Analysis of the NeflgArd Part A study population confirms Nefecon suppresses circulating levels of BAFF, APRIL, and soluble BCMA in IgA nephropathy

Nadia Nawaz, Karen Molyneux, and Jonathan Barratt

College of Medicine, Biological Sciences and Psychology, University of Leicester, Leicester, UK

C O I disclosure

presenter : *Nadia Nawaz*

I have nothing to disclose

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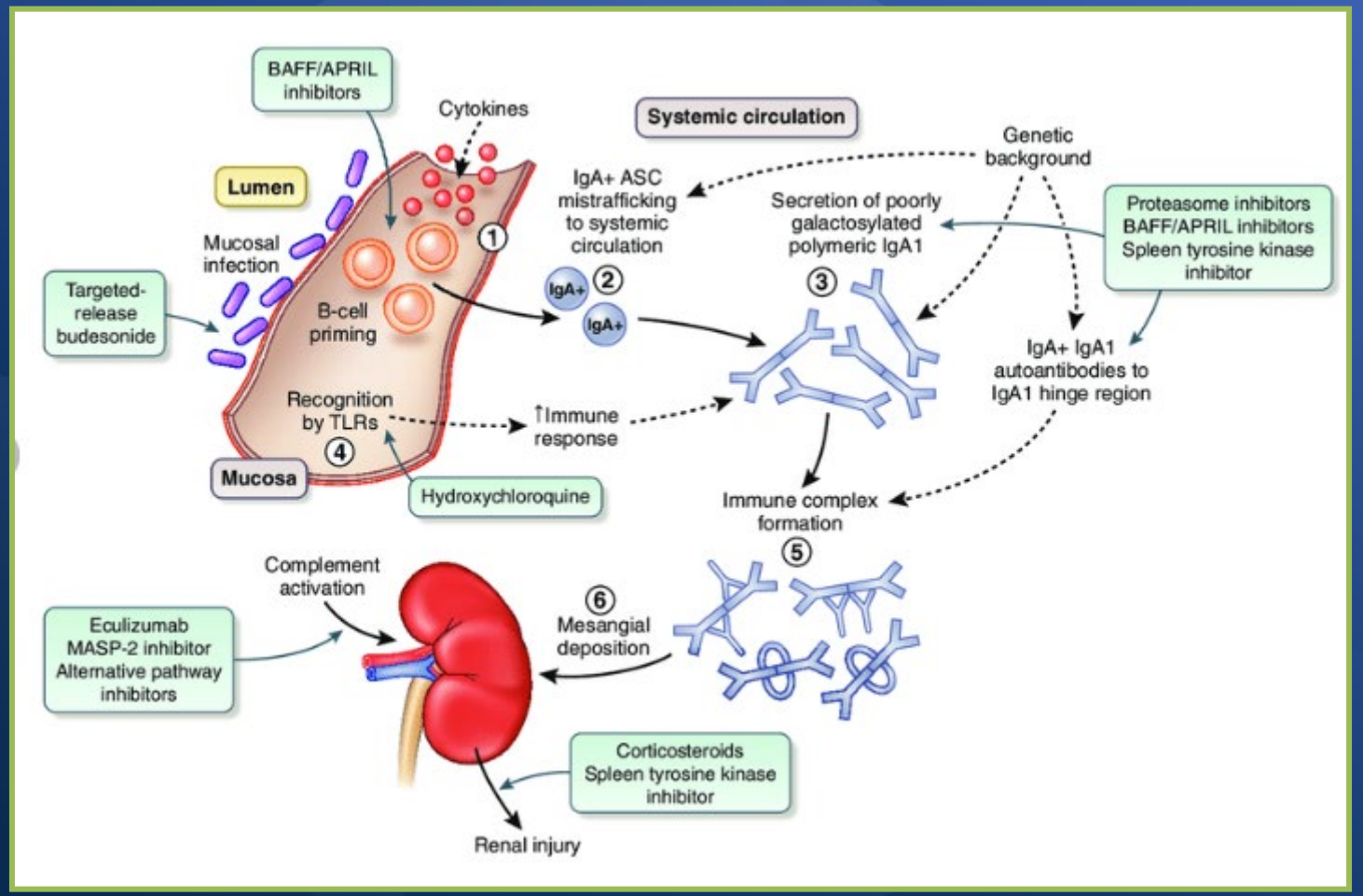
Background

Pathogenesis of IgA nephropathy



APRIL, a proliferation-inducing ligand; ASC, antibody-secreting cells; BAFF, B-cell activating factor; IgA, immunoglobulin A; MASP-2, mannan-binding lectin-associated serine protease-2; TLR, toll-like receptor.

