Supplementary Material

Summary

Table S1 – Mean liver dose by prescription dose

Prescription dose (Gy)	**Mean Liver Dose (MLD) (Gy)**
50	13
45	15
40	15
35	15.5
30	16

Figure S1. Flow diagram of patients.

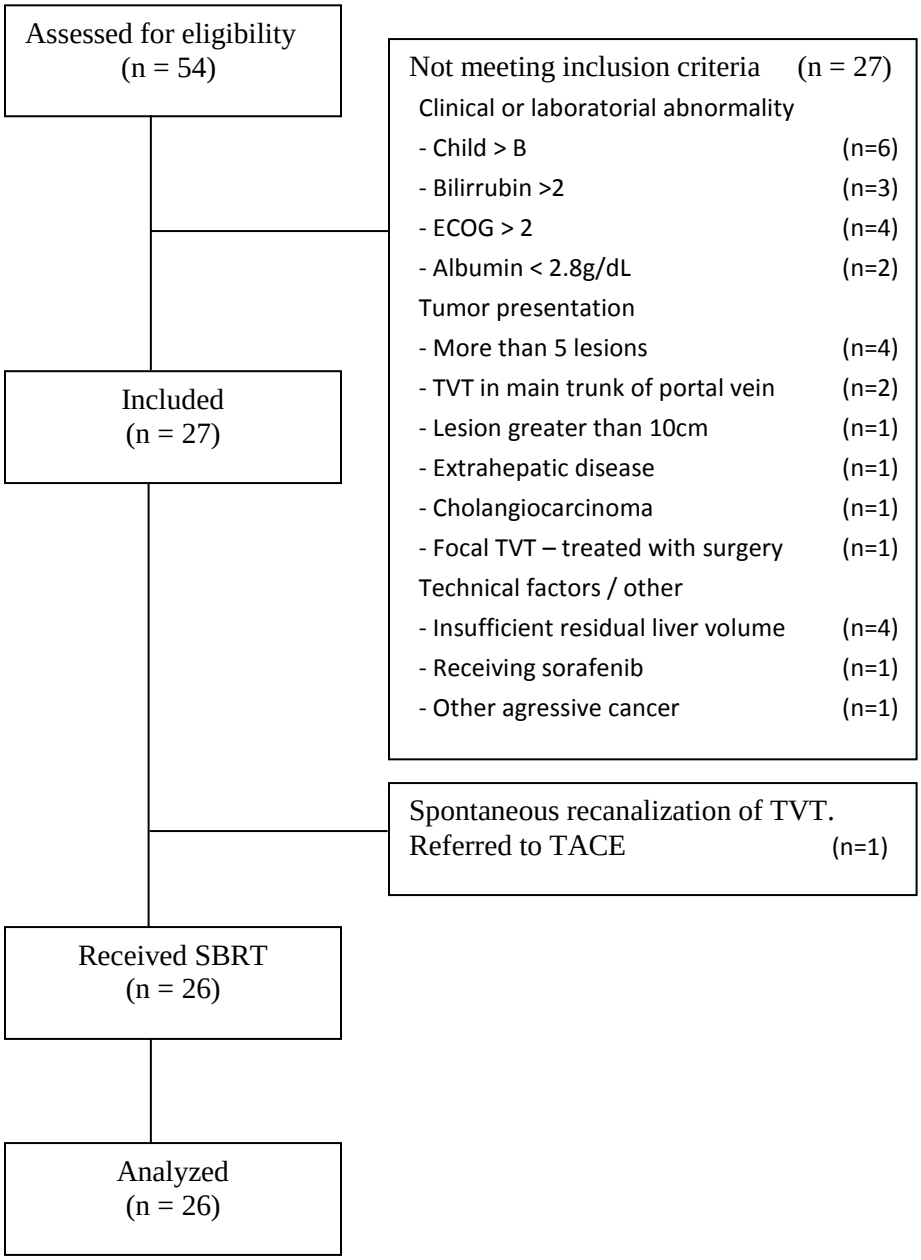


Table S2 – Best response of treated lesions according to mRECIST

Radiological Response	n	%
Complete response	14	54
Partial response	9	35
Stable disease	3	12
Total	26	100

Clinical case description of death possibly related to radiation treatment.

Here we present the case of a 70-year-old patient that had a 10 cm infiltrative HCC, tumor vascular thrombosis and AFP of 1,529 ng/mL. Gross Tumor Volume (GTV) was 554.9 cc and residual hepatic volume (liver minus GTV) was 1417.1 cc. Patient received SBRT with prescription dose of 30 Gy and mean residual liver dose of 15.8 Gy (within the protocol dose of 16 Gy).

One month later, patient was asymptomatic, with AFP of 1,448 ng/mL; sorafenib was introduced at the discretion of the clinical oncologist due to concerns about tumor burden.

