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Supplemental information

Off-the-shelf allogeneic natural killer cells for the treatment of COVID-19

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Supplemental Tables and Figures

Table S1. Summary of Adverse Events

Event Term	Dose: 100 x 10^6 (n=3)	Dose: 300 x 10^6 (n=3)	Dose: 900 x 10^6 (n=3)	All Participants (n=9)
Any Adverse Event	12	9	7	28
Allergic Reaction	0	2	0	2
Dyspepsia	0	1	1	2
Dyspnea	1	0	1	2
Epistaxis	1	1	0	2
Lung Infection	1	0	1	2
Nausea	1	0	1	2
Alanine Aminotransferase Increase	1	0	0	1
Arthralgia	0	1	0	1
Aspartate Aminotransferase Increase	1	0	0	1
Chest Wall Pain	1	0	0	1
Disseminated Intravascular Coagulation	1	0	0	1
Dizziness	0	1	0	1
Dysgeusia	1	0	0	1
Hiccups	0	1	0	1
Hyperbilirubinemia	1	0	0	1
Insomnia	1	0	0	1
Nasal Congestion	0	1	0	1
Palpitations	0	0	1	1
Phlebitis	0	1	0	1
Rash	0	0	1	1
Sepsis	1	0	0	1
Sinus Tachycardia	0	0	1	1
Adverse Event Potentially Related to Study Product	0	0	0	0
Serious Adverse Event (all unrelated)	2	0	1	3
Death	0	0	0	0

No adverse events were assessed as potentially related. There were three serious AEs in two participants with active hematologic malignancies due to sepsis with bacteremia and recurrent COVID-19 in one participant and recurrent COVID-19 in a second participant in the context of weaning of corticosteroids.

Table S2: Adverse Event Severity per Participant

Participant	CTCAE Term	Severity Grade	Relatedness to DVX201	SAE	AE Details as relevant
DVX201-001	Epistaxis	1	Not related	No	
	Nausea	1	Not related	No	
	Insomnia	2	Not related	No	
DVX201-002	Alanine aminotransferase increased	3	Not related	No	Related to underlying malignancy (ALL) and receipt of chemotherapy
	Aspartate aminotransferase increased	3	Not related	No	Related to underlying malignancy (ALL) and receipt of chemotherapy
	Disseminated intravascular coagulation	2	Not related	No	Related to underlying malignancy (ALL) and receipt of chemotherapy
	Hyperbilirubinemia	3	Not related	No	
	Sepsis	4	Not related	Yes	Admitted for neutropenic fever and bacteremia.
	Lung Infection	4	Not related	Yes	COVID-19 exacerbation requiring ICU admission
DVX201-003	Dyspnea	3	Not related	No	
	Dysgeusia	2	Not related	No	
	Chest Wall Pain	2	Not related	No	
DVX201-004	Phlebitis	2	Not related	No	
	Hiccups	1	Not related	No	
	Epistaxis	1	Not related	No	
DVX201-006	Allergic reaction	1	Not related	No	
	Dizziness	1	Not related	No	
	Dyspepsia	2	Not related	No	
	Allergic Reaction	2	Not related	No	
	Dizziness	1	Not related	No	
	Arthralgia	1	Not related	No	
	Nasal Congestion	1	Not related	No	

DVX201-008	Lung Infection	3	Not related	Yes	Hospitalization for recurrent symptoms of COVID-19.
	Palpitation	2	Not related	No	
	Dyspnea	2	Not related	No	
	Sinus tachycardia	2	Not related	No	
DVX201-009	Rash maculopapular	2	Not related	No	

