THU-083

In hepatitis C infected patients with cirrhosis squamous cell carcinoma antigen (SCCA)-IgM levels may contribute to identify the individual risk of hepatocellular carcinoma development after antiviral therapy

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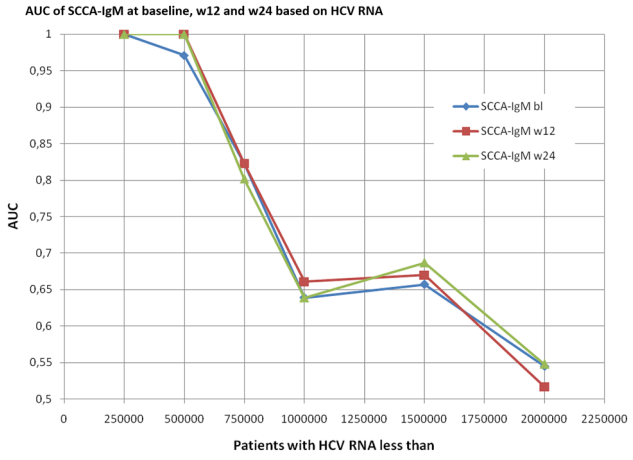
Background and Aims: In HCV infected patients with cirrhosis the risk of hepatocellular carcinoma (HCC) persists even after Direct-Acting-Antivirals (DAAs) induced HCV clearance. Therefore, biomarkers of the residual HCC risk are still an unmet need. Serum levels of squamous-cell-carcinoma antigen-immunoglobulin-M (SCCA-IgM) were associated with higher risk of HCC development. We have retrospectively evaluated the kinetics of SCCA-IgM during DAAs in HCV infected patients with cirrhosis with and without subsequent development of HCC.
Methods: Of the 572 HCV pts with cirrhosis DAAs treated according to Italian Drug Agency (AIFA) from February 2015 to August 2016 at the Hepatology Unit of Pisa University-Hospital we enrolled all 20 HCC cases (de novo or recurrence), 24 pts previously treated for HCC and 41 without HCC. Serum levels of SCCA-IgM were measured at therapy start (BL), after 12 and 24 weeks by ELISA (Hepa-IC, Xeptagen S.p.A., Venice, Italy). All pts completed DAAs treatment, 2 experienced a relapse.



Results: Overall, 9 (10.6%) and 11 (13.0%) patients were diagnosed with recurrent or newly developed HCC, after a median time of 24.9 (4.7–65.7) weeks from the end of therapy. The remaining 24 (28.2%) and 41 (48.2%) patients, with and without history of HCC, remained HCC free during a comparable follow-up. Median SCCA-IgM values were not significantly different between the four groups ($p = 0.300$) at baseline [cirrhosis without HCC = 244.0 (39.2–785.2) AU/ml; HCC de novo = 259.3 (111.0–1266.5) AU/ml; Cirrhosis with HCC = 189.0 (38.7–758.7) AU/ml; HCC recurrence = 217.1 (105.1–940.2) AU/ml], week 12 and 24 ($p = 0.448$ and $p = 0.378$, respectively) after the start of therapy. On-therapy median SCCA-IgM levels decreased similarly in all groups. None of the patients with BL SCCA-IgM values <100 AU/mL (8/85, 9.1%) developed HCC. A Receiver Operating Characteristics (ROC) analysis showed that the diagnostic performances of SCCA-IgM levels in discriminating pts with or without HCC development, improved significantly in pts with lower HCV-RNA (Figure 1) reaching the highest diagnostic accuracy (100% Sensitivity and Specificity) for a viremia below 500.000 UI/mL.
Conclusions: SCCA-IgM serum levels alone or in combination with BL HCV-RNA could contribute to better define the individual risk of HCC development in the first 18 months after DAAs treatment in HCV infected patients with cirrhosis. Our findings prompt further investigation in larger cohorts.

