One of the main goals of our clinical and research activity is to bring the personalization in the management and care of chronic liver disease patients at its highest level. To achieve this goal, the doctor should face the patient, as a scientist faces a research project, aware that the "experiment" he is studying is represented by a unique and unrepeatable subject. This approach implies the continuous adaptation of professional competence and experience on the specific nature of the disease, but it also requires the ability to adapt the monitoring and treatment programs, suggested by international guidelines, to the context of the individual person, which is characterized by the uniqueness of its clinical background.

To set the basis of a shared path toward this goal, our Hepatology group of Pisa contributed to the organization of specific congress events, starting from the 2013 AISF monothematic conference on Personalization of Treatment in Hepatology, where the foundations for the constitution of a Special Interest Group have been laid. Consequently several multicenter studies were run with the endpoint of achieving tools that can help the clinicians to personalize the management of patients with liver disease.

**Summary of the scientific achievements**

The research activity has been focused on the combined use of multiple serum biomarkers of HCC for preventive surveillance and therapy monitoring since this topic is still debated and not yet accepted by international guidelines because of the lack of a clear cut definition of clinically useful pathological cut-offs and delta variations of these biomarkers.

A collaborative study (Turin, Padua, Naples and Pisa) using standardized biomarkers of HCC, Alphafetoprotein (AFP) and des-gamma-carboxy-prothrombin (DCP or PIVKA-II), showed variable diagnostic thresholds in relation to the etiology and activity of the underlying liver disease (Ricco G et al, 2018).

On the basis of these assumptions, a model for the analysis of biomarkers fluctuations over time has been developed, aiming to overcome the concept of cut-off and introducing the more dynamic parameter of relative delta-variation. Studying the relative increase over time of an HCC biomarker may help to identify the subjects in which the biological variability underlying the "normal" fluctuations has changed, suggesting the likely onset of a neoplastic process. This approach, which represents a fine methodological analysis of the laboratory data, would also allow the identification of subjects worthy of personalized monitoring programs (Ricco G et al, AISF 2018).

A prospective multicenter study of the kinetics of AFP and PIVKA-II in single patient in HCC surveillance has collected a significant number of consecutive sera from patients who developed HCC and controls without HCC and sera will be tested within the next 6 months.

In addition exploiting the long lasting expertise of our group in bio-mathematical modelling of infected cells dynamics) by measuring circulating biomarkers in HCV and HBV infected patients that In the pre-DAAs era of Hepatitis C treatment allowed the highest cost-effective accuracy in predicting SVR at the end of treatment (Colombatto P et al, 2008, Iannazzo S et al, 2015) we developed a novel physical-mathematical model describing the dynamics of HCC neoplastic cells in vivo. Notably, the model analysis combining in a radiomic approach circulating and digital imaging biomarkers allowed to quantify the effects of sorafenib on cancer vascularization and cancer cells dynamics. Provided its validation in other cases of complete response to therapy, it might be a useful non-invasive tool to guide the clinical decision making in HCC systemic therapy (Colombatto P et al, ILC 2020).

Finally, the effort towards a greater precision/personalization of clinical decision making covered additional digital imaging biomarkers provided by the ultrasound examination of the liver. In particular, our group
developed and is currently testing in large cohorts a new multiparametric quantitative method based on artificial intelligence algorithms of digital biomarkers extracted by ultrasound images that provides an accurate and precise measurement of liver fat content. This new method is applicable in remote on simple videoclips registered by any common ultrasound equipment and provides liver fat quantification with a very high correspondence with the gold standard magnetic resonance spectrometry in ROC analyses (Di lascio N et al, 2018).

References


List of abstracts sent to National and International congress


List of Publications


