IgA Nephropathy & IgA Vasculitis

Professor Jonathan Barratt
University of Leicester, UK

Disclosure of Interests

Consultancies & Advisory Board memberships:

- Anthera
- EMD Serono
- Kancera
- Novartis
- Omeros
- Pharmalink AB
- Retrophin
- Rigel

Scientific Grant Funding:

- Anthera
- GSK
- Novartis
- Pharmalink AB

IgA Nephropathy

The commonest pattern of glomerulonephritis in the world

IgA Nephropathy

The commonest pattern of glomerulonephritis in the world

IgA Nephropathy

A pattern of glomerulonephritis

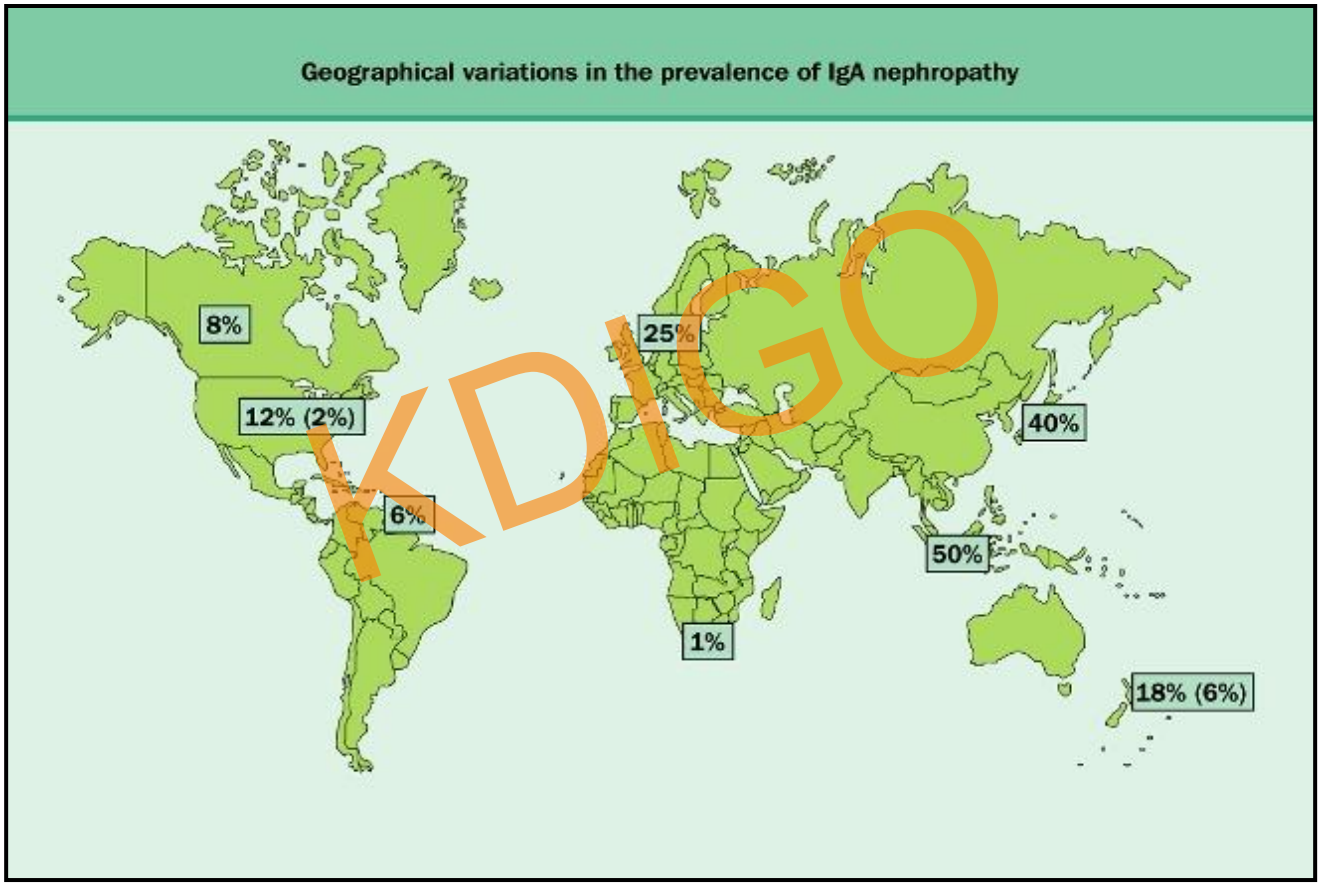
with many variants

IgA Nephropathy

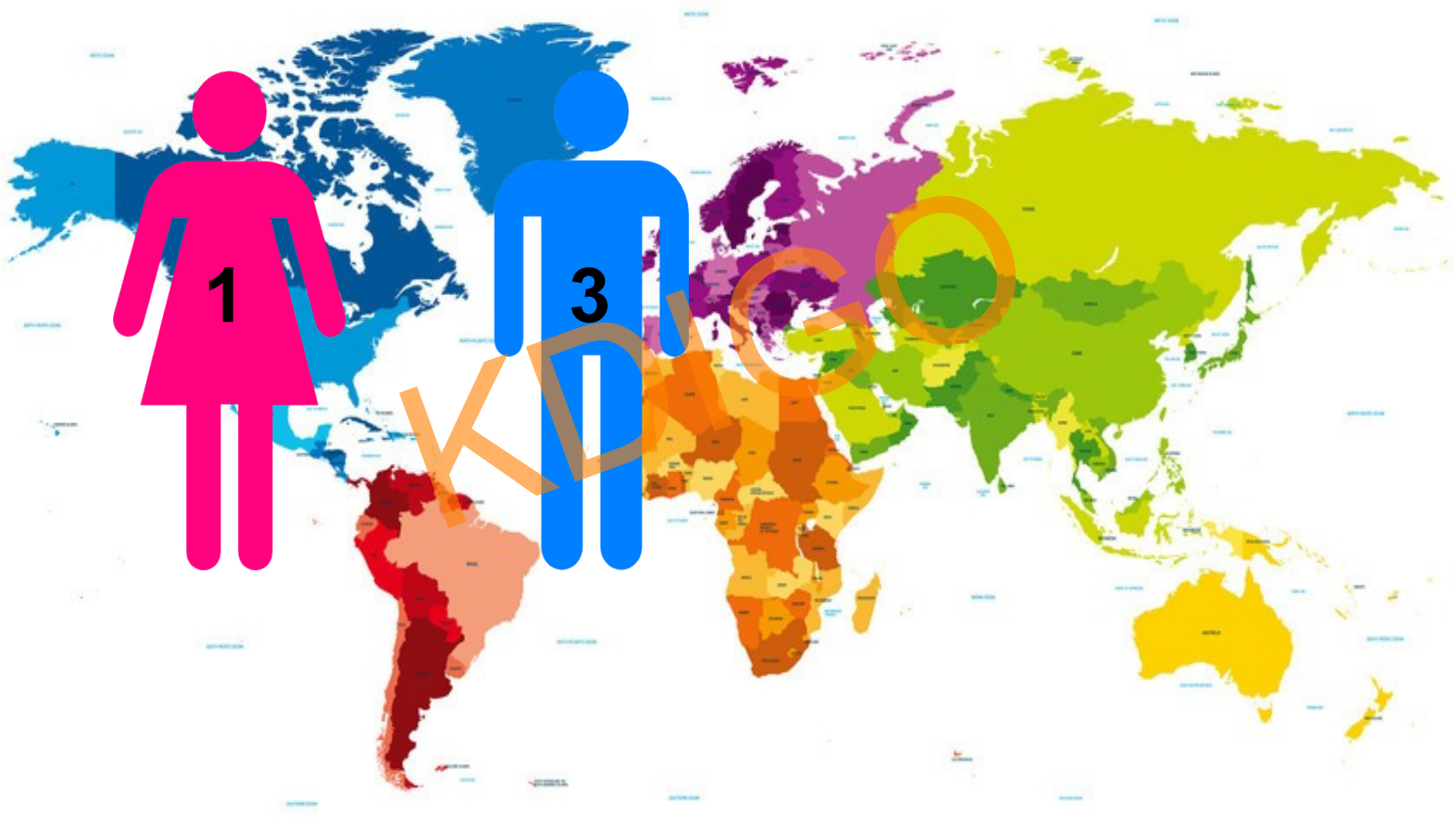
No proof that IgAN is a single 'disease'

No proof that IgAN is the same 'disease' in all parts of the world

IgA Nephropathy

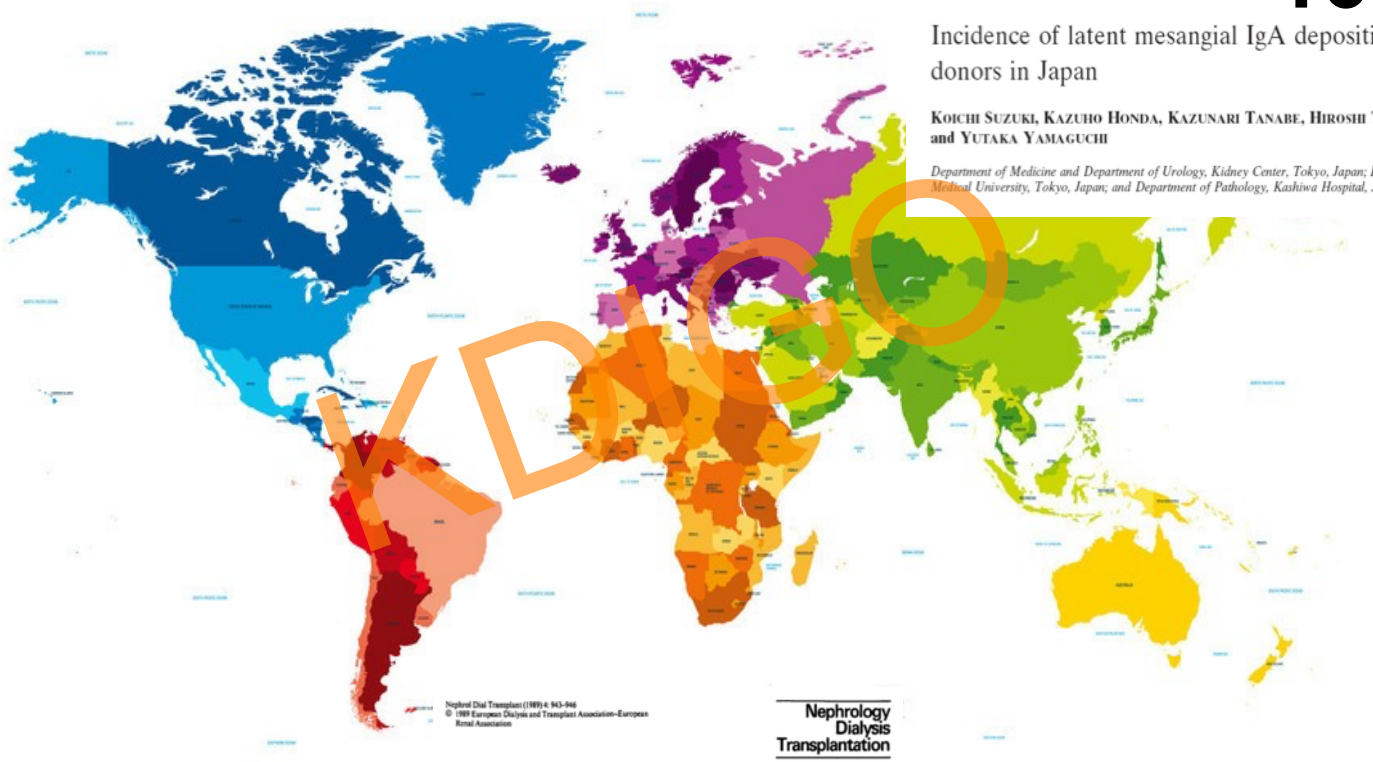


IgA Nephropathy



IgA Nephropathy

IgA Nephropathy



Kidney International, Vol. 63 (2003), pp. 2286–2294

16%

Incidence of latent mesangial IgA deposition in renal allograft donors in Japan

KOICHI SUZUKI, KAZUHO HONDA, KAZUNARI TANABE, HIROSHI TOMA, HIROSHI NIHEI, and YUTAKA YAMAGUCHI

Department of Medicine and Department of Urology, Kidney Center, Tokyo, Japan; Department of Pathology, Tokyo Women's Medical University, Tokyo, Japan; and Department of Pathology, Kashiwa Hospital, Jikei University, Chiba, Japan

