ACADEMIC INSTITUTES

Ceinge Biotecnologie avanzate s.c. a r.l. - ITALY
www.ceinge.unina.it

Erasmus Medical Centre - THE NETHERLANDS
www.erasmusmc.nl

University of Ghent - BELGIUM
www.ugent.be

University of Birmingham - UNITED KINGDOM
www.bham.ac.uk

University of Gdansk - POLAND
www.ug.gda.pl/en

The Egyptian Company for Blood Transfusion Services, Egyblood - EGYPT
www.vacsera.com

University of Oxford - UNITED KINGDOM
www.ox.ac.uk

Klinikum der Johann Wolfgang Goethe Universitaet Frankfurt - GERMANY
www.klinik.uni-frankfurt.de

University of Pisa - ITALY
www.med.unipi.it/medint

COMPANY

Novartis Vaccines & Diagnostics s.r.l. - ITALY
www.novartis.com

SMEs

Okairos S.r.l. - ITALY
www.okairos.it

ALTA Srlu - ITALY
www.altaweb.eu

HEPACIVAC

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COMMISSION

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Sixth Framework
Programme

HEPACIVAC

NEW PREVENTATIVE AND THERAPEUTIC HEPATITIS C VACCINES: FROM PRE-CLINICAL TO PHASE 1

EUROPEAN
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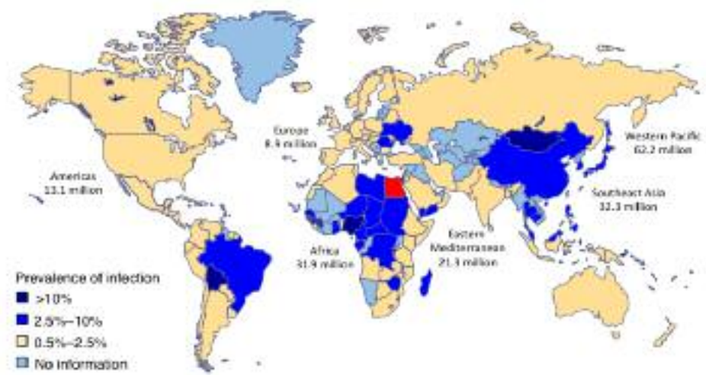
HEPACIVAC SUMMARY

Hepatitis C virus (HCV) is a major cause of liver disease globally. The virus is readily able to set up persistent infection, leading to chronic liver inflammation, cirrhosis, liver failure and liver cancer. Current treatments, although improving rapidly, are costly, imperfect and associated with major side-effects. The Centers for Disease Control estimate that there are approximately 170 million people infected worldwide. The Middle East and North Africa region suffers from high prevalence of unnecessary medical injections and transfusions, reuse of needles and syringes, needle-stick injuries among health care workers, and skin scarifications. For more than a decade, Egypt has been widely regarded as having an epidemic, with the highest recorded prevalence of HCV in the world. HCV is currently the most significant public health problem in Egypt.

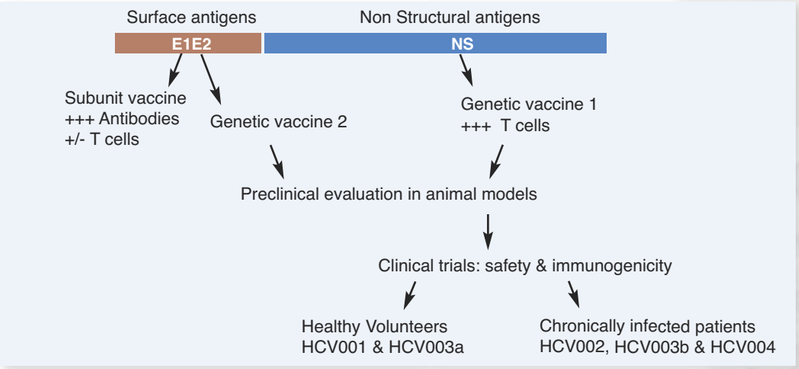
Estimated 170 Million Persons With HCV Infection Worldwide
Egypt has the highest prevalence of HCV infection in the world



Currently, there is no effective HVC vaccine; therefore the development of new preventive and therapeutic vaccines would be a major step forward.

