ABSTRACT

This research has been registered in http://www.clinicaltrials.gov/ the *21/07/2020* under the n° *NCT04481633.*

Sponsor of this research:
CHU TOULOUSE – Toulouse, France
Source of grants: PHRC

Title:
Real-life evaluation of the efficacy of pre-exposure treatment with Hydroxy-Chloroquine on the risk and severity of COVID 19 infection in patients receiving long-term treatment for systemic lupus erythematosus and/or Gougerot's disease.

Short title:
Efficacy of pre-exposure treatment with Hydroxy-Chloroquine on the risk and severity of COVID 19 infection

PREPCOV study

Brief summary:
There is a pandemic in the world by COVID 19. Currently, the pharmacological curative or prophylactic treatments for this infection are not known. Recent studies have suggested that Hydroxy-Chloroquine could be effective in vitro and in vivo against COVID 19. The main objective of this study is to assess in patients with autoimmune disease treated with long course Hydroxy-Chloroquine initiated before the pandemic COVID 19 had an independent protective effect on the risk or the severity of infection with COVID 19.
With the substantial modification and the current evolution, the main complementary objective would be to evaluate the post-vaccination Ac titer according to the treatments received or the type of pathology among the 3 large current Prepcov groups. The threshold of 140 BAU/mL being considered as the one from which a vaccine protection is effective, it could thus be evaluated the influence of the received treatment or the type of pathology in the various groups on the proportion of patients having a significant post-vaccine immunity.

Detailed description:
A pre- or post-exposure treatment strategy has been validated in some infectious diseases. In particular, in HIV infection, this type of prophylactic treatment reduces the rate of infection in at-risk populations. The first studies from Chinese show that in case of immunosuppression or immunosuppressive treatment, whatever the causal pathology, COVID19 infection is more severe. We have a population of patients with lupus (SLE) or Gougerot's disease (SGD) who are treated for a long time, with Hydroxy-Chloroquine. The protective effect against COVID19 infection of Hydroxy-Chloroquine compared to populations not exposed to this drug requires to be assessed in patients and their control groups under or without immunosuppressive treatments.
It is hypothesized that long-term treatment with Hydroxy-Chloroquine in SLE or SGD taken in its usual indication before the onset of the pandemic could decrease the number of COVID19 infections and/or the intensity of the disease.

Primary outcome:
The main objective of this study is to assess in patients with SLE or SGD, whether long-term Hydroxy-Chloroquine therapy initiated before the COVID 19 pandemic had an independent protective effect on the risk of infection with COVID 19. The diagnosis of COVID-19 past infection will be made by serology.

Secondary outcomes:
Determine whether long-term use of Hydroxy-Chloroquine initiated prior to the COVID 19 pandemic had a protective effect on the symptomatic or severe form of COVID 19 infection.

Determine whether combination with an immunosuppressant such as Azathioprine or Methotrexate has had an adverse effect on Hydroxy-Chloroquine induced protection, in terms of risk of infection and symptomatic or severe disease.

Complementary outcomes:
- Evaluate the protective effect of vaccination against Covid 19 infection according to the type of treatment and the group. The threshold of 140 BAU/mL being considered as the one from which a vaccine protection is effective, it could thus be evaluated the influence of the treatment received or the type of pathology in the various groups on the proportion of patients having a significant post-vaccine immunity.
- Evaluate the post-vaccination Ac titer as a function of the treatments received or the type of pathology in the 3 main current Prepcov groups.
- Evaluate the influence of the type of pathology on the decision to vaccinate.

Study design:
Prognostic study exposed/not exposed to Hydroxychloroquine with multicenter prospective inclusion on 12 centers comparing patients treated or not treated with Hydroxy-Chloroquine associated or not with immunosuppressive therapies.

Eligibility criteria:
Inclusion criteria:
800 patients will be included initially with 400 SLE/SGD patients treated with Hydroxy-Chloroquine (HC) with or without immunosuppressants (IS)Azathioprine, MMF (mycophénolate mofétil), corticosteroid therapyor Methotrexate (HC+ group, n=400) and an unexposed group of 400 patients without treatment with Hydroxy-Chloroquine with or without immunosuppressants (HC+ group, n=400; including HC- IS+ n=200; HC- IS-, n=200).

Exclusion criteria:
-Anti-CD20 or Cyclophosphamide taken during the six months prior to the completion of the COVID 19 serology.
- Refusal of a blood test for antibodies to COVID-19.
- Protected adults
- Recent plasma or transfusion
- Pregnant or breastfeeding women.
- Lack of health insurance coverage

Arm number :
Prognostic study exposed, unexposed to Hydroxy-Chloroquine with prospective inclusion of patients. A first group will consist of 400 SLE/SGJD patients who are routinely taking Hydroxy-Chloroquine before and during the pandemic with or without combination with an immunosuppressant such as Azathioprine or Methotrexate.
The control group will consist of 400 patients not taking Hydroxy-Chloroquine. This group will include patients seen as part of the usual follow-up for primary biliary cholangitis, or viral hepatitis C cured without significant hepatic fibrosis. Also included in this group will be patients with autoimmune hepatitis whose usual treatment is Azathioprine and patients with SLE/SGD on Azathioprine or Methotrexate but not taking Hydroxy-Chloroquine for any reason.

Intervention:
Usual follow-up of each patient in real life.

Number of subjects:
800 patients were initially planned.
The current numbers of 524 patients ensure a power greater than 90% for the response to the new main complementary objective.

Statistical analysis:
The analysis of the main objective will be based on a logistic regression model incorporating potential confounding factors together with the intake of Hydroxy-Chloroquine.
The analysis of the main complementary objective will be based on a logistic regression model incorporating potential confounding factors together with the group ((HC+, HC- IS+, HC- IS-).

Conditions :
Infectious diseases therapy

Key-words :
COVID-19 infection, prophylaxis, severity, pre-emptive therapy, Hydroxy-Chloroquine