Nephrol Dial Transplant (1989) 4: 943-946

Nephrology Dialysis Transplantation

Original Article

2.4%

Frequency of Mesangial IgA Deposits in a Non-Selected Autopsy Series*

R. Waldherr[1], M. Rambausek[2], W. D. Duncker[1] and E. Ritz[2]

Departments of [1]Pathology and [2]Nephrology, University of Heidelberg, Heidelberg, FRG

IgA Nephropathy

CMC Vellore 1994-2003

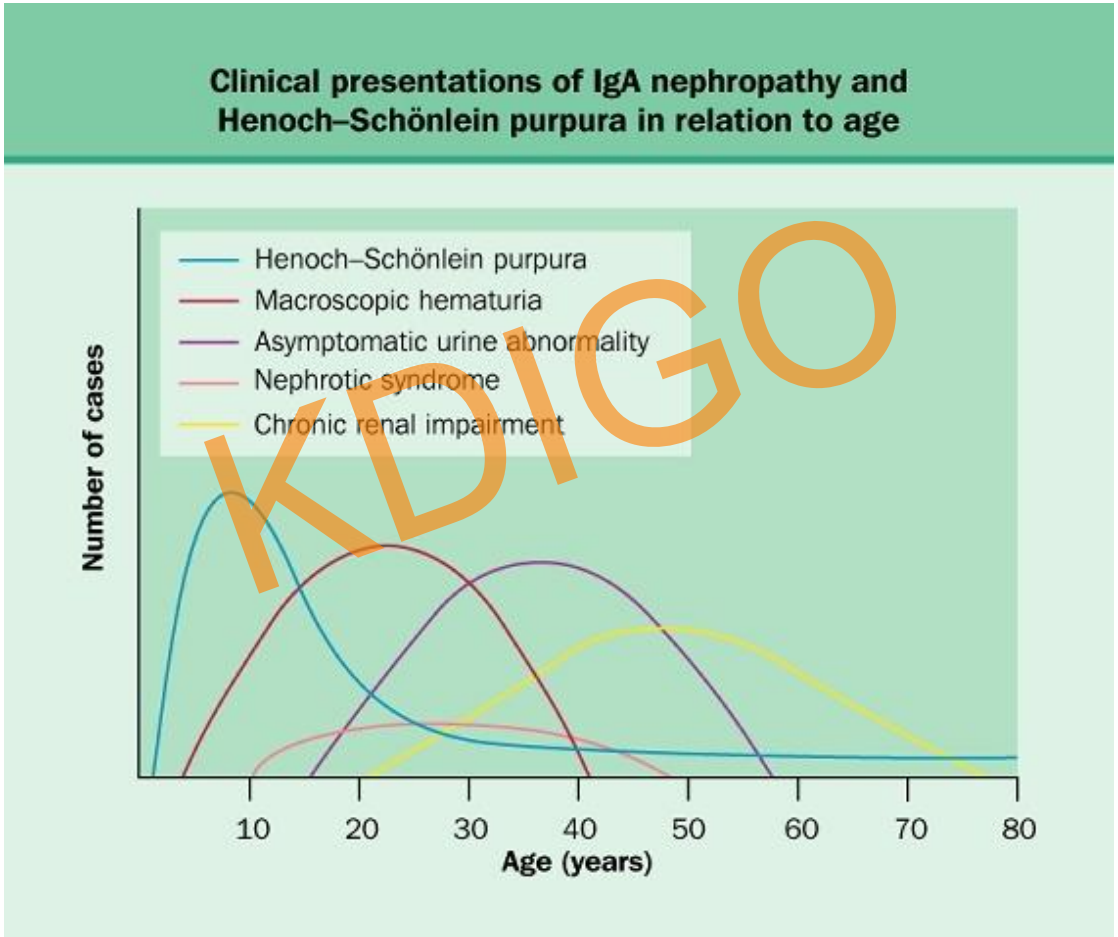
478 adults

- 55% - Nephrotic syndrome at presentation

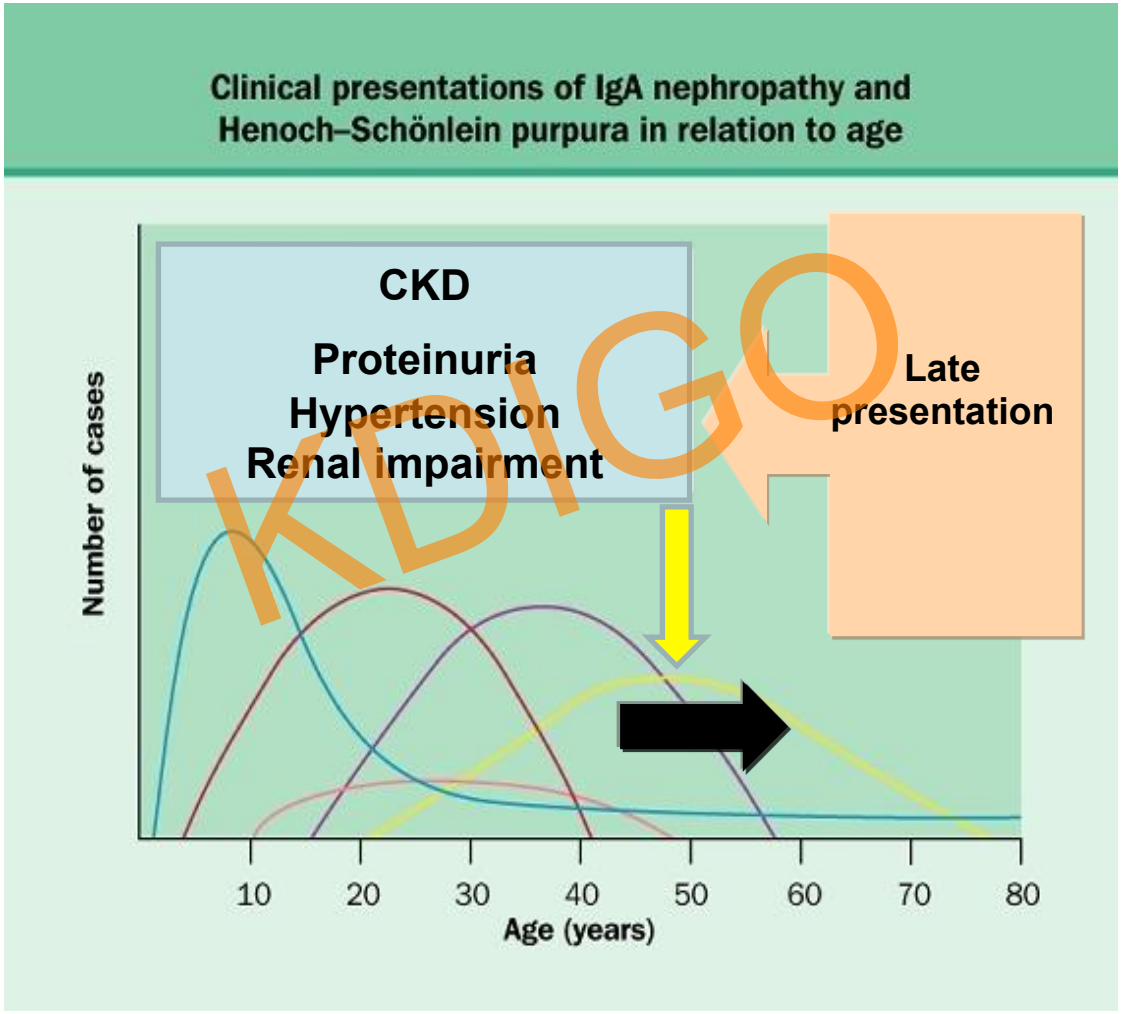
- 56% - Serum creatinine > 125µmol/L at presentation

Chacko B *et al.* Nephrology 2005; 10: 496

IgA Nephropathy



IgA Nephropathy



IgA Nephropathy

Cohort study – Toronto – 286 patients

Microscopic haematuria

plus

Proteinuria < 0.2 g/24hr

Normal BP

10 year risk
of deterioration in renal function
= ZERO

Bartosik et al. AJKD 2001;

IgA Nephropathy

Cohort study – Hong Kong

Microscopic haematuria *plus* **Proteinuria < 0.4 g/24hr**

During 7 years follow up, 44% had a 'clinical event'

