## **Description for the general public**

Viral hepatitis C is the disease that affects even 150 million people worldwide and results in a death almost 700.000 people yearly. This disorder contributes to gradual development of liver insufficiency, its cirrhosis and in a portion of patients – also hepatic cell cancer. Moreover, many patients present so called extrahepatic manifestations, mainly of autoimmune background. Among the most common are rheumatoid arthritis , progressive kidney insufficiency, skin alterations and disturbances of thyroid functions. Treatment of viral hepatitis C for about 20 years was dependent on drugs based on cytokine interferon. These therapies, however, were characterized by insufficient efficiency and prevalence of unwanted effects. Fortunately, since couple of years ,on world markets , but also in Poland are available novel noninterferon therapies, so called Directly Acting Antivirals (DAA). They can eradicate virus in almost one hundred percent efficiency with minimal adverse effects.

Long lasting persistence of HCV (virus) in the body results in a number of disturbances in the immune system of patient. Numbers and functions of many subsets of white blood cells are subject of essential change. Cytokines, signal transferring proteins among cells, show major departures from the norm. It contributes to the formation of various systemic and hepatic disturbances.

Novel DAA therapies in contrary interferon ones, act directly on virus, without participation of own immune response of patient. Initial research reports indicate the possibility that even after successful treatment, patient's immunity becomes faltered. It would mean, that even person considered cured still would remain in a group of increased risk of development liver cancer or autoimmune complications. Indeed, scientists recently postulate, that the risk of liver cancer induction or its relapse following DAA therapy, still remains increased.

Until now studies of the immune system in the course and after noninterferon therapy were carried out on small group of patients and did not attempted to search the link between patient clinical status and immunological anomalies. In the current project we wish to test these relationships. We plan to examine patients before, directly after DAA therapy and one year later. At each planned patient visit we wish to describe general clinical status of patient In detail, advancement of liver disease (including eventual cancer formation). Presence of autoimmune phenomena, patient's mood and eventual appearance of novel disorders. We will also search for metabolic diseases such as obesity, diabetes or arterial hypertension – its appearance and the course also show some link with immunological disturbances of viral hepatitis C affected patient.

At the same time we will collect blood from patients for studies on their immune system. Before onset of treatment we will assess the range and degree of departures from the norm of blood immune cells and various mediator proteins. In subsequent studies we will screen the evolution of changes-whether immune system returns to normal, or not and to what degree. The results will be referred to the general status of patient.

In each of examine d patients we will determine his or her genotype. It has been shown that some gen e variants linked with the immune system show relationship with the course of chronic viral hepatitis C. The study offering such complex evaluation of a large patient group treated by means of the most modern drugs is undoubtedly pioneering in this field. We hope that the results of our study will help to answer whether patients already virus free, are still constitute the group of increased risk of complications characteristic for disease in question. If yes, we wish to pinpoint some subgroups in which such complications are especially likely.

We wish also to demonstrate whether such factors as age, sex, accompanying diseases, some genetic variants or baseline degree of liver damage may contribute to the persistence of immune complications having an impact on health and the duration of patient life.