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Is Modified Albumin-Bilirubin (mALBI) Grade Prognostic for All Hepatocellular Carcinoma Patients Who Receive Systemic Treatment?

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Background

- Child Pugh A (CP-A) patients with hepatocellular carcinoma (HCC) who receive systemic therapy represent a heterogenous population.

- Earlier studies have shown that modified albumin-bilirubin grade (m-ALBI) can stratify prognosis in patients receiving multi-kinase inhibitors [1] [2]

- In the post-hoc subgroup analysis of IMBrave150, 1st line atezolizumab + bevacizumab had superior overall survival compared to sorafenib in ALBI G1, but not G2, or G2a/2b individually [3]

- Real world data on the predictive value of mALBI in newer HCC systemic therapies such as immunotherapy is limited

[1] Tada T et al. *Sci Rep*. 2021
[2] Ando et al. *Oncology*. 2020
[3] Kudo et al. *ILCA 2021*

Methods

- All (n=463) patients with HCC with **baseline CP-A and mALBI G1-2**, who received systemic treatment between Jan 2008 to Dec 2021 from a tertiary center in Hong Kong, China were included. Those who received unapproved first-line treatment except when used in combination with immunotherapy (IO) were excluded.

- Two first-line treatment groups were identified and evaluated: **(1) multi-kinase inhibitor group (MKI)** (total 385 patients, including 278 sorafenib and 107 lenvatinib); **(2) IO based treatment** (total 78 patients, including 30 IO monotherapy, 33 IO + multi-kinase inhibitors/anti-VEGF, and 15 dual IO therapy)

- Categorical variables were compared using chi-squared test or Fisher's exact test when appropriate. Continuous variables were compared using t-test. Kaplan-Meier and log-rank test were used for survival analysis. Cox regression was used for hazard ratio calculation. SPSS version 28 was used for statistical analysis. The study was approved by the institutional research ethics committee.

Baseline characteristics

	MKI (385)	IO based group (78)	P-value
Age (mean)	61.1 (SD 11.2)	63.1 (SD 9.6)	P=0.146
HbsAg +	269 (69.9%)	65 (83.3%)	**P=0.016**
Anti HCV+	50 (13.0%) 1 equivocal, 44 not tested	4 (5.1%) 7 not tested	**P=0.049**
Alcohol	182 (47.3%)	34 (43.6%)	P=0.552
Hypertension	131 (34.0%)	31 (39.7%)	P=0.334
Diabetes Mellitus	85 (22.1%)	11 (14.1%)	P=0.113
Tumoral Macrovascular invasion	157 (40.8%)	26 (33.3%)	P=0.220
Extrahepatic Involvement	219 (56.9%)	44 (56.4%)	P=0.939
No Liver Nodules	33 (8.6%)	8 (10.3%)	P=0.476
Solitary Liver Nodule	65 (16.9%)	9 (11.5%)	
Multiple Liver Nodules	287 (74.5%)	61 (78.2%)	
Largest Tumour Size (cm) (mean)	7.7 (SD 5.7) 26 missing	5.7 (SD 4.3) 3 missing	**P=<0.001**
Alpha fetoprotein (µg/L) (mean)	56252 (SD 210909) 2 missing	24099 (SD 81216)	**P=0.024**
Neutrophil/lymphocyte ratio (mean)	4.4 (4.8) 22 missing	3.7 (2.4) 6 missing	P=0.223
Any prior local treatment	202 (52.5%)	55 (70.5%)	**p=0.003**
Any subsequent or concurrent local treatment after systemic therapy	31 (8.1%)	11 (14.1%)	P=0.090
ECOG 0	128 (33.2%)	43 (55.1%)	**P=0.004**
ECOG 1	240 (62.3%)	33 (42.3%)	
ECOG 2	15 (3.9%)	2 (2.6%)	
ECOG 3	2 (0.5%)	0	
BCLC A	1 (0.3%)	0	P=0.218
BCLC B	39 (10.1%)	14 (17.9%)	
BCLC C	343 (89.1%)	64 (82.1%)	
BCLC D	2 (0.5%)	0	
ALBI G1	111 (28.8%)	26 (33.3%)	P=0.427
ALBI G2	274 (71.2%)	52 (66.7%)	
Child Pugh A5	201 (52.2%)	47 (60.3%)	P=0.194
Child Pugh A6	184 (47.8%)	31 (39.7%)	

mALBI grading by treatment group

|	MKI (385)	IO based group (78)
G1	111 (28.8%)	26 (33.3%)
G2a	96 (24.9%)	24 (30.8%)
G2b	178 (46.2%)	28 (35.9%)

Overall survival by mALBI for the **MKI group**

- Patients with ALBI G1 had better median overall survival (OS) than G2, 14.1 mo (10.7-17.5) versus 6.4 mo (5.5-7.3), p=<0.001, HR 0.46 (0.36-0.59).