33% proteinuria

26% hypertension

7% renal impairment

Szeto C *et al* Am J Med 2001; 110:434

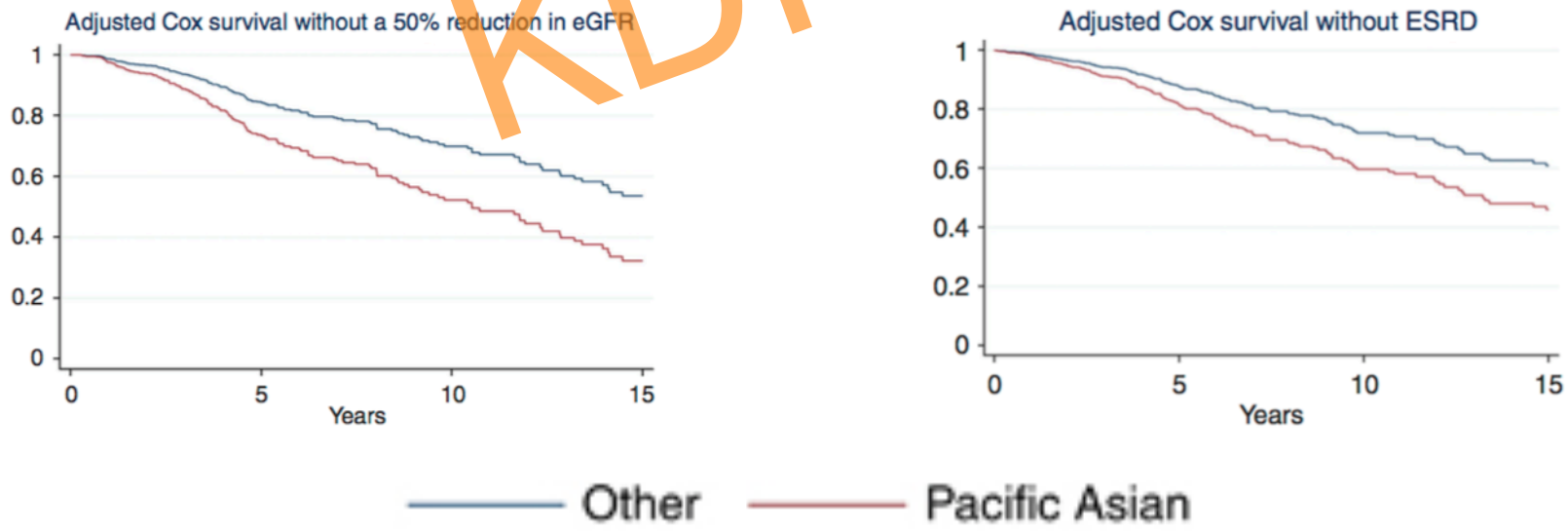
IgA Nephropathy

http://www.kidney-international.org clinical investigation

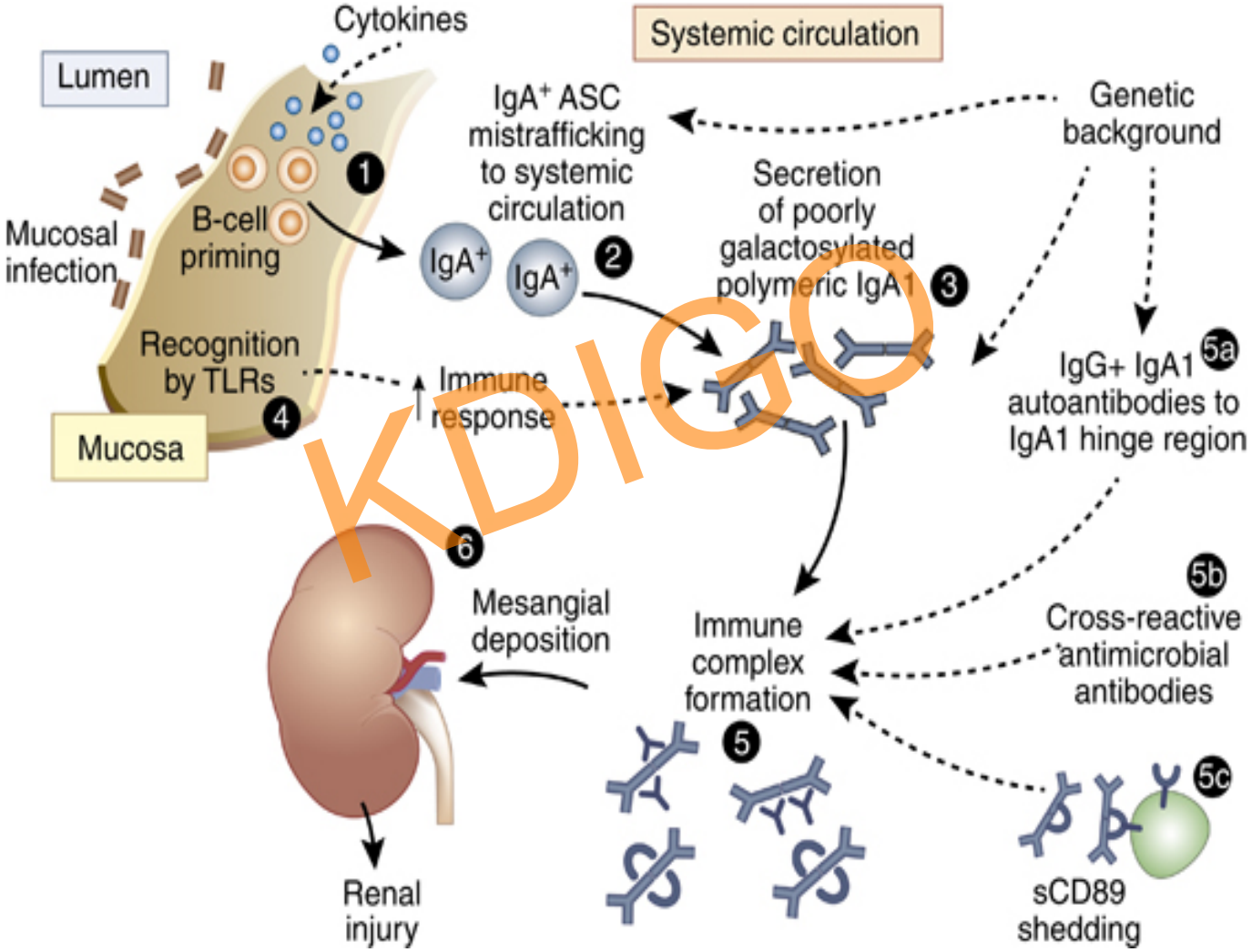
Individuals of Pacific Asian origin with IgA nephropathy have an increased risk of progression to end-stage renal disease

Sean J. Barbour[1,2,3], Daniel C. Cattran[3,4], S. Joseph Kim[4], Adeera Levin[1,2], Ron Wald[4], Michelle A. Hladunewich[3,4] and Heather N. Reich[3,4]

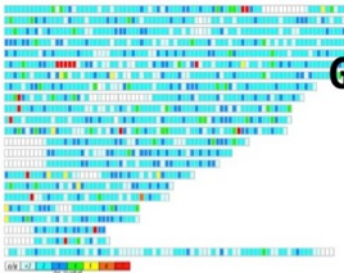
[1]Division of Nephrology, Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada; [2]British Columbia Provincial Renal Agency, Vancouver, British Columbia, Canada; [3]Toronto Glomerulonephritis Registry, University Health Network, Toronto, Ontario, Canada and [4]Division of Nephrology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada



IgA Nephropathy



IgA Nephropathy



Genome-wide Association Studies

CLINICAL RESEARCH www.jasn.org

HLA Has Strongest Association with IgA Nephropathy in Genome-Wide Analysis

John Feehally,* Martin Farrall,† Anne Boland,‡ Daniel P. Gale,§ Ivo Gut,‡ Simon Heath,‡ Ashish Kumar,† John F. Peden,† Patrick H. Maxwell,§ David L. Morris,‖ Sandosh Padmanabhan,¶ Timothy J. Vyse,‖ Anna Zawadzka,† Andrew J. Rees,** Mark Lathrop,‡ and Peter J. Ratcliffe††

ARTICLES

nature genetics

Genome-wide association study identifies susceptibility loci for IgA nephropathy

Ali G Gharavi[1], Krzysztof Kiryluk[1], Murim Choi[2], Yifu Li[1], Ping Hou[1,2], Jingyuan Xie[1,4], Simone Sanna-Cherchi[1], Clara J Men[2], Bruce A Julian[5], Robert J Wyatt[6], Jan Novak[5], John C He[7], Haiyan Wang[2], Jicheng Lv[3], Li Zhu[3], Weiming Wang[4], Zhaohui Wang[4], Kasuhito Yasuno[2], Murat Gunel[2], Shrikant Mane[2,8], Sheila Umlauf[2,8], Irina Tikhonova[2,8], Isabel Beerman[2], Silvana Savoldi[9], Riccardo Magistroni[10], Gian Marco Ghiggeri[11], Monica Bodria[11], Francesca Lugani[11,12], Pietro Ravani[12], Claudio Ponticelli[13], Landino Allegri[14], Giuliano Boscutti[15], Giovanni Frasca[16], Alessandro Amore[17], Licia Peruzzi[17], Rosanna Coppo[17], Claudia Izzi[18], Battista Fabio Viola[19], Elisabetta Prati[20], Maurizio Salvadori[21], Renzo Mignani[22], Loreto Gesualdo[23], Francesca Bertinetto[24], Paola Mesiano[24], Antonio Amoroso[24], Francesco Scolari[18], Nan Chen[4], Hong Zhang[3] & Richard P Lifton[2]

LETTERS

nature genetics

A genome-wide association study in Han Chinese identifies multiple susceptibility loci for IgA nephropathy

Xue-Qing Yu[1,2,15], Ming Li[1,2,15], Hong Zhang[3,15], Hui-Qi Low[4], Xin Wei[1,2], Jin-Quan Wang[5], Liang-Dan Sun[6,7], Kar-Seng Sim[4], Yi Li[8], Jia-Nee Foo[4], Wei Wang[1,2], Zhi-Jian Li[1,2], Xian-Yong Yin[6,7], Xue-Qing Tang[1,2], Li Fan[1,2], Jian Chen[9], Rong-Shan Li[9], Jian-Xin Wan[10], Zhang-tuo Liu[11], Tan-Qi Lou[12], Li Zhu[3], Xiao-Jun Huang[13], Xue-Jun Zhang[6,7], Zhi-Hong Liu[3] & Jian-Jun Liu[8,14]

ARTICLES

nature genetics

Discovery of new risk loci for IgA nephropathy implicates genes involved in immunity against intestinal pathogens

Krzysztof Kiryluk[1], Yifu Li[1], Francesco Scolari[2,3], Simone Sanna-Cherchi[1], Murim Choi[2,4], Miguel Verbitsky[1], David Fasel[5], Sneh Lata[1], Sindhuri Prakash[1], Samantha Shapiro[1], Clara Fischman[1], Shelly J Snyder[1], Gerald Appel[6], Claudia Izzi[3,4], Battista Fabio Viola[3], Nadia Dallera[3,5], Lucia Del Vecchio[3], Cristina Barlassina[4], Erika Salvi[4], Francesca Eleonora Bertinetto[4,10], Antonio Amoroso[4,10], Silvana Savoldi[11], Marcella Rocchietti[11], Alessandro Amore[12], Licia Peruzzi[12], Rosanna Coppo[12], Maurizio Salvadori[13], Pietro Ravani[14,15], Riccardo Magistroni[16], Gian Marco Ghiggeri[17], Gianluca Caridi[17], Monica Bodria[17], Francesca Lugani[17], Landino Allegri[18,19], Marco Delsante[20,21], Marianna Maiorana[18,19], Andrea Magnano[18,19], Giovanni Frasca[20], Emanuela Rose[20], Giuliano Boscutti[22], Claudio Ponticelli[23], Renzo Mignani[24], Carmelita Marcantoni[25], Domenico Di Landro[25], Domenico Santoro[26], Antonello Pani[27], Rosaria Polci[28], Sandro Feriani[29], Silvana Chicca[30], Marco Gallieni[30], Maddalena Gigante[31], Loreto Gesualdo[31], Pasquale Zambelli[32], Giovanni Giorgio Battaglia[33], Maurizio Gaeta[33], Dita Maixnerová[34], Vladimír Tesař[34], Frank Eitner[35,36], Thomas Rauen[36], Jürgen Floege[35], Tibor Kovacs[37,38], Judit Nagy[37,38], Krzysztof Mucha[39], Leszek Pączek[39], Marcin Zaniew[40], Małgorzata Mizerska-Wiercik[41], Maria Roszkowska-Blaim[42], Krzysztof Pawlaczyk[42], Daniel Gale[43], Jonathan Barratt[44,45], Lise Thibaudin[46], Francois Berthoux[46], Guillaume Canaud[47,48], Anne Boland[49], Marie Metzger[49,51], Ulf Panzer[52], Hitoshi Suzuki[53], Shin Goto[54], Ichiei Narita[54], Yasar Caliskan[55], Jingyuan Xie[56], Ping Hou[57], Nan Chen[56], Hong Zhang[57], Robert J Wyatt[58,59], Jan Novak[60], Bruce A Julian[60], John Feehally[61,62], Benedicte Stengel[49,51], Daniele Cusi[63], Richard P Lifton[64] & Ali G Gharavi[1]

Journal of Human Genetics (2015) 60, 573–580
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www.nature.com/jhg

ORIGINAL ARTICLE

Genome-wide association study of IgA nephropathy using 23 465 microsatellite markers in a Japanese population

Sanae Saka[1,2], Nobuhito Hirawa[2], Akira Oka[3], Keisuke Yatsu[1], Takeshi Hirukawa[4], Ryohei Yamamoto[5], Taiji Matsusaka[6], Enyu Imai[6,7], Ichiei Narita[8], Masayuki Endoh[1], Iekuni Ichikawa[9,10], Satoshi Umemura[1] and Hidetoshi Inoko[3]

nature COMMUNICATIONS

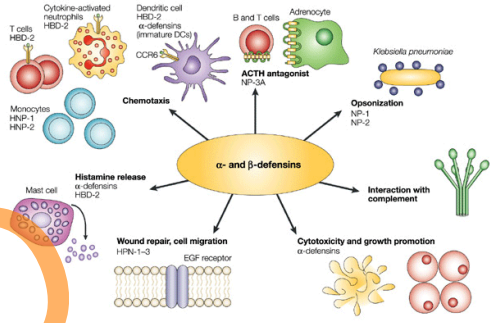
ARTICLE

Received 12 Dec 2014 | Accepted 23 Apr 2015 | Published 1 Jun 2015 DOI: 10.1038/ncomms8270 OPEN

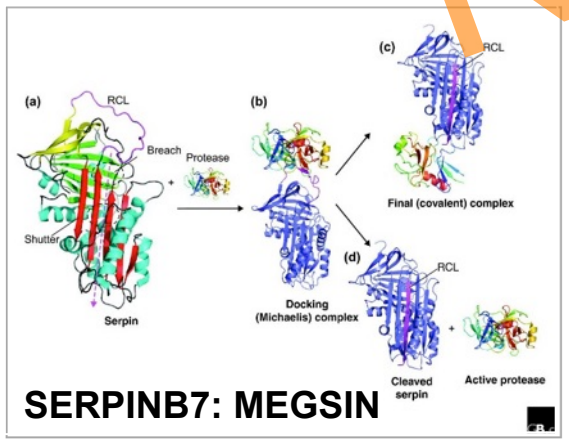
Identification of new susceptibility loci for IgA nephropathy in Han Chinese

Ming Li[1,2,*], Jia-Nee Foo[3,*], Jin-Quan Wang[4,*], Hui-Qi Low[3], Xue-Qing Tang[1,2], Kai-Yee Toh[3], Pei-Ran Yin[1,2], Chiea-Chuen Khor[3,5,6], Yu-Ren Goh[3], Ishak D. Irwan[3], Ji-Cong Xu[1,2], Anand K. Andiappan[7], Jin-Xin Bei[8], Olaf Rotzschke[7], Meng-Hua Chen[9], Ching-Yu Cheng[3,10], Liang-Dar Sun[4,10], Geng-Ru Jiang[11], Tien-Yin Wong[3,6], Hong-Li Lin[12], Tin Aung[3,6], Yun-Hua Liao[13], Seang-Mei Saw[3,6,14], Kun Ye[15], Richard P. Ebstein[16], Qin-Kai Chen[17], Wei Shi[18], Soo-Hong Chew[19], Jian Chen[20], Fu-Ren Zhang[21], Sheng-Ping Li[22], Gang Xu[23], E. Shyong Tai[24,25], Li Wang[26], Nan Chen[27], Xue-Jun Zhang[4,10], Yi-Xin Zeng[28,29], Hong Zhang[30], Zhi-Hong Liu[4], Xue-Qing Yu[1,**] & Jian-Jun Liu[3,14,31,32,**]

