European Liver Patients' Association

Box 27
Rue de la Loi 235
1040 Brussels
Belgium

ELPA Symposium 2017

On 20th April 2017, ELPA hosted its traditional symposium at the International Liver Congress™ (ILC). The ILC is the largest European gathering of liver disease experts and each year ELPA is kindly invited by the Governing Board of the European Association for the Study of the Liver (EASL) to gather renowned experts in the field of liver health to address a mixed audience composed of, among others, hepatologists, gastroenterologists, infectologists, nurses, medical students and patients.

This year's ELPA symposium, titled *New Horizons in Liver Disease* aimed to draw attention to the remarkable progress made over the last decade or so, and emphasise that liver disease remains an ongoing concern for Europe, where an estimated 29 million citizens suffer from a chronic liver condition. Chronic Viral Hepatitis B is the second major cause of both cirrhosis and liver cancer, Chronic Hepatitis C is an important risk factor for hepatocellular carcinoma, while alcohol-related liver disease and non-alcoholic fatty liver disease are both major concerns, particularly the latter, given the growing incidence of obesity in Europe. Additionally, there is an increase in rarer liver conditions such as Primary Biliary Cholangitis (PBC), Primary Sclerosing Cholangitis (PSC) and Autoimmune Hepatitis (AIH) which also deserves attention. As well as looking specifically at what progress has been made, and what the future looks like, for Hepatitis B, Hepatitis C, Autoimmune Liver Diseases, NAFLD and NASH, the symposium provided an opportunity to showcase the work ELPA carried out in 2016, highlighting in particular the Hep-CORE survey. Finally, it gave ELPA and the Symposium attendees the opportunity to review the wish list of what progress ELPA would like to see in the next 20 years of hepatology.

With Amsterdam RAI's Emerald Room full to capacity, and overflowing onto the corridor, ELPA President, Ms Tatjana Reic opened the Symposium, welcoming the more than 250 attendees noting how pleased she was that ELPA was once again able to contribute to the success of ILC by organising a symposium which gathered key opinion leaders in the field and highlighted the benefits of collaboration between the medical and scientific community and the patients represented by ELPA. Ms Reic also warned against complacency given the recent medical advances in liver disease, and emphasised the importance not only of finding cures for the different liver conditions but also of ensuring that the medical advances were available to those who needed them, indicating that HEP-Core, ELPA's flagship project for 2016, had given a better understanding, as far as hepatitis B and C were concerned, of where there had been successes and where there were still gaps. Ending her brief intervention Ms Reic proceeded to introduce ELPA Board Member Marko Korenjak, who would be introducing the speakers for the session.

As first speaker Mr Korenjak introduced Dr Anna Lok, President of the American Association for the Study of Liver Diseases (AASLD). Mr Korenjak reminded the audience that Dr Lok's research focused on natural history and treatment of hepatitis B and C, and she had published more than 450 papers viral hepatitis and liver diseases, including the AASLD Guidelines on Hepatitis B. Dr Lok's presentation was entitled "Cure for Hepatitis B: Current and Future Treatment" which she started by outlining the current goals of HBV treatment which include sustained suppression of HBV replication, decrease of hepatic inflammation, reverse liver fibrosis and reduce the risk of cirrhosis, liver failure, and hepatocellular carcinoma; before proceeding to outline the current approved HBV treatments which are either Interferons (IFN) or Nucleos(t)ide analogues. Subsequently Dr Lok spoke to the efficacy of the currently available HBV therapies (potent viral suppression, reverse hepatic fibrosis/cirrhosis, prevention of progression to liver failure) but noted the low rate of HBsAg loss and the fact that they decrease but do not eliminate incidence of HCC. Dr Lok then moved on to try and answer the question of when to start HBV treatment, outlining the AASLD Guideline recommendations and giving an overview of the different possibilities available. Dr Lok then moved on to asking whether an HBV cure was possible, and whether treatment can accomplish what nature cannot, and then

looking at the barriers to eradicating HBV. Finally, Dr Lok tried to summarise how an HBV cure could be defined, looking at "Complete Cure", "Functional Cure", "Realistic Functional Cure" and "Partial Cure". Dr Lok indicated that a realistic functional cure (simulate CHB with spontaneous HBsAg loss) is possible but will require (1) a combination of antiviral with different targets and restoration of immune response, and (2) cooperation of multiple stakeholders. In closing her presentation Dr Lok noted that a cure will only benefit patients who have been diagnosed, and have access to care.

