

Paris, 12 February 2019

Press release

Direct-acting antivirals: confirmation of their short-term clinical efficacy in "real life"

A study published in [The Lancet on 11 february 2019](#) shows that direct-acting antivirals have short-term clinical benefits in the treatment of hepatitis C virus infection. These results come from ANRS-funded interdisciplinary research conducted by clinicians, hepatologists, and epidemiologists of the Inserm, Sorbonne University and AP-HP and coordinated by Professors Fabrice Carrat and Stanislas Pol, and Dr H el ene Fontaine,¹ in 9895 patients of the ANRS CO 22 HEPATHER national cohort recruited in 32 centers in France.

The most recent treatments of hepatitis C virus (HCV) infection, the direct-acting antivirals (DAAs), are remarkably effective. Indeed, they eliminate the virus in almost all treated patients (95% in general) in 8 to 12 weeks. DAAs were first prescribed in France in 2014. Initially, priority was given to patients with advanced HCV infection, but from January 2017 DAA therapy was extended to all patients with chronic HCV infection.

The virologic efficacy of DAAs is well established, but until now prospective data on their clinical efficacy (ie, their impact on the progression of liver disease associated with HCV infection in real life) were scarce and related to highly selected patients or to patients from retrospective surveys. An ANRS-funded team of researchers has now compared clinical progression of HCV infection in patients receiving or not receiving DAA therapy. The researchers monitored clinical progression in "real life" in 9895 HCV-infected patients included between 2012 and 2015 in the ANRS CO22 HEPATHER cohort (see box below).

In these 9895 patients, who were followed up for a median period of 33 months², statistical analysis showed in the 7344 patients who received DAAs before the end of the study that this treatment was associated with reductions in mortality and in the occurrence of hepatocellular carcinoma (liver cancer). After adjustment for individual factors (age, disease staging, presence of other diseases, etc.), the patients treated with DAAs showed a 52% reduction in mortality risk and a 33% decrease in the risk of liver cancer compared with patients at a similar disease stage but not treated with DAAs.

¹ Fabrice Carrat (Institut Pierre Louis d'Epid miologie et de Sant e Publique, Sorbonne universit e, Inserm UMS-20 – unit e de sant e publique – h opital Saint-Antoine, AP-HP), Stanislas Pol (D epartement d'H epatoLOGIE, H opital Cochin AP-HP; Universit e Paris-Descartes; Inserm, Institut Pasteur), H el ene Fontaine (D epartement d'H epatoLOGIE, H opital Cochin, AP-HP).

² Median: the value that separates the higher half from the lower half of a data sample.

"We could have expected these results. It seems logical that the elimination of the virus causing the damage is linked to clinical improvement," said Prof Fabrice Carrat. "Our results show that these benefits are obtained soon after virologic control and the patients are no longer highly selected as in early trials. Our analysis reflects real-world efficacy for all patients."

The prolonged collection of data from these patients cured of an HCV infection will allow definition of the long-term benefit of DAA therapy and of the modalities needed for medical follow-up (How frequent should liver cancer screening be? How long after the cure? At what cost?). One of the difficulties sometimes encountered in this sort of study arises when patients who are cured are lost to follow-up. The "linking" of medical data from the patients of ANRS CO22 HEPATHER cohort to the national health data system (SNDS), which was validated by the French Data Protection Authority (CNIL) on 19 July 2018, should help researchers obtain exhaustive information on healthcare consumption by these patients over the long term.

This study was conducted in collaboration with the AFEF (French Hepatology Society) and supported by the ANR (French National Research Agency) in the framework of investments for the future and from industrial partners: Gilead, Abbvie, MSD, Janssen BMS, and Roche

The ANRS CO22 HEPATHER cohort initiated in 2012 in collaboration with the French Association for the Study of the Liver now includes more than 21 000 patients (6500 infected by HBV, 14 600 by HCV, and 95 by both). The main purpose of this cohort, which is coordinated by Professors Fabrice Carrat and Stanislas Pol, and Dr H el ene Fontaine, is to measure the benefits and risks associated with different therapeutic modalities in the management of hepatitis B and hepatitis C and to identify their individual, virologic, environmental, and social determinants.

Source:

"Clinical outcomes in patients with chronic hepatitis C following direct-acting antiviral therapy: a prospective cohort study".