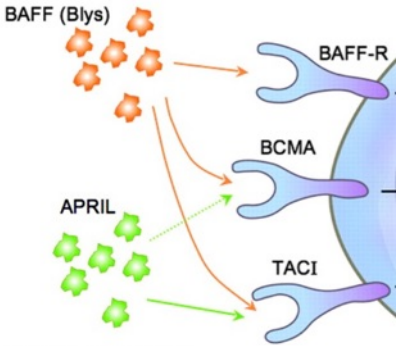
IgA Nephropathy



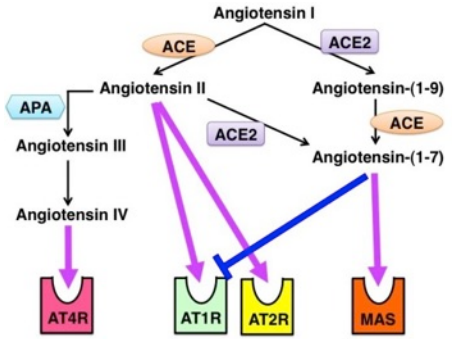
***DEFA*: DEFENSINS**



SERPINB7: MEGSIN

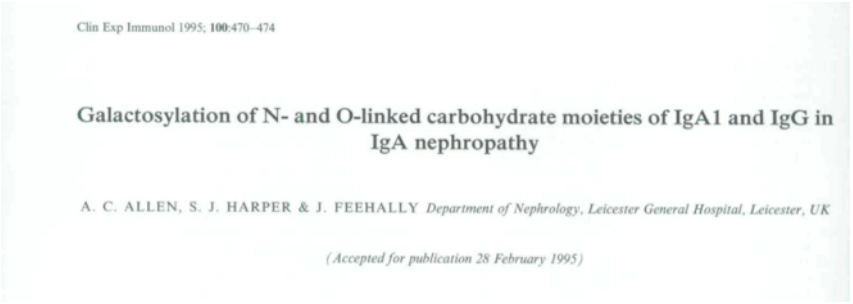


17p13 (containing TNFSF13, APRIL)



I/D polymorphisms

IgA Nephropathy



Clin Exp Immunol 1995; 100:470–474

Galactosylation of N- and O-linked carbohydrate moieties of IgA1 and IgG in IgA nephropathy

A. C. ALLEN, S. J. HARPER & J. FEEHALLY *Department of Nephrology, Leicester General Hospital, Leicester, UK*

(Accepted for publication 28 February 1995)

original article http://www.kidney-international.org

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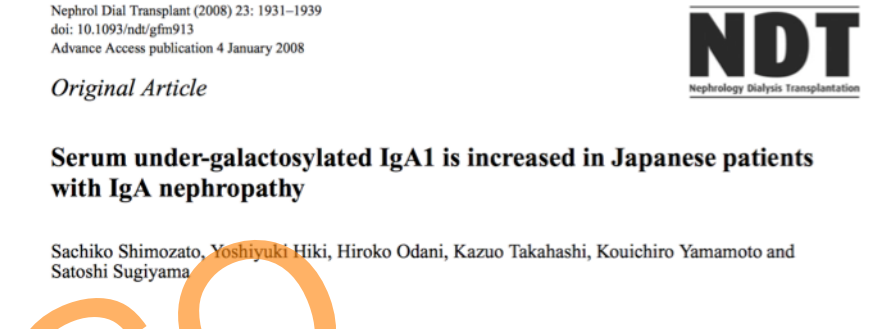
see commentary on page 1089

Patients with IgA nephropathy have increased serum galactose-deficient IgA1 levels

Z Moldoveanu[1], RJ Wyatt[2], JY Lee[3], M Tomana[3], BA Julian[1,3], J Mestecky[1,3], W-Q Huang[1], SR Anreddy[1,5], S Hall[1], MC Hastings[2], KK Lau[2,6], WJ Cook[4] and J Novak[1]



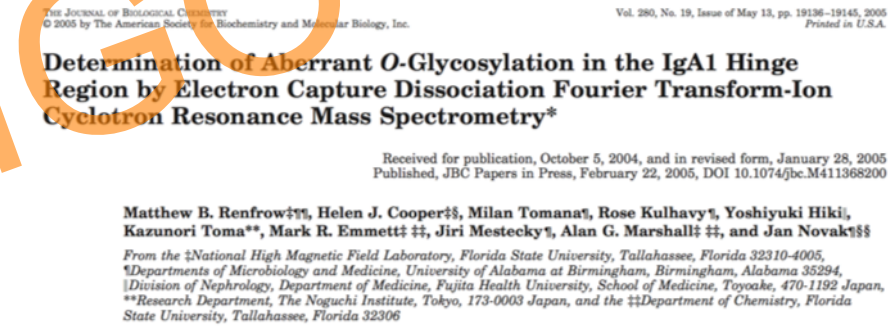
Nephrol Dial Transplant (2008) 23: 1931–1939
doi: 10.1093/ndt/gfm913
Advance Access publication 4 January 2008

NDT Nephrology Dialysis Transplantation

Original Article

Serum under-galactosylated IgA1 is increased in Japanese patients with IgA nephropathy

Sachiko Shimozato, Yoshiyuki Hiki, Hiroko Odani, Kazuo Takahashi, Kouichiro Yamamoto and Satoshi Sugiyama



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Vol. 280, No. 19, Issue of May 13, pp. 19136–19145, 2005
Printed in U.S.A.

Determination of Aberrant *O*-Glycosylation in the IgA1 Hinge Region by Electron Capture Dissociation Fourier Transform-Ion Cyclotron Resonance Mass Spectrometry*

Received for publication, October 5, 2004, and in revised form, January 28, 2005
Published, JBC Papers in Press, February 22, 2005, DOI 10.1074/jbc.M411368200

Matthew B. Renfrow‡¶¶, Helen J. Cooper‡§, Milan Tomana¶, Rose Kulhavy¶, Yoshiyuki Hiki‖, Kazunori Toma, Mark R. Emmett‡ ‡‡, Jiri Mestecky¶, Alan G. Marshall‡ ‡‡, and Jan Novak¶§§**

*From the ‡National High Magnetic Field Laboratory, Florida State University, Tallahassee, Florida 32310-4005, ¶Departments of Microbiology and Medicine, University of Alabama at Birmingham, Birmingham, Alabama 35294, ‖Division of Nephrology, Department of Medicine, Fujita Health University, School of Medicine, Toyoake, 470-1192 Japan, **Research Department, The Noguchi Institute, Tokyo, 173-0003 Japan, and the ‡‡Department of Chemistry, Florida State University, Tallahassee, Florida 32306*

CLINICAL RESEARCH www.jasn.org

Aberrant IgA1 Glycosylation Is Inherited in Familial and Sporadic IgA Nephropathy

Ali G. Gharavi,* Zina Moldoveanu,† Robert J. Wyatt,‡ Catherine V. Barker,§ Susan Y. Woodford,§ Richard P. Lifton,‖ Jiri Mestecky,† Jan Novak,† and Bruce A. Julian†§

IgA Vasculitis

Nephrol Dial Transplant (1998) 13: 930–934

Nephrology
Dialysis
Transplantation

Original Article

Abnormal IgA glycosylation in Henoch-Schönlein purpura restricted to patients with clinical nephritis

Alice C. Allen, Frank R. Willis[1], T. James Beattie[1] and John Feehally

Pediatr Nephrol (2007) 22:2067–2072
DOI 10.1007/s00467-007-0623-y

ORIGINAL ARTICLE

Serum levels of galactose-deficient IgA in children with IgA nephropathy and Henoch-Schönlein purpura

Keith K. Lau · Robert J. Wyatt · Zina Moldoveanu · Milan Tomana · Bruce A. Julian · Ronald J. Hogg · Jeannette Y. Lee · Wen-Qiang Huang · Jiri Mestecky · Jan Novak

http://www.kidney-international.org original article

see commentary on page 8

Aberrant glycosylation of IgA1 is inherited in both pediatric IgA nephropathy and Henoch–Schönlein purpura nephritis

Krzysztof Kiryluk[1], Zina Moldoveanu[2], John T. Sanders[3,4], T. Matthew Eison[3,4], Hitoshi Suzuki[2,5], Bruce A. Julian[2], Jan Novak[2], Ali G. Gharavi[1] and Robert J. Wyatt[3,4]

IgA Nephropathy (& IgA Vasculitis?)

Kidney International, Vol. 60 (2001), pp. 969–973

Mesangial IgA1 in IgA nephropathy exhibits aberrant O-glycosylation: Observations in three patients

ALICE C. ALLEN, ELAINE M. BAILEY, PAUL E.C. BRENCHLEY, KATHARINE S. BUCK, JONATHAN BARRATT, and JOHN FEEHALLY

Kidney International, Vol. 68 (2005), pp. 167–172

Aberrantly glycosylated serum IgA1 are closely associated with pathologic phenotypes of IgA nephropathy

LI-XIA XU and MING-HUI ZHAO

Renal Division & Institute of Nephrology, Peking University First Hospital, Beijing, People's Republic of China

Research article Related Commentary, page 1450

Aberrantly glycosylated IgA1 in IgA nephropathy patients is recognized by IgG antibodies with restricted heterogeneity

Hitoshi Suzuki,[1,2] Run Fan,[1,3] Zhixin Zhang,[3] Rhubell Brown,[1] Stacy Hall,[1] Bruce A. Julian,[1,4] W. Winn Chatham,[4] Yusuke Suzuki,[2] Robert J. Wyatt,[5] Zina Moldoveanu,[1] Jeannette Y. Lee,[6] James Robinson,[7] Milan Tomana,[4] Yasuhiko Tomino,[2] Jiri Mestecky,[1,4,8] and Jan Novak[1]

[1]Department of Microbiology, University of Alabama at Birmingham, Birmingham, Alabama, USA. [2]Division of Nephrology, Department of Internal Medicine, Juntendo University School of Medicine, Tokyo, Japan. [3]Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha, Nebraska, USA. [4]Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA. [5]Department of Pediatrics, University of Tennessee Health Sciences Center, Memphis, Tennessee, USA. [6]Department of Biostatistics, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA. [7]Department of Pediatrics, Tulane University, New Orleans, Louisiana, USA. [8]Institute of Microbiology and Immunology, First Faculty of Medicine, Charles University, Prague, Czech Republic.

IgA Nephropathy (& IgA Vasculitis?)

J Am Soc Nephrol 15: 622–634, 2004

Glycosylation and Size of IgA1 Are Essential for Interaction with Mesangial Transferrin Receptor in IgA Nephropathy

IVAN C. MOURA,* MICHELLE ARCOS-FAJARDO,* CHARLOTTE SADAKA,* VALÉRIE LEROY,*† MARC BENHAMOU,* JAN NOVAK,‡ FRANÇOIS VRTOVSNIK,§ ELIE HADDAD,*† KOTESWARA R. CHINTALACHARUVU,‖ and RENATO C. MONTEIRO*

**INSERM E-0225, Bichat Medical School, Paris, France; †Pediatric Nephrology Unit, Robert-Debré Hospital, Paris, France; ‡Department of Microbiology, University of Alabama at Birmingham, Birmingham, Alabama; §Bichat-Claude Bernard Hospital, Paris, France; and ‖Department of Microbiology, Immunology and Molecular Genetics and The Molecular Biology Institute, University of California, Los Angeles, California*

munology 1994 **81** 137–141

Glycosylation of IgA is required for optimal activation of the alternative complement pathway by immune complexes

W. ZHANG & P. J. LACHMANN *Molecular Immunopathology Unit, MRC Centre, Cambridge*

Human IgA Activates the Complement System Via the Mannan-Binding Lectin Pathway[1]

Anja Roos,[2]* Lee H. Bouwman,* Daniëlle J. van Gijlswijk-Janssen,* Maria C. Faber-Krol,* Gregory L. Stahl,† and Mohamed R. Daha*

IgA Nephropathy (& IgA Vasculitis?)

