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# Hepatology Today and in the Future : A Summary of the Highlights of the Paris Hepatology Conference 2019

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## Q. What is the Paris Hepatology Conference?

The Paris Hepatology Conference (PHC) is an international conference entirely focused on the management of patients with liver disease. The PHC was created in 2004 by the APHC (Association for the Promotion of Hepatologic Care), a not-for-profit association. The main objectives of the APHC are the promotion of education, research, awareness and healthcare in liver diseases. Educational activities include annual meetings: the Paris Hepatology Conference (PHC) and the Young European Hepatologists Course (YEHC).

The PHC is a widely recognized annual "rendez-vous" of international specialists and scientists interested in all the fields of Hepatology. The concept of this two-day conference is to provide the state-of-the art in Hepatology and how to apply the up-to-date knowledge for the optimal management of patients with liver disease in real life. For this purpose, the PHC addresses the major issues in all chronic liver diseases including hepatitis C, hepatitis B, NASH, cholestatic and auto-immune liver diseases, end-stage liver disease, HCC and liver transplantation.
The DNA of the PHC is to create the appropriate friendly atmosphere to favour discussions and exchanges between the attendees and the international experts. To achieve this aim, interaction is encouraged during the plenary sessions (round table discussions) as well as interactive lunch workshops (discussion of clinical cases).

The Faculty of the PHC consists of 80 selected speakers from among the best international experts presenting the state-of-the-art and through interactive exchanges provide clinically relevant information for daily practice.

The PHC is an independent and high-level postgraduate educational program, designed for specialists caring for patients with chronic liver disease, worldwide. Since the first edition in 2004, attendance has steadily increased: 1000 specialists from 70 countries from all continents now participate in the PHC every year.

This year, thanks to the outstanding Faculty, the presentations and discussions during the 12th edition of PHC reflected the remarkable recent advances in all fields of Hepatology.

## Q. Can you update us on hepatitis C?

In Hepatitis C, we can tell our patients, thirty years after the discovery of the virus, that they have almost a 100% chance of cure with pangenotypic DAAs. Treatment is highly effective whatever the stage of the disease and the associated comorbidities. The rare patients who relapse with resistance associated substitutions after DAA therapy are cured with appropriate retreatment. There are so far no concerns about the safety of current therapies, however potential interactions with other drugs and adherence require attention. Cure means eradication of HCV infection with improved quality of life and outcome with a lower risk of complications and a higher survival rate. Successful antiviral therapy reduces, but does not eliminate, the risk of HCC in patients with cirrhosis. The challenge remains the treatment of patients with decompensated cirrhosis who are the most difficult to treat and need careful indication and management. Patients with HBV coinfection need anti-HBV NUC to prevent HBV reactivation during or after DAA

treatment. Nowadays, the main issue is how to achieve global elimination of hepatitis C. The WHO HCV program with the goal of elimination of hepatitis C by 2030, even difficult to achieve, is nevertheless accompanied by active national programs worldwide. Numerous examples of successful programs indicate that removing barriers and improving access to care is possible.

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## Q. And the advances in hepatitis B?

In Hepatitis B, we can tell our patients that they have a 100% chance of viral suppression. Long-term studies of patients under last generation NUCs demonstrate sustained complete viral supression without resistance, disapearance of necroinflammation and regression of fibrosis, even at the stage of cirrhosis. Long-term NUC therapy is safe. Modest changes of GFR and/or bone marrow density have been observed with tenofovir with a smaller decrease associated with TAF. TAF and ETV are recommended for patients with risk for renal or bone disease. Sustained remission is associated with an improved outcome with a decreased risk of evolution to cirrhosis, decompensation and HCC. The problem is that NUCs should be administered indefinitely since HBsAg loss occurs only in a small minority of patients. Even if stopping treatment can be associated with a favourable outcome, this is not recommended because of the risk of flares that can be severe or even fatal. The combination of PEG IFN with TDF can be effective in a sub-group of patients with an accelerated decline of HBsAg and a higher rate of HBsAg loss. Quantitative HBsAg has been confirmed to be a useful tool for the prognosis and the monitoring of treatment. The next objective is the cure defined as HBsAg loss, even if it does not mean complete viral eradication. This objective  now seems realistic with the development of numerous promising drugs against different viral targets, including viral proteins, RNAs and cccDNA. Future treatments will certainly consist of combinations adapted to the different phases of hepatitis B. Among an estimated 250 million chronic carriers, only 30 million are diagnosed and 5 million are receiving treatment, with a great geographic disparity. WHO has set priorities for achieving global goals including more effective vaccination and easy access to therapy programs. However, progress is needed in hepatitis B awareness, adequate vaccination, screening, diagnosis and access to treatment.