The second speaker of the afternoon was Prof. Jean-Michel Pawlotsky, a long-term supporter of ELPA who has fought against viral hepatitis for over 25 years. Prof Pawlotsky is a Professor of Medicine at Henri Mondor Hospital, University of Paris-Est in Creteil, France, and Director of the National Reference Centre for Viral Hepatitis B, C and D, and has also been Associate Editor of *Hepatology and Gastroenterology.* In his presentation, which focused on hepatitis C Prof Pawlotsky started by providing an overview of the prevalence of HCV infection worldwide, before moving on to looking at the strategies to eliminate/control HCV by 2030, specifically the Prevention Targets (100% of blood donations screened, 90% access to safe injections), Testing Targets (90% of people aware of infection) and Treatment Targets (80% of HCV patients treated, 90% of HCV patients cured) as outlined by WHO. Prof Pawlotsky stressed that the conditions for broadening access to HCV therapy are awareness, screening, diagnosis, adequate medical environment, affordable drugs and simplified access and monitoring. Following on from his overview on targets that needed to be achieved by 2030 Prof. Pawlotsky looked at HCV diagnosis and treatment rates in Europe and the tools available to improve HCV screening, providing the example of the dried blood spot testing in drug services in Scotland before moving on to give a comprehensive overview of the the WHO HCV Testing Guidelines, and presenting a slide which showed the ideal birth Cohorts to screen by country. Prof. Pawlotsky summarised this first part of his presentation by saying that a major effort was needed, through national action plans, to improve screening, diagnosis, prevention, linkage to care and cascade of care. In the second part of his presentation Prof. Pawlotsky focused on the remaining issues which included drug-drug interactions,

HBV reactivations, HCV recurrence/occurrence, and treatment failures, resistance and re-treatment.

Moving on from hepatitis B and C, Marko Korenjak introduced Mr Robert Mitchell-Thain, Head of Education and Development at the PBC Foundation, an international patient organisation based in the UK. Mr Mitchell-Thain, a leader in the field of self-management, is trained in counselling and coaching techniques and is also an ELPA Board Member. Mr Mitchell-Thain's presentation focused on the three big autoimmune liver diseases: PBC, PSC and AIH. He noted that Primary Biliary Cholangitis (PBC) patients were 90% female, with an age of presentation of 35 - 55 years and that 50-60% were asymptomatic at diagnosis. Both first and second line therapies exist but PBC is incurable and 42% of those affected have at least one other autoimmune condition. Mr Mitchell-Thain indicated, on the other hand, that Primary Sclerosing Cholangitis (PSC) mainly affected males (60%), who were diagnosed in their 20s and 30s, with 44% being asymptomatic at diagnosis. Contrary to PBC, with PSC there was a lack of agreed therapies, although the disease was also incurable, with the median survival being 12 years. He also noted that 80% of PSC patients were affected by IBD. In contrast Mr Mitchell-Thain indicated that for Autoimmune hepatitis the diagnosis was by exclusion and the treatment was Prednisolone then Azathioprene and there was a strong chance of remission with risks and side effects from medication and usually life-long immunosuppression. Continuing his presentation Mr Mitchell-Thain noted there were a number of oddities when it came to autoimmune liver diseases, for example PSC and AIH overlap, as do PBC and AIH but there was still disagreement regarding the overlaps. Looking to the future, Mr Mitchell-Thain indicated that easy diagnosis was needed, as were improved treatments with less side-effects, together with information, support and joined up care. Finally, in closing his presentation, Mr Mitchell-Thain looked at the challenges that were presented (symptoms/side-effects, OP and diabetes) but also highlighted the opportunities which presented themselves in the form of clinician/patient partnerships and the European Reference Network.