BASIC RESEARCH www.jasn.org

Galactosylation of IgA1 Is Associated with Common Variation in *C1GALT1*

Daniel P. Gale,* Karen Molyneux,† David Wimbury,† Patricia Higgins,† Adam P. Levine,‡ Ben Caplin,* Anna Ferlin,* Peiran Yin,§ Christopher P. Nelson,‖ Horia Stanescu,* Nilesh J. Samani,‖ Robert Kleta,* Xueqing Yu,§ and Jonathan Barratt†

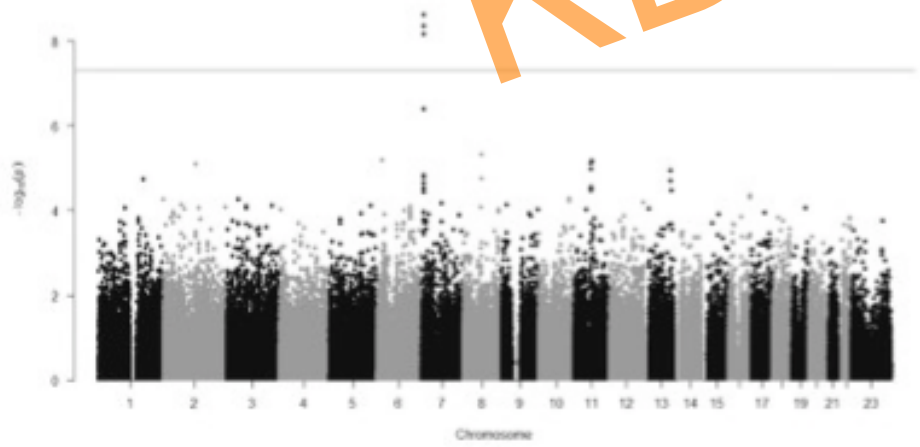
*Centre for Nephrology and †Division of Medicine, University College London, London, United Kingdom; †Department of Infection, Immunity and Inflammation, University of Leicester, Leicester, United Kingdom; §Department of Nephrology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China; and ‖Department of Cardiovascular Sciences, University of Leicester and National Institute for Health Research Leicester Cardiovascular Biomedical Research Unit, Leicester, United Kingdom

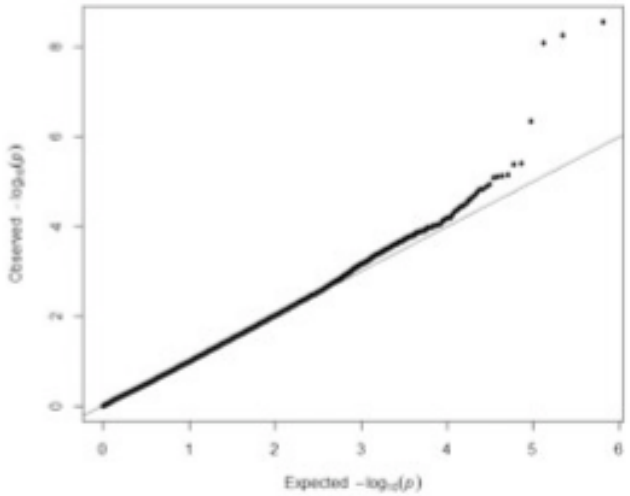
PLOS | GENETICS

RESEARCH ARTICLE

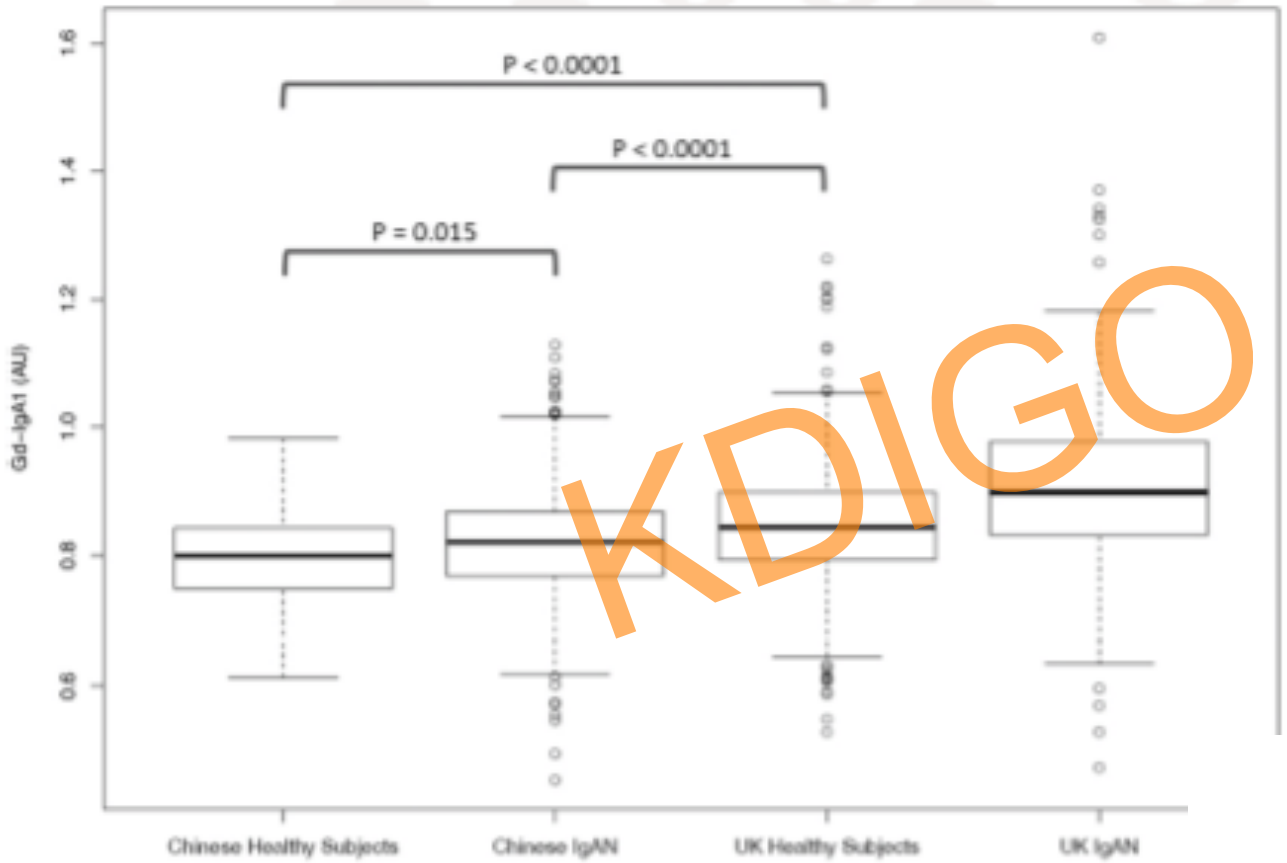
GWAS for serum galactose-deficient IgA1 implicates critical genes of the *O*-glycosylation pathway

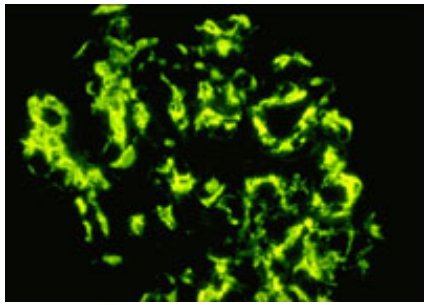
Krzysztof Kiryluk[1]*, Yifu Li[1], Zina Moldoveanu[2], Hitoshi Suzuki[3], Colin Reily[2,4], Ping Hou[5], Jingyuan Xie[6], Nikol Mladkova[1], Sindhuri Prakash[1], Clara Fischman[1], Samantha Shapiro[1], Robert A. LeDesma[1], Drew Bradbury[1], Iuliana Ionita-Laza[7], Frank Eitner[8,9], Thomas Rauen[8], Nicolas Maillard[10], Francois Berthoux[10], Jürgen Floege[8], Nan Chen[6], Hong Zhang[5], Francesco Scolari[11,12], Robert J. Wyatt[13,14], Bruce A. Julian[2,4], Ali G. Gharavi[1], Jan Novak[2]





IgA Nephropathy (& IgA Vasculitis?)





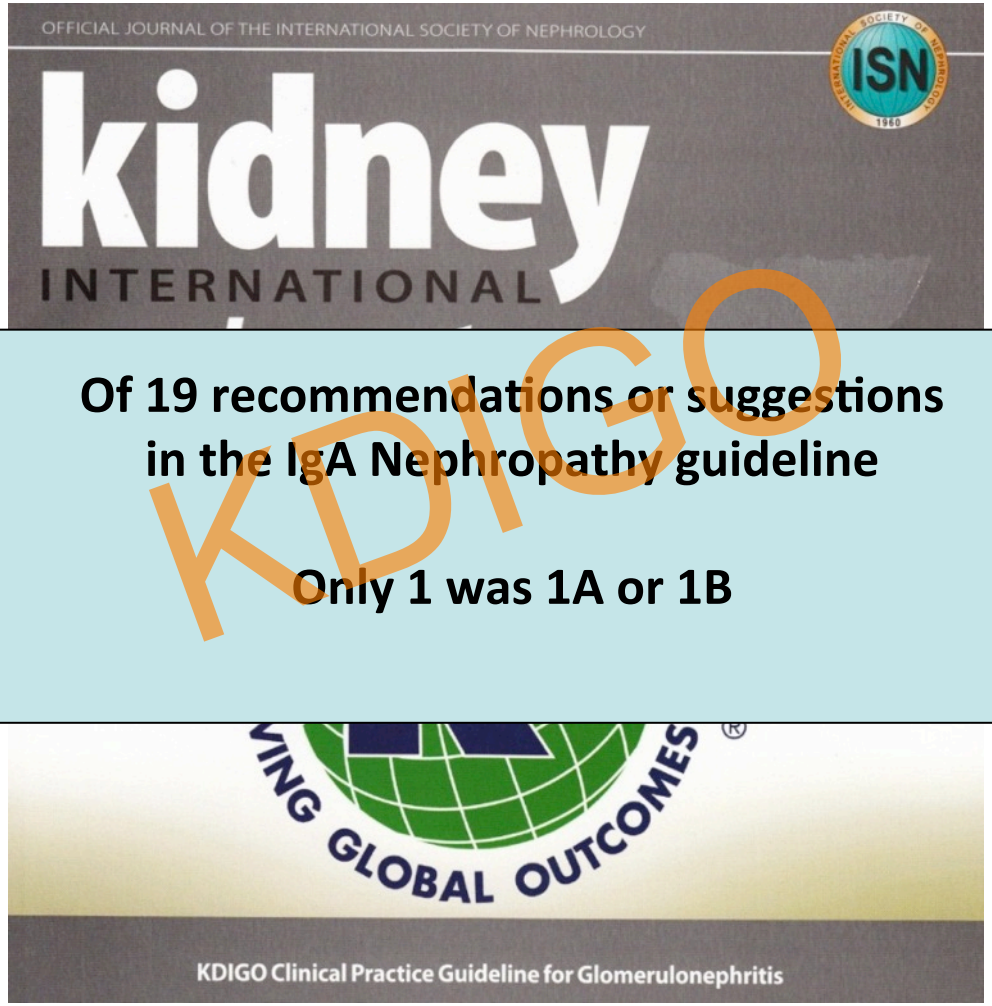
IgA Nephropathy

No proof that IgAN is a single 'disease'

