

Cabaletta Bio[®]

A microscopic view of several cells, likely T-cells, with prominent red internal structures, possibly nuclei or organelles, set against a white background. The cells are slightly out of focus, with one in the foreground being more detailed.

CAR T-cells to treat autoimmunity

CD19 CAR T-CELLS FOR SLE

Disclaimer

The following presentation, including any printed or electronic copy of these slides, the talks given by the presenters, the information communicated during any delivery of the presentation and any question and answer session and any document or material distributed at or in connection with the presentation (collectively, the "Presentation") has been prepared by Cabaletta Bio, Inc. ("we," "us," "our," "Cabaletta" or the "Company") and is made for informational purposes only. This Presentation does not purport to be a prospectus, to be complete or to contain all of the information you may desire. Statements contained herein are made as of the date of this Presentation unless stated otherwise, and this Presentation shall not under any circumstances create an implication that the information contained herein is correct as of any time after such date or that information will be updated or revised to reflect information that subsequently becomes available or changes occurring after the date hereof. This Presentation may contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, and include, but are not limited to, express or implied statements regarding our current beliefs, expectations and assumptions regarding: our business, future plans and strategies for our CAAR T and CARTA technologies and CABA™ platform; Cabaletta's ability to grow its autoimmune-focused pipeline; the ability to capitalize on and potential benefits resulting from the translational research partnership with Professor Georg Schett and the exclusive license agreement with IASO Bio; the timing of our planned submission of an Investigational New Drug application (IND) for CABA-201 to the U.S. Food and Drug Administration as well as other planned regulatory filings for our development programs; the progress and results of our DesCAARTes™ Phase 1 trial, including the significance and impact around reported safety and clinical and translational data of cohorts from our DesCAARTes™ trial; the therapeutic potential and clinical benefits of our product candidates; the expectation that Cabaletta may improve outcomes for patients suffering from mucosal pemphigus vulgaris, myasthenia gravis, or other autoimmune diseases; our ability to escalate dosing as high as 10 to 15 billion cells in cohort A6m, initiate dosing in a combination cohort or otherwise; Cabaletta's plans to implement a pre-treatment regimen and the potential ability to enhance *in vivo* DSG3-CAART exposure; our ability to advance dose escalation in the DesCAARTes™ Phase 1 trial at the current dose ranges for the current cohorts and any projected potential dose ranges for future cohorts, and to optimize our targeted cell therapy; our ability to evaluate, and the potential significance of, the relationship between DSG3-CAART persistence and potential clinical responses in patients with mPV; our ability to safely retreat additional patients and whether we will continue to observe a lack of immune-mediated clearance of DSG3-CAART cells after retreatment and repeat dosing of patients; our ability to successfully complete our preclinical and clinical studies for our product candidates, including CABA-201, our ongoing Phase 1 DesCAARTes™ trial, and our ongoing Phase 1 MuSK-CAART, including our ability to enroll the requisite number of patients, dose each dosing cohort in the intended manner, and progress the trial; the ability of MuSK-CAART to target B cells that differentiate into antibody secreting cells, which produce autoantibodies against muscle-specific kinase; our ability to obtain and maintain regulatory approval of our product candidates, including our expectations regarding the intended incentives conferred by and ability to retain Orphan Drug Designation and Fast Track Designation for DSG3-CAART for the treatment of pemphigus vulgaris and Orphan Drug Designation and Fast Track Designation for MuSK-CAART to improve activities of daily living and muscle strength in patients with MuSK antibody-positive myasthenia gravis; the further expansion and development of our modular CABA™ platform across a range of autoimmune diseases; our ability to contract with third-party suppliers and manufacturers, implement an enhanced manufacturing process and further develop our internal manufacturing strategy, capabilities and facilities; our potential commercial opportunities, including value and addressable market, for our product candidates; our expectations regarding our use of capital and other financial results; and our ability to fund operations into the first quarter of 2025. Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements.

Various risks, uncertainties and assumptions could cause actual results to differ materially from those anticipated or implied in our forward-looking statements. Such risks and uncertainties include, but are not limited to, risks related to the success, cost, and timing of our product candidate development activities and preclinical studies and clinical trials, risks related to our ability to demonstrate sufficient evidence of safety, efficacy and tolerability in our preclinical studies and clinical trials of CABA-201, DSG3-CAART and MuSK-CAART, the risk that the results observed with the similarly-designed construct employed in the recent *Nature Medicine* publication are not indicative of the results we seek to achieve with CABA-201, our plans to evaluate additional cohorts in the DesCAARTes™ trial, including a cohort implementing a pre-treatment regimen, the risk that signs of biologic activity or persistence may not inform long-term results, the risk that persistence observed with effective CART-19 oncology studies in combination with lymphodepletion is not indicative of, or applicable to, clinical responses in patients with mPV, risks related to clinical trial site activation or enrollment rates that are lower than expected, our ability to protect and maintain our intellectual property position, risks related to our relationship with third parties, uncertainties related to regulatory agencies' evaluation of regulatory filings and other information related to our product candidates, our ability to retain and recognize the intended incentives conferred by any Orphan Drug Designation and Fast Track Designations, the risk that any one or more of our product candidates will not be successfully developed and commercialized, the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies, the impact of COVID-19 on the timing, progress, interpretability of data, and results of ongoing or planned clinical trials and risks relating to as a result of extraordinary events or circumstances such as the COVID-19 pandemic, and any business interruptions to our operations or to those of our clinical sites, manufacturers, suppliers, or other vendors resulting from the COVID-19 pandemic or similar public health crisis. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, you are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ materially from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in our other filings with the Securities and Exchange Commission. Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. The Company is the owner of various trademarks, trade names and service marks. Certain other trademarks, trade names and service marks appearing in this Presentation are the property of third parties. Solely for convenience, the trademarks and trade names in this Presentation are referred to without the ® and TM symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Overview

- Autoimmune diseases background
- Treatment options
 - B cell depletion – why it works and why it doesn't
 - Is it possible to “cure” autoimmune disease?
 - Developing curative cellular therapies for patients with autoimmune disease
- CD19 CAR T for Autoimmune disease
 - Emerging data in SLE
 - Unique considerations

Autoimmune Disease – Global Impact

- An estimated 4.5% of the world's population lives with autoimmune disease¹
- Estimated economic burden of >\$100 billion²
- Incidence is increasing^{3,4}
 - Environmental factors
 - Improved surveillance and diagnoses
- Represents a global unmet medical need for which new therapies are needed

1. Hayter and Cook (2012) Updated assessment of the prevalence, spectrum and case definition of autoimmune disease. *Autoimmune Rev*

2. AARDA (2011) The Cost of Autoimmune Disease.

3. Dinse *et al* (2020) Increasing Prevalence of Antinuclear Antibodies in the United States. *Arthritis Rheumatol*

4. Rose (2016) Prediction and Prevention of Autoimmune Disease in the 21st Century. *Am J Epidemiol*

Current Treatment Modalities for Autoimmune Disease

Therapies listed in **bold** represent standard of care therapies commonly used to treat SLE

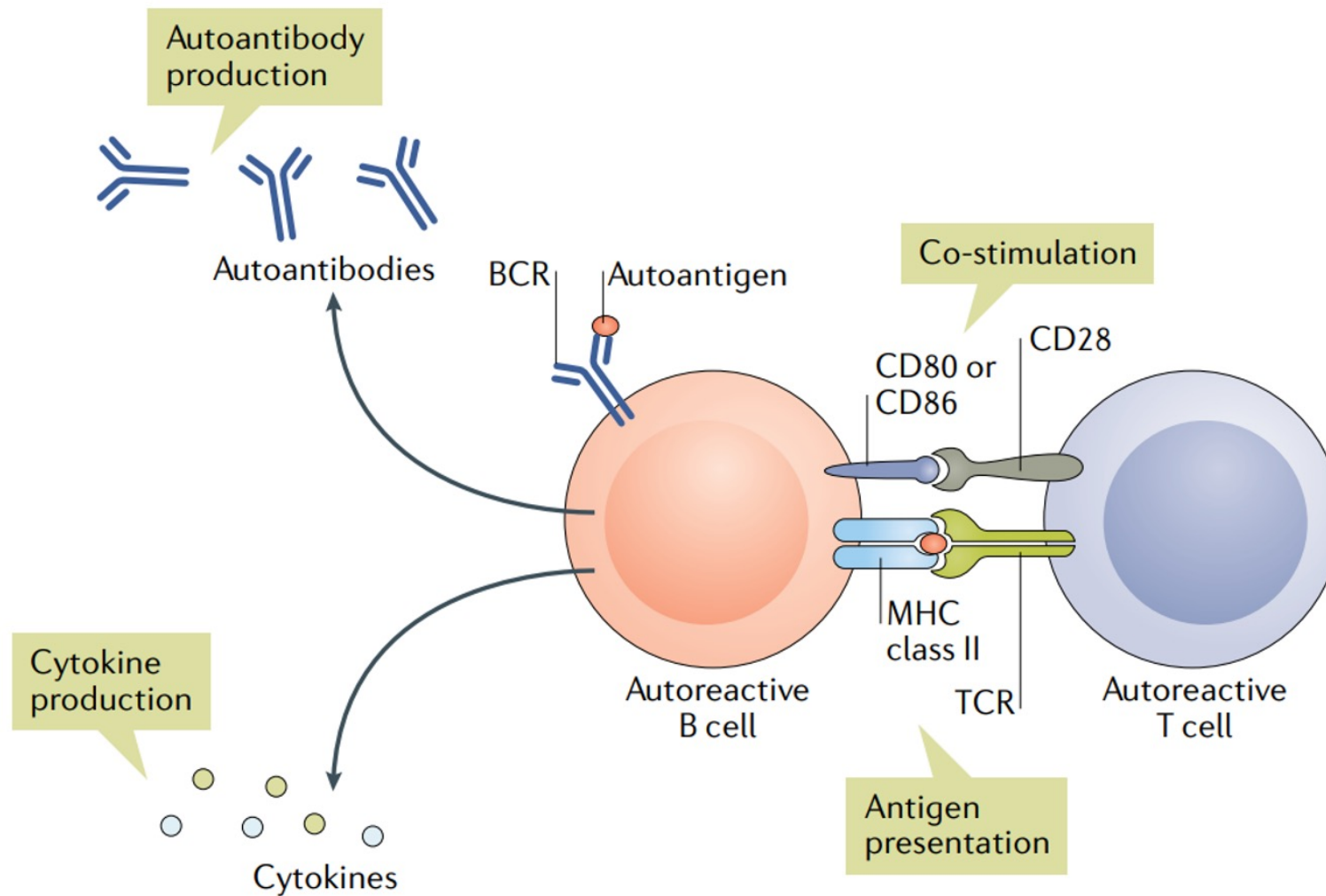
- Systemic therapies
 - Metabolic inhibitors: **mycophenolate mofetil** and methotrexate
 - Immune suppressants: **hydroxychloroquine**, and corticosteroids (**prednisone**), **voclosporin**
 - Cytotoxic therapies: cyclophosphamide
- Targeted therapies
 - B cell depletion: rituximab¹
 - Cytokine blockers: **belimumab** (anti-BAFF) and **anifrolumab** (anti-IFNAR1)
 - T and B cell signaling blockade: BTK and JAK inhibitors
- These therapies remain largely non-curative, requiring chronic therapy