Floege J, *et al. Kidney Int* 2019;95:268-280.

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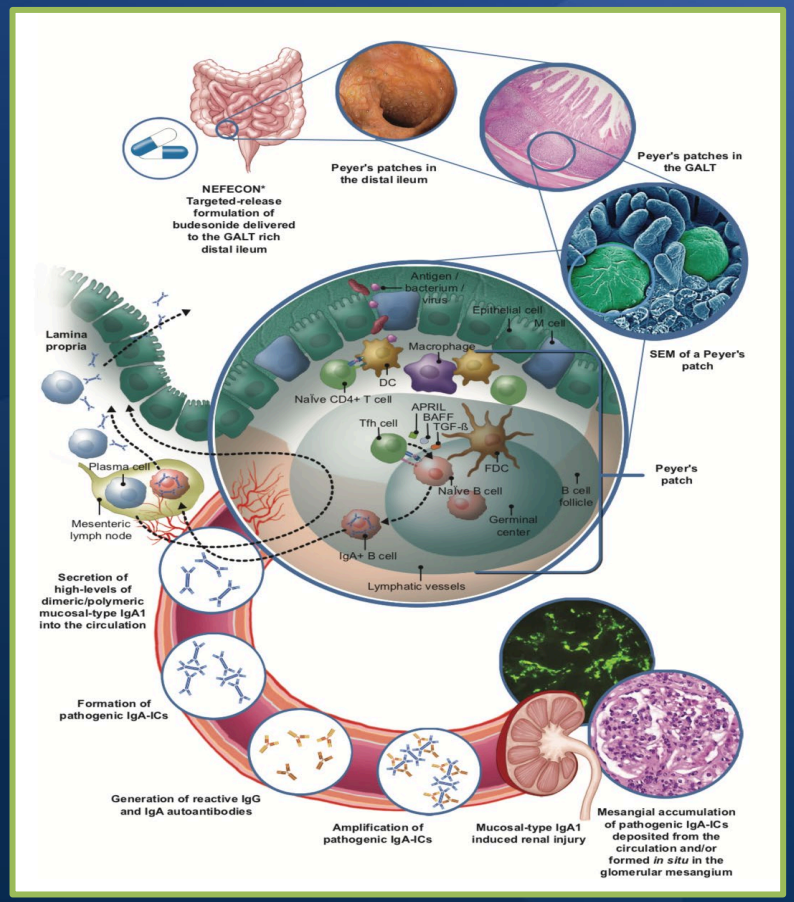
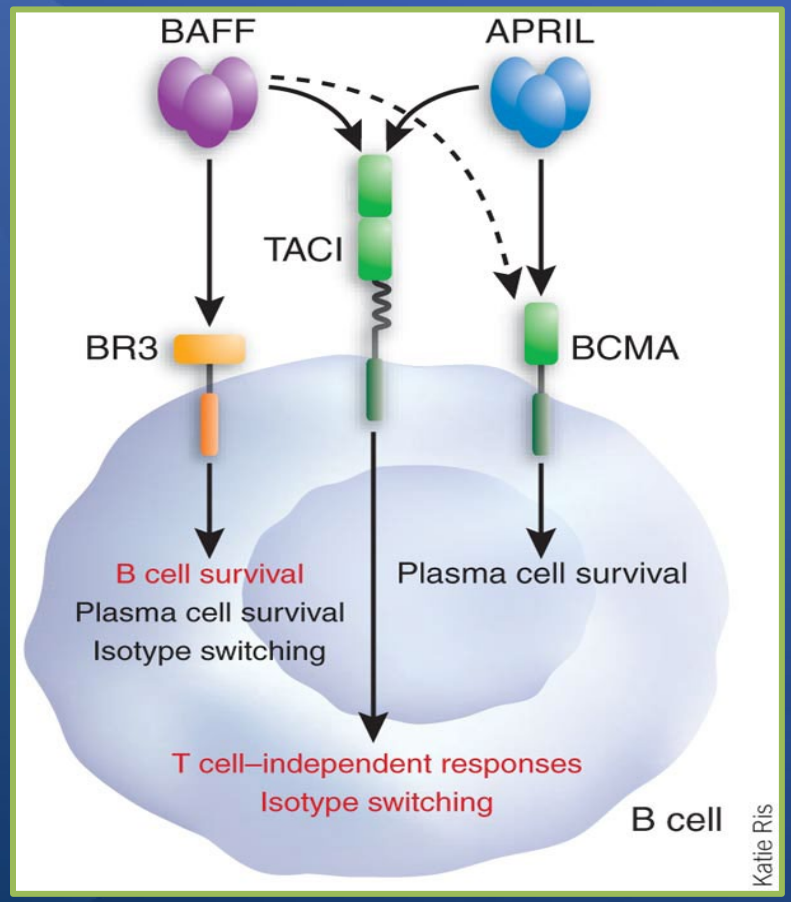
Background