- G2a patients had numerically superior mOS of 6.9 mo (5.1-8.7) vs G2b of 5.8 mo (4.6-7.1), p=0.085, HR 0.80 (0.61-1.03)

mALBI G1 vs G2

P=<0.001
HR 0.46 (0.36-0.59)

mALBI G2a vs G2b

P= 0.085
HR 0.80 (0.61-1.03)
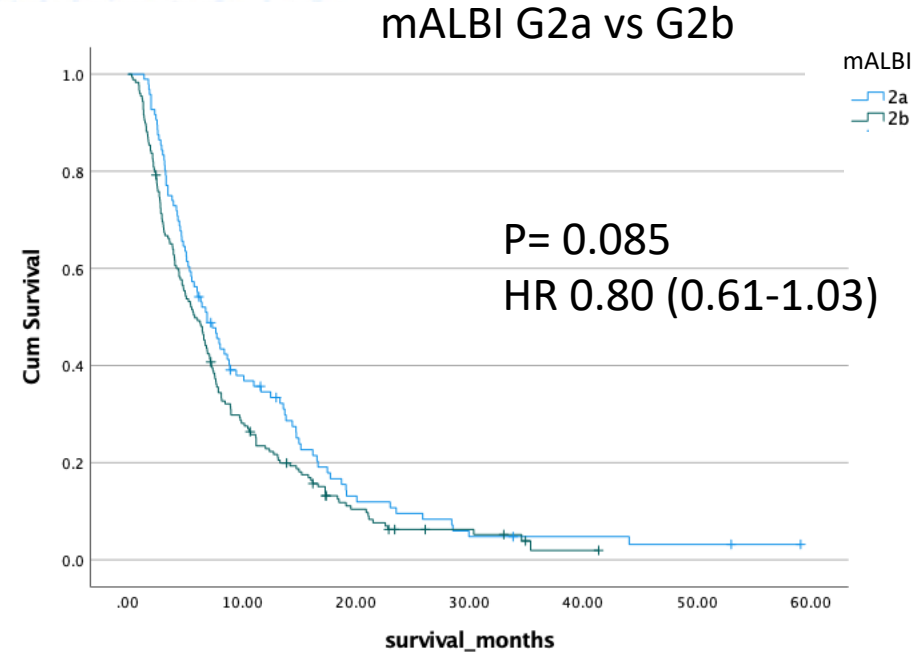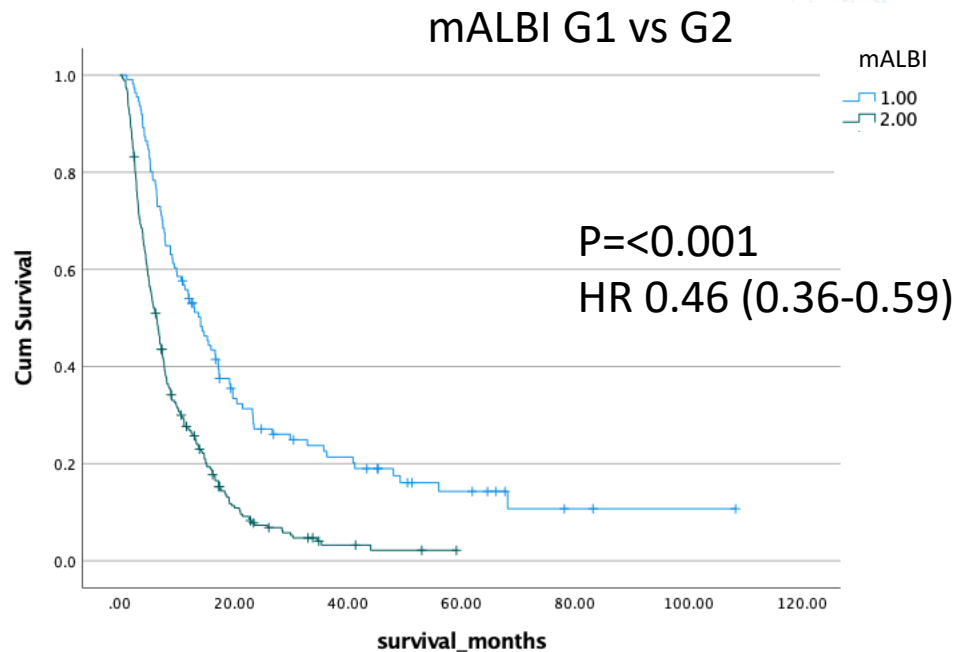
Overall survival by mALBI for the **IO based group**

- Patients with G1 had similar median OS to G2, 24.4 mo (14.8-34.0) vs 20.6 mo (13.3-27.8), p=0.554.