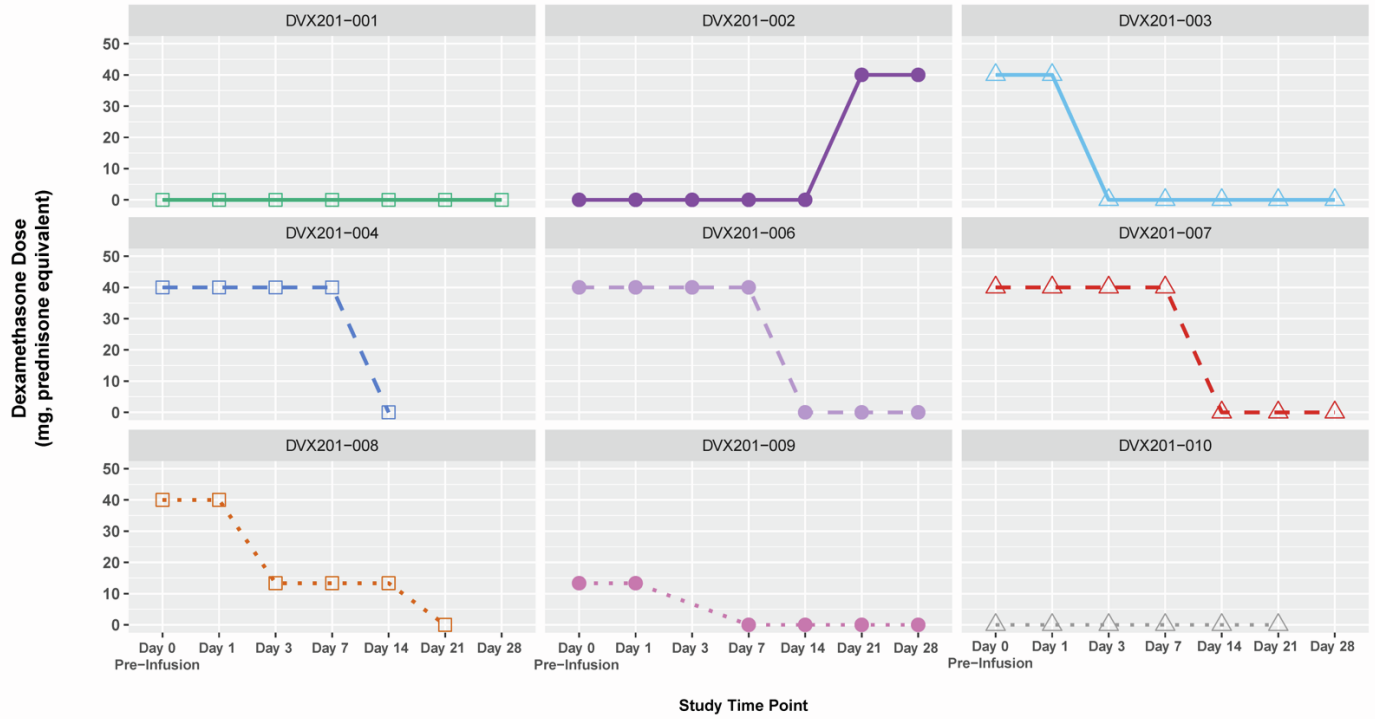

Figure S1: Corticosteroid use by participants during the study

Participant-level plots of the dexamethasone dose (in prednisone equivalence) at each study timepoint.