1. Kaegi *et al* (2019), Safety and Efficacy of Rituximab in Treating Immune-Mediated Disorders, *Front Immunol*.

B cell depletion is effective in diseases caused by both T and B cells

WHY?....

....because B cells play a central role in driving (autoreactive) T cell responses¹



Rituximab is not Commonly Curative

WHY?...

- ...because Rituximab does not deplete all B cells within tissues¹
 - Difficulty in tissue penetration
 - Requirement for effector mechanisms to deploy cytotoxic effect
 - Therefore, requires repeat administration
 - This induces prolonged B cell aplasia
- Newer generations of anti-B cell depleting agents are emerging – may work better²

Organs	Diseases	RTX regimen	Other therapies	Delay between last RTX infusion and analysis	Number of patients	Residual B-cell populations	Reference no.
Bone marrow	ITP	4 weekly doses of 375 mg/m ²		3 mo	1	None	38
	RA	2 doses of 1000 mg (2 wk apart)		3 mo	6	Presence of residual CD19 ⁺ cells (0.1% to 3.25% in the lymphoid gate), mainly precursors and immature B cells	39
	RA	2 doses of 1000 mg (2 wk apart)		3 mo	25	8 of 25 patients (32%) had residual CD19 ⁺ cells (median 2.21%). No CD20 ⁺ cells	40
	RA	2 doses of 1000 mg (2 wk apart)		3 mo	8	No significant reduction in CD19 ⁺ cells numbers	41
	RA	2 doses of 1000 mg (2 wk apart)		1 to 3 mo	24	Presence of immature and/or transitional B cells (CD38 ⁺⁺ CD24 ⁺⁺) and CD27 ⁺ IgD ⁻ B cells, while IgD ⁺ cells were completely depleted	42
Spleen	ITP	4 weekly doses of 375 mg/m ²		3 mo	1	None	38
	ITP	4 weekly doses of 375 mg/m ²	i.v. Ig (4 of 15)	3 to 6 mo	15	CD19 ⁺ cells represented 0.06% to 1% of CD45 ⁺ cells, including 75% plasma cells. Remaining CD19 ⁺ cells were mostly CD27 ⁺ IgD ⁻ memory B cells. No residual germinal center	19
	AIHA	2 doses of 1000 mg (2 wk apart)	High-dose steroids	4 to 5 mo	4	CD19 ⁺ cells represented 1.45% of CD45 ⁺ cells, including 70% plasma cells. Remaining CD19 ⁺ cells were mostly CD27 ⁺ IgD ⁻ memory B cells. No residual germinal center	43
	ITP	4 weekly doses of 375 mg/m ² or 2 doses of 1000 mg (2 wk apart)	i.v. Ig (8 of 10) Steroids (1 of 10)	3 to 15 mo	10	CD19 ⁺ cells represented 5.1% of splenocytes, but some patients had already reconstituted their B cells	44
Lymph nodes	Prevention or treatment of antibody-mediated rejection	Single dose of 375 mg/m ²	Tacrolimus, mycophenolate mofetil, steroids, i.v. Ig, and rATG	2 to 45 d	7	Presence of few residual CD20 ⁺ CD79a ⁺ cells in some patients	45
	Prevention of antibody-mediated rejection	Single dose of 500 mg	Tacrolimus, mycophenolate mofetil, steroids	1 mo	5	20% of lymphoid cells were CD19 ⁺ (but not CD20 ⁺), mainly CD27 ⁺ IgD ⁻ memory B cells	46
	Prevention of antibody-mediated rejection	Single dose of 375 mg/m ²	Tacrolimus, mycophenolate mofetil, steroids, i.v. Ig	1 mo	4	35% of lymphoid cells were CD19 ⁺ (but not CD20 ⁺), mainly CD27 ⁺ IgD ⁻ memory B cells	47
Salivary glands	RA	2 doses of 1000 mg (2 wk apart)		1 mo	14	10% of lymphoid cells were CD19 ⁺ , mainly CD27 ⁺ IgD ⁻ memory B cells	48
	Sjögren syndrome	2 doses of 1000 mg (2 wk apart) then 1000 mg every 6 mo		6 mo	19	No CD20 ⁺ B cells. Ectopic germinal centers reduced from 53% to 5%	49
Synovial tissue	Sjögren syndrome	2 weekly doses of 375 mg/m ²		4 mo	8	No residual B cells	50
	RA	2 doses of 1000 mg (2 wk apart)		1 mo	17	Presence of residual CD22 ⁺ B cells	51
	RA	2 doses of 1000 mg (2 wk apart)		2 to 6 mo	17	Presence of CD20 ⁺ B cells in 2 of 17 patients (22%) and of CD79a ⁺ B cells in all patients	40
	RA	2 doses of 1000 mg (2 wk apart)		1 and 4 mo	16	Presence of residual CD22 ⁺ B cells	52

1. Table excerpted from: Crickx et al (2020) Anti-CD20-mediated B-cell Depletion in autoimmune diseases
 2. Furie RA, et al (2022) B-cell depletion with obinutuzumab for the treatment of proliferative lupus nephritis: a randomised, double-blind, placebo-controlled trial. Ann Rheum Dis

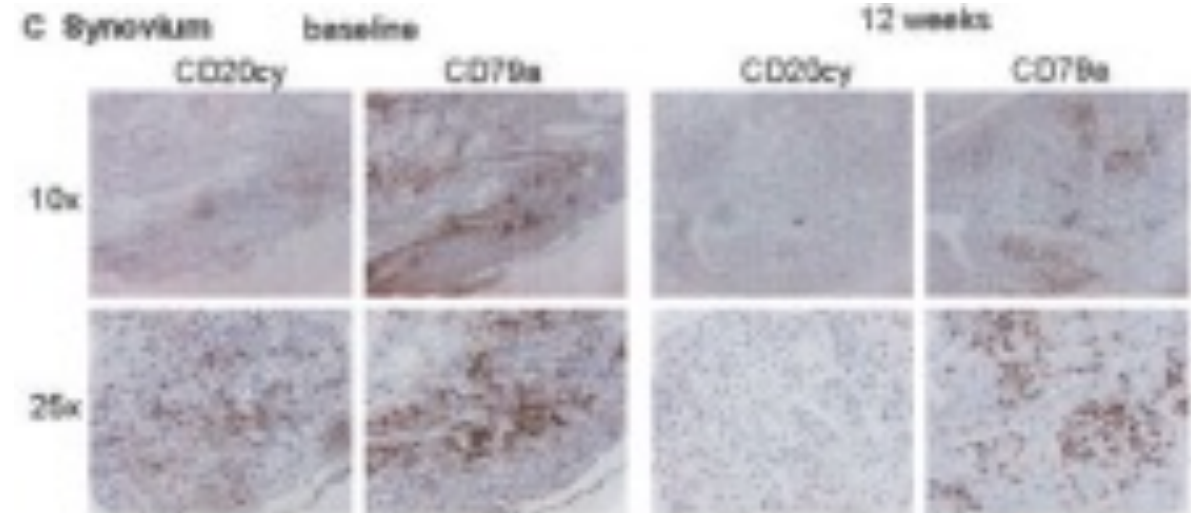
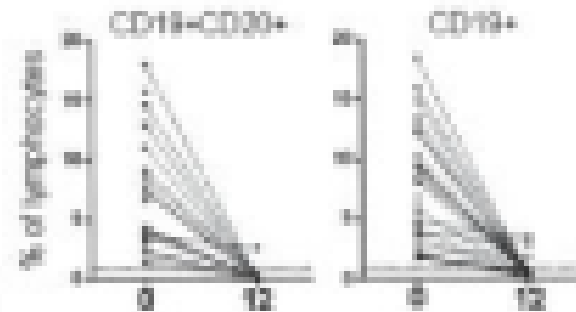
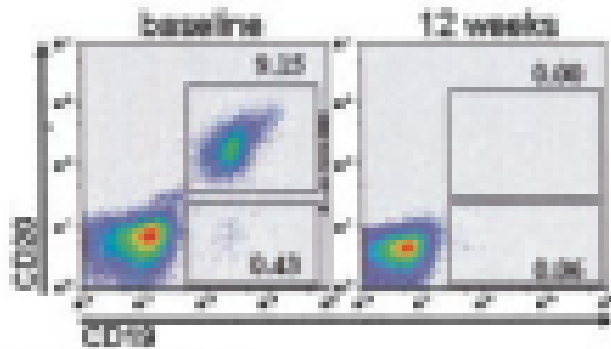
Rituximab has limited tissue penetrance