THU-084

Predictors for successful downstaging in patients with BCLC intermediate stage hepatocellular carcinoma

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Background and Aims: Liver transplantation (LT) after downstaging therapy for hepatocellular carcinoma (HCC) is still controversial. Several studies have been performed to assess the outcome after LT in patients with HCC initially outside Milan criteria (MC) who achieved successful downstaging. However, little is known about factors that may predict successful response to downstaging therapies or intention-to-treat outcome of downstaging therapy.
Methods: Medical records of 220 consecutive patients diagnosed with BCLC intermediate stage HCC between 2005 and 2011 in five Dutch tertiary care centres were retrospectively reviewed. According to the radiologic response to downstaging therapy, patients were classified into 2 groups: successfully downstaged (SD) and not-successfully downstaged (NSD). SD was defined as >3 months fulfilling MC. Student's t, chi-square and Wilcoxon test were used to compare groups. A competing risks model was used to estimate the cumulative incidence for time to success. To study the effect of risk factors on time to success, a multivariate Cox proportional hazards model censoring patients dying without success was employed. Risk factors associated with overall survival were estimated with a multivariate Cox model with transplantation and successful downstaging as time dependent covariates.
Results: At baseline, significant differences were found between the SD (n = 64, 29%) and NSD (n = 154) group in the median AFP (19 vs. 62 ng/mL, $p = 0.005$), number of lesions (2.6 vs. 4.0, $p < 0.001$), diameter of the largest tumor (5.1 vs. 7.0 cm, $p < 0.001$). Also therapies applied differed significantly between groups ($p < 0.001$). After 15 months 95% of the patients in the SD group were downstaged successfully, while 68% of the NSD group had deceased (Figure). Hepatitis B/C as underlying aetiology, lower number of lesions and diameter of the largest tumor were independent predictors for successful downstaging (all $p \leq 0.03$). Importantly, successful downstaging was predictive for a better survival ($p = 0.004$). A high age at diagnosis, MELD score, number of lesions, diameter of the largest tumour and AFP > 100 ng/mL were all associated with a significantly worse survival (all $p \leq 0.006$).
Conclusions: Hepatitis B/C as underlying aetiology, number of lesions and maximum diameter of the largest tumour independently predict successful downstaging of HCC. Moreover, patients with intermediate stage HCC have a survival benefit from downstaging therapies.

failure. The loss of productivity was considered in 42% of the patients who worked, estimated as a mean of €926 and in 10% of patients with caregivers, estimated as a mean of €498.
Conclusions: Real life data, based on the PITER platform, indicate that about 3.6% of patients, mainly treated in the advanced liver disease stage, failed to achieve HCV viral eradication after first line interferon free DAA regimens, part of them considered as suboptimal to date. Clinical and economic burden of this unfavorable event is significant and treatment appropriatness need to be better addressed.

FRI-281

Relapse after direct-acting antivirals (DAAs) in cirrhotic patients with hepatitis C is highly related to development of liver cancer