The Peyer's patch and mucosal IgA synthesis



Control of B cells/T cells in the Peyer's patches



APRIL, a proliferation-inducing ligand; BAFF, B-cell activating factor; BCMA, B-cell maturation antigen; BR3, B lymphocyte stimulator receptor 3; CD, cluster of differentiation; DC, dendritic cells; FDC, follicular dendritic cells; GALT, gut-associated lymphoid tissue; IgA, immunoglobulin A; IgG, immunoglobulin G; IgA-IC, immunoglobulin A immune complex; SEM, scanning electron micrograph; TACI, transmembrane activator and calcium modulating ligand interactor; TGF-β; transforming growth factor beta; Tfh, T follicular helper cell.

Barratt J, *et al. Kidney Int Rep* 2020;5:1620-1624.

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J Nephrol. Jul-Aug 2013;26(4):683-90. doi: 10.5301/jn.5000218. Epub 2012 Oct 4.

Serum BAFF is elevated in patients with IgA nephropathy and associated with clinical and histopathological features

Gang Xin [1], Wei Shi, Li-Xia Xu, Yun Su, Li-Jun Yan,

Clinical TRANSPLANTATION
The Journal of Clinical and Translational Research

ORIGINAL ARTICLE

A proliferation-inducing ligand increase precedes IgA nephropathy recurrence in kidney transplant recipients

Luis Martín-Penagos, Adalberto Benito-Hernández, David San Segundo, Cristina Sango,
Javier Gómez-Román, Gema Fernández-Fresnedo, Marcos López-Hoyos, Juan C. Ruiz,

BAFF induces a hyper-IgA syndrome in the intestinal lamina propria concomitant with IgA deposition in the kidney independent of LIGHT

Douglas D. McCarthy, Sidney Chiu, Yunfei Gao, Leslie E. Summers-deLuca, Jennifer L. Gommerman *

Department of Immunology, University of Toronto

Received 26 May 2
Available onl

Research article

Mice overexpressing BAFF develop a commensal flora–dependent, IgA-associated nephropathy

Douglas D. McCarthy,[1] Julie Kujawa,[2] Cheryl Wilson,[2] Adrian Papandile,[2] Urjana Poreci,[2]
Elisa A. Porfilio,[1] Lesley Ward,[1] Melissa A.E. Lawson,[3] Andrew J. Macpherson,[3] Kathy D. McCoy,[3]
York Pei,[4] Lea Novak,[5] Jeannette Y. Lee,[6] Bruce A. Julian,[5] Jan Novak,[5] Ann Ranger,[2]
Jennifer L. Gommerman,[1] and Jeffrey L. Browning[2]

APRIL and TALL-1 and receptors BCMA and TACI: system for regulating humoral immunity

Gang Yu, Tom Boone, John Delaney, Nessa Hawkins, Michael Kelley, Meena Ramakrishnan, Susan McCabe, Wan-rong Qiu, Masayo Kornuc, Xing-Zhong Xia, Jane Guo, Marina Stolina, William J. Boyle, Ildiko Sarosi, Hailing Hsu, Giorgio Senaldi & Lars E. Theill

Nature Immunology **1**, 252–256(2000) | Cite this article

nature research

OPEN

Analysis of the receptor BCMA as a biomarker in systemic lupus erythematosus patients

Diana Celeste Salazar-Camarena[1],
Miguel Marín-Rosales[2] & José Franci

Contents lists available at ScienceDirect

Cellular Immunology

journal homepage: www.elsevier.com/locate/ycimm

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A proliferation-inducing ligand (APRIL) induced hyper-production of IgA from tonsillar mononuclear cells in patients with IgA nephropathy

Miki Takahara[a,*], Toshihiro Nagato[a], Yui Nozaki[a], Takumi Kumai[b], Akihiro Katada[a],
Tatsuya Hayashi[b], Yasuaki Harabuchi[a]

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Expression profile of BAFF in peripheral blood from patients of IgA nephropathy: Correlation with clinical features and Streptococcus pyogenes infection

Authors: Nuoyan Zheng, Jinjin Fan, Bing Wang
Qiongqiong Yang, Xueqing Yu

Abstracts

P0344

NEFECON® (BUDESONIDE) SELECTIVELY REDUCES CIRCULATING LEVELS OF BAFF (BLYS) AND SOLUBLE BCMA AND TACI IN IGA NEPHROPATHY

Karen Molyneux[1], David Wimbury[1], Jonathan Barratt[1]
[1]*University of Leicester, Mayer IgA Nephropathy Laboratory, Department of Cardiovascular Sciences, Leicester, United Kingdom*