RA patients treated with rituximab have incomplete tissue B cell depletion

B cells mostly depleted in peripheral blood post-rituximab Tx

Limited synovial B cell depletion post-rituximab Tx

A Peripheral Blood



Systemic Lympho-ablation is Potentially Curative,

- A series of randomized controlled studies have been conducted to test lympho-ablation followed by stem cell rescue for refractory autoimmune disease^{1,2}
 - Over 3000 reported stem cell transplants worldwide
 - Efficacy reported in Severe systemic sclerosis and juvenile sclerosis, MS, SLE, juvenile idiopathic arthritis, multiple sclerosis, NMO and others
- Durable (>3 year) complete remissions off therapy occurred in large numbers of patients^{3,4}
 - 23-71%
 - Suggests curative potential by resetting the immune system

1. Ramalingam and Shah (2021), Stem cell therapy as a Treatment for Autoimmune Disease, *Current Allergy and Asthma Reports*

2. Swart *et al* (2017), Haematopoietic stem cell transplantation for autoimmune disease, *Nature Reviews*

3. Sullivan *et al* (2009), Hematopoietic cell transplantation for autoimmune disease, *Biol Blood Marrow Transplant*

4. Farge *et al* (2010), Autologous hematopoietic stem cell transplantation for autoimmune diseases, *Haematologica*

Systemic Lympho-ablation is Potentially Curative, but Toxic

- A series of randomized controlled studies have been conducted to test lympho-ablation followed by stem cell rescue for refractory autoimmune disease^{1,2}
 - Over 3000 reported stem cell transplants worldwide
 - Efficacy reported in Severe systemic sclerosis and juvenile sclerosis, MS, SLE, juvenile idiopathic arthritis, multiple sclerosis, NMO and others
- Durable (>3 year) complete remissions off therapy occurred in large numbers of patients^{3,4}
 - 23-71%
 - Suggests curative potential by resetting the immune system
- Toxicity was unacceptable with high intensity* lympho-ablative regimens (11% mortality)
 - *Containing TBI or high dose busulfan
- Reduced toxicity with intermediate conditioning** regimens, while maintaining efficacy
 - **Utilizing cyclophosphamide with anti-thymocyte globulin

1. Ramalingam and Shah (2021), Stem cell therapy as a Treatment for Autoimmune Disease, *Current Allergy and Asthma Reports*

2. Swart *et al* (2017), Haematopoietic stem cell transplantation for autoimmune disease, *Nature Reviews*

3. Sullivan *et al* (2009), Hematopoietic cell transplantation for autoimmune disease, *Biol Blood Marrow Transplant*

4. Farge *et al* (2010), Autologous hematopoietic stem cell transplantation for autoimmune diseases, *Haematologica*

What We Know.... (a brief summary)

- Autoimmune disease is a major global unmet need
- B cells play a central role in the many autoimmune diseases
- Antibody mediated clearance of B cells is incomplete and without durable responses
- Many autoimmune disease may be “cured” with deep lympho-ablation
 - Toxicity of deep lympho-ablation severely limits use of stem cell transplant

Engineered T cells (in Oncology):

- *Can traffic through all tissues to effect cytotoxicity*
- *Have established clinical efficacy for the systemic eradication of B cells*
- *Can be administered without the toxicity related to deep lymphoablative preconditioning*

CD19 CAR-T therapy for autoimmune disease

In the past two years, several papers have shown CD19 CAR-T efficacy in autoimmune disease

CORRESPONDENCE



CD19-Targeted CAR T Cells in Refractory Systemic Lupus Erythematosus

CD19-targeted
CAR T cells in refractory
antisynthetase
syndrome

nature
medicine

ARTICLES

<https://doi.org/10.1038/s41591-022-02017-5>

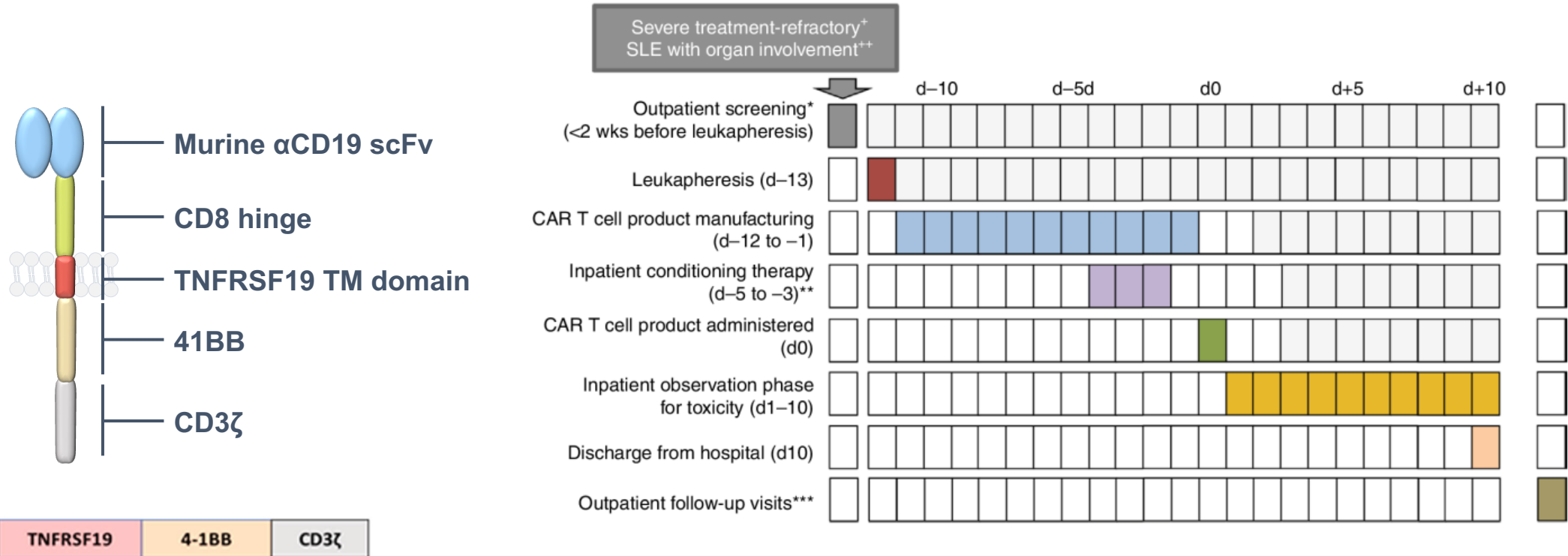


Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus

1. Mackensen et. al (2022), Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus, *Nature Medicine*
2. Mougiakakos et. al (2021) CD19-Targeted CAR T Cells in Refractory Systemic Lupus Erythematosus, *New England Journal of Medicine*
3. Muller et. al (2023) CD19-targeted CAR T cells in refractory antisynthetase syndrome, *The Lancet*

Anti-CD19 CAR-T in SLE

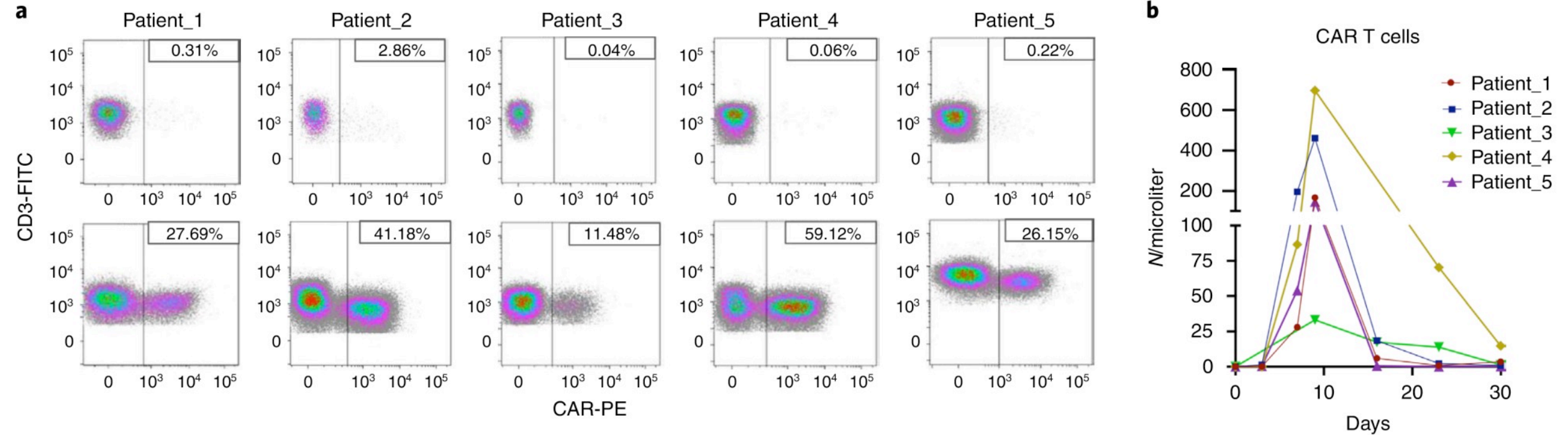
Patient treatment schema overview from FAU compassionate use protocol



