SAFETY AND EFFICACY OF SARS-COV-2-SPECIFIC T CELLS AS ADOPTIVE IMMUNOTHERAPY FOR HIGH-RISK COVID-19 PATIENTS: A PHASE I/II, RANDOMIZED CLINICAL TRIAL

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Background & Aim: SARS-CoV-2 pandemic poses an urgent need for the development of effective therapies. We report the feasibility of creating a bank of immediately available off-the-shelf SARS-CoV-2-specific T cells (CoV-2-STs) from convalescents and preliminary results of a randomized phase I/II trial (EudraCT 2021-001022-22) using CoV-2-STs in high-risk COVID-19 patients.

Methods, Results & Conclusion: We prepared ~480 clinical doses of CoV-2-STs from 30 convalescent donors. Peripheral blood mononuclear cells were exposed to peximix spanning SARS-CoV-2 antigens (spike/membrane/NCAP) and expanded for 10 days in G-Rex to produce a median of 6x10^6 T-cells/donor (2-11x10^7). The cell products were polyclonal, enriched in CD4+ (78±2%) cells expressing memory markers and high specificity against SARS-CoV-2 (2428±109 spot forming cells/SFC/2x10^6) and its variants (WT 1873±481 /alpha 2182±582/beta 2177±624/delta 1549±463 SFC/2x10^6). At least 1 HLA mediating CoV-2-ST specificity was identified in 29/30 products. Hospitalized COVID-19 patients within 6 days from the symptoms onset with pneumonia, lymphopenia (CD3±650/µl) and ≥1 elevated biomarker (D-dimers, ferritin, CRP, LDH) were enrolled and followed for 8 weeks. Patients were evaluated for recovery by the WHO 8-point Ordinal Scale (OS). Safety was demonstrated during phase I where 6 patients received dose escalated (15x10^6,2x10^6/µl) CoV-2-STs sharing at least 1 HLA mediating specificity. In phase II, 90 randomized (2:1) high-risk patients were enrolled; 57 received the standard of care (SoC) plus partially HLA-matched CoV-2-STs and 30 received the SoC (control arm). Three withdrew consent and 1 from the CoV-2-ST arm was allocated to control arm as referred to ICU prior to receiving SoC. On day 60 (d60) the add-on treatment resulted in 51% lower risk of mortality than SoC alone (24.6% [14/57] vs 50.0% [15/30]; risk ratio (RR); 0.49;p=0.016) with crude hazard ratio (HR) 2.42 (1.17, 5.05;p=0.018) in favor of CoV-2-STs. The benefit on survival was confirmed by multiple analysis after adjustment for confounding factors [HR:2.16(1.02, 4.60);p=0.04]. On d30, 67% had recovered (OS≤3) in the CoV-2-ST arm vs 37% in the control arm (RR; 1.82;p=0.02) with HR 0.48 (0.24, 0.94;p=0.03). CoV-2-ST-treated patients were more likely to recover by d30 even after adjustment for confounding factors [HR:0.46(0.23,0.92);p=0.03]. Overall, off-the-shelf immunotherapy with CoV-2-STs can serve as a safe and effective treatment in a real world environment for severe COVID-19.

40 Immunotherapy

A NOVEL GMP PROTOCOL USING THE HUMAN THYMUS AS A NEW SOURCE OF REGULATORY T CELLS (THYtREG) TO BE EMPLOYED AS AN AUTOLOGOUS CELLULAR THERAPY IN HEART TRANSPLANTED CHILDREN

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Keywords: Cell therapy, Treg, Clinical Trial.

Background & Aim: Immune allograft rejection continues to be the main obstacle to definitive successful transplants. Due to their suppressive capacity, adoptive transfer of regulatory T cells (Treg) has acquired growing interest in achieving indefinite graft survival. Limited Treg recovery and reduced quality (in terms of survival, suppressive capacity and phenotype stability) remain the main obstacles in current protocols where Treg are obtained from adult peripheral blood. To overcome these limitations, we have developed a novel GMP-com-