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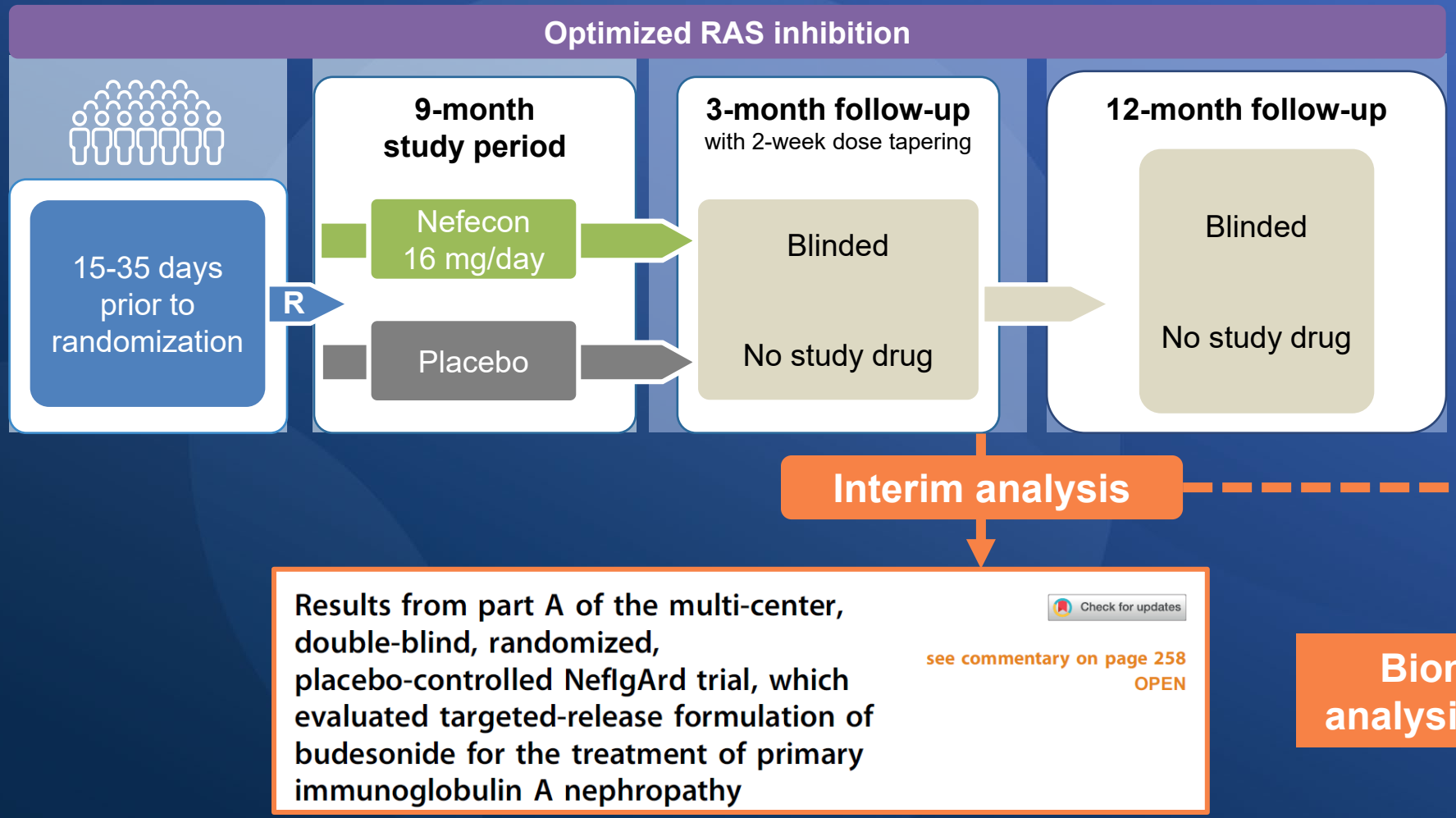
NeflgArd trial



Results from part A of the multi-center, double-blind, randomized, placebo-controlled NeflgArd trial, which evaluated targeted-release formulation of budesonide for the treatment of primary immunoglobulin A nephropathy

Check for updates

see commentary on page 258

OPEN

RAS, renin–angiotensin system.

Barratt J, *et al. Kidney Int* 2022;103:391-402. Lafayette R, *et al. Lancet* 2023;402:859-870.