1. Maschan et. al (2021), Multiple site place-of-care manufactured anti-CD19 CAR-T cells induce high remission rates in B-cell malignancy patients, *Nature Communications*
 2. Mackensen et. al (2022), Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus, *Nature Medicine*

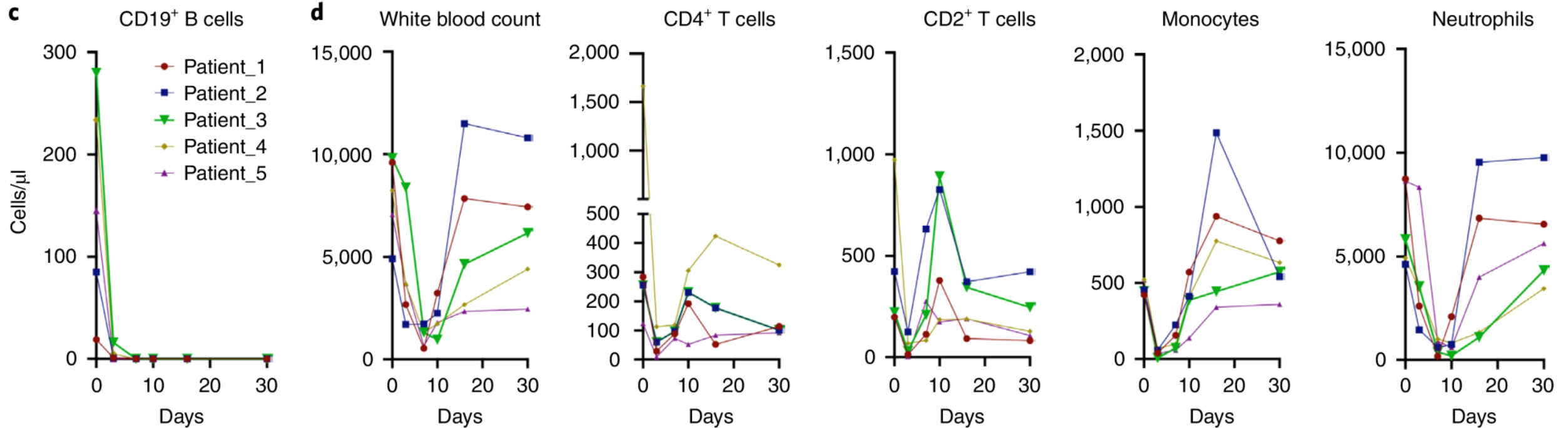
Robust T cell expansion observed post-infusion

Similar kinetics as observed with CD19 CAR T-cell therapy in hematologic malignancies



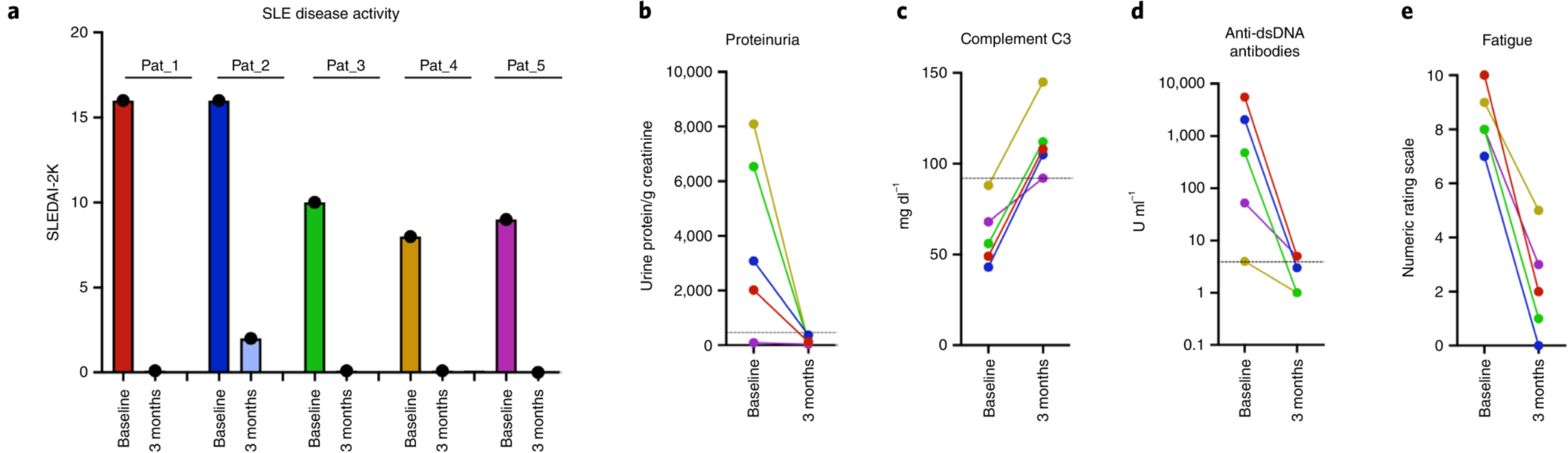
Specific CD19⁺ B cell aplasia observed for 30 days post-infusion

Rapid recovery of non-B cell leukocyte populations post-lymphodepletion



Remission or near complete remission observed at 3 months

Selected clinical biomarkers change dramatically by 3 months

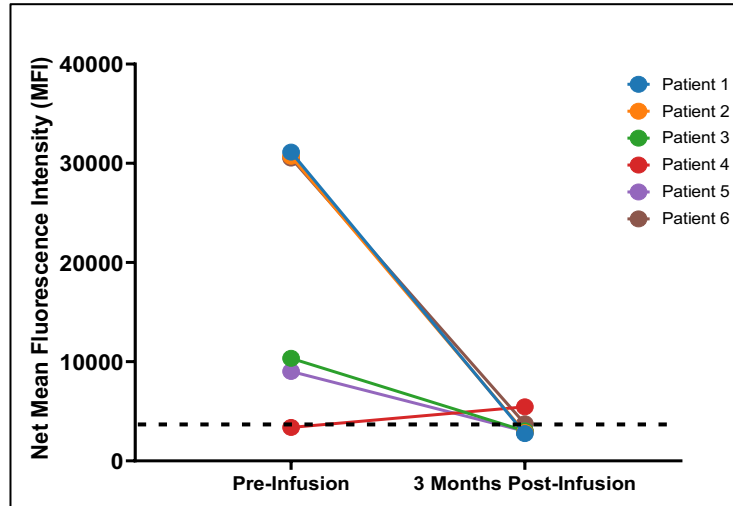


Reduction observed in SLE associated antibodies

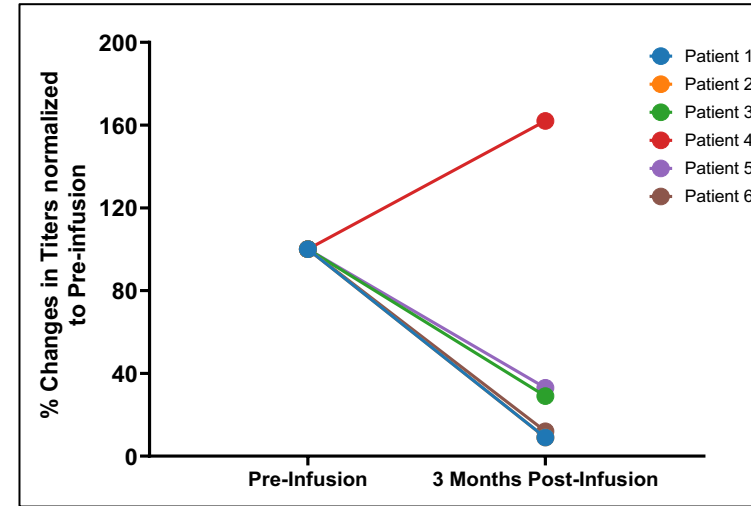
Most patients show a decrease following CAR-T infusion – patient #4 appears to be an outlier

