Transarterial Chemo-embolisation with degradable starch microspheres(DSM-TACE) in intermediate/advanced HCC patients dismissing or inelegible for Sorafenib

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Aims and objectives

According to BCLC staging system, HCC patients with well preserved liver function (Child Pugh A-B), portal vein tumor thrombosis or extrahepatic spread are classified as "advanced" or stage C and they present dismal prognosis. In these kind of patients and in those tumors progressing upon loco-regional therapies, the treatment of choice is represented by Sorafenib, an oral multikinase inihibitor that significant prolongs time to progression but without significant differences in time to symptomatic progression. In particular, about 80% of patients present adverse events (hand-foot syndrome, gastrointestinal symptoms) leading to permanent discontinuation in 11% of cases. In patients ineligible to or dismissing Sorafenib there is no available second-line therapy.

Based on this background, the aim of our study is to evaluate safety, feasibility and effectiveness of transarterial chemoembolisation with degradable-starch-microspheres (DSM-TACE), in the treatment of patients with advanced HCC dismissing or ineligible for multikinase-inhibitor chemotherapy administration (Sorafenib) due to unbearable side effects or clinical contraindications.

DSM-TACE consists in degradable particles loaded with doxorubicin that allows the temporary occlusion of the smaller arterial vessels, improving the therapeutic effect (by reducing the immediate wash-out of the cytostatic agent) and decreasing the risk of systemic toxicity and post-embolic syndrome.

Methods and materials

A single-center phase II study was conducted on 24 consecutive HCC patients (13 intermediate-stage non responder and 11-advanced stage stage) dismissing Sorafenib due to unbearable side effects or worsened clinical conditions (deteriorated liver function), who underwent DSM-TACE.

Under local anesthesia, through femoral approach, the treatment was performed after selective lobar hepatic artery catheterization. Based on extent and distribution of the disease and according to the protocol, each cycle of therapy consists into two consecutive treatments performed within one month. In particular, in case of unilobar disease, patients underwent two session treatment in one month while in case of bilobar disease they underwent four session treatment, two for each lobe with a two week interval between sessions.

Tumor response was evaluated, according to mRECIST criteria, with MDCT exam performed 1 month after complete treatment and every 3 months thereafter.

Primary endpoints were safety, tolerance and overall disease control (ODC); secondary endpoints were progression free survival (PFS) and overall survival (OS).

Results

A total of 86 treatments were performed. Technical success, defined as the ability to deliver the total planned dose or to obtain stop flow, was achieved in all patients. No intra- or peri-procedural complications occurred and in particular no signs of liver failure or systemic toxicity were detected. At 1-month follow-up, an objective response rate (ORR) of 45.9% and overall disease control (ODC) of 79.2% were observed. In nine patients with ODC and residual viable tumor higher than 50%, a repeated DSM-TACE treatment was performed. During the mean follow-up of 18.2 months an ODC of 45.8% was registered. PFS, calculated using the Kaplan-Meier method, was 5.8 months with a median OS of 10.8 months (**Fig. 1**; **Fig.2**).

When considering the subgroup evaluation (**Fig.3**), significant longer overall survival was obtained for BCLC-B intermediate Child-Pugh A patients compared with BCLC-C advanced Child-Pugh B patients. The outcome justifies the prognostic pivotal role of liver functional reserve in intermediate/advanced HCC patients with liver cirrhosis which has been previously described by other groups.

Images for this section:

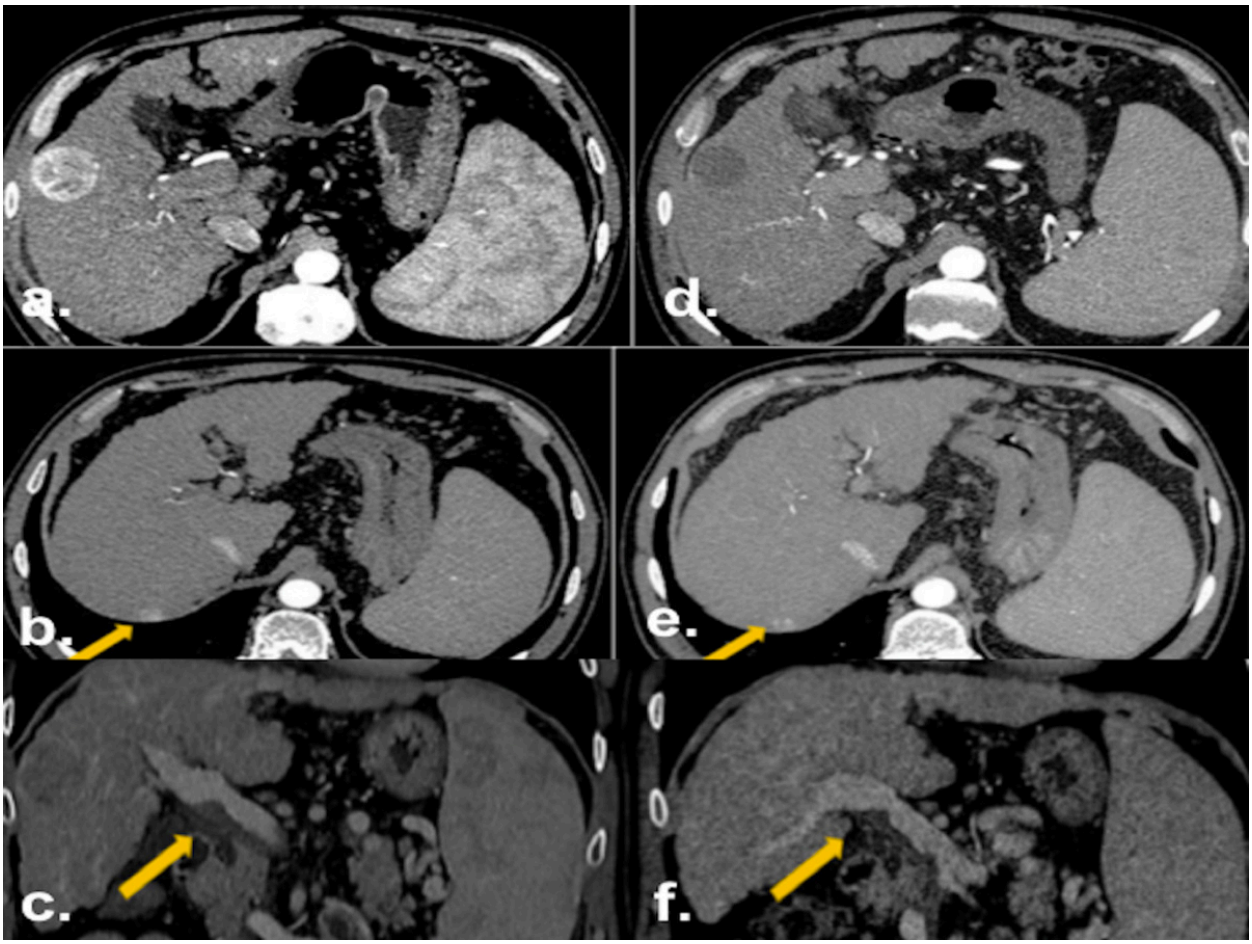

Fig. 1: A 52 yo male patient with advanced multinodular HCC: the main lesions of 3.7 cm in diameter in the V segment (a) and 1 cm in VII segment (arrow in b) with portal vein tumor thrombosis (PVTT) (arrow in c). Two right lobar DSM-TACE were performed with a 4-weeks interval. CT performed on 6-months (d-f), demonstrates a complete necrosis of the main nodule in sV (d) and of the multiple nodules in the right lobe; it also is demonstrates stability of the lesion in the sVII segment (e) and of the portal vein thrombosis (f). We obtained a substantial downstaging of disease and the patient underwent liver transplant.

