

The need for surveillance: How to implement it?

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Era of direct-acting antivirals



- HCV treatment changed incredibly
- DAAs are very effective
- Failure occurs in small proportions
 - Link with resistance associated mutations



Nomenclature



- Only for this presentation

Resistance associated mutations



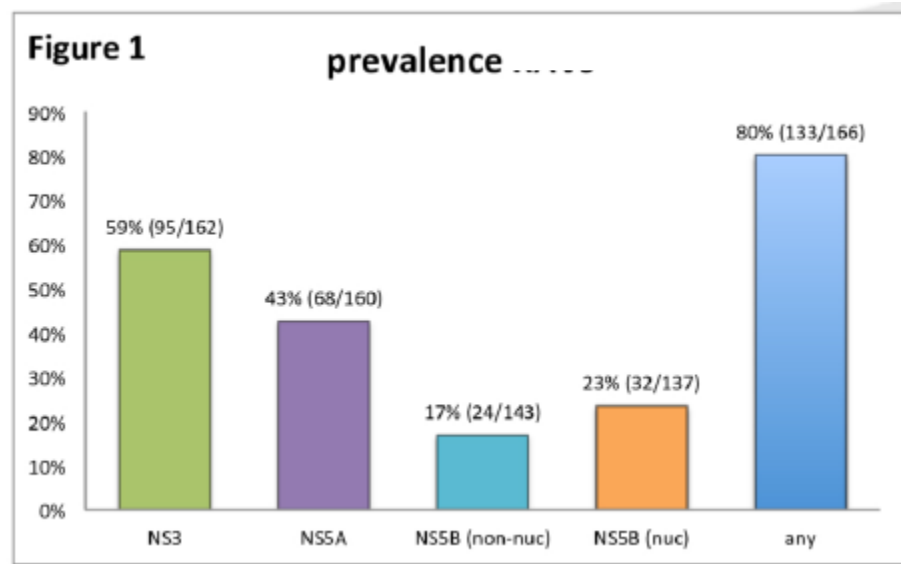
Prevalence of resistant associated mutation



- Difference in prevalence over
 - Genotype
 - Geographic region
 - Method of sequencing
- Limited studies with real-life data



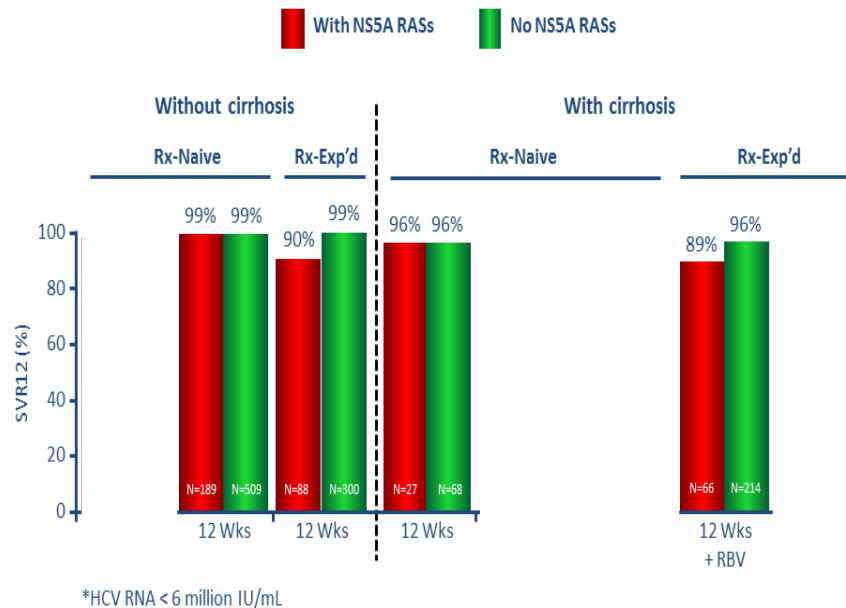
133/166 patients with GT 1 had a baseline resistance associated mutation



H. Peiffer, S.Susser et al. EASL 2016



SVR changes in the presence of baseline resistant associated mutations



S. Zeuzem et al. AASLD 2015



Why is surveillance important?



- Resistance has influence on DAA treatment
 - C.Hezode et al. EASL 2016 – first incurable patient
- Important to understand the mechanism of resistance



HCV sequence can provide important information



- Occurrence of resistance associated DAA treatment failure
- Mutations patterns associated with DAA treatment failure



Collaboration is key



- Large datasets are required
- A combined European effort is essential to gain more insight into occurrence of DAA failure



Hepcare: a European registry for clinical cases of DAA treatment failure



HepCare



2014 implemented in the Netherlands

- European multicenter study
 - Clinical cases of failure
- Part of ESAR
 - Sister of the SPREAD database
- Central Database at International Health institute in Luxembourg



European society for translational antiretroviral research - ESAR

- More than 33 countries
- Combines the efforts of virologists, clinicians and epidemiologists
- Extensive experience with collaboration
 - SPREAD (HIV)
 - CAPRE (HBV)



Benefits of contributing



- Part of joint publications
-



L.E. Hermans, V. Svicher et al. 2015 Journal of infectious diseases



Combined Analysis of the Prevalence of Drug-Resistant Hepatitis B Virus in Antiviral Therapy-Experienced Patients in Europe (CAPRE)