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Background and Aims: The clinical outcome of cases with chronic hepatitis C and cirrhosis treated with the direct-acting antiviral (DAAs) are still controversial, particularly regarding the development of hepatocellular carcinoma (HCC). Some reports appeared in the recent literature that would confirm the inability of DAAs to prevent the cancer in patients at risk and the characteristics of this unfavorable cases are still unknow. We prospectively analized a real life study population with HCV related cirrhosis to compare diagnostic performances during development of HCC.
Methods: One-hundred and 87 out-patients (aged 59 ± 11 yrs;103 males;101 experienced) treated with DAAs (72% SOF-based) were monitored from March 2015 to October 2016 to assess sustained virologic response at week-12 post-therapy (SVR12). Stage of liver disease was F4, F3 and F1-F2 in 160 (108/52 ChildA/B), 23 and 4 cases, respectively. Development of HCC was confirm by MRI with hepatospecific contrast. All cases were tested for alfa-fetoprotein (AFP) and SCCA-IgM levels in serum by XEPTAGEN (Italy), Squamous Cell Carcinoma Antigen variants immune complexes ELISA kit and monitored for biochemical parameters and determination of HCV-RNA by real time PCR (sensitivity 10,5 UI/mL) monthly.
Results: SVR12 was achieved in 170 cases (91%), while 15 relapsed and 2 dropped-out. Twenty cases developed HCC (11%; 14 *de novo*/6 recurrence) with a multifocal stage in 75% and a mean time of diagnosis from therapy initiation of 7,3 ± 4,5 mos. In cases with relapse 53% (8/15) developed HCC, respect to 7% (12/170 cases) of the patients with SVR12 ($p < 0.001$). AFP (ug/L) and SCCA-IgM (AU/mL) mean levels were 4,2 ± 3,0 and 138 ± 145 in cases without HCC respect to 64 ± 160 and 378 ± 312, respectively in cases with HCC development. AFP showed a diagnostic performance with a cut-off >20 μg/L only in 4 patients (Sens.20%; Spec. 99%), while SCCA-IgM diagnosed 80% of cases (16/20) with HCC with a cut-off >200 AU/mL (Sens.80%, Spec.83%).
Conclusions: Viral reactivation after suppression of HCV-RNA during DAA is highly associated to the development of HCC, particularly in cases with *de novo* HCC occurence and Child A cirrhosis, showing a more aggressive clinical outcome. SCCA-IgM levels seem more powerful in the early diagnosis of this type of liver cancer compared to AFP. The DAAs do not seem to prevent this kind of liver tumor. It is assuming that these drugs can't influence this new kind of oncogenetic related mechanisms.

FRI-282

Genotype 3 infection in DAA era: reports of a real life Northern Italy network for viral hepatitis after 2 years by the start

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Background and Aims: In this new era, HCV genotype 3 has emerged as a difficult-to-treat viral strain, achieving response rates lower than other genotypes. The Lombardy Region Network (34 prescribing centres from North Italy) collected data on HCV Gen. 3 treatments since May 2015. We aimed to explore the real life outcome of genotype 3-infected patients treated with DAAs.
Methods: We retrospectively/prospectively analyzed the data of 806 patients with genotype 3 HCV infection. 30%, 66% and 4% of pts received respectively: SOF + RBV, SOF + DAC ± RBV, PEG + SOF + RBV. Treatment duration was 24 weeks in 85% or 12 wks in 12%.
Results: 85,8% of patients were cirrhotic of whom 82% were well compensated and the remaining were waitlisted for LT. Pts treated with DAC + SOF + RIBA were older, with a higher rate of cirrhosis. Overall, 21 SAEs (3,28%), unrelated to therapy, were observed during treatment or follow-up. 1 pt died during treatment for heart attack. Another patient died for end stage liver disease at week 8th of antiviral therapy. At the time of the analysis, **639 patients** had completed the treatment and **433 could be evaluated for SVR 12.** By ITT analysis, the overall SVR12 was 88,4% (375/424). No differences were observed in SVR rate by stratifying the patients according to: presence or absence of cirrhosis, HIV co-infection and treatment duration. SVR rates in pts treated with SOF + RBV (81%) were significantly lower ($p < 0.005$) than in pts treated with SOF + DAC (89%), SOF + DAC + RBV (97%) and PEG + SOF + RBV (90%). In cirrhotic patients SVR12 was 87,54%: a significant MELD score improvement was observed (median EOT MELD score 6 vs median baseline MELD score 9: $p < 0.005$); the patients which presented a MELD improvement were statistically younger (median age 51 yrs vs 54 yrs) ($p < 0.005$).
Conclusions: In our cohort, overall SVR12 in G3 patients was: 88.4%. The highest SVR rates were achieved with SOF + DAC + RIBA. No significant differences were observed in SVR rate by stratifying Genotype 3 patients according to the presence or absence of cirrhosis (94% in F4 patients vs 100% in F3) for DAC + SOF + RIBA. Among cirrhotic patients, a MELD score improvement was observed in 49.3% of patients.

FRI-283

The old patient in DAA era: real life reports on 5925 patients from the Lombardy HCV Network

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