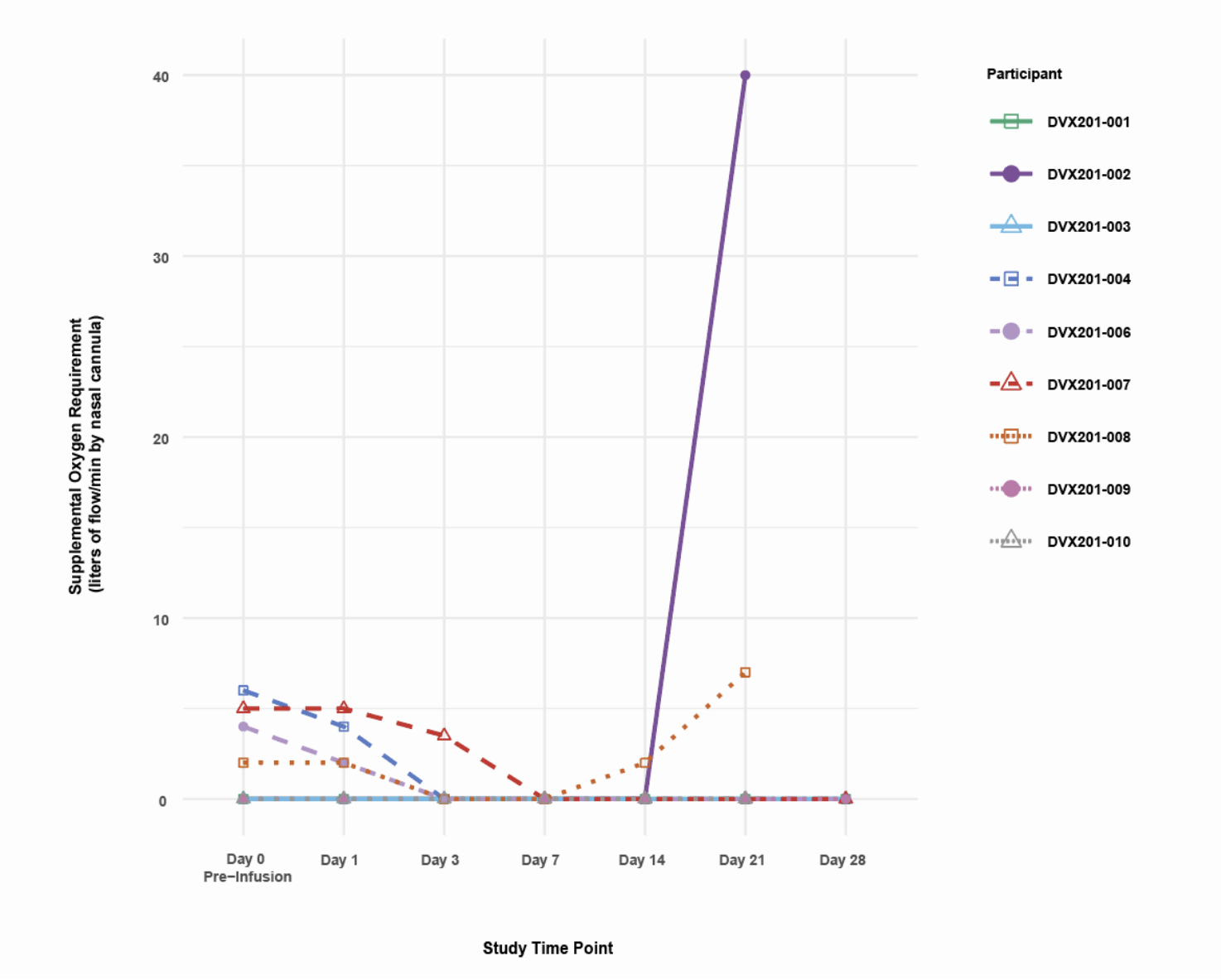

Figure S2: Kinetics of supplemental oxygen use

Spaghetti plot of the supplemental oxygen requirement in liters at each study timepoint. Each line represents an individual participant. Participants DVX201-002 and DVX201-008 were readmitted for worsening respiratory symptoms attributed to recurrent/persistent COVID-19.

