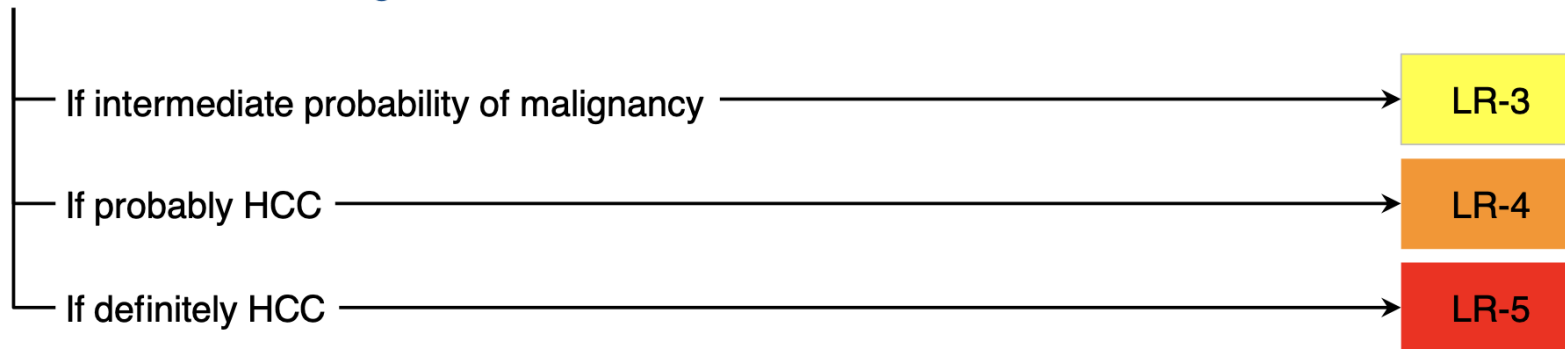


CT/MRI LI-RADS[®] v2018 CORE

Untreated observation without pathologic proof in [patient at high risk for HCC](#)



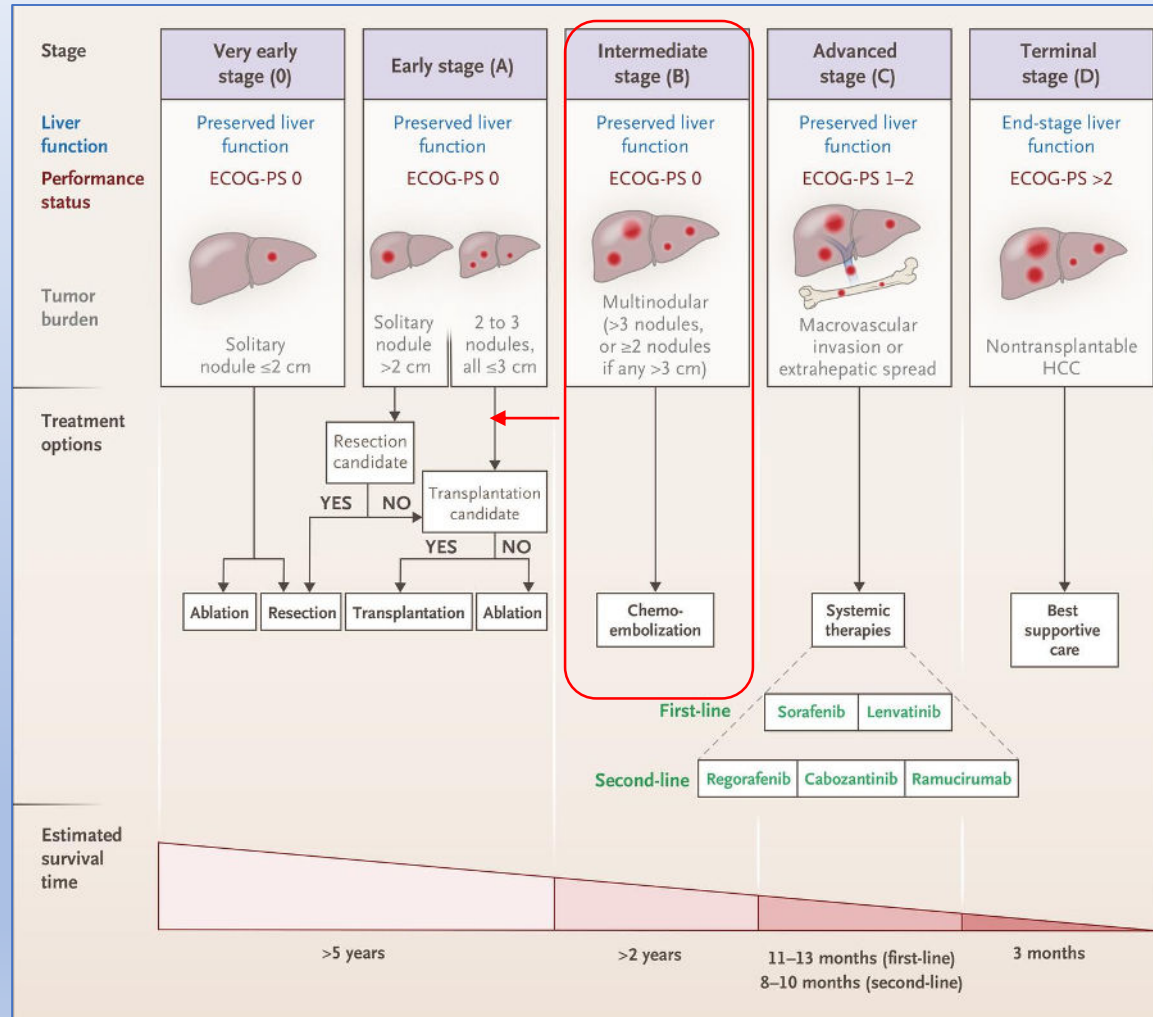
Otherwise, use CT/MRI diagnostic table below