Nucleosome

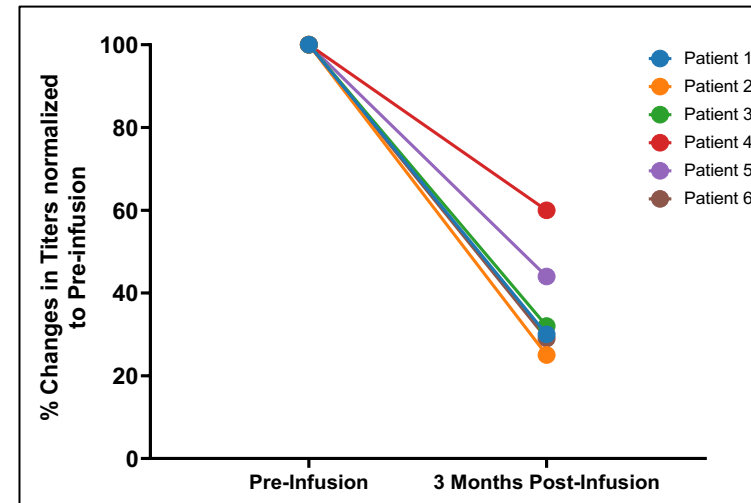
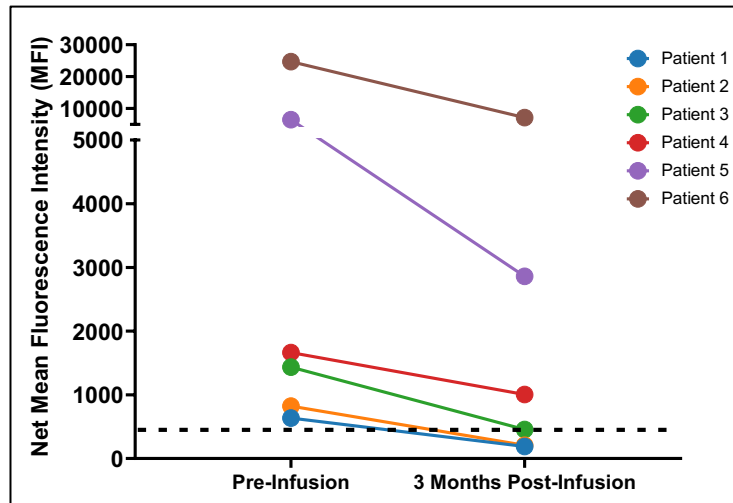
Raw Values



% Change



Sm(D3)

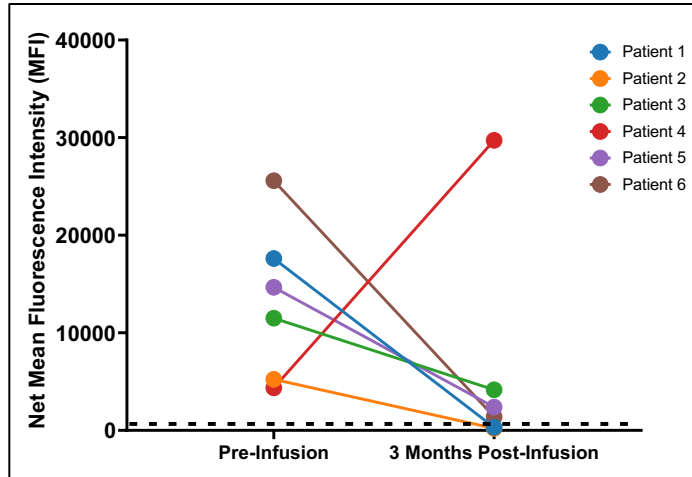


Reduction observed in SLE associated antibodies

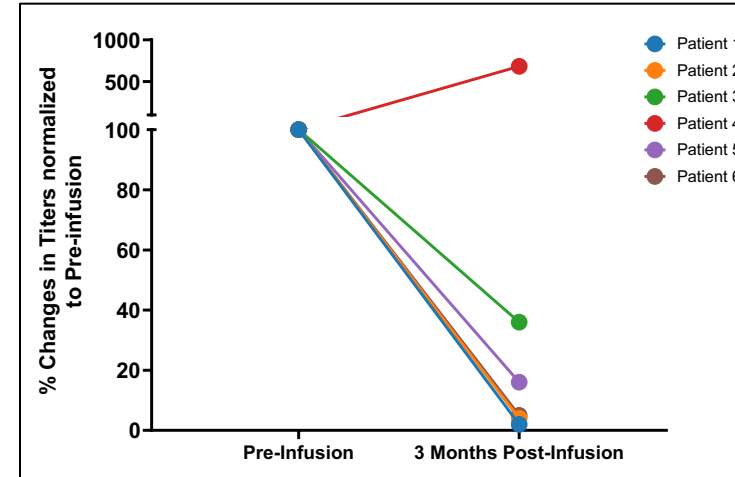
Patient #4 continues to remain an outlier

Histone

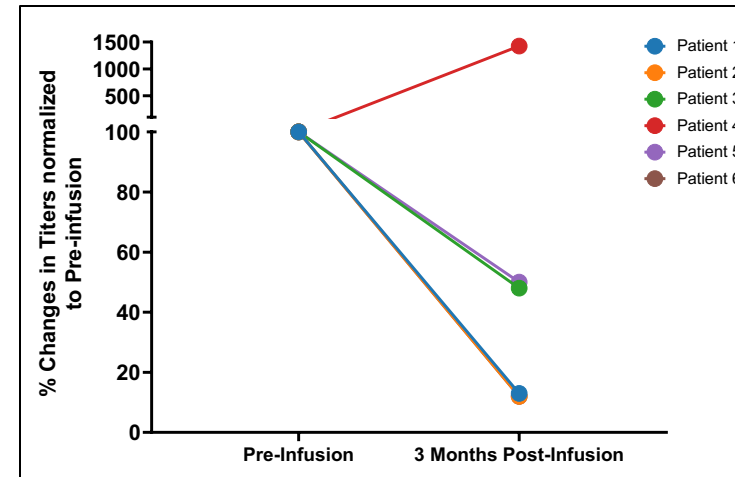
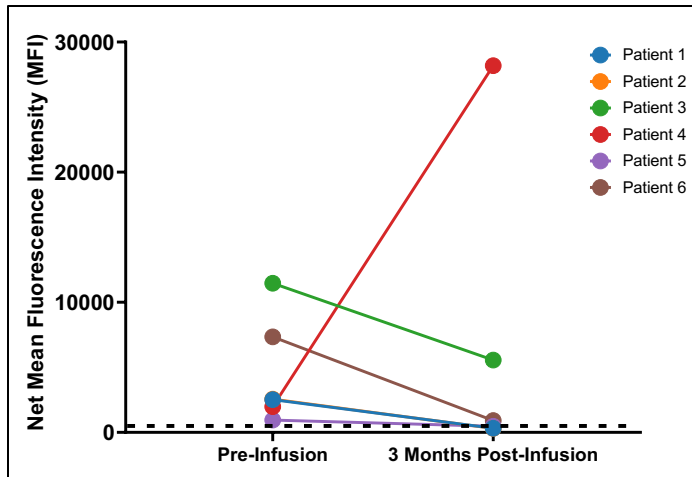
Raw Values



% Change



H1

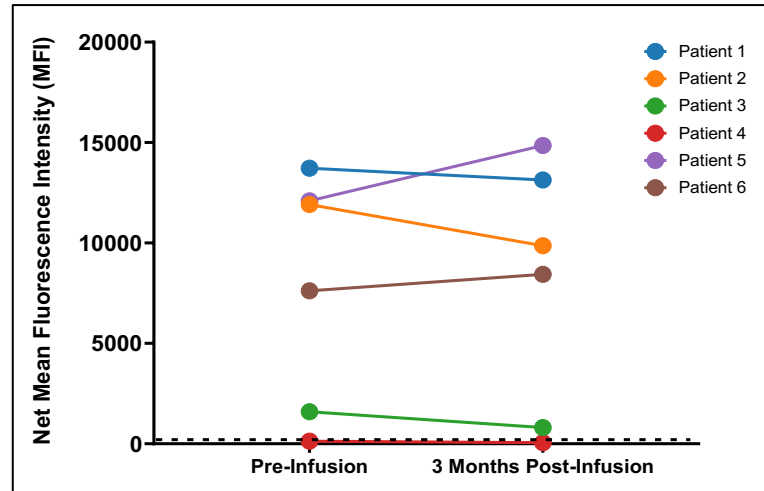


Preservation of pre-infusion vaccine antibodies

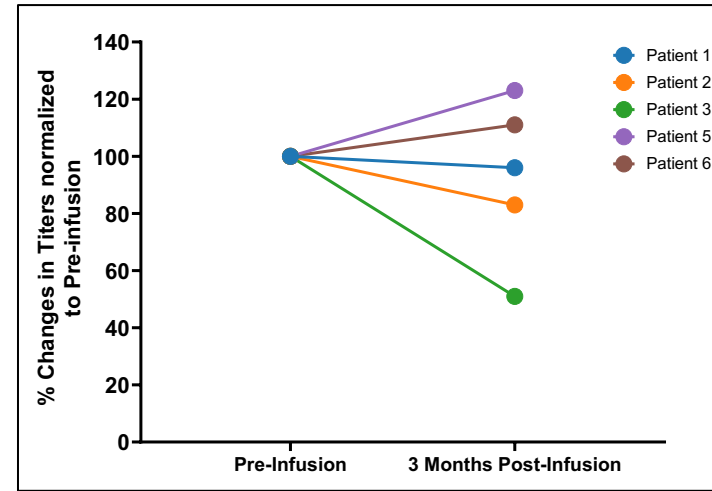
Representative titers shown: most patients remain stable or have minimal changes pre/post-infusion