No proof that IgAN is the same 'disease' in all parts of the world

IgA Nephropathy & IgA Vasculitis

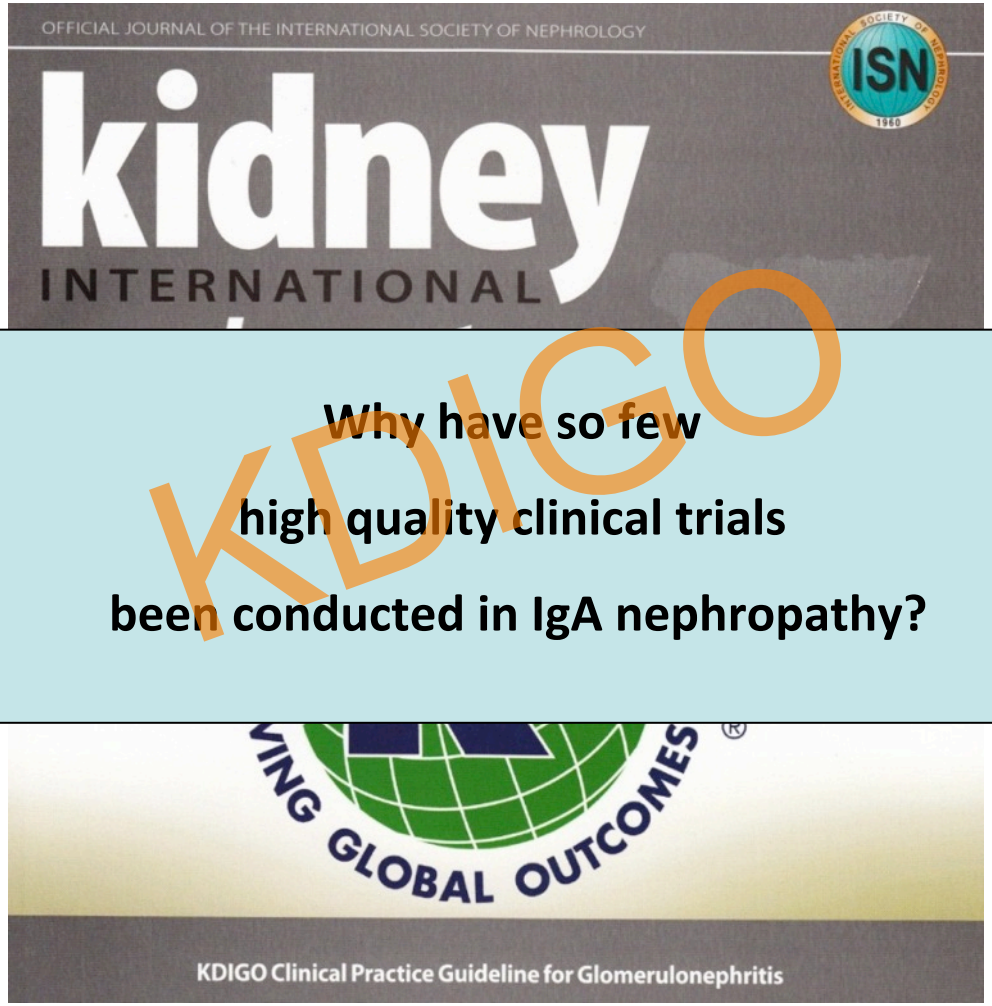
IgA Nephropathy



Of 19 recommendations or suggestions in the IgA Nephropathy guideline

Only 1 was 1A or 1B

IgA Nephropathy

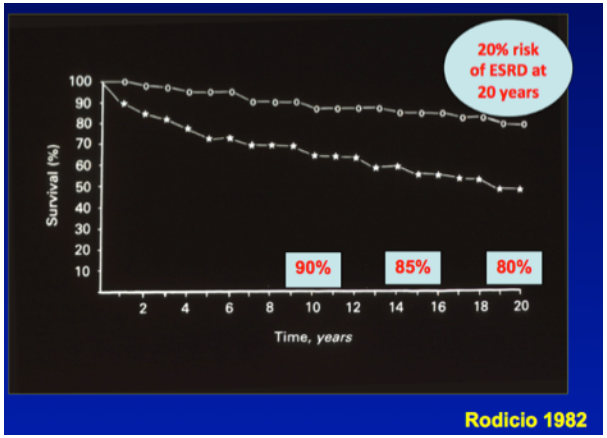


Why have so few

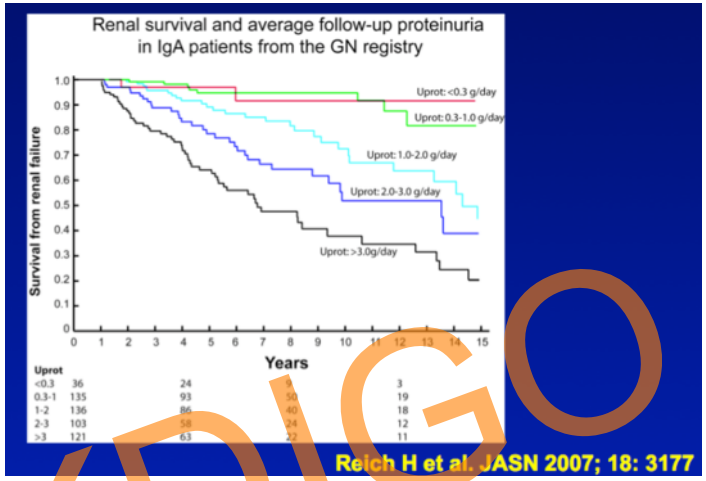
high quality clinical trials

been conducted in IgA nephropathy?

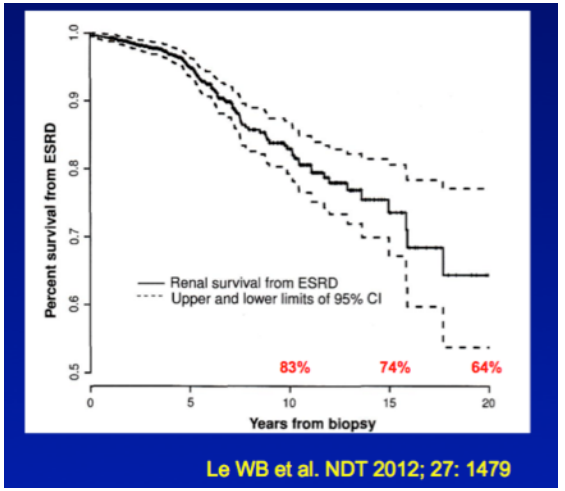
IgA Nephropathy



Rodicio 1982

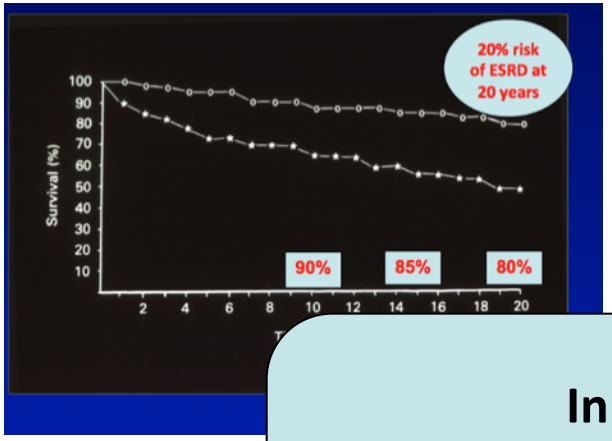


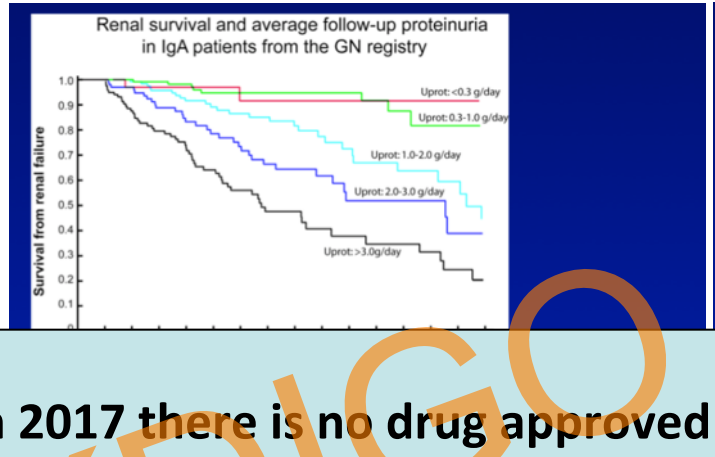
Reich H et al. JASN 2007; 18: 3177

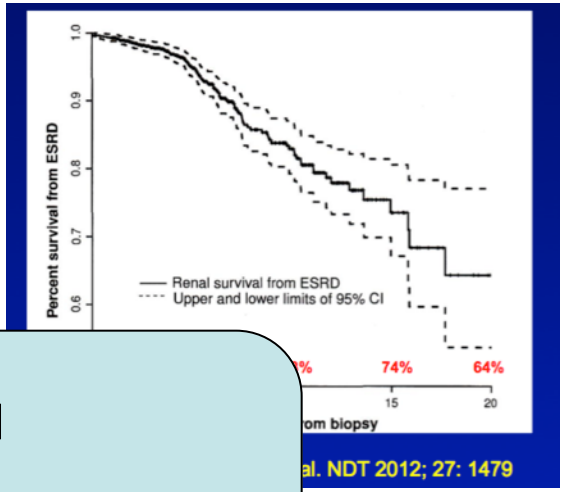


Le WB et al. NDT 2012; 27: 1479

IgA Nephropathy



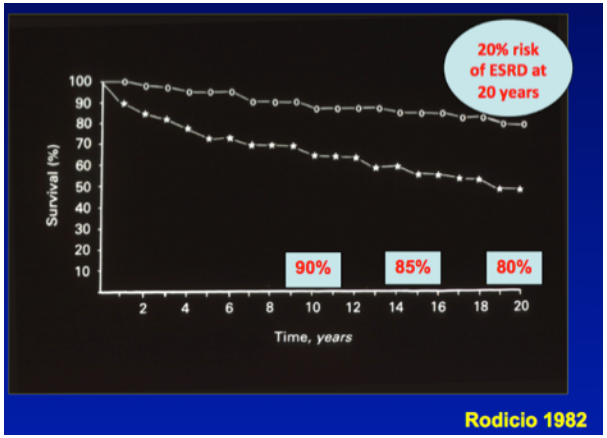




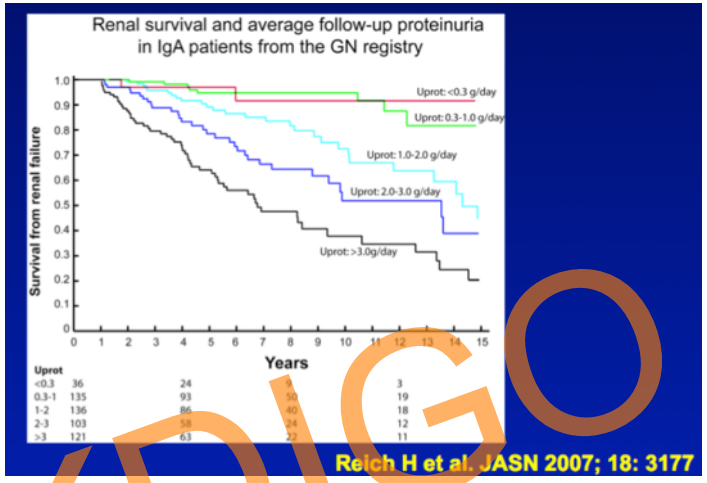
In 2017 there is no drug approved

for the treatment of IgA nephropathy

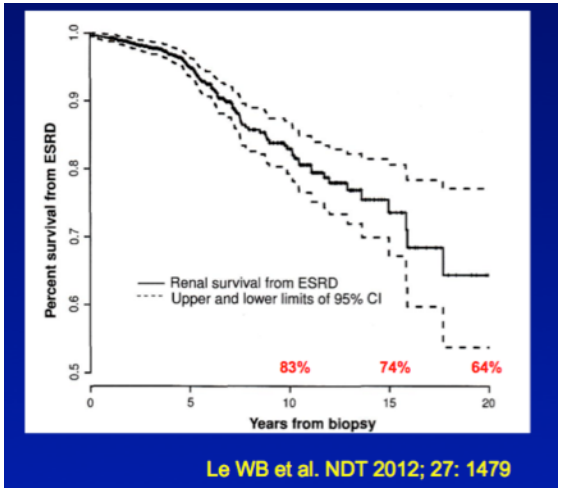
IgA Nephropathy



Rodicio 1982



Reich H et al. JASN 2007; 18: 3177



Le WB et al. NDT 2012; 27: 1479

We need robust surrogate biomarkers of future risk of ESRD to allow the use of surrogate endpoints in clinical trials for regulatory approval?