Two months after SBRT (one month after the start of sorafenib), the patient presented asymptomatic mild elevated hepatic enzymes (< 5 x ULN), elevated bilirubin, and reduced albumin. AFP had dropped to 85.6 ng / ml. Laboratory exams resumed to baseline values after 4 months, compatible with transient alterations after RT.

Three months after SBRT (two months after initiation of sorafenib), the patient presented with diarrhea and dehydration that was attributed to sorafenib; the medication was discontinued 10 days later.

During the 4th month, patient had multiple episodes of infectious colitis,

attending the emergency room with diarrhea and dehydration. At the end of the month, patient presented worsening of liver function (from Child A to B).

In the 5th month, patient lost performance (ECOG 3) and developed refractory ascites requiring repeated paracentesis. At the time, MRI

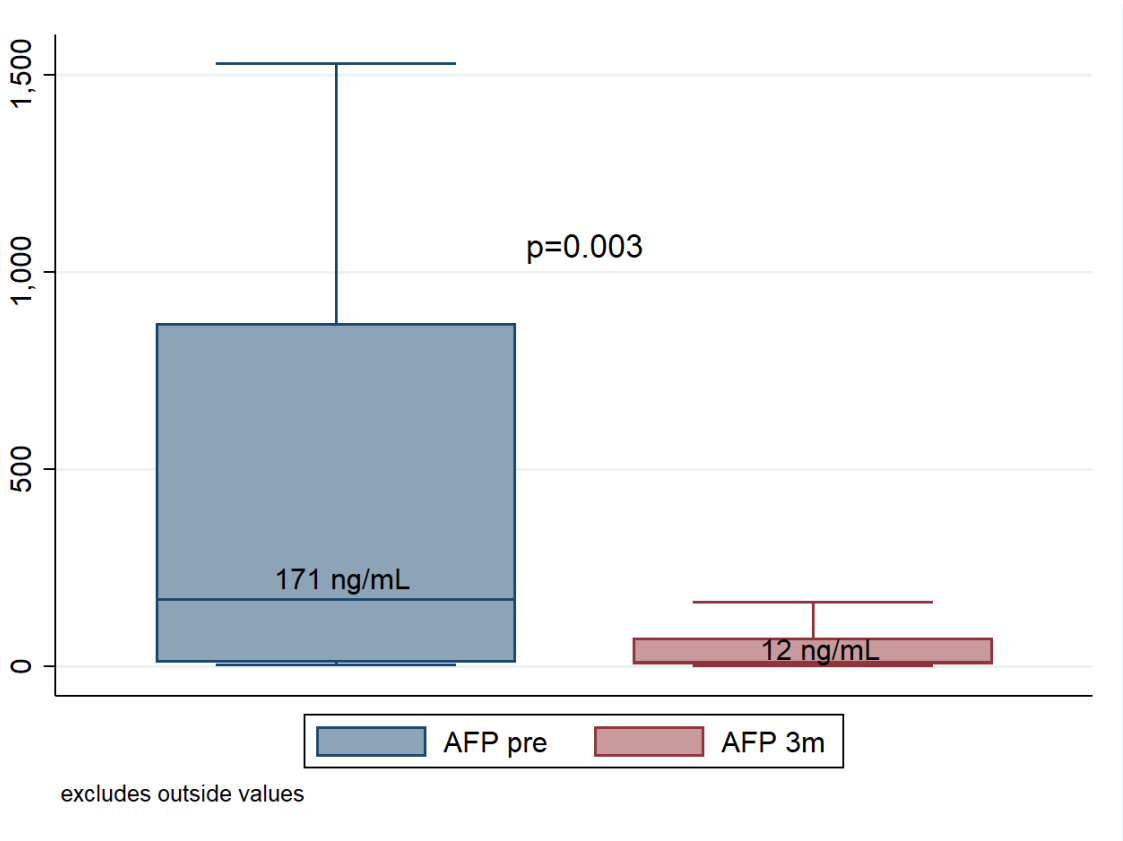
revealed complete response of the treated lesion and no sign of new lesions;

AFP was 15.0 ng/mL.

In the 6th month, patient had upper gastrointestinal bleeding, pre-renal acute renal failure, and died without signs of HCC progression.

After multidisciplinary discussion, we considered death as not directly related to radiotherapy, but possibly related.

Figure S2. Response by AFP reduction



Boxplot diagram showing response to treatment by alpha-fetoprotein (AFP) levels. To the left, pretreatment AFP levels; Median AFP 171 ng/mL. To the right, levels 3 months after treatment; median AFP 12 ng/mL. (p = 0.003; Wilcoxon rank-sum test for paired samples). Outliers not shown to facilitate graphical representation.