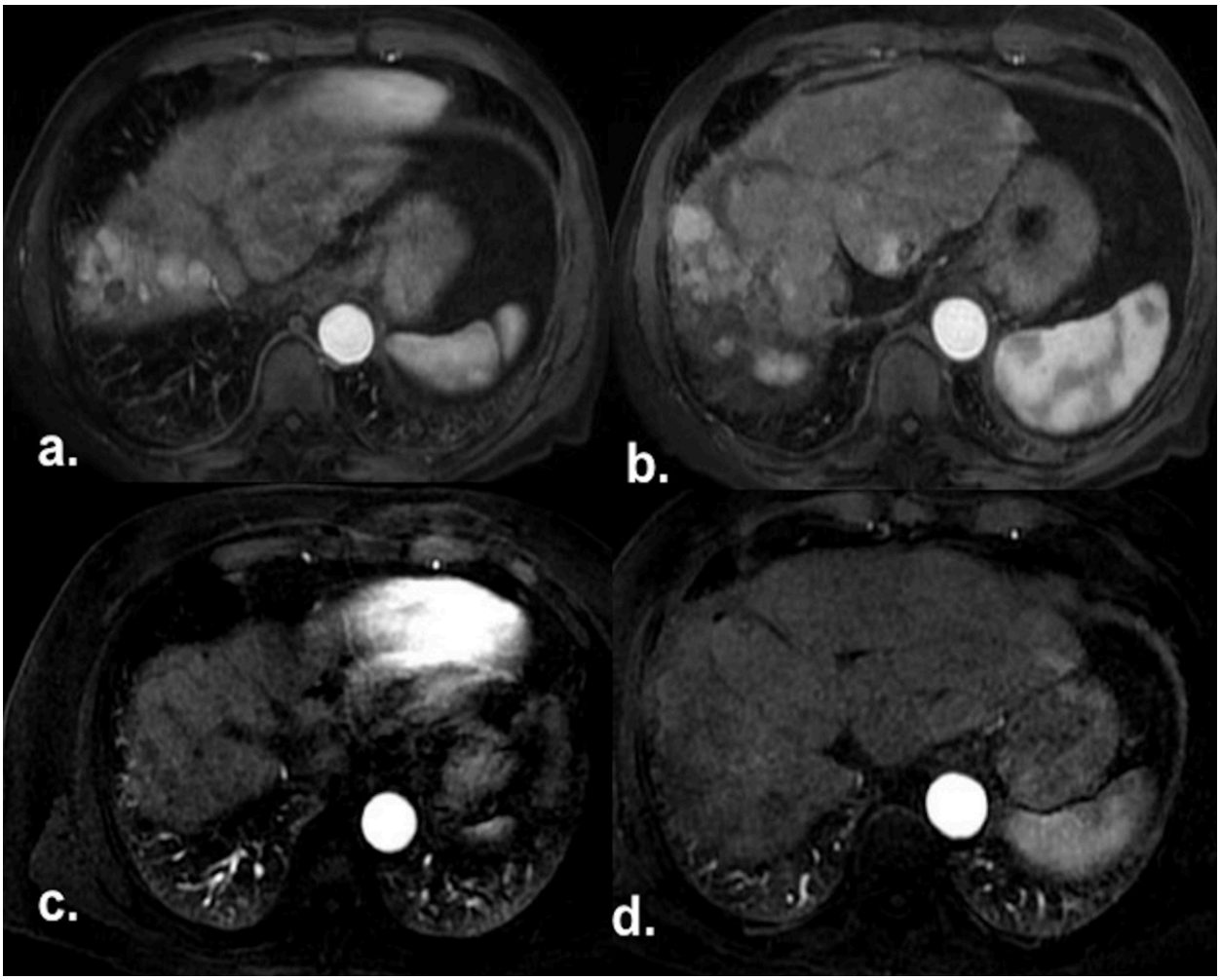

Fig. 2: A 76 yo male patient, BCLC- B (intermediate stage), progressing upon loco-regional treatment, in therapy with Sorafenib and dismissing it due to unbearable side effects; MRI shows multiple bilobar HCC nodules (a, b). After two DSM-TACE treatment performed for each lobe, on one year follow up, a complete response, evaluated with MRI and according to mRECIST criteria, is obtained (c, d).

	6-month Survival Rate (%)	1-year SurvivalRate (%)	Median OS (months)
BCLC B	61,5	53.8	11.2
BCLC C	81,8	54,5	8.6
CHILD A	77,8	56,7	12.3
CHILD B	66,7	46,7	8.1
BCLC B - CHILD A	80	60	12.4 *
BCLC B - CHILD B	50	50	8.5
BCLC C - CHILD A	75	55	8.7
BCLC C - CHILD B	85,7	42,8	6.5

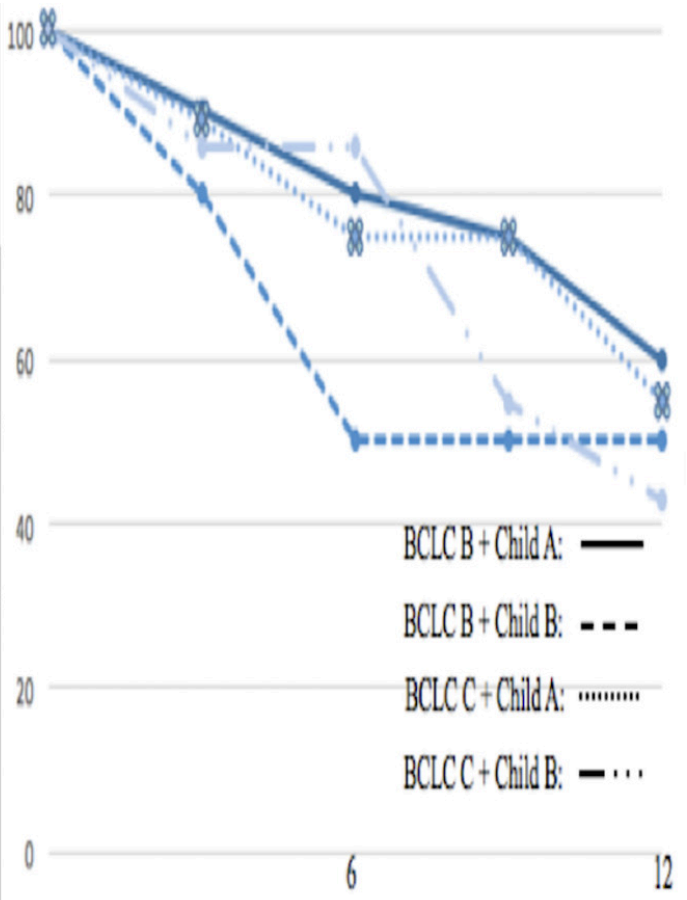

Fig. 3

Conclusion

DSM-TACE seems to be a promising option for intermediate and advanced HCC patients ineligible for Sorafenib administration or dismissing it due to progressive disease or unbearable side effects.

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