Abstract 472: Plasma hPG_{80} (circulating progastrin) as a novel prognostic biomarker for hepatocellular carcinoma at early to intermediate stages (BCLC 0 to B)

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Background/Goal of the study

- Alpha-fetoprotein (AFP) is the most widely used biomarker for hepatocellular carcinoma (HCC) prognosis. However, AFP is not useful in establishing a prognosis for patients with a tumor in the early stages.
- hPG_{80} (circulating progastrin) is a tumor promoting peptide present in the blood of patients with various cancers including HCC, even at early stages.
- In this study, we evaluated the prognostic value of plasma hPG_{80} in patients with HCC at early and intermediate stages.

Methods

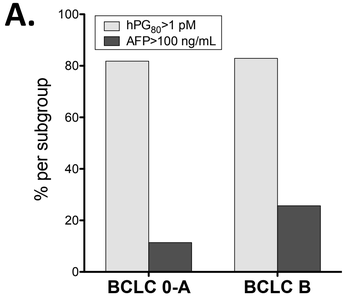
- The ELISA DxPG$_{80}$.lab kit (ECS-Progastrin) was used to measure hPG_{80} levels in all plasma EDTA samples according to the manufacturer's instruction. The limit of detection is 1 pM.
- The blood-based biomarker AFP concentrations were centrally measured using Cobas E411 (Roche Diagnostic) with Elecsys AFP (Roche).
- An optimal cutoff value of hPG_{80} was identified at 4.5 pM by calculating the minimal p-value based on the log-rank method.
- For AFP, a cutoff of 100 ng/mL was used as for liver transplantation (Notarpaolo, 2016).

Study demographics

Clinical and pathological characteristics for HCC patients		N (%) n = 79
Age, years	Median (range)	67 (27-84)
Gender	Male	72 (91.1%)
	Female	7 (8.9%)
BCLC	0 - A	44 (55.7%)
	B	35 (44.3%)
hPG_{80} (cutoff:4.5 pM) and AFP (cutoff: 100 ng/mL) levels	hPG_{80}-/AFP-	28 (36.3%)
	hPG_{80}-/AFP+	5 (6.5%)
	hPG_{80}+/AFP-	35 (45.5%)
	hPG_{80}+/AFP+	9 (11.7%)

Detection rates for hPG_{80} and AFP according to the BCLC score

A.



B.

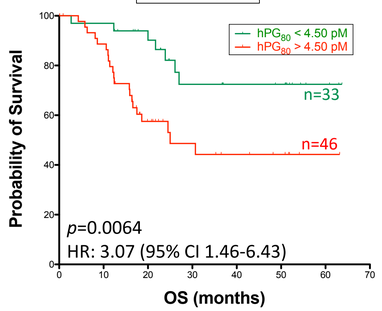
		BCLC 0-A (n=44)	BCLC B (n=35)	Control cohorts (n=252)
hPG_{80}	Median (IQR), pM	5.7 (1.7-22.4)	6 (1.5-22.2)	1.5 (0.0-3.1)
	Mean (SE), pM	17.8 (3.5)	28.7 (11.3)	3.82 (0.55)

		BCLC 0-A (n=43)	BCLC B (n=34)
AFP	Median (IQR), ng/mL	5 (3.3-9.9)	12.7 (6.2-129.5)
	Mean (SE), ng/mL	80.9 (40.4)	530.7 (315.6)

hPG_{80} was detected in 81.8% of HCC patients (threshold = 1 pM, corresponding to the limit of detection of the DxPG$_{80}$. lab kit) at stages BCLC 0 to A and 82.9% at stage BCLC B by contrast to AFP present in only 11.4% and 25.7% patients, respectively (threshold = 100 ng/mL).

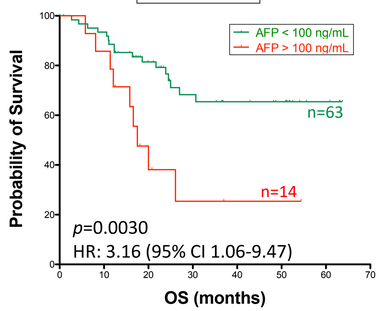
Overall survival of HCC patients according to hPG_{80} levels, AFP levels or combined hPG_{80} and AFP levels

hPG_{80}



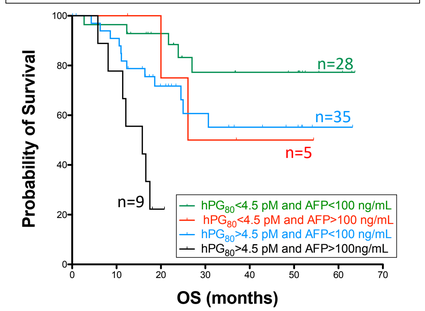
	hPG_{80}<4.5 pM	hPG_{80}>4.5 pM
Median OS (months)	Not reached	25

AFP



	AFP<100 ng/mL	AFP>100 ng/mL
Median OS (months)	Not reached	17.5

hPG_{80} combined with AFP levels



	AFP<100 ng/mL	AFP>100 ng/mL	
hPG_{80}<4.5 pM	Not reached	40.25	*p*=ns HR: 2.94 (95% CI 0.37-23.57
hPG_{80}>4.5 pM	Not reached	15.80	*p*=0.0052 HR: 6.38 (95% CI 1.74-23.41)

- Median OS for hPG_{80}+ patients (>4.5pM) was significantly shorter than that of hPG_{80}- patients (25 months vs not reached).
- AFP+ patients (>100 ng/mL) were significantly correlated with poorer OS (17.5 months vs not reached).
- hPG_{80}- patients with AFP+ had a tendency of worse OS than those with AFP- (40.25 months vs not reached).
- hPG_{80}+ patients with AFP+ had a worse OS than that of patients with AFP- (15.8 months vs not reached).

Conclusions

- **hPG_{80} could serve as a new prognostic biomarker for HCC patients at early to intermediate stages.**
- **Following validation in a prospective study, it opens the possibility to use hPG_{80} as a biomarker for HCC patients at early stage at a time they can be treated to be cured.**