The fourth speaker at the symposium was Prof. Ali Canbay from Germany. Prof. Canbay is Director of the Department of Gastroenterology, Hepatology and Infectious Diseases at the University of Madgeburg's Faculty of Medicine. Mr Korenjak noted, when introducing Prof. Canbay, that his specialties include endoscopy, endocrinology, hepatobiliary carcinogenesis and transplantation hepatology. Prof Canbay's presentation related to NAFLD and NASH. Prof. Canbay opened his presentation by emphasising that 34.6% of the european population is overweight i.e. has a BMI above 25. As outlined in *HEPAMAP: A roadmap for hepatology research in Europe: an overview for policymakers (EASL, 2015)* out of the total population 20 – 30% were affected by NAFLD, 3% by NASH which he then compared with HCC which affected 0.2% - 0.5% of the population. Prof. Canbay gave an overview of the global prevalence of NAFLD, noting that in general NAFLD is, probably wrongly, thought to be a benign condition but that retrospective studies have shown a 58% consistency in diagnostic findings, 3.6% improvement and 46% progression, with 1/3 showing liver cirrhosis. Prof. Canbay then discussed the diagnostic procedure for NAFLD, and the separation of NAFLD and NASH by Fetuin A. Furthermore, he indicated that there are multiple factors involved in the causes of metabolic syndrome and NAFLD, with interplay of environment, genetics, and possibly gut microbiome composition. The main cause of obesity and subsequent insulin resistance being the "western lifestyle" of high calorie food combined with low physical activity, with the adipose tissue insulin resistance and inflammation together with the altered adipokine and fatty acid secretion promoting NAFLD. Prof. Canbay indicated the possible role of the gut microbiome in the development of obesity/metabolic syndrome but noted that the cause/effect relationship was not yet clear. Furthermore, Prof. Canbay highlighted in his presentation that the rising prevalence of metabolic syndrome gave cause of concern as obesity and metabolic syndrome promote alterations in hepatic lipid and glucose metabolism which are linked to the pathophysiology of NAFLD and liver cancer, with lipid accumulation and fatty acid oxidation important mechanisms in liver damage, repair and regeneration. He also indicated that NAFLD increases risk for cardiovascular disease, diabetes and chronic kidney disease. In concluding his presentation, Prof. Canbay stated that the first line therapy remained increased physical

activity but a number of therapies were currently undergoing clinical trials, some of which were already in phase III.

For the second half of the symposium, the speakers concentrated on ELPA's role as an umbrella patient organisation, and looking at what ELPA is doing at international, national and local level. Four speakers took it in turns to outline the aspects of ELPA's work they were focused on:

- Ms Livia Alimena, ELPA's Public Affairs Director, spoke about ELPA University (the Impact Programme) which had been composed of four modules leading to key learnings and outcomes for students and where sessions had taken place in Belgrade, Lisbon, Warsaw and Sarajevo; the Time to DeLiver campaign which focused on hepatic encephalopathy (HE) and had outcomes such as a patient leaflet (translated into 11 languages and providing an overview of what HE is, symptoms, summary of available treatment options as well as signposting patients to further information and support); a European Factsheet (providing an overview of the burden of HE in the U, an outline of the barriers that need to be overcome to improve the lives of people living with HE and a summary of ELPA's call to action); an Advocacy Toolkit which provides practical tips to support ELPA members' in their HE-related work; and a Patient Passport created to help patients keep track of important information relating to their condition, and to facilitate conversations with healthcare providers. Ms Alimena then moved on to outlining ELPA's launch of Hep-CORE and its communications plan for 2017. Finally, in closing her presentation, Ms Alimena spoke to the upcoming EU NASH NAFLD Policy Summit, the first of its kind which would be held in Brussels on 31 May, hosted by Alojz Peterle MEP, and organised jointly by ELPA and EASL.