Methods

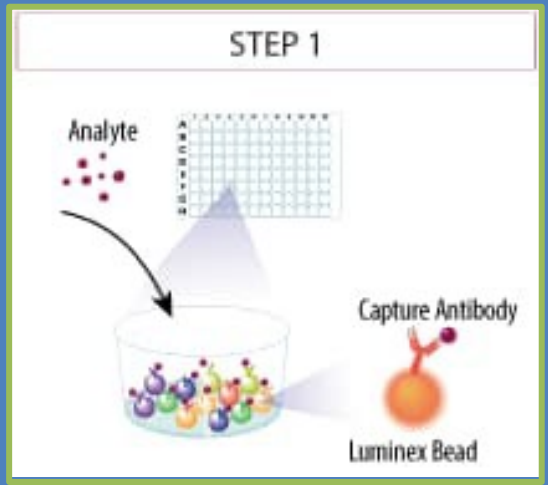
Samples Analysed

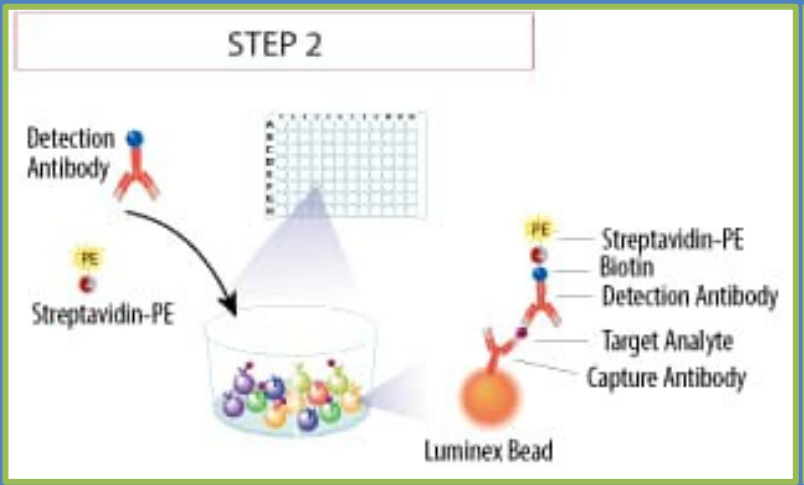
9-month study period

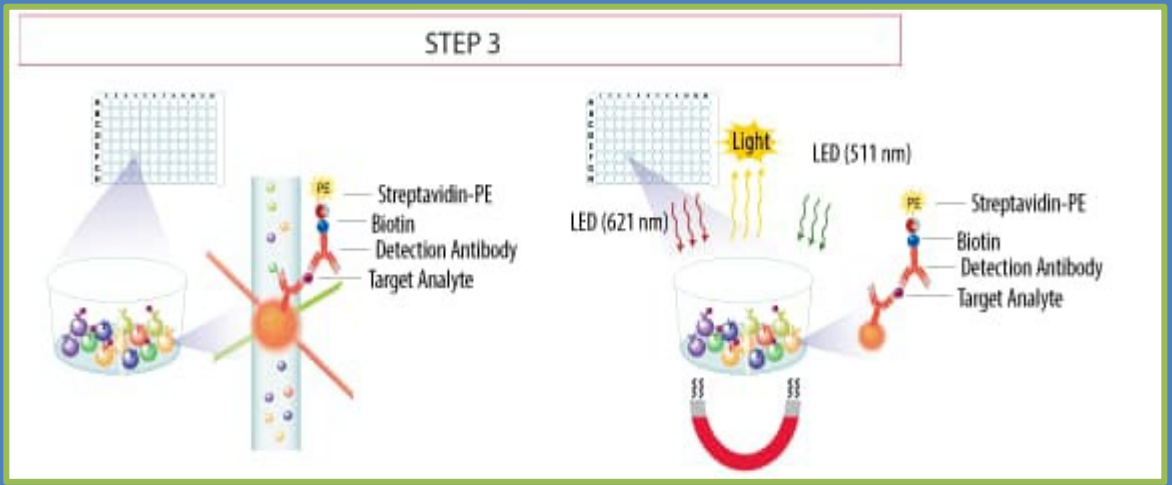
- Nefecon 16 mg/day
- Placebo

Serum Samples Collected at:

- 3 Months
- 6 Months
- 9 Months

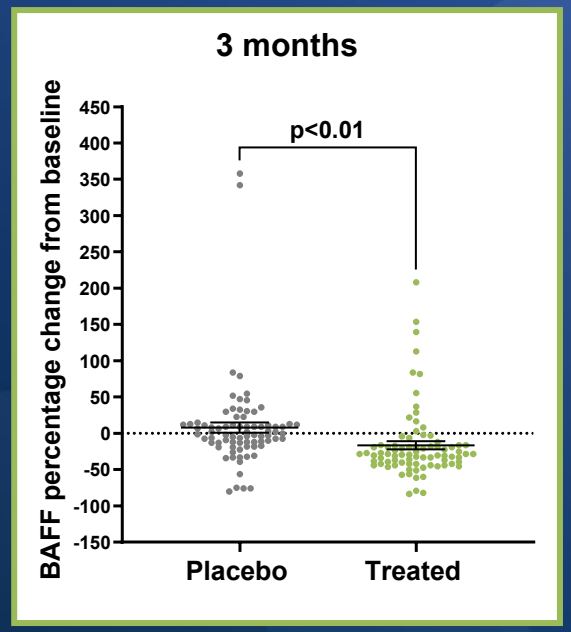


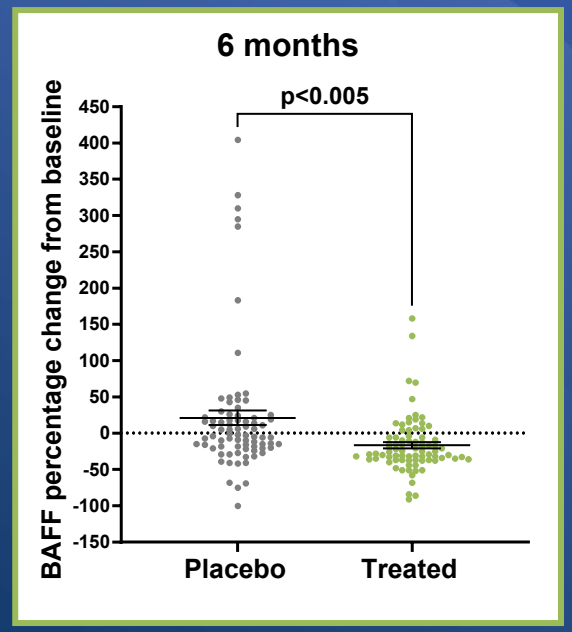


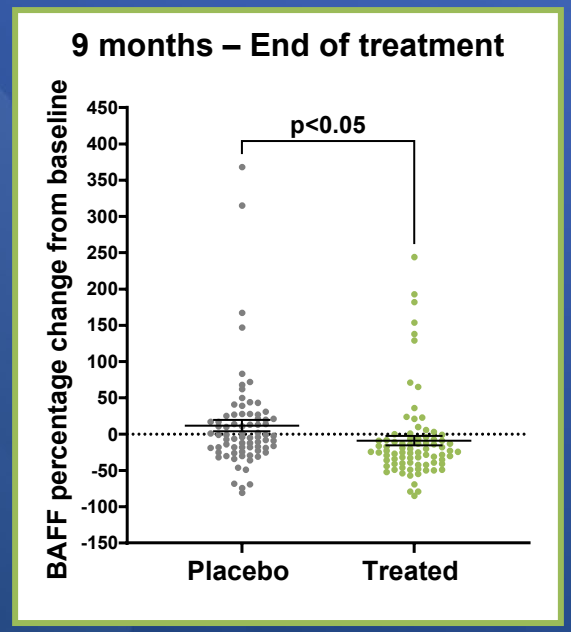


LED, light emitting diode; PE, phycoerythrin.