IgA Nephropathy

KHI Current Project

Identifying Surrogate Endpoints for Clinical Trials in IgA Nephropathy

Workgroup:

CHAIRS:

Patrick Nachman, MD
University of North Carolina Kidney Center

Aliza Thompson, MD
Division of Cardiovascular and Renal Products Center for Drug Evaluation and Research, FDA

MEMBERS:

Jonathan Barratt, PhD, FRCP
University of Leicester, United Kingdom

Annamaria T. Kausz, MD, MS
Allena Pharmaceuticals

Kevin J. Carroll, PhD
KJC Statistics Limited

Alex Mercer, PhD
Pharmalink AB

Daniel Cattran, MD
University of Toronto, Canada

Heather Reich, MD, CM, PhD, FRCPC
University of Toronto, Canada

Jürgen Floege, MD
University of Aachen, Germany

Brad H. Rovin, MD
The Ohio State University

Barbara S. Gillespie, MD, MMS, FASN
Quintiles Global CRO

KIDNEY HEALTH INITIATIVE

IgA Nephropathy

Chapter 10: Immunoglobulin A nephropathy

10.1: Initial evaluation including assessment of risk of progressive kidney disease

10.1.1: Assess all patients with biopsy-proven IgAN for secondary causes of IgAN. (*Not Graded*)

10.1.2: Assess the risk of progression in all cases by evaluation of proteinuria, blood pressure, and eGFR at the time of diagnosis and during follow-up. (*Not Graded*)

10.1.3: Pathological features may be used to assess prognosis. (*Not Graded*)

IgA Nephropathy

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IgA Nephropathy

original article

http://www.kidney-international.org

see commentary on page 477

The Oxford classification of IgA nephropathy: rationale, clinicopathological correlations, and classification

A Working Group of the International IgA Nephropathy Network and the Renal Pathology Society: Daniel C. Cattran[1,†], Rosanna Coppo[2,†], H. Terence Cook[3,†], John Feehally[4,†], Ian S.D. Roberts[5,†], Stéphan Troyanov[6,†], Charles E. Alpers[7], Alessandro Amore[2], Jonathan Barratt[4], Francois Berthoux[8], Stephen Bonsib[9], Jan A. Bruijn[10], Vivette D'Agati[11], Giuseppe D'Amico[12], Steven Emancipator[13], Francesco Emma[14], Franco Ferrario[15], Fernando C. Fervenza[16], Sandrine Florquin[17], Agnes Fogo[18], Colin C. Geddes[19], Hermann-Josef Groene[20], Mark Haas[21], Andrew M. Herzenberg[22], Prue A. Hill[23], Ronald J. Hogg[24], Stephen I. Hsu[25], J. Charles Jennette[26], Kensuke Joh[27], Bruce A. Julian[28], Tetsuya Kawamura[29], Fernand M. Lai[30], Chi Bon Leung[31], Lei-Shi Li[32], Philip K.T. Li[31], Zhi-Hong Liu[32], Bruce Mackinnon[19], Sergio Mezzano[33], F. Paolo Schena[34], Yasuhiko Tomino[35], Patrick D. Walker[36], Haiyan Wang[37], Jan J. Weening[38], Nori Yoshikawa[39] and Hong Zhang[37,*]

http://www.kidney-international.org original article

The Oxford IgA nephropathy clinicopathological classification is valid for children as well as adults

A Working Group of the International IgA Nephropathy Network and the Renal Pathology Society: Rosanna Coppo[1], Stéphan Troyanov[2], Roberta Camilla[1], Ronald J. Hogg[3], Daniel C. Cattran[4], H. Terence Cook[5], John Feehally[6], Ian S.D. Roberts[7], Alessandro Amore[1], Charles E. Alpers[8], Jonathan Barratt[6], Francois Berthoux[9], Stephen Bonsib[10], Jan A. Bruijn[11], Vivette D'Agati[12], Giuseppe D'Amico[13], Steven N. Emancipator[14], Francesco Emma[15], Franco Ferrario[16], Fernando C. Fervenza[17], Sandrine Florquin[18], Agnes B. Fogo[19], Colin C. Geddes[20], Hermann J. Groene[21], Mark Haas[22], Andrew M. Herzenberg[23], Prue A. Hill[24], Stephen I. Hsu[25], J. Charles Jennette[26], Kensuke Joh[27], Bruce A. Julian[28], Tetsuya Kawamura[29], Fernand M. Lai[30], Lei S. Li[31], Philip K. Li[32], Zhi H. Liu[31], Sergio Mezzano[33], F. Paolo Schena[34], Yasuhiko Tomino[35], Patrick D. Walker[36], Haiyan Wang[37], Jan J. Weening[38], Norishige Yoshikawa[39] and Hong Zhang[37,*]

original article

http://www.kidney-international.org

Validation of the Oxford classification of IgA nephropathy

Andrew M. Herzenberg[1,6,7], Agnes B. Fogo[2,6], Heather N. Reich[1,6], Stéphan Troyanov[3,6], Nuket Bavbek[2], Alfonso E. Massat[4], Tracy E. Hunley[2], Michelle A. Hladunewich[2], Bruce A. Julian[5], Fernando C. Fervenza[4] and Daniel C. Cattran[2]

Article

Validation Study of Oxford Classification of IgA Nephropathy: The Significance of Extracapillary Proliferation

Ritsuko Katafuchi, Toshiharu Ninomiya,† Masaharu Nagata,‡ Koji Mitsuiki,‡ and Hideki Hirakata‡*

clinical investigation

http://www.kidney-international.org

OPEN

Validation of the Oxford classification of IgA nephropathy in cohorts with different presentations and treatments

Rosanna Coppo[1,7], Stéphan Troyanov[2,7], Shubha Bellur[3,8], Daniel Cattran[4,7], H. Terence Cook[5,7], John Feehally[6,7], Ian S.D. Roberts[3,7], Laura Morando[8], Roberta Camilla[8], Vladimir Tesar[8], Sigrid Lunberg[8], Loreto Gesualdo[8], Francesco Emma[8], Cristiana Rollino[8], Alessandro Amore[8], Manuel Praga[8], Sandro Feriozzi[8], Giuseppe Segoloni[8], Antonello Pani[8], Giovanni Cancarini[8], Magalena Durlik[8], Elisabetta Moggia[8], Gianna Mazzucco[8], Costantinos Giannakakis[8], Eva Honsova[8], B. Brigitta Sundelin[8], Anna Maria Di Palma[8], Franco Ferrario[8], Eduardo Gutierrez[8], Anna Maria Asunis[8], Jonathan Barratt[8], Regina Tardanico[8] and Agnieszka Perkowska-Ptasinska[8], on behalf of the VALIGA study of the ERA-EDTA Immunonephrology Working Group[8]

IgA Nephropathy

meeting report www.kidney-international.org

Oxford Classification of IgA nephropathy 2016: an update from the IgA Nephropathy Classification Working Group

Hernán Trimarchi[1], Jonathan Barratt[2], Daniel C. Cattran[3], H. Terence Cook[4], Rosanna Coppo[5], Mark Haas[6], Zhi-Hong Liu[7], Ian S.D. Roberts[8], Yukio Yuzawa[9], Hong Zhang[10] and John Feehally[2] on behalf of the IgAN Classification Working Group of the International IgA Nephropathy Network and the Renal Pathology Society[1]; for Conference Participants[11]

www.kidney-international.org clinical investigation

Evidence from the Oxford Classification cohort supports the clinical value of subclassification of focal segmental glomerulosclerosis in IgA nephropathy

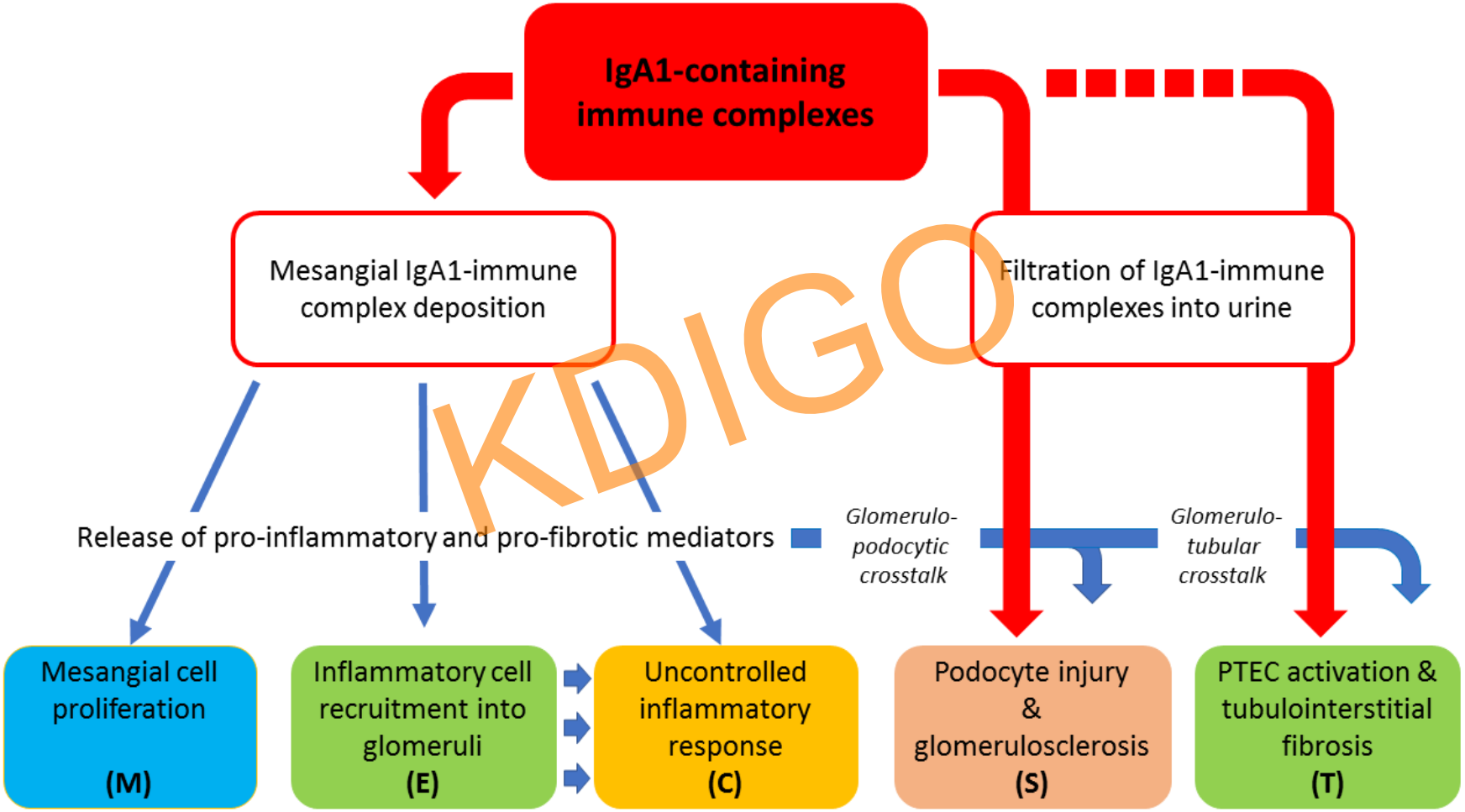
Shubha S. Bellur[1], Fanny Lepeytre[2], Olga Vorobyeva[1], Stéphan Troyanov[2], H. Terence Cook[3] and Ian S.D. Roberts[1], on behalf of the International IgA Nephropathy Working Group

CLINICAL RESEARCH www.jasn.org

A Multicenter Study of the Predictive Value of Crescents in IgA Nephropathy

Mark Haas,* Jacobien C. Verhave,† Zhi-Hong Liu,‡ Charles E. Alpers,§ Jonathan Barratt,‖ Jan U. Becker,¶ Daniel Cattran,** H. Terence Cook,†† Rosanna Coppo,‡‡ John Feehally,‖ Antonello Pani,§§ Agnieszka Perkowska-Ptasinska,‖‖ Ian S.D. Roberts,¶¶ Maria Fernanda Soares,*** Hernan Trimarchi,††† Suxia Wang,‡‡‡ Yukio Yuzawa,§§§ Hong Zhang,‖‖‖ Stéphan Troyanov,¶¶¶ and Ritsuko Katafuchi****

IgA Nephropathy



IgA Nephropathy

Chapter 10: Immunoglobulin A nephropathy

10.1: Initial evaluation including assessment of risk of progressive kidney disease

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10.1.2: Assess the risk of progression in all cases by evaluation of proteinuria, blood pressure, and eGFR at the time of diagnosis and during follow-up. (*Not Graded*)

10.1.3: Pathological features may be used to assess prognosis. (*Not Graded*)

IgA Nephropathy

The derivation and validation of an international risk prediction tool in IgAN

Sean Barbour
Assistant Professor
University of BC, Division of Nephrology

IgA Nephropathy

1. Derive a prediction model for renal outcome in IgAN that includes the MEST-C score and clinical risk factors at the time of biopsy, using cohorts from Europe, Japan and China.
2. Externally validate the prediction model in a separate multi-ethnic international cohort.
3. Update the prediction model for application in pediatric populations using a multi-ethnic international cohort

IgA Nephropathy

- Merged the following datasets:
  - VALIGA (with new/post VALIGA), Tokyo, Nanjing
  - Total N=3067
- Inclusion criteria:
  - Adults age ≥ 18 years
  - Did not have ESRD at the time of biopsy
  - Available eGFR at biopsy and ≥ 1 after biopsy
  - Total N=2784
- Primary outcome:
  - Time from biopsy to a ≥ 50% reduction in eGFR or ESRD (dialysis, transplantation, eGFR ≤ 15)
  - Censored: death, end of follow-up
  - Modeled using Cox PH survival models

