HCC

#P12 - Characterization of the intratumoral immune microenvironment of hepatocellular carcinoma before selective intrahepatic radiation therapy and study of its prognostic value on response to treatment

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Background & Aims
Internal selective radiation therapy (SIRT) is a validated treatment of hepatocellular carcinoma (HCC). The role of local immune response in achievement of response remains elusive. This study was designed to characterize the HCC immunological status before SIRT and its impact on therapeutic response (primary endpoint) and survival.

Methods
Ninety-one patients from 8 University Hospitals (7 French, 1 Italian), affected by histologically proven HCC and treated with SIRT, were enrolled in the study. Patient's clinical, biological and radiological data were collected at the diagnosis of HCC and during follow-up. Patients were defined as "responders" or "not responders" according to radiological tumor response (mRECIST criteria) evaluated 3 and 6 months after SIRT. RNA sequencing was analyzed to study genes expression differences in the intra-tumoral microenvironment.

Results
Twenty-seven patients (81.5% male, median age 63 years, 67% with cirrhosis) were analyzable for primary endpoint. HCC distribution across BCLC stage was: 4 A (15%), 10 B (37%), 13 C (48%). Ten patients were classified «responders» (1 complete/9 partial response), 17 «not responders» (3 stable/14 progressive disease). Median overall survival (OS) of patients was 15.9 months. According to RNA sequencing analysis, unsupervised hierarchical clustering identified two clusters (10 C1, 17 C2) of patients with different genes expressions. Most «responders» were in C2. Clusters were significantly different for cirrhosis, albumin, AFP levels, histological differentiation, subtype of HCC and OS (C1: 10.6 months; C2: 18.0 months; p = 0.047). Supervised analysis showed 480 genes down- and 1121 over-expressed in C1 vs C2. Gene set enrichment analysis showed that C1 was associated with genes involved in immune responses while C2 with genes involved in proliferation/differentiation liver cells. By Microenvironment Cell Populations counter method, we identified an abundance of immune infiltrates (monocytes, myeloid dendritic cells, cytotoxic lymphocytes, T and B cells) in C1 vs C2.

Conclusions
These results suggest that presence of a pro-inflammatory intratumoral immune infiltrate appears predictive of a worse OS with a trend of bad response to SIRT in HCC patients. SIRT, in analogy with external radiotherapy, could trigger the release of pro-inflammatory mediators and increase tumour-infiltrating immune cells. This phenomenon may enhance the efficacy of combined treatments with immunotherapy.