Antiviral and Immunomodulatory Interferon-Beta in high-risk COVID-19 patients: a phase II clinical study

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The rapid and devastating outbreak of Coronavirus disease 2019 (COVID-19) pandemic highlighted the need of developing therapeutic options to control or prevent virus spreading. Most of the efforts focused on the repurposing of existing antiviral agents, thus shortening the timelines needed for clinical experimentation (1). Among the many drugs under evaluation all over the world, type I Interferons (IFN-I) have been considered and are presently being evaluated in clinical trials, either as monotherapy or in combination with other compounds. In particular, IFN-β proved effective in alleviating COVID-19 symptoms when used in combination with lopinavir and ritonavir (2) and in reducing mortality when combined with hydroxychloroquine and other antivirals (3). When given as monotherapy, subcutaneous IFN-β1a had no significant effect in hospitalized COVID-19 patients at advanced disease stage, although elderly patients seemed to benefit with respect to adult patients (4). Instead, inhaled IFN-β1a attenuated the clinical consequences of COVID-19 (5). An ensemble of studies, some of them carried out in our laboratories, revealed that, in addition to the antiviral activity, IFN-I exhibit important immunoregulatory effects, including the increase of neutralizing antibodies and the induction of both innate and adaptive cellular immunity (6). Based on these premises and on the evidence of a defective IFN-I production/response in high-risk patients (6), we designed a phase II clinical trial to explore the efficacy of IFN-β1a in reducing the risk of progressing to severe COVID-19 in SARS-CoV-2-infected elderly patients with mild symptoms. Our study foresees four discontinuous subcutaneous administration of low doses of IFN-β1a in the early phase of infection, considered the best time window to exploit its immune activating properties in addition to its antiviral effects. Sixty patients either hospitalized or at home will be enrolled and randomized in 2:1 ratio to receive subcutaneous IFN-β1a (3×10^6 MIU, at day 1, 3, 7 and 10) or standard of care. Exploratory analysis on patients' blood samples will assess treatment-induced modulations of IFN-I signalling status, as well as of the frequency, activation status and functionality of defined leucocyte subsets and inflammatory markers expected to occur as a consequence of immunomodulatory effects of IFN-β. The clinical protocol has been approved by AIFA and by the national COVID-19 Ethic Committee. The start-up phase is now proceeding and the study is expected to start in January 2021 and complete the enrolment by the end of April. Overall, this clinical study may support a treatment option for high-risk elderly patients experiencing mild symptoms, for which no approved therapy is available so far, and will generate preliminary evidence on the underlying immune-based mechanisms of IFN-β in SARS-CoV-2 infection.

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