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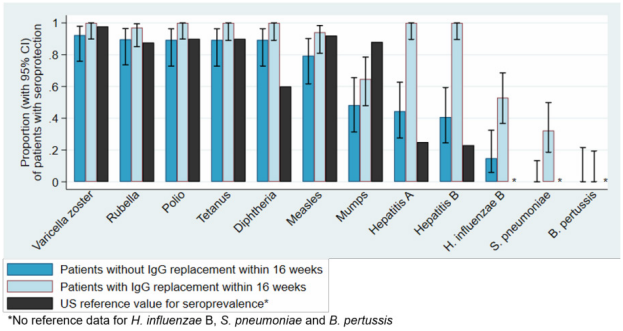
Background: Chimeric antigen receptor-modified T (CAR-T) cell immunotherapy for B cell hematologic malignancies results in prolonged B cell depletion. Little is known about the effects of CAR-T cell therapy on pre-existing pathogen-specific humoral immunity.

Methods: We conducted a prospective, cross-sectional study of children and adults treated with CD19- or BCMA-CAR-T cell therapy. Eligible patients were ≥ 6 months post-CAR-T cell infusion and in remission without subsequent chemoimmunotherapy. We measured total immunoglobulin G (IgG), pathogen-specific IgG levels for 12 vaccine-preventable infections, and B cell subsets from blood. Seroprotective antibody titers were based on standard thresholds. We described the proportion of patients with seroprotective titers and tested for associations between clinical factors and seroprotection using generalized estimating equations.

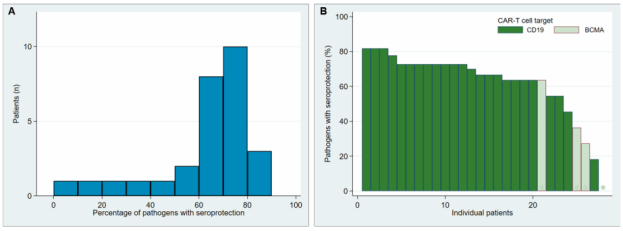
Results: We enrolled 65 patients who received CD19- (n=54) or BCMA- (n=11) CAR-T cell therapy. Seven patients were < 18 years old. Samples were collected a median of 20 months (range, 7–68) after CAR T cell infusion. Seroprotection to vaccine-preventable pathogens was generally comparable to the U.S. population (**Fig 1**) even though blood CD19+ B cell counts were low (< 20 cells/mm^3) in 60% of patients. Among 30 patients without IgG replacement in the prior 16 weeks (4 half-lives of IgG), 27 (90%) had hypogammaglobulinemia. Despite this, these individuals had seroprotection to a median of 67% (IQR, 59%-73%) of tested pathogens (**Fig 2A**). The proportion of patients with seroprotection was lowest for mumps, hepatitis A and B, *H. influenzae* type B (Hib), *S. pneumoniae,* and *B. pertussis*. Patients receiving BCMA-CAR-T cells had seroprotection to fewer pathogens than those receiving CD19-CAR-T cells (**Fig 2B**), but the difference did not reach statistical significance (**Fig 3**). There were no significant differences by other variables.

Figure 1. Proportion of CAR-T cell recipients with seroprotection to vaccine-preventable infections compared to the U.S. population, stratified by receipt of IgG replacement in the previous 16 weeks.



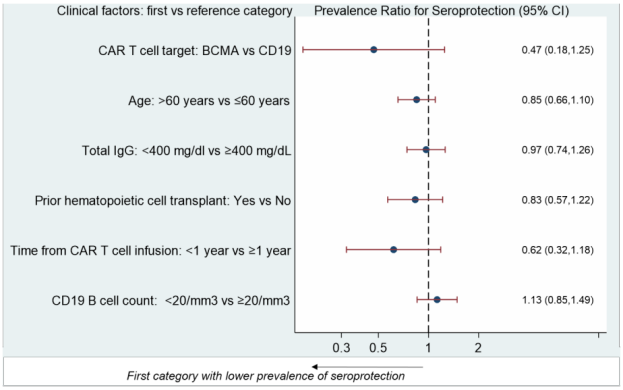
*No reference data for *H. influenzae* B, *S. pneumoniae* and *B. pertussis*

Figure 2 A-B. Percentage of pathogens with seroprotective antibody titers among patients without IgG replacement in the previous 16 weeks.



