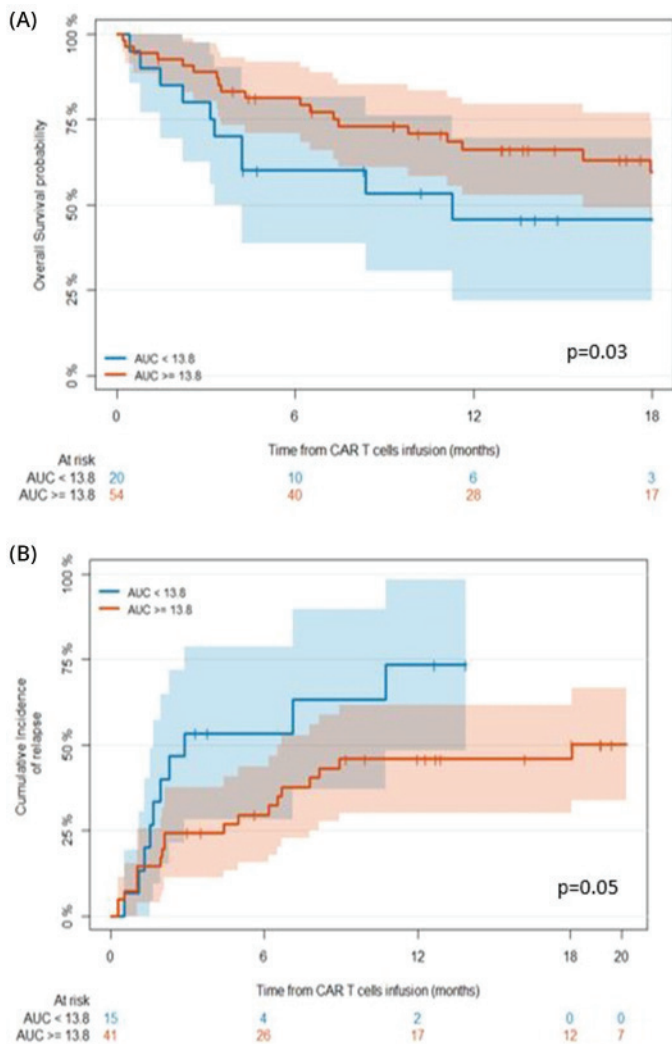




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**Fig. 3** (abstract 21) (A) Overall survival in patients with high pre-treatment disease burden using a fludarabine AUC of 13.8 mg.hr/L. (B) Cumulative incidence of relapse using a fludarabine AUC of 13.8 mg.hr/L in patients with high disease burden.

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### Immunotherapy: Non-malignant

#### A PHASE I/II DOSE-ESCALATION SINGLE CENTER STUDY TO EVALUATE THE SAFETY OF INFUSION OF MEMORY T CELLS AS ADOPTIVE THERAPY IN CORONAVIRUS PNEUMONIA AND /OR LYMPHOPENIA (RELEASE)

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**Keywords:** SARS-CoV-2 specific Memory T lymphocytes, Lymphopenia, COVID-19.

**Background & Aim:** Effective treatments to reduce the severity of symptoms and mortality for moderate/severe COVID-19 patients are needed. We have shown the presence of SARS-CoV-2 specific T cells within the CD45RA<sup>+</sup> memory T cells of the blood from convalescent donors. These memory T cells may be an alternative to treat SARS-CoV-2 pneumonia and/or lymphopenia. A wide number of doses can be easily manufactured and stored to generate a biobank of “living drugs” immediately available that can cover the country population based on the HLA genotype. In this study, we conducted a first-in-human phase 1 clinical trial, dose-escalation study to evaluate the safety of a single infusion of CD45RA<sup>+</sup> memory T cells containing SARS-CoV-2 specific T cells from a COVID-19 convalescent donor as adoptive cell therapy against moderate/severe cases of COVID-19.

**Methods, Results & Conclusion:** Hospitalized participants suffering from COVID-19 pneumonia and lymphopenia were enrolled based on HLA-match with donor and following the protocol inclusion/exclusion criteria. Participants were sequentially enrolled to receive a single infusion of CD45RA<sup>+</sup> memory T cells in a dose-escalating manner and the standard of care. Primary outcomes were to determine the safety of a single infusion of memory T cells and the dose-limiting toxicity. Secondary outcomes were to evaluate time to lymphopenia recovery and immune dysregulation.

Nine patients were enrolled. The first 3 patients received  $1 \times 10^5$  cells/kg, the next 3 received  $5 \times 10^5$  cells/kg and the last 3 patients received  $1 \times 10^6$  cells/kg of CD45RA<sup>+</sup> memory T cells. Patients' clinical status showed an improvement 6 days after infusion by NEWS and 7-category point ordinal scales. The median time of hospitalization after the infusion was 8 days in the low dose group, 7 in the intermediate dose group, and 4 days in the high dose group. The inflammatory parameters were stabilized and they all showed lymphocyte recovery two weeks after infusion. Donor microchimerism was observed at least for 2 weeks after infusion.

Despite the small sample size, our study supports the idea that treatment of COVID-19 patients with moderate/severe symptoms using CD45RA<sup>+</sup> memory T cells is feasible, safe, and it is associated with quick clinical improvement and short hospitalization stays. Neither patient had an infusion reaction, inflammatory impairment, or other serious adverse reaction. We are now opening a multicentre phase 2 study to show treatment efficacy.

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### Immunotherapy: Non-malignant

#### GM-CSF DISRUPTION IN CART CELLS AMELIORATES CART CELL ACTIVATION AND REDUCES ACTIVATION-INDUCED CELL DEATH

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