Experience with COVID-19 infection and vaccination in combined kidney/HSCT

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BACKGROUND

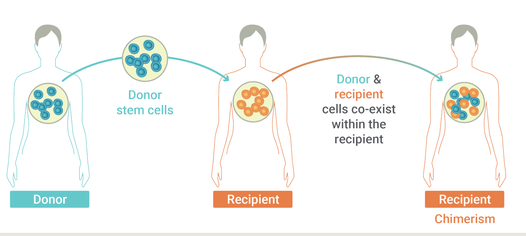
Transplant and the COVID-19 experience

- Kidney transplant (KTx) recipients are at increased risk of COVID-19–related complications because of comorbidities and because the use of chronic immunosuppression (IS) often impairs the ability to fight viral infection[1]
- KTx patients who have undergone an investigational allogeneic stem cell therapy to induce tolerance and are able to discontinue IS are a unique cohort regarding SARS-CoV-2 susceptibility, clinical course following infection, and vaccination response
  - These patients participated in a Phase 2 trial to induce KTx tolerance through the establishment of durable donor whole blood and T-cell chimerism using FCR001, an investigational allogeneic cell therapy[2]
  - Durable tolerance that allowed withdrawal of IS was established in 26 of 37 highly mismatched recipients of combined FCR001/living-donor kidney transplant (LDKT) with a low incidence (5.4%) of graft-vs-host disease (GvHD)[3]

FCR001

- FCR001 is derived from donor-mobilized peripheral blood cells, processed to contain an optimized number of hematopoietic stem cells (HSCs), facilitating cells, and αβTCR+ T cells that may induce chimerism and immune tolerance[4] (Figure 1)
  - Facilitating cells promote stem cell engraftment in unmatched recipients, prevent GvHD in mouse models, and induce antigen-specific T_{reg} and B_{reg}

Figure 1. Establishing chimerism



HSCT, hematopoietic stem cell transplantation.

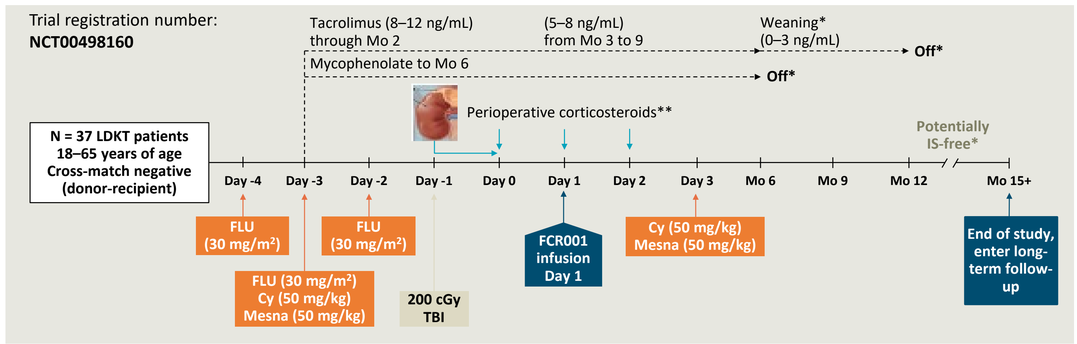
OBJECTIVE

- The objective of this retrospective analysis was to evaluate SARS-CoV-2 vaccine response in and the impact of COVID-19 infection on combined FCR001/LDKT recipients

METHODS

- A chart review was conducted to evaluate patient response to COVID-19 infection and vaccination, using data collected from Dec 4, 2021 to April 20, 2022
  - Variables of interest included:
    - Demographic data
    - Clinical course
    - Virologic assays
- Patients were drawn from a Phase 2 study at Northwestern University, in which they received nonmyeloablative conditioning and LDKT followed the next day by infusion of cryopreserved FCR001, produced from the same donor as the kidney (**Figure 2**)[2]
- Immunosuppression consisting of mycophenolate and tacrolimus was weaned and discontinued in the presence of sustained donor T-cell chimerism (>50%), stable renal function, and no evidence of biopsy-proven rejection

Figure 2. Transplant and treatment timeline



*Assuming no biopsy-proven acute rejection; stable kidney function; >50% donor chimerism; no GvHD.
**Methylprednisolone 500 mg IV on Day 0; 250 mg on Day 1 and 125 mg on Day 2.
cGy, centigray; Cy, cyclophosphamide; FLU, fludarabine; GvHD, graft-vs-host disease; IS, immunosuppression; IV, intravenous; LDKT, living-donor kidney transplant; Mesna, mercapto-ethyl sulfonate; Mo, month; TBI, total body irradiation.