Tetanus

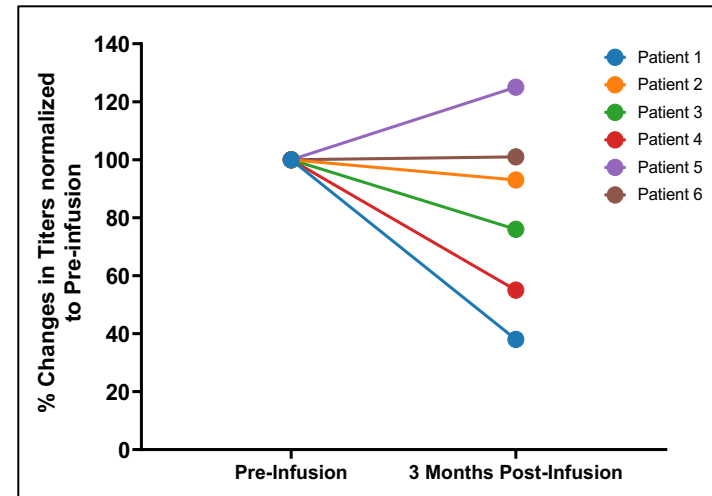
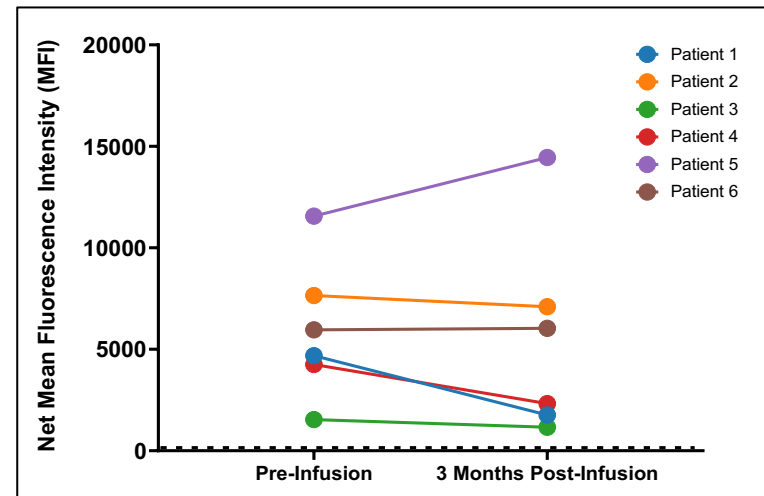
Raw Values



% Change



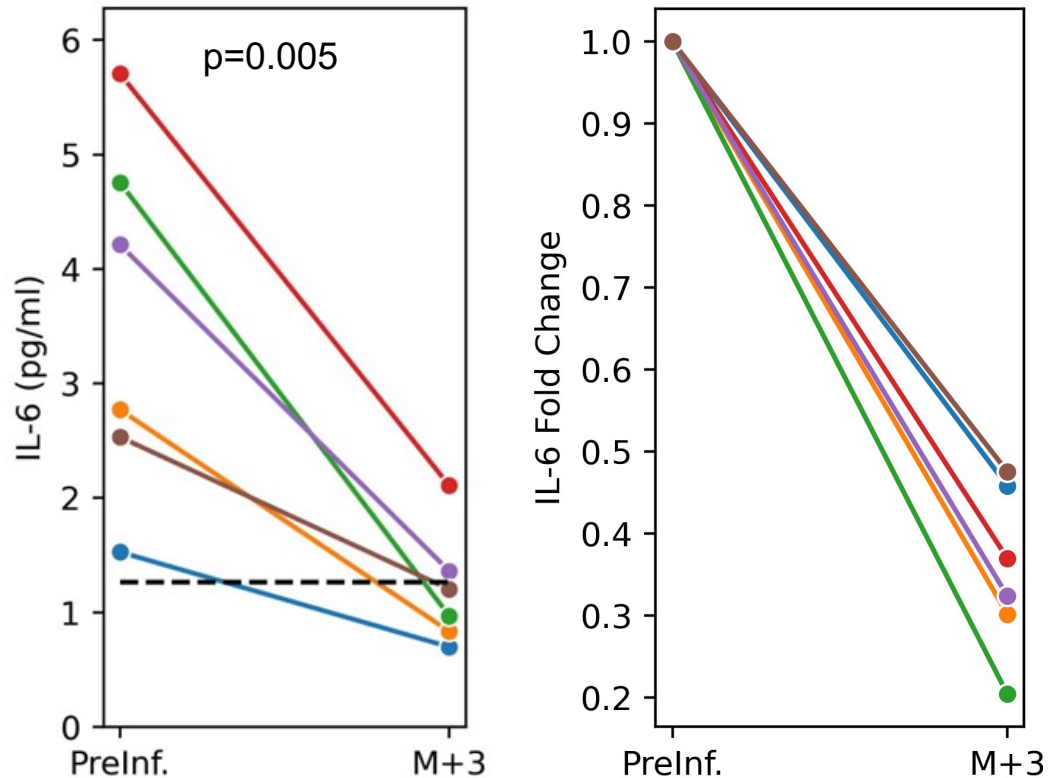
Diphtheria



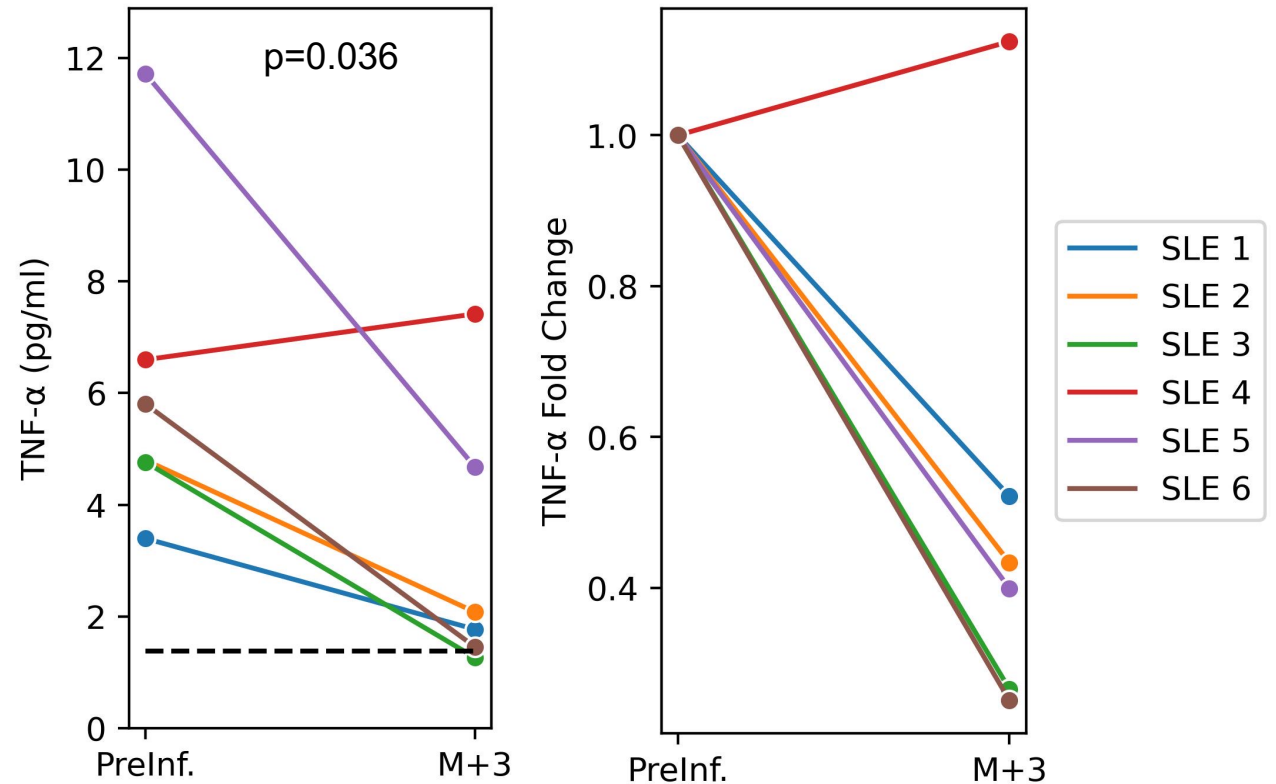
Many markers of systemic inflammation decreased at 3 months

B cell cytopenia could drive drop in IL-6 and TNF α either through direct secretion or via T cell activation