(A) Distribution of the percentage of pathogens for which patients have seroprotective antibody titers (B) Percentage of pathogens with seroprotective antibody titers per patient. (A-B) Results of 28 patients with >5 valid test results are shown. Pertussis results are excluded due to incomplete test series.

Figure 3. Association of clinical factors with seroprotection to vaccine-preventable infections among patients without IgG replacement in the previous 16 weeks (n=30)



A prevalence ratio <1 represents lower prevalence of seroprotection among pathogens in the first vs the reference category; BCMA-CAR-T cell recipients had fewer seroprotective antibody titers compared to CD19-CAR-T cell recipients but this difference did not reach statistical significance

Conclusion: Seroprotection for vaccine-preventable infections after CD19-CAR-T cell therapy was comparable to the general population. BCMA-CAR-T cell recipients may benefit most from replacement IgG. Vaccinations after CAR-T cell therapy should be considered and prioritized for *S. pneumoniae*, Hib, hepatitis viruses, and *B. pertussis*.

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197. Dengue Virus Infection Among Renal Transplant Recipients in Singapore: A 15-year Single Center Retrospective Review

Sophie Tan Seine Xuan, MBBS[1]; Quan Yao Ho, MBBS, MRCP, MMed, FAMS[2]; Sobhana Thangaraju, MBBS, MRCP (UK)[2]; Thuan Tong Tan, MBBS[3]; Terence Kee, MBBS (Aust), MRCP (UK), FAMS, FRCP, FASN, GDipHML[2]; Jasmine Chung Shimin, MBBS (Hons)(Australia), MRCP (UK)[2]; [1]Singapore General Hospital, Singapore, Singapore, Not Applicable, Singapore; [2]Singapore General Hospital, SingHealth Duke-NUS Transplant Centre, Singapore, Singapore, Not Applicable, Singapore; [3]Singapore General Hospital, Singapore, Not Applicable, Singapore

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Background: Dengue is a mosquito-borne viral infection endemic in Singapore. Its clinical course in the immunocompetent host is well characterised but its impact in renal transplantation is not well described. We aim to characterise the clinical presentation and outcomes of dengue virus infection in renal transplant recipients treated at a tertiary center in Singapore.

Methods: We conducted a 15 year retrospective review of dengue in renal transplant patients treated at Singapore General Hospital between January 2005 to October 2019. The diagnosis of dengue was made if there were a compatible clinical syndrome and a positive dengue diagnostic assay, either Dengue NS1 antigen, IgM or PCR.

Results: Thirty-two renal transplant patients were diagnosed with dengue, 18 (56.3%) were deceased donor recipients. The median age at time of diagnosis was 53 [IQR 42,61] years; 16 (50%) were males. The median time to diagnosis of dengue was 95.5 [IQR 15.0,95.5] months from transplant; and the median duration of clinical illness was 7 [IQR 5,7] days. The most common clinical symptoms were fever (84.4%), myalgia (40.6%), gastrointestinal symptoms (37.5%) and headache (25.0%). Based on the WHO 2009 dengue classification, 20 (62.5%) had dengue without warning signs, 9 (28.1%) had dengue with warning signs, and 3 (9.4%) had severe dengue; 19 (59.3%) had graft dysfunction and 1 (3.1%) required dialysis. Of the patients who had graft dysfunction, 18 (94.7%) had recovery of graft function at time of dengue resolution. Dengue mortality rate was 3.1%. There were 2 possible cases of donor derived dengue infections, occurring within 2 weeks of deceased donor transplantation.

Conclusion: Dengue in renal transplant is usually community acquired; donor derived infections are uncommon. The clinical presentation of dengue is similar to the immunocompetent host, however graft dysfunction is common and fluid management in this population is important. Severe dengue is less common.

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