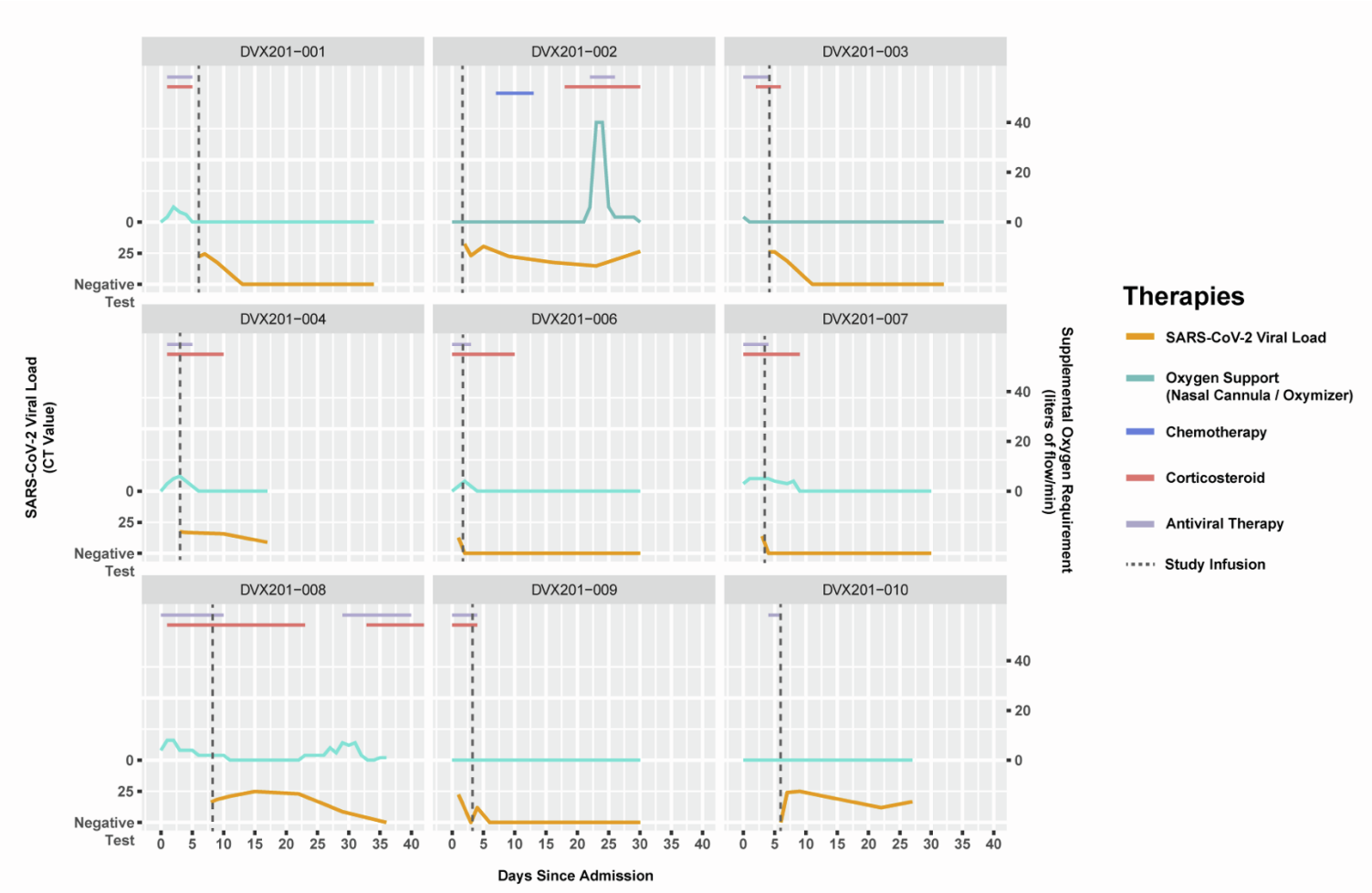

Figure S3. Dual-axis spaghetti plots of the kinetics of supplemental oxygen usage, SARS-CoV-2 detection, and concurrent therapies per day after hospital admission

For SARS-CoV-2 viral loads, the figure depicts the cycle threshold (CT) value, wherein a lower CT value indicates a higher viral load. Participant DVX201-002 also received casirivimab/imdevimab (Regeneron) on Day 1.