IL-6

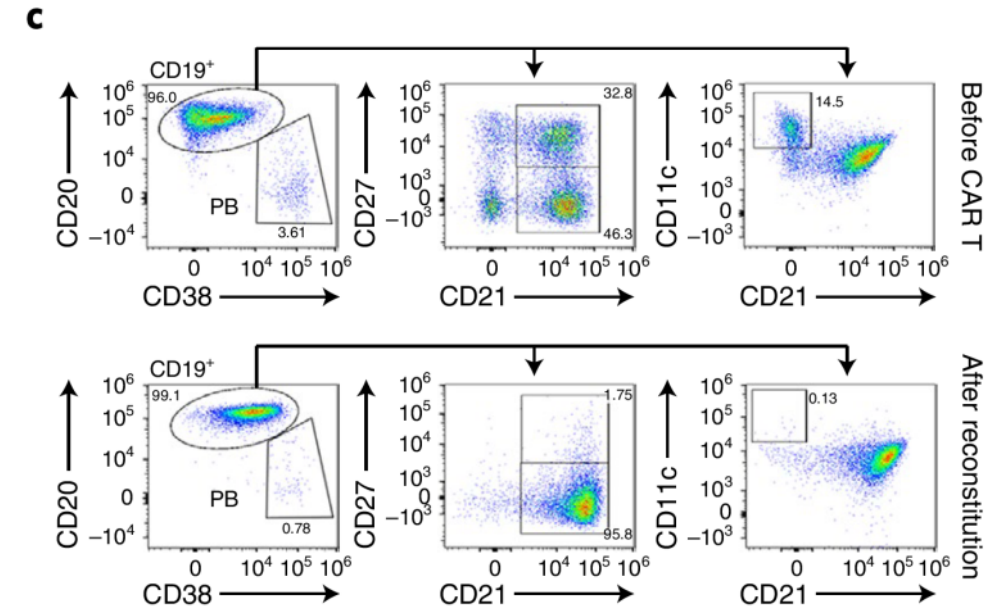
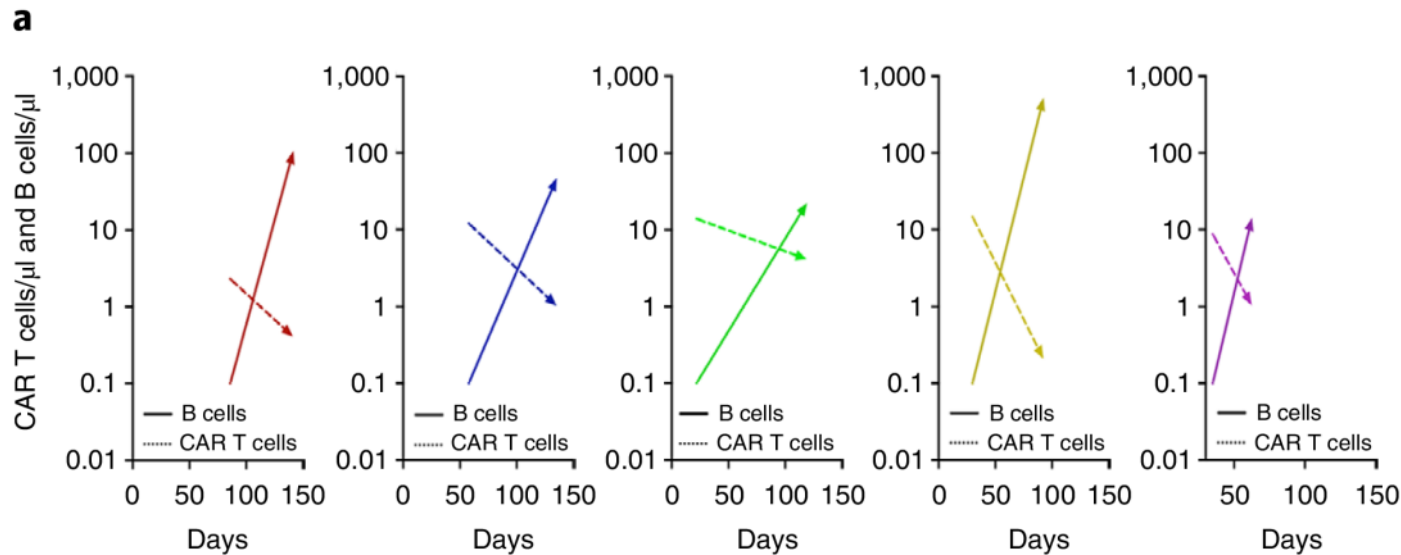


TNF α



CD19⁺ B cell recovery observed within 150 days post-infusion

Naïve B cells are the predominant population returning to the periphery post-infusion



Takeaways from initial exploration of CD19 CAR-T in SLE

CD19 41BBz CAR-T appears to have promising efficacy and safety in refractory SLE

- Safety

- No CRS > grade 1 reported across 5 patients
- No ICANs of any grade reported
- Non-B cell cytopenias appear to be due to cyclophosphamide and fludarabine < 14 to 21 days
- Vaccine and infectious disease antibodies are largely intact

- Efficacy

- All patients experienced complete or near-complete remission by 3 months
- No relapses to date: duration of remission has lasted ~ 1 to 2 years (data shared at ACR last Nov)
- Patients currently off all other immune suppressive therapies
- Preliminary evidence suggests immune reset across most patients

Active clinical trials exploring CAR-T in autoimmune disease

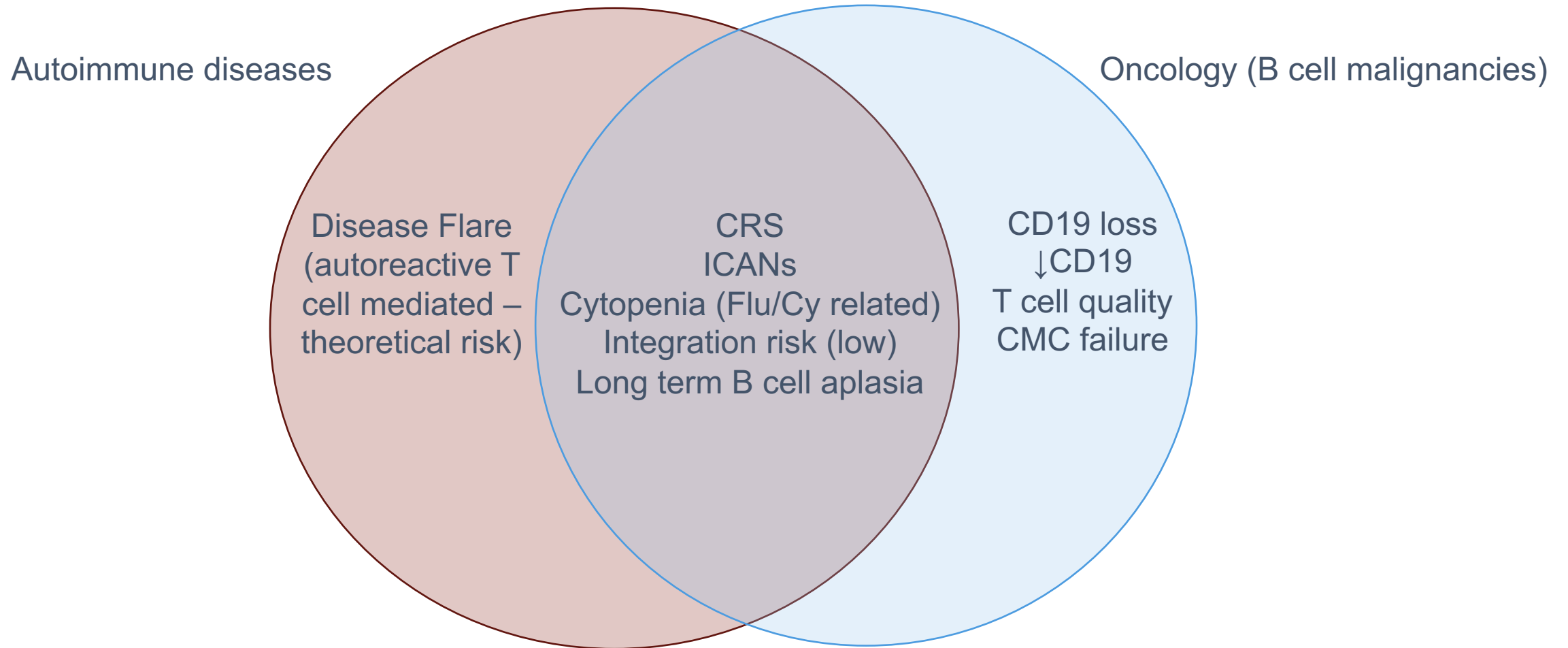
List below includes CD19 and BCMA CAR-T approaches (search date of 4.21.2023)

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Recruiting	CAR-T Cells Targeting Autoimmune Diseases	<ul style="list-style-type: none"> Autoimmune Diseases 	<ul style="list-style-type: none"> Biological: 4SCAR T cells 	<ul style="list-style-type: none"> Shenzhen Geno-immune Medical Institute Shenzhen, Guangdong, China Gulin Hospital of Chinese Traditional and Western Medicine Gulin, Guangxi, China
2	<input type="checkbox"/>	Recruiting	Clinical Study of Targeting CD7 CAR-T Cells in the Treatment of Autoimmune Diseases	<ul style="list-style-type: none"> Crohn Disease Ulcerative Colitis Dermatomyositis (and 2 more...) 	<ul style="list-style-type: none"> Biological: CD7 CAR T-cells 	<ul style="list-style-type: none"> The first affiliated hospital of medical college of zhejiang university Hangzhou, Zhejiang, China
3	<input type="checkbox"/>	Recruiting	A Study of CD19/BCMA Chimeric Antigen Receptor T Cells Therapy for Patients With Refractory Systemic Lupus Erythematosus	<ul style="list-style-type: none"> Systemic Lupus Erythematosus Autoimmune Diseases 	<ul style="list-style-type: none"> Biological: Assigned Interventions CD19/BCMA CAR T-cells 	<ul style="list-style-type: none"> The First Affiliated Hospital, College of Medicine, Zhejiang University Hangzhou, Zhejiang, China
4	<input type="checkbox"/>	Recruiting	A Study of CD19/BCMA Chimeric Antigen Receptor T Cells Therapy for Patients With Refractory Sjogren's Syndrome	<ul style="list-style-type: none"> Sjogren's Syndrome Autoimmune Diseases 	<ul style="list-style-type: none"> Biological: Assigned Interventions CD19/BCMA CAR T-cells 	<ul style="list-style-type: none"> The First Affiliated Hospital, College of Medicine, Zhejiang University Hangzhou, Zhejiang, China
5	<input type="checkbox"/>	Recruiting	A Study of CD19/BCMA Chimeric Antigen Receptor T Cells Therapy for Patients With Refractory Scleroderma	<ul style="list-style-type: none"> Scleroderma Autoimmune Diseases 	<ul style="list-style-type: none"> Biological: Assigned Interventions CD19/BCMA CAR T-cells 	<ul style="list-style-type: none"> The First Affiliated Hospital, College of Medicine, Zhejiang University Hangzhou, Zhejiang, China
6	<input type="checkbox"/>	Recruiting	A Study of CD19/BCMA Chimeric Antigen Receptor T Cells Therapy for Patients With Refractory Immune Nephritis	<ul style="list-style-type: none"> Immune Nephritis Autoimmune Diseases Lupus Nephritis 	<ul style="list-style-type: none"> Biological: Assigned Interventions CD19/BCMA CAR T-cells 	<ul style="list-style-type: none"> The First Affiliated Hospital, College of Medicine, Zhejiang University Hangzhou, Zhejiang, China
7	<input type="checkbox"/>	Recruiting NEW	An Open-label, Study to Assess Safety, Efficacy and Cellular Kinetics of YTB323 in Severe, Refractory Autoimmune Disorders	<ul style="list-style-type: none"> Systemic Lupus Erythematosus Lupus Nephritis 	<ul style="list-style-type: none"> Drug: YTB323 	<ul style="list-style-type: none"> Novartis Investigative Site Barcelona, Catalunya, Spain
8	<input type="checkbox"/>	Recruiting	Safety and Efficacy of CT103A Cells for Relapsed/Refractory Antibody-associated Idiopathic Inflammatory Diseases of the Nervous System	<ul style="list-style-type: none"> Autoimmune Diseases Autoimmune Diseases of the Nervous System Neuromyelitis Optica Spectrum Disorder (and 3 more...) 	<ul style="list-style-type: none"> Biological: CT103A cells Drug: Cyclophosphamide and fludarabine 	<ul style="list-style-type: none"> Tongji Hospital affiliated to Tongji Medical College of Huazhong University of Science and Technology Wuhan, Hubei, China