Nefecon supresses BAFF levels



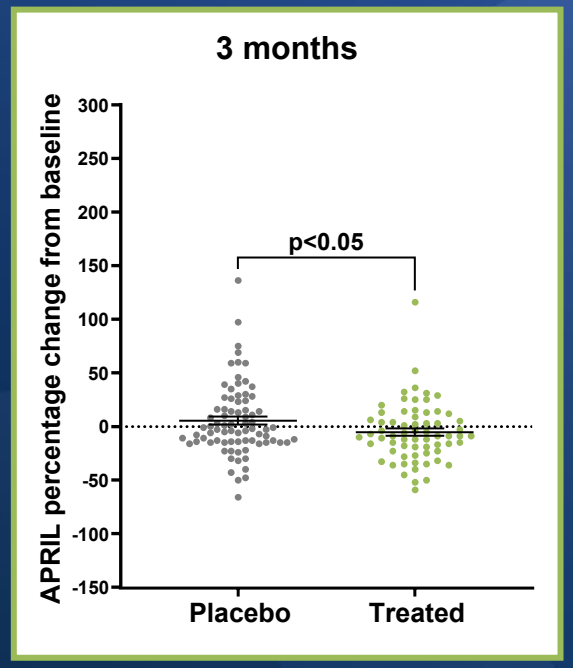


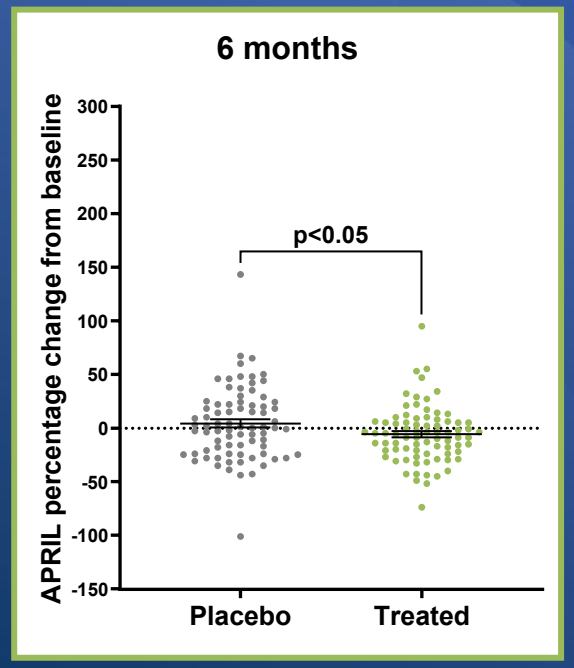


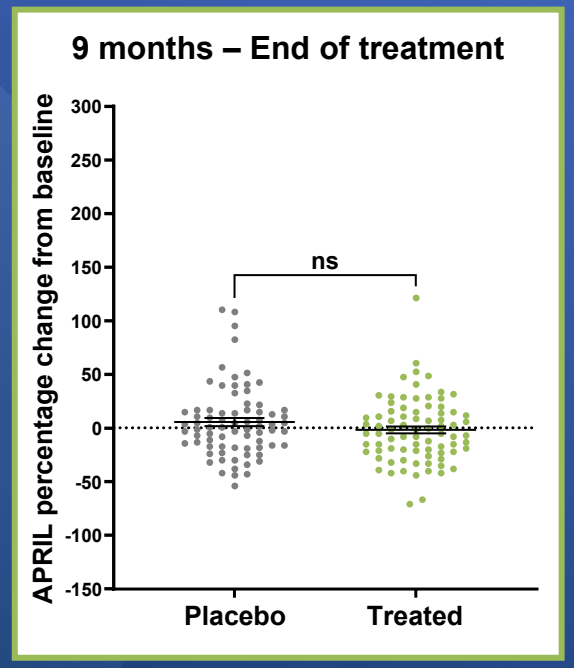
Reduction in levels of BAFF

BAFF data for Phase 2b trial were presented at ASN 2022.
ASN, American Society of Nephrology; BAFF, B-cell activating factor.