The final aim of the HEPACIVAC project was to develop efficacious prophylactic and therapeutic vaccines to HCV. For this purpose, two vaccine companies in Europe, Okairos (a Biotech company created as a spin-off from Merck Inc.) and Novartis Vaccines & Diagnostics, have joined their efforts with several European groups and one institution from Egypt. Okairos, in collaboration with CEINGE, has developed a gene based HCV vaccine candidate, which encodes for the HCV Non Structural region and utilizes adenoviral vectors for delivery. This vaccine elicits potent T cell responses and, in animal models, was shown to be very efficacious in the prevention of HCV acute and chronic infection. A second vaccine candidate, previously developed by Novartis and based on the capacity of the HCV envelope glycoproteins to elicit neutralizing antibodies was studied at preclinical level.

The goal of the HEPACIVAC project was to develop these two HCV vaccine components both at the pre-clinical level by testing safety, tolerability and immunogenicity, and at the clinical level by testing the two vaccines in healthy volunteers for safety and dose optimization and in chronically infected patients with and without the gold standard therapy.
During the course of the project it was decided to “merge” the two candidate vaccines into a single technological platform, whereby both the structural proteins (Okairos’ vaccine) and the envelope proteins (Novartis’ Vaccine) were encoded into highly immunogenic adenoviral vectors. Following administration of adenoviral vectors by intramuscular injection was possible to elicit both arms of the immunological response.
The Okairos vaccine was successfully tested in five separate Phase I clinical trials under supervision of the PIs from the University of Oxford and University of Pisa and yielded excellent safety and immunogenicity results. Interestingly, the quality of the results prompted the initiation of a large Phase II clinical trial to test the efficacy of the prophylactic HCV vaccine, sponsored by NIH and approved by FDA, which is now ongoing in USA.



The ambitious but realistic goals of this unique project have required the expertise, the optimal organization and the strong coordination that can be provided by the successful collaboration of industrial institutions like Novartis and Okairos, and the excellent academic partners (CEINGE, University of Oxford, Erasmus Medical Center, University of Ghent, University of Birmingham, University of Gdansk, Egyblood, University of Frankfurt, University of Pisa) and the scientific know-how of the collaborators experience both in pre-clinical studies and in clinical trials.

HEPACIVAC OUTCOME

The HEPACIVAC project allowed testing of two promising vaccines alone and in combination in preclinical studies and performing Phase I clinical trials of the genetic vaccine expressing the HCV Non Structural antigens:

1. Prophylactic trials, in healthy volunteers for safety and dose optimization;
2. Therapeutic trials, in chronically infected patients with and without anti-viral therapy.

Moreover, this project aimed at standardizing the procedures for pre-clinical and clinical trials for HCV vaccines.

- **Two Clinical studies in healthy volunteers (HCV001 & HCV003a) for safety, dose and administration regimens optimization demonstrated that the *vaccine is very safe & highly immunogenic***

- **Three Clinical studies in chronically infected patients (HCV002, HCV003b & HCV004) with and without the gold standard therapy are still in progress; *interim data showed that the vaccine is safe and immunogenic***

HEPACIVAC ALLIANCE

The HEPACIVAC consortium was composed by twelve partners from seven countries. The main characteristic of this Consortium was the presence of two vaccine companies in Europe: OKAIROS and Novartis joined forces for the development of two of the most promising HCV vaccine so far available worldwide. CEINGE has lead the project and, together with Okairos and Novartis Vaccines & Diagnostics, has ensured an objective oriented industrial approach and guaranteed the full exploitation of the achieved results.

The two companies were flanked by important European partners for the basic research necessary to develop and standardize pre-clinical and clinical trials. These participating groups have been carefully chosen for their technical expertise and scientific excellence. The most excellent scientists in the field of vaccine design and development have taken part to this project. Some of them have already cooperated in many other projects within EU Programs and other initiatives. In addition, in the HEPACIVAC project it was also involved one partner for the Mediterranean area, Egypt with strong interest and commitment to HCV prevention and therapy due to the very high prevalence of infection in Egypt.

This project has contributed to the training of young scientists in the diverse methodologies employed and transfer of knowledge between participants groups.