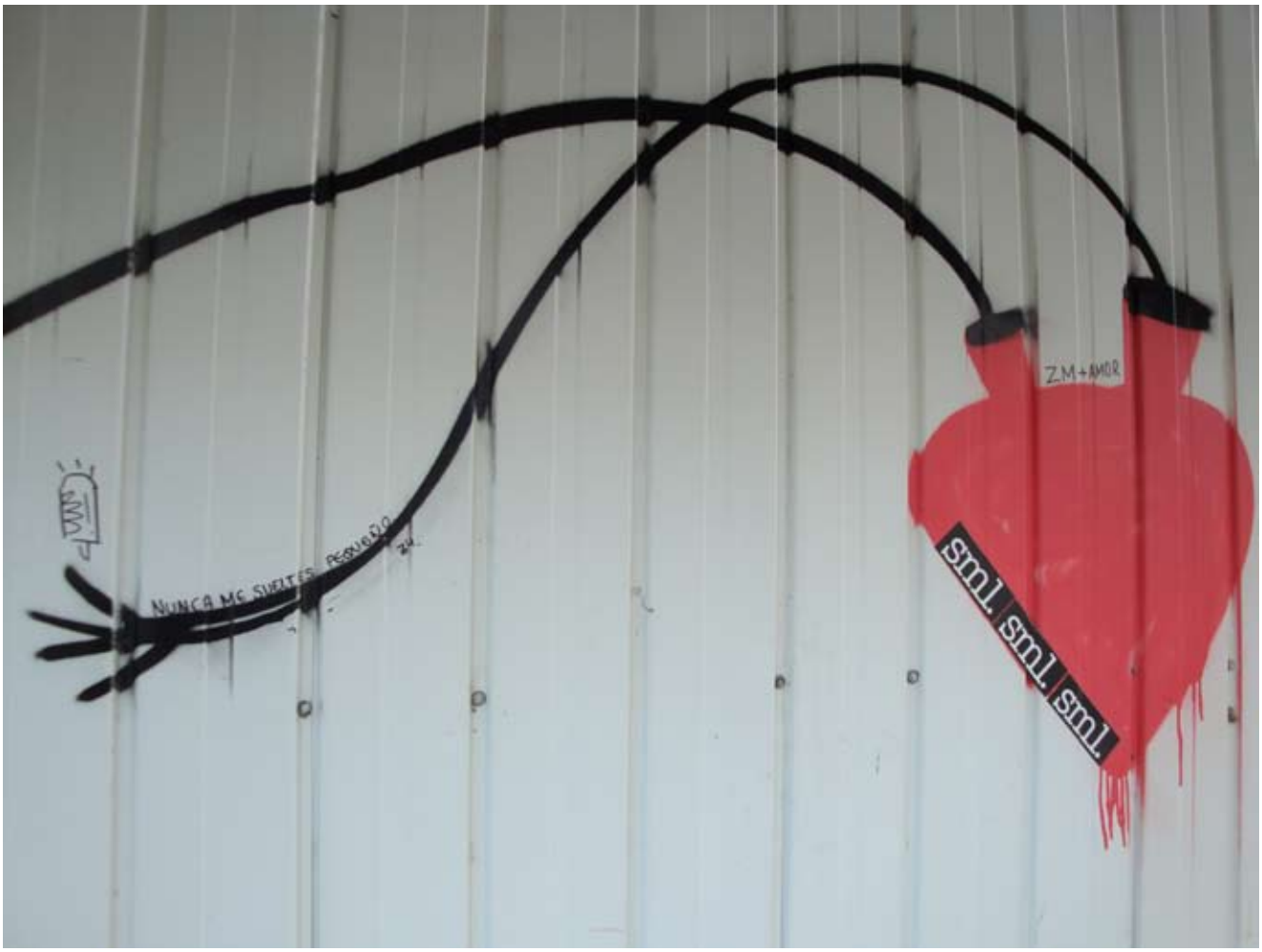
Hepatitis and stakeholders in Europe

Interview with Markus Peck-Radosavljevic

"We are considering the stakeholders that are involved in the management of the clinical condition of hepatitis": well said Markus Peck-Radosavljevic, Associate Professor of Medicine at the Department of Gastroenterology and Hepatology at the Medizinische Universität Wien, Austria, in the speech he gave during EASL meeting in Barcellona, where I met him.
A medical doctor usually works on patients or on scientific perspectives directly related to an agent that causes the disease. Why is it important to think about stakeholders, when you are speaking about hepatitis?
As a medical doctor, my main interest is my patient but, as a official of a scientific organization that is engaging not only in science, but also in political action and lobbying for a certain disease, like in our case liver disease, for me it also important to talk about the other stakeholders. This is the reason why EASL is becoming more and more interested also in things like epidemiology and therefore we are interested in public action, in political action and in also teaming up with other people involved in the field like patients organizations.

Numbers and figures about viral hepatitis are absolutely impressive. We need to understand the facts that are beyond these figures…

The numbers are fairly high but the numbers are also highly variable, even within Europe and especially globally. If we concentrate on Europe you will find countries where you have not such a high burden of viral hepatitis, especially, with incidences or preva-



lences of below 0.5%, but we have also countries where the prevalence is 10%. Some countries are just ahead in the management of those diseases, and this has historic reasons.