RESULTS

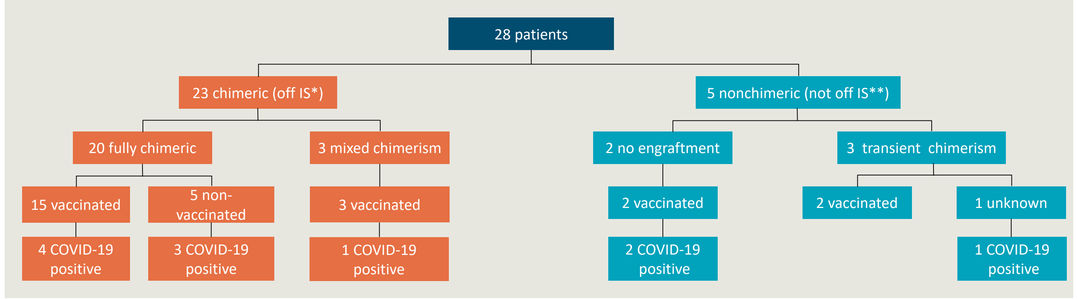
- 28 patients within the cohort with available data were identified (**Table 1, Figure 3**)

Table 1. Demographics and available data

	FCR001/LDKT patients, N = 28
Age range, y	28–73 years
Male	25
Race, white	25
Fully vaccinated*	22
Pfizer-BioNTech	16
Moderna	3
Johnson & Johnson	3
Positive PCR test	11
Serology performed	4

*At least 2 doses of Pfizer BioNTech or Moderna vaccines or 1 dose of the Johnson & Johnson vaccine.
LDKT, living donor kidney transplant; PCR, polymerase chain reaction.

Figure 3. Patient outcomes



*Range, 51.5−139.4 months.
**1 patient was on low-dose mTOR-based IS.
HSC, hematopoietic stem cell; IS, immunosuppression; mTOR, mammalian target of rapamycin.

- Vaccination was well tolerated with no loss of donor HSC engraftment
- Of **11** infected patients, none were hospitalized
  - 3 patients received casirivimab/imdevimab
  - Symptoms during COVID-19 infection are summarized in **Table 2**

Table 2. COVID-19 symptoms

Signs and symptoms	COVID-19–positive patients, N = 11, n (%)
Cough	5 (45%)
Fatigue	4 (36%)
Body aches	3 (27%)
Fever	2 (18%)
Loss of smell	2 (18%)
Sore throat	2 (18%)
Runny nose	1 (9%)
Headache	1 (9%)
Diarrhea	1 (9%)
Shortness of breath	1 (9%)

- No change in peripheral blood chimerism was seen in infected tolerant patients
- No evidence of kidney function impairment as a result of COVID-19 infection (**Table 3**)

Table 3. Kidney function

	Average eGFR
Pre-infection	68.1 mL/min/1.73 m²
Post-infection	65.6 mL/min/1.73 m²

eGFR, estimated glomerular filtration rate.

- Four patients had serology performed (**Table 4**)

Table 4. COVID-19 serologic results in 4 FCR001/LDKT patients

Subject	Antibody test	Result	Time point	Subject details
NU17	Siemens Advia Centaur SARS-CoV-2 Total Assay	>10.00 Index (ref ≤1.00)	28 days postvaccination with Pfizer-BioNTech	Off all IS, mixed chimera
NU27	Siemens Advia Centaur SARS-CoV-2 Total Assay	>10.00 Index (ref ≤1.00)	176 days postvaccination with Johnson & Johnson	Off all IS, with h/o GvHD
NU22	Siemens Advia Centaur SARS-CoV-2 Total Assay	>10.00 Index (ref ≤1.00)	15 days postvaccination with Pfizer-BioNTech	Off all IS, mixed chimera
	Beckman Access SARS-CoV-2 IgG	7.02 Index (ref ≤1.00)	177 days postvaccination with Pfizer-BioNTech	Off all IS, mixed chimera
NU11	Quest Diagnostics SARS-CoV-2 Total Antibody, Spike, Semi-Quantitative	35.5 U/mL (ref <0.8 U/mL)	222 days postvaccination with Moderna	On CNI-based IS, transient chimerism

CNI, calcineurin inhibitors; GvHD, graft-vs-host disease; h/o, history of; IgG, immunoglobulin G; IS, immunosuppression; LDKT, living-donor kidney transplant; ref, reference.

CONCLUSIONS

- SARS-CoV-2 vaccination resulted in strong humoral responses and did not result in the loss of chimerism or allograft dysfunction
- None of the infected FCR001/LDKT recipients developed severe COVID-19
- Infection in patients off IS was not associated with loss of chimerism

References

1) Nahi, et al. *PLoS One*. 2021; 2) Leventhal, et al. *Sci Transl Med*. 2012; 3) Leventhal, et al. [abstract]. *Am J Transplant*. 2020; 4) Leventhal, et al. *Hum Immunol*. 2018.

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Disclosures

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