- There was no difference in OS between G2a 20.9 mo (5.0-36.9) vs G2b patients 19.4 mo (12.3-26.5), p=0.956, and between G1 and 2b, p=0.611.

mALBI G1 vs G2 — P=0.554

mALBI G2a vs G2b — P=0.956
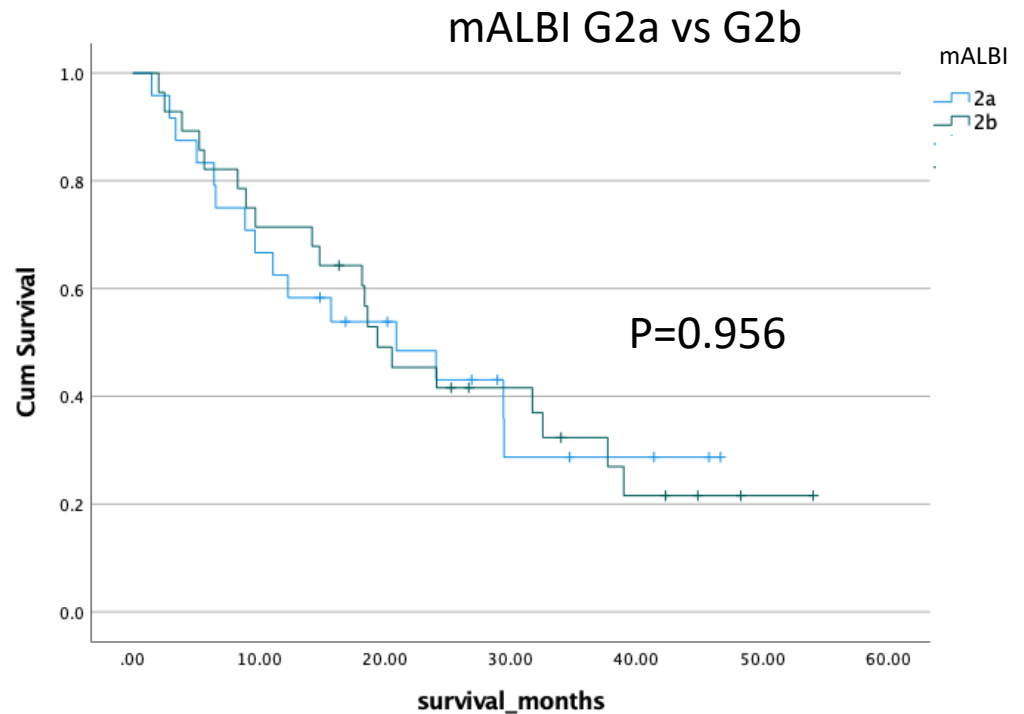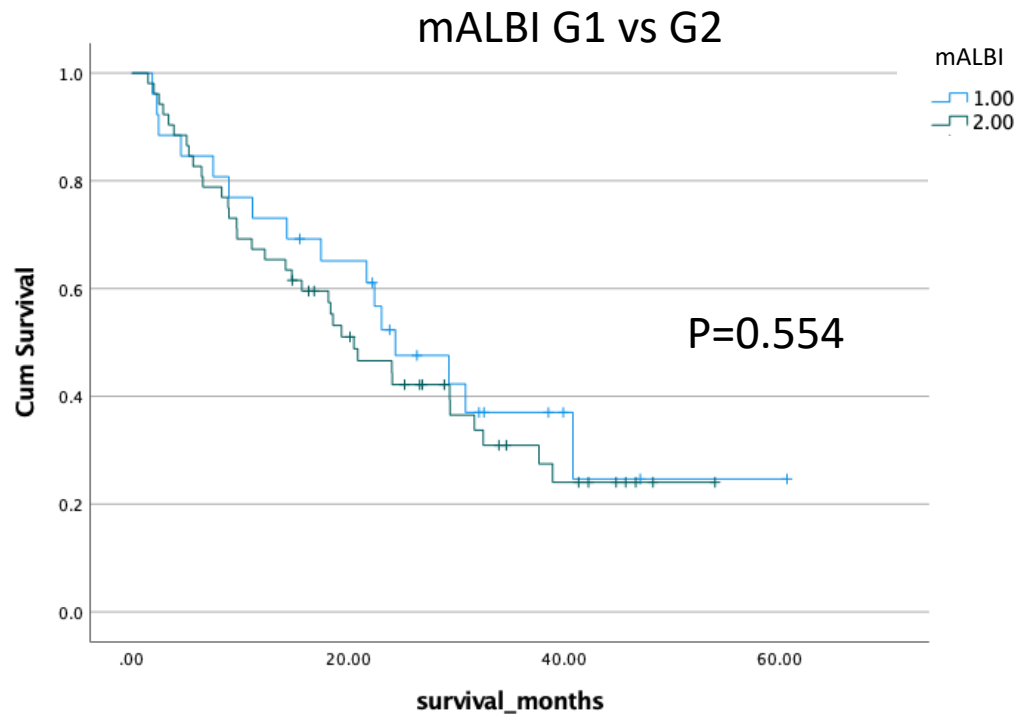
Conclusion

- mALBI was not a significant prognostic factor for CP-A HCC patients who receive first-line IO-based treatment.

- However, mALBI G1 vs 2 was significantly prognostic for patients who receive first-line MKI and may be prognostic for G2a vs G2b.

- The study may be limited by its retrospective nature and the relatively smaller and heterogenous IO-based group.

- Better prognostic markers are needed to determine which patients will benefit from upfront immunotherapy-based treatments.