Lucas Etienne Hermans^{1,2,a}, Valentina Svicher^{3,a}, Suzan Diepstraten Pas², Romina Salpini³, Marta Alvarez⁴, Ziv Ben Ari⁵, Greet Boland¹, Bianca Bruzzone⁶, Nicola Coppola⁷, Carole Seguin-Devaux⁸, Tomasz Dyda⁹, Federico Garcia⁴, Rolf Kaiser¹⁰, Sukran Köse¹¹, Henrik Krarup¹², Ivana Lazarevic¹³, Maja M. Lunar¹⁴, Sarah Maylin¹⁵, Valeria Micheli¹⁶, Orna Mor¹⁷, Simona Paraschiv¹⁸, Dimitrios Paraskevis¹⁹, Mario Poljak¹⁴, Elisabeth Puchhammer-Stöckl²⁰, François Simon¹⁵, Maja Stanojevic¹³, Kathrine Stene-Johansen²¹, Nijaz Tihic²², Pascale Trimoulet²³, Jens Verheyen²⁴, Adriana Vince²⁵, Nina Weis²⁶, Tülay Yalcinkaya²⁷, Snjezana Zidovec Lepej²⁵, Carlo Perno³, Charles A. B. Boucher² and Annemarie M. J. Wensing¹ on behalf of the HEPVIR working group of the European Society for Translational Antiviral Research (ESAR)

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L.M. Hofstra et al. 2016

Clinical infectious diseases



Transmission of HIV Drug Resistance and the Predicted Effect on Current First-line Regimens in Europe

L. Marije Hofstra^{1,2}, Nicolas Sauvageot¹, Jan Albert^{3,4}, Ivailo Alexiev⁵, Federico Garcia⁶, Daniel Struck¹, David A. M. C. Van de Vijver⁷, Birgitta Åsjö⁸, Danail Beshkov⁵, Suzie Coughlan⁹, Diane Descamps¹⁰, Algirdas Griskevicius¹¹, Osamah Hamouda¹², Andrzej Horban¹³, Marjo Van Kasteren¹⁴, Tatjana Kolupajeva¹⁵, Leondios G. Kostrikis¹⁶, Kirsi Liitsola¹⁷, Marek Linka¹⁸, Orna Mor¹⁹, Claus Nielsen²⁰, Dan Otelea²¹, Dimitrios Paraskevis²², Roger Paredes²³, Mario Poljak²⁴, Elisabeth Puchhammer–Stöckl²⁵, Anders Sönnernborg^{3,4}, Danica Staneková²⁶, Maja Stanojevic²⁷, Kristel Van Laethem²⁸, Maurizio Zazzi²⁹, Snjezana Zidovec Lepej³⁰, Charles A. B. Boucher⁷, Jean–Claude Schmit¹, and Annemarie M. J. Wensing² for the SPREAD Program

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Benefits of contributing



- Submit your own research question
 - Access to HepCare data
- Use HepCare data as a reference
- Contribute into better patient care



Governance



- Submission does not affect ownership
- Permission will be requested when new research question is submitted
- We encourage to publish your own data first



HepCare inclusion criteria



- > 18 years old
- HCV infection
- Failure/relapse on a DAA regimen
- Sample available



Minimal requirements

- Patient demographics
- Fibrosis stage

- Viral load
- Antiviral therapy response

- Genotypic resistance test result at failure
- Encourage a baseline sequence



How to submit

← →  www.esar-society.eu



<http://www.esar-society.eu/>

Transmission of HIV Drug Resistance and the Predicted Effect on Current First-line Regimens in Europe.

Hofstra LM, Sauvageot N, Albert J, Alexiev I, Garcia F, Struck D, Van de Vijver DA, Åsjö B, Beshkov D, Coughlan S, Descamps D, Griskevicius A, Hamouda O, Horban A, Van Kasteren M, Kolupajeva T, Kostrikis LG, Liitsola K, Linka M, Mor O, Nielsen C, Otelea D, Paraskevis D, Paredes R, Poljak M, Puchhammer-Stöckl E, Sönnnerborg A, Staneková D, Stanojevic M, Van Laethem K, Zazzi M, Zidovec Lepej S, Boucher CA, Schmit JC, Wensing AM; SPREAD Program. *Clin Infect Dis.* 2016 Mar 1;62(5):655-63.

The CAPRE study by the HEPVIR working group has been published in *The Journal of Infectious Diseases* August 15th.

An interesting article about the CAPRE study has been written by Reuters. Please find the article [here](#).

**SPREAD Database
& Interactive map**

HepCare Database

How to submit



- Web-based submission form
- For login
 - K.G.Siebelt@umcutrecht.nl
- Larger dataset?
 - data dump is available

HepCare
Hepatitis C antiviral therapy
failure registry

username:

password:

login

[\(support\)](#)



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Closing remarks



- A combined European effort is essential to gain more insights into the clinical correlates and mechanisms of DAA failure
- Hepcare is the DAA Failure registry database provided by ESAR
- Contribution leads to joint publication and does not affect data ownership