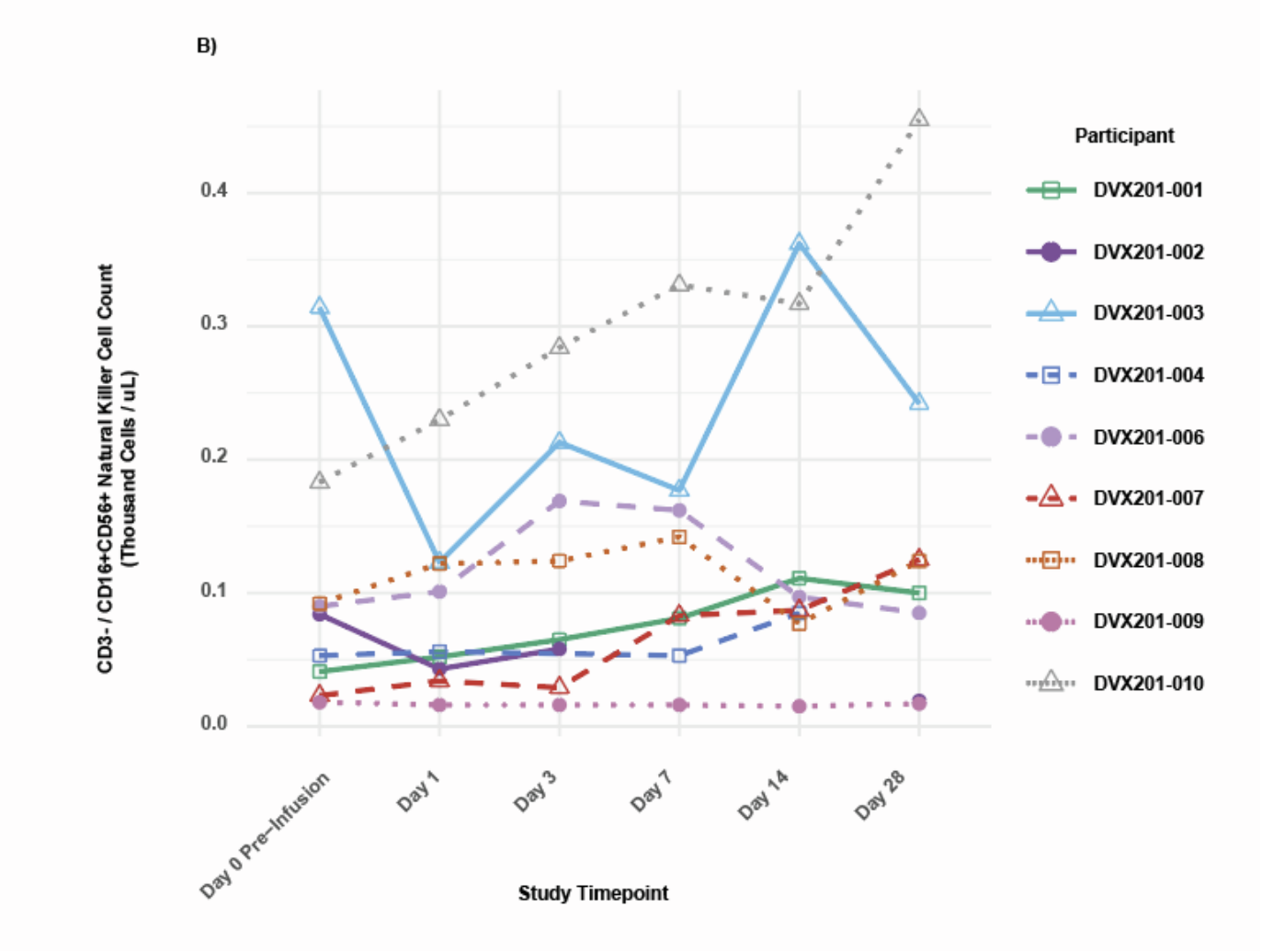

Figure S4. Kinetics of CD3- / CD16+CD56+ NK cell counts

Spaghetti plots of NK cell counts at each study timepoint per participant.