EASL puts emphasis on societal liver disease burden in Europe. What it means?

If we refer to numbers and figures, the two most important clinical condition related to liver are alcoholic liver disease and viral hepatitis, and the third most common is probably non-alcoholic fatty liver disease. Those are the three diseases that make up the vast majority of patients with liver disease in Europe. We feel that we really have to work for all of them, but especially in viral hepatitis there is also other parties who are very active, like the industry and the patients organizations. In other areas, like in alcohol and non-alcoholic fatty liver disease, there is not so much interest from other stakeholders and for that reason we are very actively engaged in those areas.

Speaking about viral hepatitis, what kind of dimensions are evaluated in order to define the societal burden?
On the one hand the problem is that we don't have a clear idea how many patients are really affected by viral hepatitis. On the other hand, viral hepatitis, as opposed to other causes of liver disease, is fairly easy to detect because screening just works with a little blood, as opposed to alcoholic liver disease and non-alcoholic liver disease, where you don't have a simple test. So, that means actually if you want to start a screening and an early detection effort, viral hepatitis is actually an ideal candidate because we have a very good and easy, not very expensive test and with that we could find probably most of the patients if we would try.

We know that now we are treating only the peak of an iceberg. One hundred years ago the Titanic crashed because of an iceberg, now we are in the condition to treat, thanks to the new drugs, people with hepatitis C but the risk is that the financial crisis and the cost of the drugs cause a crash for public health…

Well, there is some danger but I don't think there is immediate danger and, for one very important thing: not every patient with viral hepatitis needs treatment. It's estimated that only 20 to 30% of those patients actually will ever suffer any harm from their liver disease. The problem at the moment is that it's not so easy to define who will actually run into problems and who will not. Of course the search is also on for other markers, to better define patients at risk vs. patients not at risk, but this is something also for the future. For the moment, at the present, it would be already very good to detect all the patients and then we can consider whom we want to treat. I really want to point out that actually by an Italian study that has been featured here at the Conference it was clearly shown that most of the cost that comes from treating patients with liver disease, more than half of them comes from hospitalizations, and hospitalizations always occur late in the disease stage. That means yes, it's going to be more expensive if you find more patients and treat them early, but you will also save significant cost because you will have a lot less patients with advanced-stage liver disease, so in the long run I think it will really pay off to do this.

Efforts of researcher are focusing on the possibility to define markers that could shorten the period in order to define as early as possible the results of the efficacy of the therapy…

Well, you know, everybody is trying to shorten treatment, because all these treatments cause side effects. If you have them for shorter periods of time, it's much more easy to take for the patients. Shortening the follow-up has also an advantage for drug development, because if your follow-up is shorter you get your results earlier and that means you can move on with drug development much faster. So, the combination of shortened treatment durations plus shortened follow-up will help us a lot in finding out which of all these new substances are actually really good treatments and which of these substances are not worth pursuing.

Now we are speaking about 4 weeks...

Yes. think this has to be validated, I mean you have to compare the outcome of SVR4 with SVR12 and with SVR24, but I think there is a good indication that for the direct-acting antiviral drugs SVR4 could also be a good time plan and, if this holds true, it will be great.

The problem we have now is there is a lot of population still in need of therapy are not elegible to these drugs, or at least we don't have enough data…I am thinking about patients co-infected with HIV or transplant patients or people that are in advanced-stage of the disease.

Yes. For those patients the problem are the drug-drug interactions, so this has to be rigorously tested, so we understand that there is a great need and we really would like to treat those patients, however it has to be done safely. As we know for the two drugs that are protease inhibitors that are in the market right now, especially for one of them, it has a lot of drug-drug interactions, so it's really important to check out what can be really used for treatment of these patients. But as treatments durations will get

shorter, for example for the co-infected cohort, you could also think about like stopping your antiretroviral treatment for 3 months treating hepatitis C and then continue with the antiretroviral treatments. This approach is feasible, at least for the co-infected cohort. Of course, in liver transplantation you need your immunosuppression: you cannot stop that for three months, at least not without significant risks. For those patients we really have to define which substances can be combined with which, but there is actually very active research ongoing in this area as well.

Three year ago we were at EASL in Vienna the day before of the declaration by the World Health Organization that hepatitis is a global problem and emergency for public health. In the last three years we had witnessed big changes, WHO hepatitis, two DAAs in the market, many new compound are coming and we are thinking about a therapy without interferon. From your point of view, how can you explain all these shifts in a such short time?

I think there were two very important findings that helped this. First of all, hepatitis C research is really tremendously benefitting from HIV research because a lot of what is known about viral kinetics and so on was learned from the HIV community. The second and really major breakthrough for hepatitis C research was the so-called "replicon system" at the turn of the century, developed in 1999 actually. Before that it was not able to grow the virus in culture, so it was not able to test targeted agents in a culture system which made drug development incredibly difficult because you could only grow the virus in chimpanzees outside the human beings. Now, with the replicon system, out of a sudden you could test drugs in a petri dish and that's what started the revolution because the companies were starting to employ a rational drug design to develop all these drugs against the different components of the virus and that's when it started off and from then on it's just a blast. ■

Andrea Tomasini