CT with dynamic triphasic protocol

- 7.4 x 6.5 cm lesion with arterial enhancement and washout identified (LIRADS 5) at segment 5/6, 3.8 x2.7 cm LIRADS 5 at segment 8

Staging BCLC



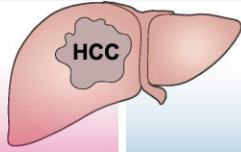
Intermediate stage lesion

- Beyond Milan criteria
- Other concern for OLT candidacy
 - Lung emphysema
- Referred to clinical trial consideration
- Received TACE (in combination with immunotherapy) as part of clinical trial on 11/2020

Trial Name	Line of therapy	Active agent	Control	Primary end-point	Results
SHARP	First-line	Sorafenib	Placebo	OS	10.7vs7.9 HR 0.69 (95% CI 0.55-0.87)
REFLECT	First-line	Levatinib	Sorafenib	OS	13.6 vs 12.3 HR 0.92 (95% CI 0.79-1.06)
RESORCE	Second-line	Regorafenib	Placebo	OS	10.6 vs 7.8 HR 0.63 (95% CI 0.50-0.79)
CELESTIAL	Second- and third-line	Cabozantinib	Placebo	OS	10.2 vs 8.0 HR0.76 (95% CI 0.63-0.92)
REACH-2	Second-line and AFP>400 ng/mL	Ramucirumab	Placebo	OS	8.5 vs 7.3 HR 0.71 (95%CI 0.531-0.949)
Checkmate-440	Second-line	Nivolumab	None	ORR, OS, safety	17%, 15.0
KEYNOTE-224	Second-line	Pembrolizumab	None	ORR, OS, safety	17%, 12.9
KEYNOTE-240	Second-line	Pembrolizumab	Placebo	PFS, OS	PFS 3.0 vs 2.8 HR 0.718 (95%CI 0.570-0.904) OS 13.9 vs 10.6 HR 0.781 (95%CI 0.611-0.998)
Checkmate-459	First-line	Nivolumab	Sorafenib	OS	16.4 vs 14.7 HR 0.85 (95%CI 0.72-1.02)
IMbrave150	First-line	Atezolizumab + bevacizumab	Sorafenib	OS% 12 mo., PFS	PFS 6.8 vs 4.8 HR 0.59 (95%CI 0.47-0.76) OS 67.2% vs 54.6% (95%CI 45.2-64.0)

Follow up image dynamic CT

Follow up dynamic CT with area of residual tumor of 3.7cm identified on segment 5 consistent with partial response (2/18)



	Proliferation class ~50%	Non-proliferation class ~50%
Molecular subclasses	<p style="text-align: center;">Cluster A/Proliferation</p> <p>G1/S2/iCluster 1 "progenitor" S1/iCluster 3 "TGFβ-Wnt"</p> <p style="margin-left: 150px;">G2 G3</p>	<p style="text-align: center;">Cluster B/S3/iCluster 2</p> <p>G4 CTNNB1</p> <p style="margin-left: 50px;">Unannot IFN Poly7 G5 G6</p>
Pathological & IHC features	<p>Stem cell: CK19+ & EPCAM+; p-ERK+ Macro-trabecular massive</p> <p style="text-align: center;">p-RPS6+</p>	<p>Steatohepatic CRP+ Cholestasis GS+ / nuclear β-catenin</p>
Genetic features	<p style="text-align: center;">Chromosomal instability</p> <p style="text-align: center;">TP53 mut</p> <p style="text-align: center;">11q13 amplification (FGF19/CCND1)</p> <p style="margin-left: 100px;">AXIN1 mut TSC1-TSC2 mut</p> <p style="margin-left: 50px;">RPS6KA3 mut</p>	<p style="text-align: center;">Chromosomal stability</p> <p style="text-align: center;">Chr 7 ampl</p> <p style="text-align: center;">CTNNB1 mut TERT promoter mut</p>
Main signalling pathways	<p style="text-align: center;">Cell cycle, mTOR, RAS-MAPK, MET signaling</p> <p>IGF1R signaling Wnt-TGFβ signaling</p> <p style="margin-left: 100px;">AKT signaling Cell cycle nucleus pore</p> <p>Progenitor features: IGF2, AFP, EPCAM+</p>	<p>IL6-JAK-STAT signaling Wnt-β-catenin signalling ++</p> <p style="margin-left: 150px;">+</p>
Epigenetic features	<p style="text-align: center;">Global DNA hypomethylation</p>	<p style="text-align: center;">Extensive promoter hypermethylation (CDKN2A, CDH1)</p>
Immunological features	<p style="text-align: center;">Immune exhaustion</p>	<p>Immune active Immune exclusion</p>
Prognosis	<p style="text-align: center;">More aggressive tumours</p>	<p style="text-align: center;">Less aggressive tumours</p>
Differentiation	<p style="text-align: center;">Poor</p>	<p style="text-align: center;">Well-moderate (hepatocyte-like)</p>
Vascular invasion	<p style="text-align: center;">↑ High frequency</p>	<p style="text-align: center;">↓ Low frequency</p>
Serum AFP	<p style="text-align: center;">↑ High levels</p>	<p style="text-align: center;">↓ Low levels</p>
Aetiology	<p style="text-align: center;">HBV</p>	<p style="text-align: center;">Alcohol - HCV</p>

Discussion

- Role of liver biopsy on diagnosis and management of HCC
- Role of locoregional therapy approach to HCC
- Role of combination of locoregional therapies and systemic/ target therapies
- Availability of molecular classifications of tumors