Nefecon supresses APRIL levels



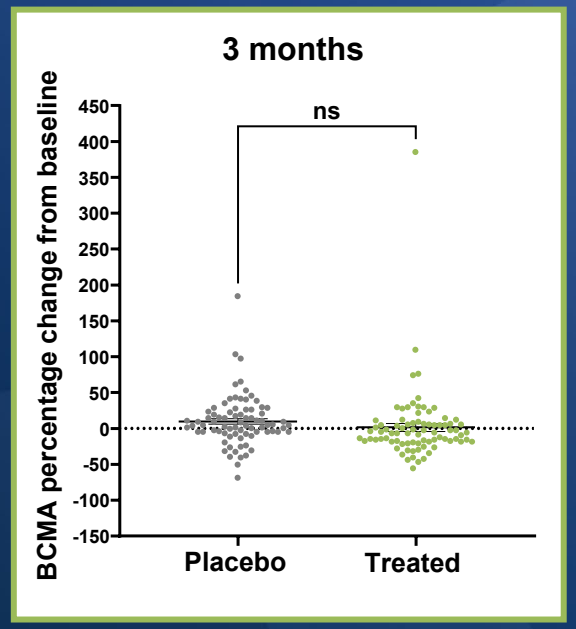


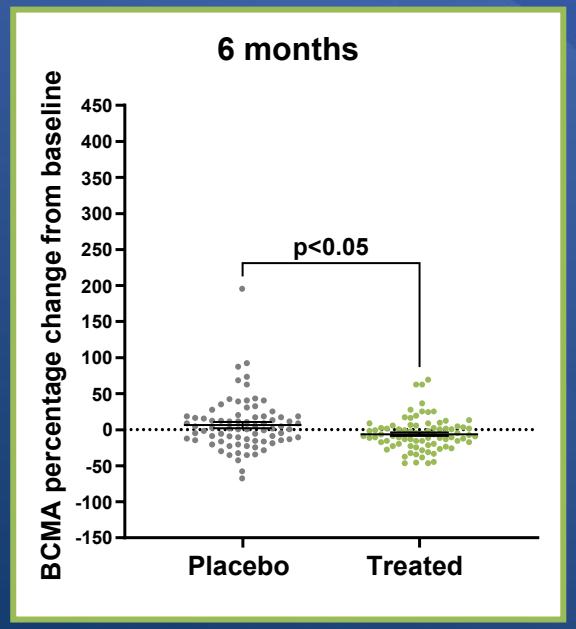


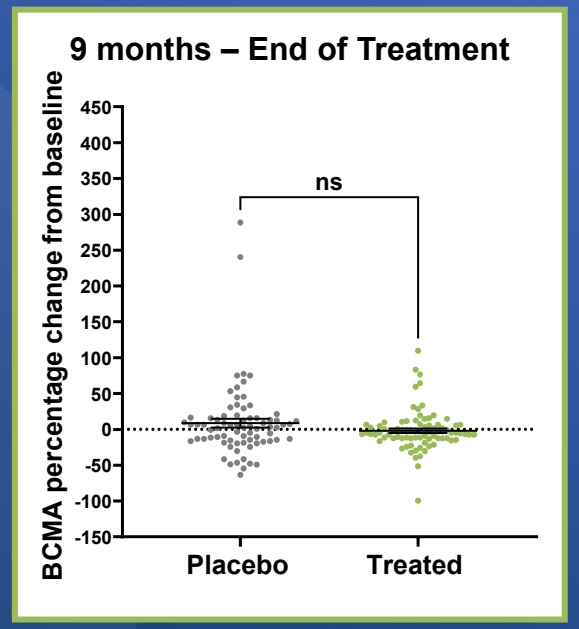
Reduction in levels of APRIL

APRIL data for Phase 2b trial were presented at ASN 2022.
ASN, American Society of Nephrology; APRIL, a proliferation-inducing ligand; ns, not significant.

Nefecon supresses BCMA levels







Reduction in levels of soluble BCMA

BCMA data for Phase 2b trial were presented at ASN 2022.
ASN, American Society of Nephrology; BCMA, B-cell maturation antigen; ns, not significant.

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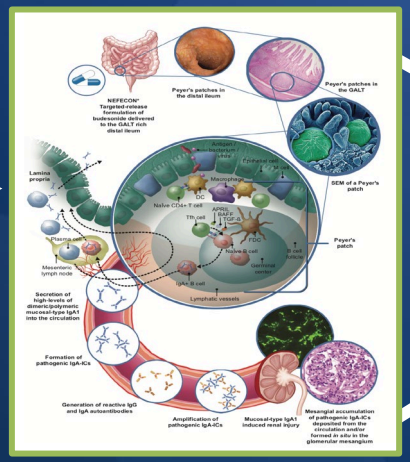
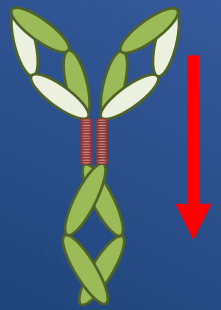
Discussion

Nefecon

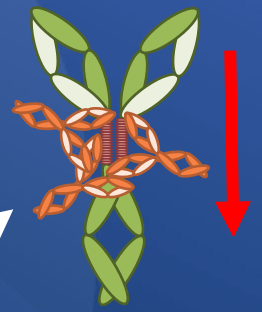
Mucosal dysregulation



*Galactose-deficient IgA1

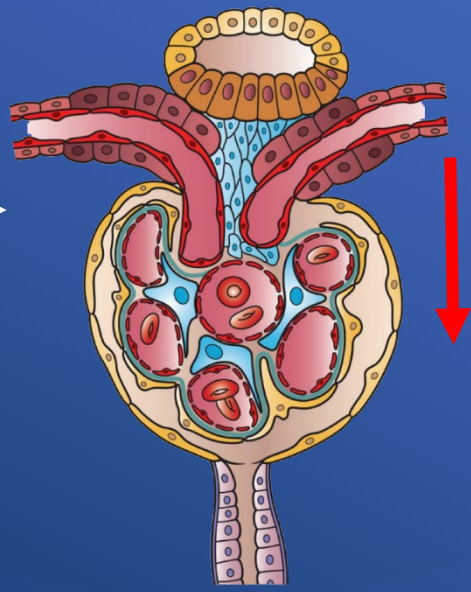


Immune complex formation



Anti-glycan antibodies

Mesangial deposition



Renal injury

*Galactose-deficient IgA1 data were presented at ASN 2022.
ASN, American Society of Nephrology; IgA1, immunoglobulin A type 1.

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Acknowledgments

The Mayer Family Foundation

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