## Q. Can you update us on hepatitis delta?

In hepatitis delta, we can tell our patients that new treatments are coming soon. PEG IFN therapy induces only 25-40% of sustained virological response with undetectable HDV RNA and possible subsequent HBsAg loss. More effective and user-friendly drugs are urgently needed. Several drugs are under development on different targets : nucleic acid polymers (RP129), farnesyl-transferase inhibitor (lonafarnib), entry inhibitor (myrcludex). Phase 2 studies have demonstrated their effects on HDV RNA and HBsAg decline. Ongoing phase 3 trials should confirm their efficacy. The future treatment of hepatitis delta will certainly be a combination of these drugs with an interferon such as interferon lambda. Hepatitis delta is a neglected problem with high prevalences, underestimated so far, in many countries in all continents. Moreover, the incidence is increasing, favoured by population migrations. Effective actions including screening, diagnosis and treatment are needed.

## Q. News on NAFLD and NASH

In NAFLD, we can better counsel our patients, however treatment is hardly needed. In this emerging liver disease, affecting 25% of the global population, we know that lifestyle counselling is effective only in a minority. NASH is an important and increasing cause of cirrhosis, HCC and an increasing indication for liver transplantation. The key issue is to differenciate NASH from simple steatosis. Where is the red line ? As, we learned from non-A, non-B hepatitis, before discovering the virus, our ignorance explains the problems we face in NAFLD. The treatment of NASH is complicated by the lack of markers and the multifactorial causes. There is a long way to go to understand the physiopathology and the natural history of the disease in order to develop appropriate markers and effective treatments targeting oxidative stress and apoptosis, fibrosis, inflammation and metabolic disturbances. Several drugs are being currently evaluated and results of phase 3 studies will be available soon. Drugs need to show a significant superiority as compared with lifestyle counselling and management of metabolic disorders. The control of Nash is and will be the most important challenge in Hepatology.

## Q. Hepatocellular carcinoma

In HCC, more patients will be stabilized or cured. Professor Massimo Colombo, who received the PHC Award this year for his outstanding accomplishments in clinical research and education, delivered a remarkable state-of-the art lecture on the advances in the management of HCC. Obviously, HCC is the current and future most important challenge to face. With the improvement of diagnosis and characterization of tumours, treatment may be improved. Furthermore, new drugs showed promising results and others are coming. Four agents have been added to sorafenib as systemic therapeutic options based on positive randomized trials : lenvatinib, regorafenib, cabozantinib and ramucirumab. Effective combinations may be expected soon. New technologies, including genomic and proteomic will help to develop more effective and personalized therapeutic strategies.

In transplanted patients, nowadays both mortality and morbidity have considerably improved. The indications for transplantation have markedly changed during the last decade with increasing rates in HCC, alcohol and NASH and decreasing rates in HCV and HBV. The indications and the management of patients pre-transplantation have been refined and allow transplantation in better selected patients with a better outcome.

## PHC Wrap-up:

Hepatology is in a very active and promising phase of development in all areas. No doubt that the use of new digital technologies and artificial intelligence will revolutionize Hepatology. We are entering a new era of precision Hepatology and more efficient personalized management of our patients with liver disease.

Acknowledegements : We are very grateful to the members of the Faculty of PHC 2019.

To consult the program, the videos, slides and abstracts of the presentations of PHC 2019, please visit the site www.aphc.info

The 2020 edition of PHC will be held on January 13-14 with a program covering new advances in the treatment of NASH, chronic hepatitis B and delta, as well as HCC. Special sessions will be dedicated to the role of innovative technologies in Hepatology.