HAART
HIV correlated pathologies
and other infections

KFactor

Editorial

Future is not what it used to be

Directly from the future, the following dialogue occurred inside a rocket ship, flying in the space. It was between medical doctors, nurses and others heroes. Despite it happened in the future, now it is old. Please, read it carefully, and after I will try to be more.. clear and adherent to our times.

"Four dead… the others in coma! And nothing we can do but watch them go.. one by one!
"Flash!"
"This could be! Interferon! It knocked out the virus in the lab animals!"
"Hurry!"
(the physician injects the Interferon in the patient's arm)
"Well doctor…?"
"The Interferon works! The fever is going down"
"Nurse – check their temperature every thirty minutes! We'll try injections again".

The above dialogue was published in a comic strip about half century ago: Flash Gordon cartoon has depicting the 'first' human use of interferon in 1960. It happened three years after the paper in which Isaacs and Lindenmann (1) described the phenomenon of viral interference: interferon is the substance that is released by infected cells and when it is added to uninfected cells it interferes to some extent with subsequent virus infection. This is the reason why Flash Gordon and friends were so enthusiastic about this new drug. We have to consider also that Flash Gordon is a cartoon published since January 1934 and it represented in some way the collective hopes and imaginations about a possible heroic future: a

mission in the space, the future new border. Flash has been popular in any medium during his history with -let's say a decadence- in recent years. We can suggest that it happened because science fiction 'cartoons, films literature and stories- adopted a more complex characters and plot, and also our everyday life is changed and changing faster and faster: now we are more skeptical regarding naïve stories and Flash Gordon, a simple black and white strip doesn't fit in the present, modern way of storytelling.

The same destiny seems to have been granted to interferon: patients and clinicians are looking to different solution in order to avoid hard to manage side effects, improve adherence and make simpler take care of ourself. Now the aim –or at least the hope- of patients and clinicians dealing with hepatitis C is to set up a therapy without interferon. This revolution starts now thanks a new drugs class that still needs peginterferon as backbone: the two first protease inhibitors that enrich the therapeutical armamentarium for patients and clinicians. The progress and the hope starts now, thanks to boceprevir and telaprevir. And many others new drugs are coming in the next years, for HCV and HBV, This is the reason way we say that future is not what it used to be. And the impact could be really impressive if we look at the numbers.

HCV is a blood-borne infectious that affects the liver and it is a leading cause of chronic liver disease, transplant and failure: with an estimate 170 million people infected worldwide and three to four million people newly infected each year, HCV puts a significant burden on patients and society. In the United States, an estimated 4.1 million Americans have been infected with HCV, of which approximately 3.2 million had chronic HCV infection. Chronic HCV infection is the cause of an estimated 8000 to 10000 deaths annually in the United States. The majority – about 75 to 85 percent- of HCV cases will develop into chronic infection. It is estimated 20 percent of patients with chronic HCV will develop cirrhosis within 20 years of infection. The mortality rate after cirrhosis has developed is 2-5 percent per year.

Estimations indicate that HCV caused more than 86.000 deaths and 1,2 million disability-adjusted life –years (DALYs) in the WHO European Region in 2002. Most of the DALYs (95%) were accumulated by patients in preventable disease stages. Chronic infections with HCV can lead to liver cancer and other serious and fatal liver diseases. About one-quarter of the liver transplants performed in 25 European countries in 2004 were attributable to HCV. The previously accepted standard treatment for HCV is peginterferon alfa combined with ribavirin, however this only cures 40-50 percent of genotype-1 chronic HCV patients. The majority of patients with hepatitis C have viral genotypes 1 and 4, which are generally less responsive to therapy than other genotype. There is a real need for more effective treatment options – specially for genotype 4, as no oral direct-acting antiviral are approved to treat this patient population.

About chronic hepatitis B estimates show us that approximately 350 million people worldwide are chronically infected with hepatitis B (approximately 5% of the world's population) and 75% of these cases occur in the Asia-Pacific region. Most people with chronic hepatitis B show no signs or symptoms, so many of those chronically infected are unaware of their status. A blood test can diagnose chronic hepatitis B. Patients should speak with their doctor about options available for this condition.

Now AASLD guideline for the hepatitis C includes telaprevir or boceprivir as add on to the standard care.

During the Liver Meeting in San Francisco Raymond T. Chung, professor at Department of Medicine Massachusetts General Hospital, Harvard medical School, Boston, gave a speech about how to use these new drugs. He said that "are very good drugs but use it smart". Summarizing his presentation, he underlined that this first generation PI influenced incredibly HCV care, because their potency. Resistance concerns limit to use these drugs with peginterferon plus ribavirin in genotype 1 HCV (not all genotypes created equal: there is 1b-1a disparity). Adherence is a key issue and PK and toxicities demand vigilance. Stopping rules- stated Chung- are clear: do not continue a failing regime. Costs are also a hard to manage issue. But we cannot forget that the new PI generation anticipates Direct Antiviral Agent (DAA) combos with improved potency, PK, tolerability and genotype coverage that could imply also freedom form interferon. According to prof. Chung speech the profile of the ideal oral DAA must include high potency, high barrier to resistance, not overlapping resistance profiles; it must be pangenotypic, with minimal adverse events (interferon sparing) and a good PK (once a day) in order to let a short therapy duration. It is next future.

For the present, in the last 2011 issue of HAART we decided to collect interviews and articles from the two international most relevant conference –EASL in Berlin and AASLD in San Francisco- in order to provide en overall picture of the DAA against the viruses responsible of hepatitis. In a next issue we are planning to provide an in-deep-report from the Italian "planet" of Hepatitis. AISF, FIRA and EpaC are doing a wonderful job and the goal of having a National Hepatitis Plan is behind the corner. Lets' say that really, future is going to be different.

Andrea Tomasini

[1] Isaacs, A. & Lindenmann, J. (1957). Virus interference: I. The interferon. Proc R Soc Lond Ser B Biol Sci 147, 258–267.