Prof. Fabrice CARRAT, PhD,1,2 H el ene FONTAINE, MD,3 C eline DORIVAL, PhD,1 M elanie SIMONY, MS,4 Alpha DIALLO, MD,5 Prof. Christophe HEZODE, MD6 Prof. Victor DE LEDINGHEN, MD,7 Prof. Dominique LARREY, MD,8 Georges HAOUR, MSc,1 Prof. Jean-Pierre BRONOWICKI, MD,9 Prof. Fabien ZOULIM, MD,10 Prof. Tarik ASSELAH, MD,11 Prof. Patrick MARCELLIN, MD,11 Prof. Dominique THABUT, MD,12 Prof. Vincent LEROY, MD,13 Prof. Albert TRAN, MD,14 Prof. Fran ois HABERSETZER, MD,15 Prof. Didier SAMUEL, MD,16 Prof. Dominique GUYADER, MD,17 Prof. Olivier CHAZOUILLERES, MD,18 Prof. Philippe MATHURIN, MD,19 Sophie METIVIER, MD,20 Prof. Laurent ALRIC, MD,21 Ghassan RIACHI, MD,22 J er ome GOURNAY, MD,23 Prof. Armand ABERGEL, MD,24 Prof. Paul CALES, MD,25 Prof. Nathalie GANNE, MD,26 Prof. V eronique LOUSTAUD-RATTI, MD,27 Louis D'ALTEROCHE, MD,28 Xavier CAUSSE, MD,29 Claire GEIST, MD,30 Anne MINELLO, MD,31 Isabelle ROSA, MD,32 Moana GELU-SIMEON, MD,33 Isabelle PORTAL, MD,34 Prof. Fran ois RAFFI, MD,35 Marc BOURLIERE, MD,36 Prof. Stanislas POL, MD37 for the French ANRS CO22 Hepather cohort

The Lancet Published online the 11 February [http://dx.doi.org/10.1016/S0140-6736\(18\)32111-1](http://dx.doi.org/10.1016/S0140-6736(18)32111-1)

➤ Scientific contact:

Fabrice Carrat

fabrice.carrat@iplesp.upmc.fr

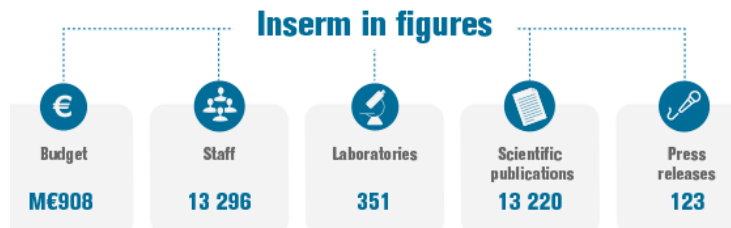
➤ ANRS press contact

S everine Ciancia

01 53 94 60 30 - information@anrs.fr

The ANRS is a funding body that coordinates research on HIV/AIDS and hepatitis. The ANRS runs, evaluates, coordinates, and finances research programs, whatever the scientific field concerned (basic, clinical, public health, or vaccine research). The ANRS brings together in France and abroad researchers from all disciplines. Its annual budget of around 50 million euros is provided mainly by the ministry of research and the ministry of health. The ANRS has been an autonomous agency of Inserm since 2012.

The AP-HP, or the Paris university hospitals, is an internationally recognized stakeholder in clinical research in France and the rest of Europe. Every year, its 39 hospitals provide care for 8.3 million patients, at consultations, in emergency departments, during scheduled admissions, and in the home care setting. The AP-HP takes pride in its duty to make public healthcare available to everyone 24/7. It is the leading employer in the Paris Ile-de-France Region: 100 000 people – doctors, researchers, paramedics, administrative staff, and workers



Sorbonne University *By joining two leading universities* at the center of Paris, an exceptional center of knowledge has been recreated under the world-renowned Sorbonne name.* Sorbonne University is a world-class research university, presenting the comprehensive disciplinary range of arts, humanities, social sciences, natural sciences, engineering and medicine. Sorbonne University is at the crossroads of knowledge and capable of responding to the intellectual and scientific challenges of the 21st century. The University offers its 55,600 students the best educational opportunities for success in each of their personal and professional projects, through mono-disciplinary, bi-disciplinary and interdisciplinary programs. Sorbonne University research draws on more than 3,400 professor-researchers and another 3,000 researcher partners from the major French research organizations. In addition to Nobel Prizes and other awards, the university has exceptional transdisciplinary institutes and is the headquarters for the European Marine Biological Research Centre. International co-operation at Sorbonne University enables its students, academic staff and researchers to increase their exchanges with the rest of the world.

* Paris-Sorbonne and Pierre & Marie Curie (UPMC) Universities