**Supplementary Methods**

Immunohistochemistry

Briefly, formalin-fixed paraffin-embedded liver tissue samples, explanted during transplantation or recurrence, were obtained. The samples were then deparaffinized and rehydrated. Antigen unmasking was performed using 1 mM EDTA buffer pH 8 at 98°C for 15 min. The sections were then incubated in methanol 5% and H2O2 1% for 5 min to block endogenous peroxidases and nonspecific sites were blocked using a blocking solution reagent with BSA 3% for 30 min at room temperature. The sections were then incubated with the primary antibody goat anti-Angiopoietin-2 (AF623) (R&D Systems, Inc., Minneapolis, MN, USA) at a dilution of 1:50 and anti-VEGF (A-20):sc-152 (Santa Cruz Biotechnology, Inc., Dallas, Texas 75220 USA) at a dilution of 1:50. Sections were then incubated with the secondary antibody OmniMap anti-goat HRP peroxidase-conjugated prediluted (Ventana Medical Systems, Inc., Tucson, AZ, USA) for 20 min in a humidity chamber, followed by detection kit reagents (UltraView Universal HRP multimer and diaminobenzidine (DAB) Chromogen, Ventana Medical Systems, Inc., Tucson, AZ, USA) following the manufacturer’s instructions. The sections were counterstained with hematoxylin, dehydrated, and permanently mounted for microscopic examination. Images of the stained liver tissue were processed using ImageJ software (http://rsbweb.nih.gov/) to obtain the medium intensity value of the DAB signal.

Transcriptomic signature

Transcriptomic signature was evaluated by RT/PCR as previously published (Villa E, Critelli R, Lei B, Marzocchi G, Cammà C, Giannelli G, et al. Neoangiogenesis-related genes are hallmarks of fast-growing hepatocellular carcinomas and worst survival. Results from a prospective study. Gut. 2016;65:861-9. doi: 10.1136/gutjnl-2014-308483). cDNA synthesis was performed from total RNA total RNA isolated from non tumor (NT) and tumor (T) liver tissues using the NucleoSpin® miRNA kit (Macherey-Nagel, Duren, Germany). Subsequently, qRT-PCR was performed on a LightCycler® 480 Real-Time PCR System (Roche, Mannheim, Germany) using TaqMan gene expression assays (Applied Biosystems). The thermal cycling conditions were as follows:50°C for 2 min, 95°C for 20 s, 40 cycles of denaturation at 95°C for 3 s, and annealing and extension at 60°C for 30 s. All qRT-PCR reactions were performed in duplicates. The relative gene expression was determined using the 2-ΔΔCt method. The levels of the five target genes were normalized to the average expression levels of ACTB and GAPDH, and to the corresponding non tumor liver tissue.