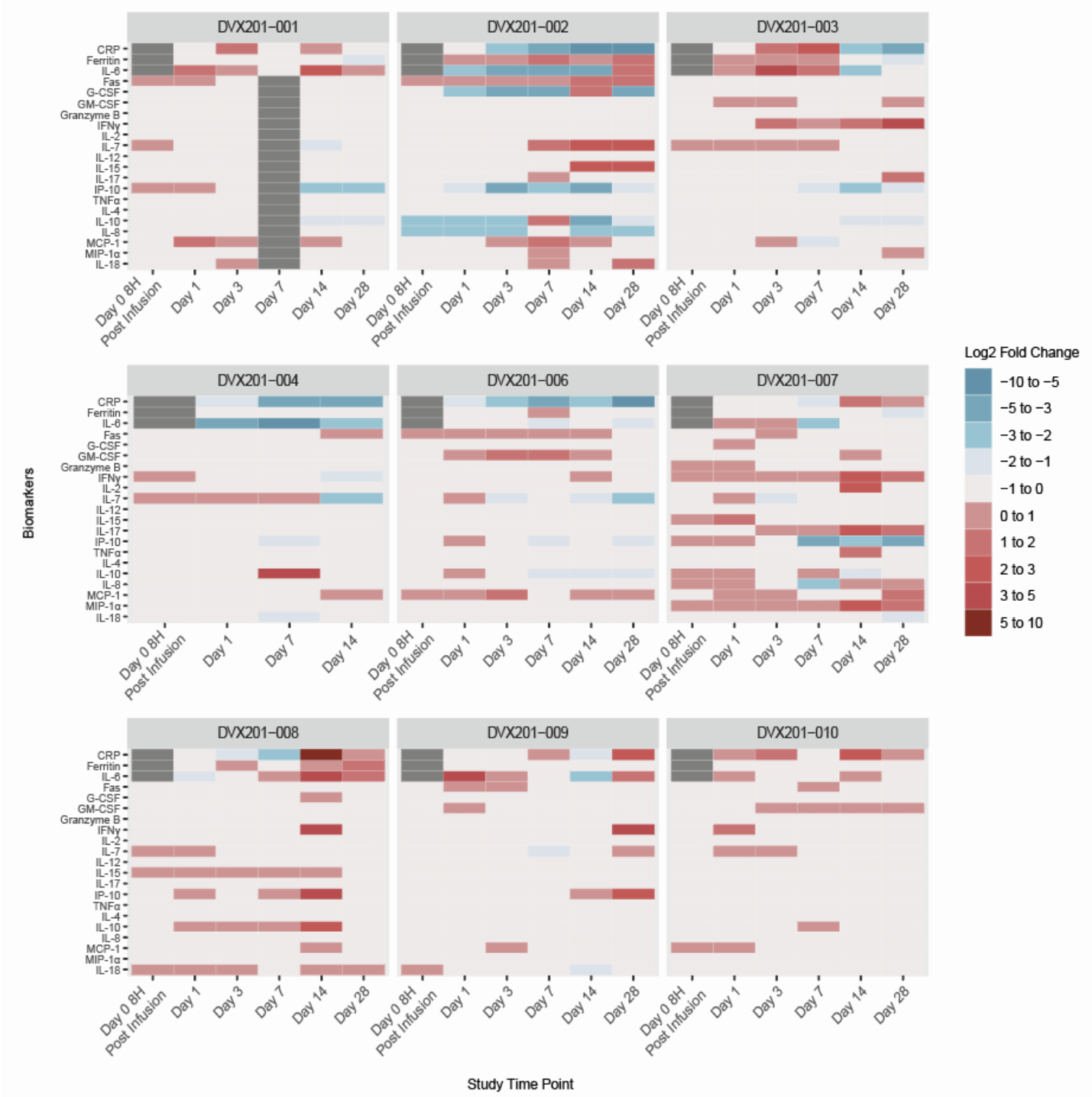

Figure S5. Heat map of the kinetics of exploratory cytokines and/or inflammatory biomarkers based on fold changes compared to baseline time points.

Heat maps for each participant are depicted in separate panels in order of dose level (3 participants pre increasing dose level). The heat maps depict fold changes (log_2) for each time point relative to the Day 0 (pre-

infusion) baseline sample per participant. Biomarkers are displayed in each panel in order of (top to bottom) cytokines, chemokines, enzymes, growth factors, acute phase proteins, and cell surface receptors.
Red colors indicate an increase and blue colors indicate a decrease in values.

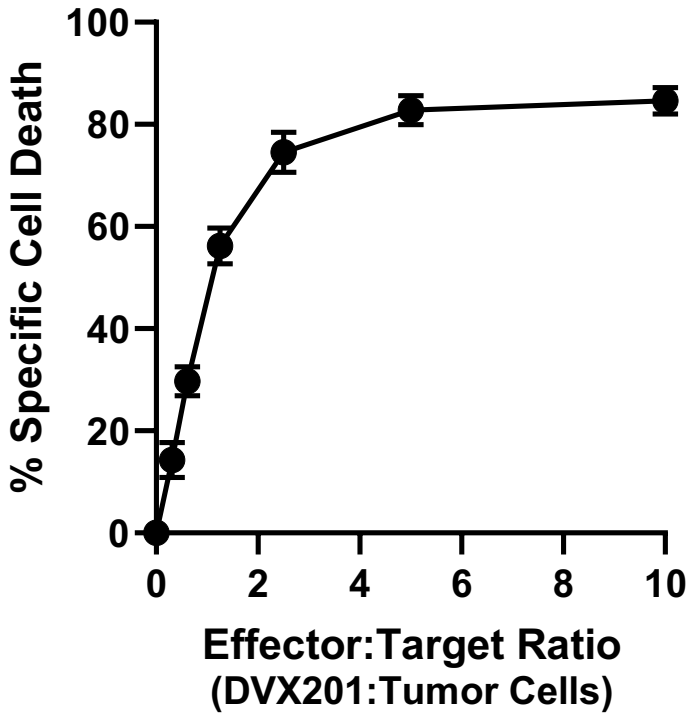

Figure S6. Functionality of four unique batches of DVX201 NK cell product using an in vitro cytotoxicity assay. A constant number of GFP-expressing Kasumi-1 target cells were co-cultured with DVX201 effector cells in a range of effector-to-target cell ratios for 24hrs in a 37°C incubator. Cells were labeled with DAPI at the end of incubation and assessed by flow cytometry for the percentage of dead/dying DAPI+ GFP+ Kasumi-1 cells. Results from these assays were generated for information only as part of the batch records. Specific cell death of the target cells was determined using the following equation:
[(% Sample Cell Death – % Spontaneous Cell Death) / (100 – % Spontaneous Cell Death)] x 100 = % Specific Cell Death