- Mr Marko Korenjak focused on European funding, the NoHEP movement and the HCV Community Summit 2017. Beginning his presentation Mr Korenjak outlined the aims of the Hepatitis C Community Summit and noted that five ELPA members presented the Hep-CORE country specific data at the summit (Germany, Romania, Turkey, Macedonia and Sweden). Secondly, he set out the Q1 highlights of the NoHEP movement which included 50% increase in offline and online NoHEP actions reaching over 6m people, the development of NoHEP national groups, the ongoing pledges at national level, and the confirmation of the NoHEP ambassador. Ending his presentation Mr Korenjak provided key information and pointers relating to the ongoing EU Horizon 2020 programme which had a budget of approx. 75 billion Euros, and highlighted why ELPA is an excellent partner for the scientific community when applying for EU grants under this particular programme. Mr Korenjak noted that ELPA was already involved in two successful

projects (LIVERHOPE and GALAXY) and that there were an additional 3 projects pending (RELIEF, LIVERSCREEN, CIRROTRANS) with ELPA's role firmly focused on the dissemination of the results of each of the projects.

- Prof. Pere Gines from the Liver Unit at the Hospital Clinic in Barcelona, added to the presentation made by Mr Korenjak by providing some key information regarding one of the EU projects ELPA is collaborating on, the LIVERHOPE project which is ongoing (2017 – 2021). The objective of LIVERHOPE is to (1) perform two trials to investigate the safety, tolerability and efficacy of the combination of simvastatin plus rifaximin in patients with decompensated cirrhosis to halt progression to ACLF, decrease complications of the disease, reduce hospital readmissions, improve cost-effectiveness, improve patients quality-of-life, and increase survival, (2) identify biomarkers of response to treatment and disease progression that can be useful in clinical practice, (3) adequately disseminate the results of the study so that the information reaches the patient population, (4) increase awareness about chronic liver disease so that preventive measures can be put in place to minimise the burden of disease and (5) reduce the social stigmatisation of patients with chronic liver disease.

- Prof Jeffrey V. Lazarus, Associated Researcher at ISGlobal, CHIP, Rigshospitalet, University of Copenhagen WHO Collaborating Centre on HIV and Viral Hepatitis, Editor in Chief, *Hepatology, Medicine and Policy* provided an overview of the 2016 Hep-CORE report which monitored the European policy responses to viral hepatitis and aimed to evaluate the extent to which ELPA member countries follow key international recommendations for good practices in addressing viral hepatitis. Prof Lazarus noted that the investigative framework for Hep-CORE was drawn from *Hepatitis B and C: an action plan for saving lives in Europe*. With the participation of 27 ELPA member countries, Prof Lazarus indicated the Hep-CORE study is key as it provides the only European viral hepatitis policy monitoring tool, uniquely it is patient-led and it casts a wide net to gather a comprehensive for each country's situation, and for the 25 European and 2 additional Mediterranean countries' situation as a whole. Among the results presented, Prof Lazarus highlighted the fact that 11 countries have a written HBV and/or HCV strategy, 24 countries have national clinical guidelines for the diagnosis and treatment of HCV, in 16 countries there are HCV testing/screening sites outside of hospitals for high-risk populations but 20 countries indicated they did not have the option for HCV patients to be treated outside the hospital setting, Concluding his presentation Prof Lazarus said that the key takeaways from Hep-CORE indicated that global elimination of HCV was now a possibility but changes need to be made (1) moving from individual management of HCV to population management (2) strengthening partnerships between healthcare professionals, policy-makers, and industry to develop and implement local strategies.

Concluding the ELPA symposium, the stage was given to Mr Ingo van Thiel, an ELPA member representative, who outlined how patients would like to see the future in liver disease through his presentation entitled "*The next 20 years of hepatology: a patient wish list*".

Mr van Thiel started by stating that many things have already been achieved and then moved on to outline the different items on the liver disease patient's wish list:

- Increased patient group involvement in the science and clinical trial set up
- Affordable and accessible diagnostics and treatments
- Improved symptom management – disease specific and general
- A cure for chronic hepatitis B
- A protective vaccine for hepatitis C
- A European vaccine and screening of blood products for HEV-RNA
- Restore immune tolerance in Autoimmune liver diseases (AILD)
- Drugs to prevent/revert fibrosis
- 3D printed human organs
- New imaging tools to replace biopsy
- Repairing genetic defects
- Target treatments that destroy cancer cells

Concluding his presentation Mr van Thiel noted that there was one thing that patients were sure of

hepatology after hepatitis C would not be boring!

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