9	<input type="checkbox"/>	Unknown †	A Study of CD19 Redirected Autologous T Cells for CD19 Positive Systemic Lupus Erythematosus (SLE)	<ul style="list-style-type: none"> Systemic Lupus Erythematosus (SLE) 	<ul style="list-style-type: none"> Drug: cyclophosphamide Drug: anti-CD19-CAR.T cells 	<ul style="list-style-type: none"> Shanghai Jiaotong University School of Medicine, Renji Hospital Shanghai, China
10	<input type="checkbox"/>	Withdrawn	Treatment of Relapsed and/or Refractory AQP4-IgG Seropositive NMOSD by Tandem CAR T Cells Targeting CD19 and CD20	<ul style="list-style-type: none"> Neuromyelitis Optica Spectrum Disorder 	<ul style="list-style-type: none"> Biological: Corticosteroids & tanCAR19/20 	<ul style="list-style-type: none"> People's Liberation of Army General Hospital (PLAGH) Beijing, Beijing, China
11	<input type="checkbox"/>	Recruiting	Descartes-08 CAR-T Cells in Generalized Myasthenia Gravis (MG)	<ul style="list-style-type: none"> Myasthenia Gravis, Generalized 	<ul style="list-style-type: none"> Drug: Descartes-08 	<ul style="list-style-type: none"> The Research Center of Southern California Carlsbad, California, United States University of California Irvine Irvine, California, United States SFM Clinical Research, LLC Boca Raton, Florida, United States (and 6 more...)
12	<input type="checkbox"/>	Recruiting	A Clinical Study of CD19/BCMA CAR-T Cells in the Treatment of Refractory POEMS Syndrome, Amyloidosis, Autoimmune Hemolytic Anemia, and Vasculitis	<ul style="list-style-type: none"> POEMS Syndrome Amyloidosis Autoimmune Hemolytic Anemia Vasculitis 	<ul style="list-style-type: none"> Biological: CD19/BCMA CAR T-cells 	<ul style="list-style-type: none"> The first affiliated hospital of medical college of zhejiang university Hangzhou, Zhejiang, China
13	<input type="checkbox"/>	Recruiting	BCMA-CD19 cCAR T Cell Treatment of Relapsed/Refractory Systemic Lupus Erythematosus (SLE)	<ul style="list-style-type: none"> Relapsed/Refractory, Systemic Lupus Erythematosus (SLE) 	<ul style="list-style-type: none"> Biological: BCMA-CD19 cCAR T cells 	<ul style="list-style-type: none"> Zhongshan People's Hospital Zhongshan, Guangdong, China
14	<input type="checkbox"/>	Unknown †	Stem Cells From Human Exfoliated Teeth in Treatment of Diabetic Patients With Significantly Reduced Islet Function	<ul style="list-style-type: none"> Type1diabetes 	<ul style="list-style-type: none"> Biological: Stem cells from human exfoliated teeth 	<ul style="list-style-type: none"> Changhai hospital Shanghai, Shanghai, China
15	<input type="checkbox"/>	Recruiting	Open-label Study to Determine the Maximum Tolerated Dose of DSG3-CAART in Mucosal-dominant PV Patients (mPV)	<ul style="list-style-type: none"> Mucosal-Dominant Pemphigus Vulgaris 	<ul style="list-style-type: none"> Biological: DSG3-CAART 	<ul style="list-style-type: none"> Stanford University, Dept. of Dermatology Redwood City, California, United States UC Davis, Dept. of Dermatology Sacramento, California, United States Northwestern University Chicago, Illinois, United States (and 7 more...)
16	<input type="checkbox"/>	Recruiting	Open-label Study to Evaluate the Safety of Various Dosing Regimens of MuSK-CAART for MuSK Myasthenia Gravis	<ul style="list-style-type: none"> MuSK Myasthenia Gravis 	<ul style="list-style-type: none"> Biological: MuSK-CAART 	<ul style="list-style-type: none"> UC Irvine, Department of Neurology Orange, California, United States UC Davis, Department of Neurology Sacramento, California, United States Oregon Health & Science University (OHSU) Portland, Oregon, United States

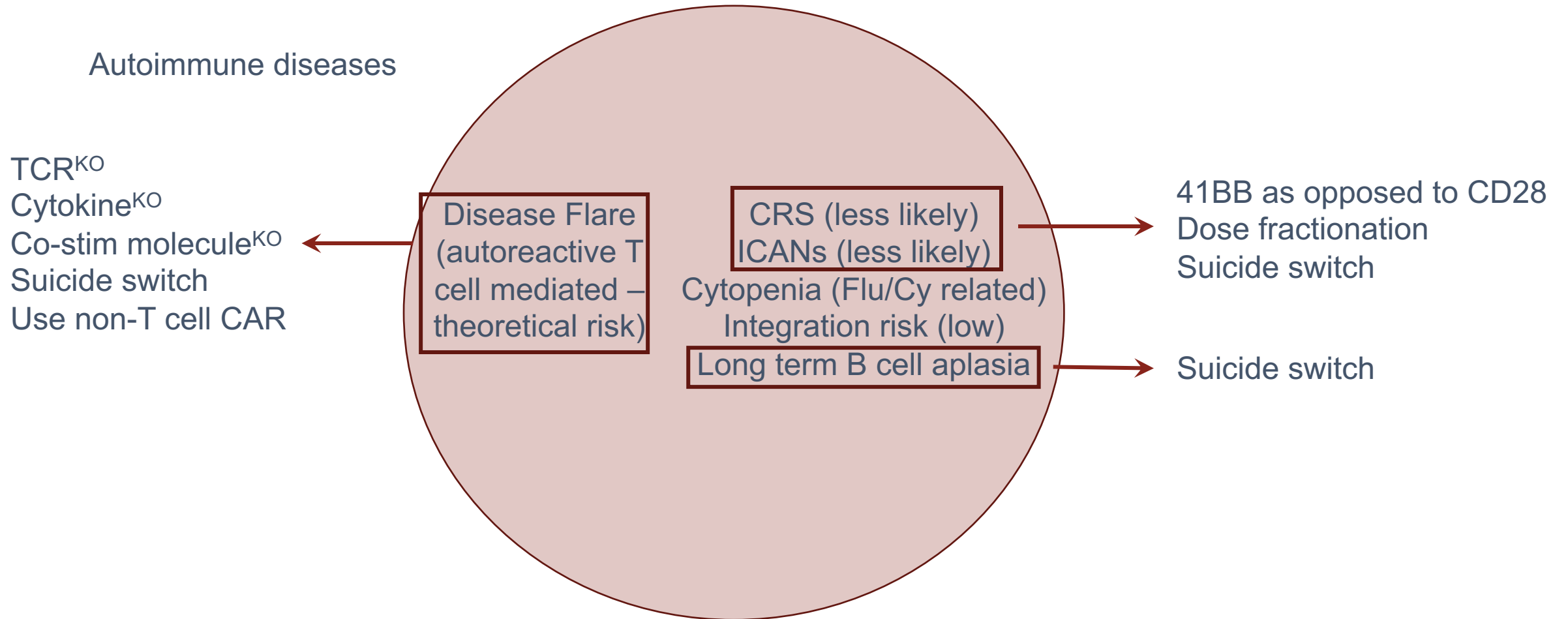
Unique considerations for CAR-T in autoimmune disease

Safety, Efficacy, Manufacturing considerations (not exhaustive)



Potential mitigation strategies

Not exhaustive



Summary

CD19 (FMC63) 41BBz CAR-T for SLE (in FAU compassionate use protocol)

- B cells are a major driver of autoimmune disease
 - Antibody secreting function
 - As an antigen presenting cell
 - Secretes pro-inflammatory cytokines as an APC
- CD19 CAR T-cells have been observed to eliminate all B cells in SLE patients
 - Superior penetrance as compared to standard biologics approaches
 - Can provide safe and durable complete responses up to two years so far
- Unique considerations in employing CD19 CAR T-cells in autoimmune disease
 - Mitigation strategies exist for potential roadblocks

Acknowledgments

- Cabaletta

Jenell Volkov
Daniel Nunez
Mallory Fouch
Zach Vorndran
Darshil Patel
Steve Wong

Cabaletta Bio™



- FAU

Georg Schett
Andreas Mackensen

