HepatoPredict

A PROGNOSTIC TOOL SUPPORTING THE DECISION OF LIVER TRANSPLANTATION IN HEPATOCELLULAR CARCINOMA

TECHNICAL SHEET HEPATOPREDICT

The HepatoPredict kit is an *in vitro* diagnostic product produced by Ophiomics and distributed by Biocartis. The HepatoPredict kit is used in hepatocellular carcinoma (HCC) formalin-fixed paraffin embedded (FFPE) biopsies obtained from HCC patients, candidate to liver transplantation. This test should be used as a complementary tool for the tumor board to assess whether a patient will benefit from liver transplantation.

FEATURES

HepatoPredict Kit

Gene expression signature	CAPNS1
	DPT
	SPRY2
	CLU
Clinical variables	Tumor number
	Tumor size (largest nodule)
	Tumor volume (TTV)

HepatoPredict is based on the expression of 4 target genes and 3 clinical variables, which are integrated and combined with HepatoPredict.AI through MyOphiomics platform.

Specimen Requirements

Sample type:

- Tumor needle biopsy
  1. 2 FFPE sections with 5 μm thickness
  2. 1 H&E slide with the tumor identified and marked by a pathologist (to guide macrodissection)
  3. Tumor area: Minimum 20 mm^2. If 2 x 5 μm sections are not sufficient for 20 mm^2 use extra section(s).
  4. Tumor cells: 100%

Ophiomics PRECISION MEDICINE

Distributed by BIOCARTIS

Performance

Analytical sensitivity (LoD of each target included in HepatoPredict kit)

Target	GAPDH	TBP	RPL13A	DPT	CLU	CAPNS1	SPRY2	Chr3
Cq value	36.32	34.75	35.75	35.11	35.35	36.89	34.93	34.00*

*For the assay to be valid, the Cq values for the Chr3 target should be undetermined or above 34.

HepatoPredict algorithm robustness

Acceptable variation range for each variable to assure a 95% confidence of the HepatoPredict algorithm performance:

	Variable	Variation Range
Gene Expression	CAPNS1	+/- 1.7 Cq
	DPT	+/- 0.4 Cq
	SPRY2	+/- 1.5 Cq
	CLU	+/- 2 Cq
Clinical Variables	Tumor number	+ 2 Units
	Tumor size	+/- 50%
	Tumor volume (TTV)	+/- 12%

Turnaround time

Total time: < 24 hours
Hands-on time: < 5 hours

Accuracy

Clinical performance evaluation

HepatoPredict demonstrates an overall better performance than clinical criteria.

	Precision (PPV)		**Recall**		**Accuracy**		**n**
	criteria	*HP**	*criteria*	*HP**	*criteria*	*HP**	
Milan	88.1%	88.5%	75.2%	99.1%	72.5%	89.1%	138
UCSF	86.5%	88.5%	82.6%	99.1%	76.1%	89.1%	138
Up to 7	80.3%	88.5%	93.6%	99.1%	76.8%	89.1%	138
AFP criteria	90.0%	92.3%	90.0%	100%	82.0%	92.5%	67
Metroticket 2.0	90.1%	92.3%	91.7%	100%	83.5%	92.5%	67
TTV	82.9%	88.7%	95.1%	100%	80.0%	89.6%	125
TTV AFP	91.7%	92.2%	93.2%	100%	86.4%	92.4%	66

*HP: HepatoPredict

Pinto Marques and Cardoso et al. Annals of Surgery, 2022

Results Reporting

HepatoPredict kit results are reported regarding the outcome of liver transplantation for an HCC patient:

1) Good Prognosis (with confidence level)
2) Bad Prognosis

HepatoPredict List of Publications

Pinto-Marques H, Cardoso J, Silva S, Neto JL, Gonçalves-Reis M, Proença D, Mesquita M, Manso A, Carapeta S, Sobral M, Figueiredo A, Rodrigues C, Milheiro A, Carvalho A, Perdigoto R, Barroso E, Pereira Leal JB (2022) A gene expression signature to select hepatocellular carcinoma patients for liver transplantation. Annals of Surgery. (https://pubmed.ncbi.nlm.nih.gov/35916378/)

Gonçalves-Reis M, Proença D, Frazão L, Neto JL, Silva S, Pinto-Marques H, Pereira Leal JB, Cardoso J. (2022) Analytical validation of HepatoPredict kit to assess hepatocellular carcinoma prognosis prior to a liver transplant. *Submitted*

Cardoso, J., Pinto Marques, H., Mesquita, M., Manso, A., Carapeta, S., Sobral, M., Silva, S., Rodrigues, c., Carvalho, A., Milheiro, A., Perdigoto, R., Barroso, B., Pereira-Leal, J. (2022) New criteria in liver transplantation for hepatocellular carcinoma: a combined molecular and clinical predictor of survival. [Oral presentation]. *Transplantation.* https://ilts.org/education/abstracts

Cardoso, J., Pinto Marques, H., Mesquita, M., Manso, A., Carapeta, S., Sobral, M., Silva, S., Rodrigues, c., Carvalho, A., Milheiro, A., Perdigoto, R., Barroso, B., Pereira-Leal, J. (2021) A new tool for predicting survival in liver transplantation for hepatocellular carcinoma combining molecular and clinical variables [Poster Presentation]. *Journal of Hepatology,* 75(2), S475. https://doi.org/10.1016/S0168-8278(21)01843-2