	DOMANDA DI PROGETTO 2020-2021	

DATI DEL RICHIEDENTE

Lions Club **Distretto**	**DISTRETTO 108 Ta1**
Persona richiedente (Presidente; Segretario-a; Socio Lions)	**Governatore**
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Altri Lions Clubs partecipanti:	
Altri partner di progetto : **(Privati, associazioni, uffici pubblici e.a.)**	Istituto di Ricovero e Cura a Carattere Scientifico "Sacro Cuore" - Negrar (VR)

DATI DEL PROGETTO

Denominazione progetto / titolo:	COVER study (COVid ivERmectin): a randomized, double-blind, multi-centre clinical trial on **ivermectin** for the early treatment of COVID-19

Contenuti del progetto: Il progetto corrisponde ai seguenti criteri : - Seguire i principi dell´etica lionistica - Rispettare lo Statuto di ALC § 10. pti. 1 -10. - Dimostrare un´ orientamento sociale/culturale - Estendersi possibilmente su ambito Club/Distretto/Regione - La dimensione del progetto esige probabilmente la collaborazione di vari Lions Clubs - Progetto con ripercussione verosimile oltre i limiti della propria zona - Destinazione prevalente, ma non esclusiva alle Regioni dell´Arco Alpino	
Quali sono i contenuti in particolar modo eccellenti del progetto presentato?	

Situazione di partenza/attuale: - Quale situazione ha portato allo sviluppo e alla proposta di questo progetto?	Recently **ivermectin**, one of the most widely used medicines in tropical area, whose discovery resulted in the Nobel Prize for Medicine in 2015, has been proven effective in vitro in reducing the viral load of SARS-CoV 2 infected Vero cells (Caly et al. 2020). Ivermectin is an "old drug" (Omura 2008) extensively used on hundred millions people for over 35 years for a wide range of parasitic infections, and with a broadening range of potential indications in recent years. Caly et al. hypothesized that the antiviral action against the SARS-CoV-2 in vitro was through the inhibition of the IMPα/β1 heterodimer-mediated nuclear import of viral proteins. However, the IC-50 for this antiviral effect was approximately 2.5 μM, equivalent to 2,190 ng/mL, that is about 50-fold higher than the peak concentration (Cmax) achieved in plasma after the single dose of 200 μg/kg, normally used as anti-parasitic drug in clinical practice (Muñoz et al. 2018; Buonfrate et al. 2019; Naquira et al. 1989). This difference raised concern on the likelihood of a successful use of ivermectin for the treatment of COVID-19 (Chaccour et al. 2020), even using doses 10-

	fold higher than the approved one (Schmith et al., 2020). However, the following points suggest that five daily doses of 600 and 1200 μg/kg in a fasted state, i.e. the schedule envisaged in the present CT, might allow to reach clinically relevant drug concentrations at the target organ (lung). Antiviral drugs can probably play a role in the first phase of the infection as it has been demonstrated for remdesivir (but not for other antiviral medicines like lopinavir), by reducing the viral load before clinical complications arise. A viral load reduction is a pre-requisite for a possible clinical effect.

Fini del progetto: - Quali traguardi si vorranno raggiungere con la conclusione positiva del progetto?	Expected results are that ivermectin is safe also at planned "antiviral" dosages in adults and efficacious in significantly reducing the SARS-CoV-2 viral load and consequently minimizing the risk of hospitalization and complications of COVID-19. In case of positive results, ivermectin could be recommended (also in low-income countries) as part of the therapeutic strategy for COVID-19.

Come si sviluppera´ il progetto: (singoli passi, contenuti o capitoli)	The project is aimed: 1) at defining if ivermectin, administered at dosage of 600 µg/kg or 1200 µg/kg QD for five consecutive days, is safe in patients with initial, asymptomatic or oligosymptomatic SARS_CoV-2 infection, 2) at defining if ivermectin, administered at the dosage(s) found to be safe, decreases the viral load of SARS-CoV-2 at Day 7. To assess 1. the temporal profile of viral load at baseline, day 7, 14 and 30 2. the time to clinical cure (for symptomatic patients) 3. the proportion of patients with virological clearance at day 14 and 30. 4. the hospitalization rate. 5. the COVID-19 Severity Score at day 14 and 30 To reach the study objectives we estimated the need of a sample size of at least 60 patients (for the safety analysis), up to 130 patients (for the efficacy analysis).
La partenza del progetto e´ prevista per: (dopo conferma dal Board ALC)	January 2021

Tempistica dei singoli contenuti del progetto: (Tappe, settimane, mesi, anni)	The rapid evolution of COVID-19 pandemic and the concerning epidemiological curves, together with the disappointing lack of therapeutic weapons, calls for an acceleration of the enrolment process in order to reach **as soon as possible** relevant results. The study has been already registered in clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT04438850) and has received ethical clearance by the competent Ethical Committees. The only sponsor of the project is the IRCCS Sacro Cuore Hospital and investigators of the DITM already began with enrollement of the first patients. Therefor we are ready to conduct the project in real time.
Conclusione prevista del progetto entro: (mass. tre anni dopo conferma da parte del Board ALC)	12 months
Preventivo dettagliato:	**a budget of 35.000 euros could cover the expenses planned for personnel, patient follow-up and testing.**

Ev. copertura spese non coperte dal contributo ALC, da parte di (indicare anche le somme dei singoli capitoli): - fondi del proprio Club - sponsor - agevolazioni da parte di … - altri fonti	
<u>Contributo richiesto da parte di ALC :</u>	**35.000 €**
Lions/Persona responsabile (di contatto e/o coordinatore di progetto) dall´inizio fino alla fine, compresa relazione finale e presentazione contabilita´del progetto:	Prof.Zeno Bisoffi - Direttore Dipartimento di Malattie Infettive-Tropicali e Microbiologia - IRCCS Negrar (VR)
Luogo e data della domanda :	SAN BONIFACIO 24.10.2020
Firma del coordinatore/responsabile del progetto con dati contatto:	
Dichiaro di aver letto le condizioni del bando ALC per i progetti e di averli presi a conoscenza:	
Acconsento alla pubblicazione del progetto in ogni sua parte:	