IgA Nephropathy

	Total	VALIGA[1]	Nanjing	Tokyo
Patients	2784	1194	1021	569
Follow-up (years)	4.79	6.62	4.34	3.92
Age (years)	35.6	38.7	34.0	34.7
Race:				
Caucasian	1169 (42%)	1169 (97.9%)	0 (0%)	0 (0%)
Japanese	570 (20.5%)	2 (0.2%)	0 (0%)	568 (99.8%)
Chinese	1021 (36.7%)	0 (0%)	1021 (100%)	0 (0%)
eGFR (ml/min/ 1.73m^2)	82.95	69.35	87.92	103.09
Proteinuria (g/d)	1.2	1.4	1.28	0.68
MAP (mmHg)	96.7	100.0	95.0	88.0
BMI (kg/m^2)	23.8	25.5	22.6	21.9

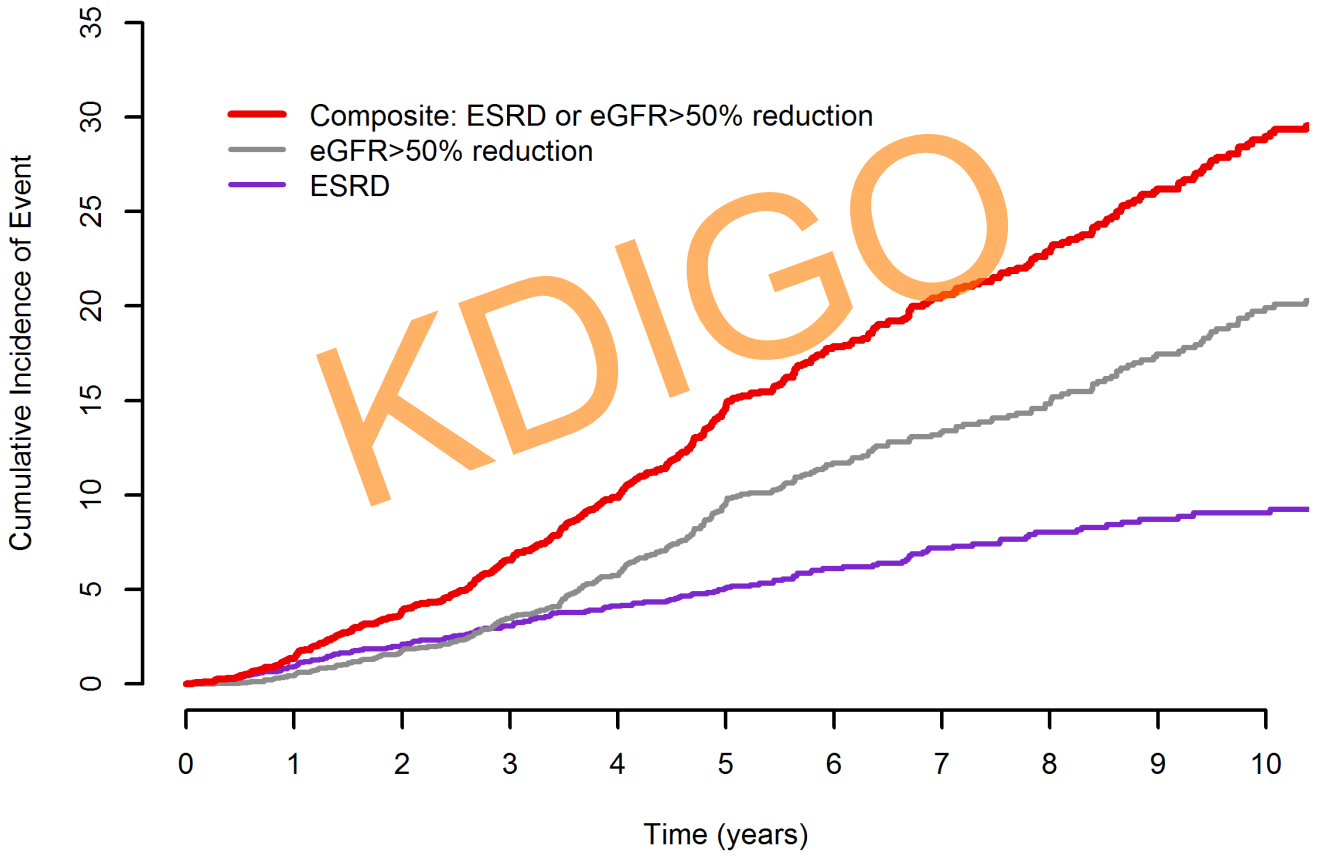
[1]Includes VALGIA, post-VALIGA and new-VALIGA

IgA Nephropathy

	Total	VALIGA[1]	Nanjing	Tokyo
Pathology				
M1	1057 (38%)	424 (35.5%)	435 (42.6%)	198 (34.8%)
E1	479 (17.2%)	159 (13.3%)	113 (11.1%)	207 (36.4%)
S1	2139 (76.8%)	875 (73.3%)	852 (83.4%)	412 (72.4%)
T1	688 (24.7%)	256 (21.4%)	247 (24.2%)	185 (32.5%)
T2	129 (4.6%)	68 (5.7%)	33 (3.2%)	28 (4.9%)
C	954 (34.3%)	155 (13%)	458 (44.9%)	341 (59.9%)
RASB at biopsy	862 (31%)	472 (39.5%)	230 (22.5%)	160 (28.1%)
RASB during follow-up	2402 (86.3%)	1093 (91.5%)	931 (91.2%)	378 (66.4%)
IS during follow-up	1212 (43.5%)	501 (42%)	341 (33.4%)	370 (65%)
Primary outcome events	495 (17.8%)	288 (24.1%)	151 (14.8%)	56 (9.8%)

[1]Includes VALGIA, post-VALIGA and new-VALIGA

IgA Nephropathy



IgA Nephropathy

International IgAN study investigators and collaborators

- Data access and study support
- D Cattran, H Reich, S Troyanov (Canada)
- J Ding (Beijing, China)
- J Feehally (Leicester, UK)
- M Hattori, Y Suzuki and K Matsuzaki (Tokyo, Japan)
- R Katafuchi (Fukuoka, Japan)
- R Coppo and ML Russo (Torino, Italy)
- H Zhang and S Shi (Beijing, China)
- H Trimarchi (Buenos Aires, Argentina)
- R Wyatt (Memphis, US)
- N Yoshikawa and Y Shima (Wakayama, Japan)
- ZH Liu and C Zheng (Nanjing, China)
- VALIGA and new-VALIGA site investigators and study coordinators

IgA Nephropathy

10.2: Antiproteinuric and antihypertensive therapy

10.2.1: We recommend long-term ACE-I or ARB treatment when proteinuria is >1 g/d, with up-titration of the drug depending on blood pressure. (*1B*)

10.2.2: We suggest ACE-I or ARB treatment if proteinuria is between 0.5 to 1 g/d (in children, between 0.5 to 1 g/d per 1.73 m^2). (*2D*)

10.2.3: We suggest the ACE-I or ARB be titrated upwards as far as tolerated to achieve proteinuria <1 g/d. (*2C*)

10.2.4: In IgAN, use blood pressure treatment goals of <130/80 mm Hg in patients with proteinuria <1 g/d, and <125/75 mm Hg when initial proteinuria is >1 g/d (see Chapter 2). (*Not Graded*)

RESEARCH RECOMMENDATION

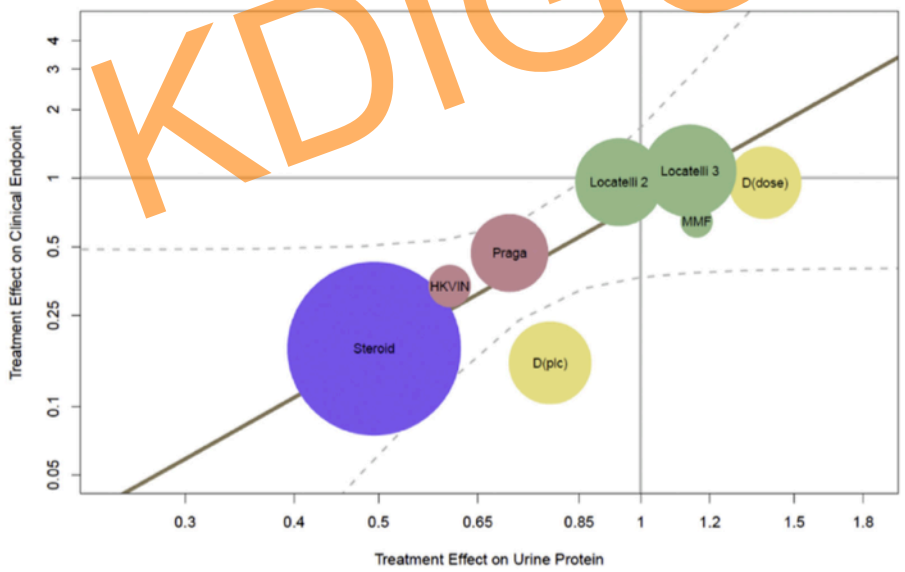
- RCTs are needed to compare the efficacy in proteinuric IgAN of combination therapy using ACE-I and ARBs to monotherapy using either alone.

IgA Nephropathy

AJKD
Original Investigation

Early Change in Urine Protein as a Surrogate End Point in Studies of IgA Nephropathy: An Individual-Patient Meta-analysis

Lesley A. Inker, MD, MS,[1] Hasi Mondal, MPH,[1] Tom Greene, PhD,[2] Taylor Masaschi, BA,[1] Francesco Locatelli, MD,[3] Francesco P. Schena, MD,[4] Ritsuko Katafuchi, MD,[5] Gerald B. Appel, MD, PhD,[6] Bart D. Maes, MD,[7] Philip K. Li, MD,[8] Manuel Praga, MD,[9] Lucia Del Vecchio, MD,[3] Simeone Andrulli, MD,[3] Carlo Manno, MD,[4] Eduardo Gutierrez, MD,[9] Alex Mercer, PhD,[10] Kevin J. Carroll, PhD,[11] Christopher H. Schmid, PhD,[12] and Andrew S. Levey, MD[1]



KDIGO Controversies Conference on Glomerular Diseases
November 16-19, 2017 | Singapore

IgA Nephropathy

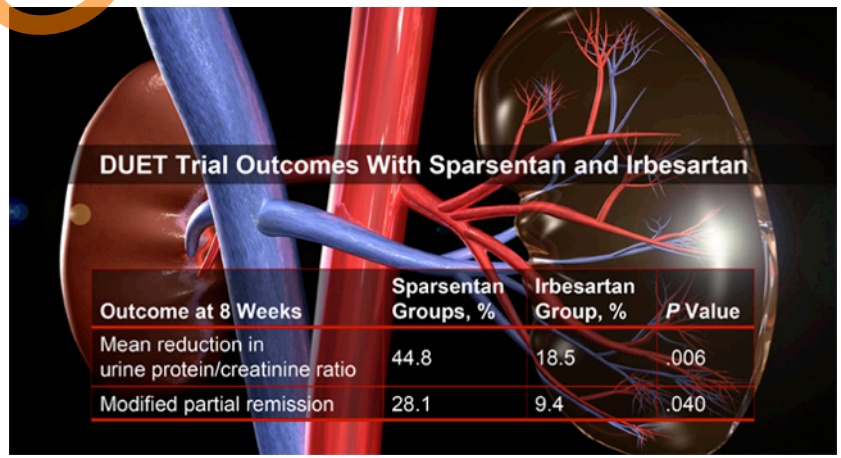
TABLE 1 Drugs for Direct Manipulation of the Renin–Angiotensin–Aldosterone System[1,2,18,20–24]

Class	Generic Names[a]	Mechanism of Action
Renin inhibitors	Aliskiren	Interfere with the first rate-limiting step in the synthesis of Ang I from angiotensinogen
ACE inhibitors	▸ Benazepril[b] ▸ Captopril ▸ Enalapril[b,c] ▸ Imidapril ▸ Lisinopril ▸ Ramipril	Inhibit the conversion of Ang I into Ang II
Angiotensin receptor antagonists	▸ Candesartan ▸ Irbesartan ▸ Losartan ▸ Valsartan	Block the binding of Ang II to AT1 receptors
Aldosterone antagonists	Spironolactone[b]	Block the binding of aldosterone to principal cells of the renal collecting ducts

Articles

Anti-albuminuric effect of the aldosterone blocker eplerenone in non-diabetic hypertensive patients with albuminuria: a double-blind, randomised, placebo-controlled trial

Katsuyuki Ando, Hiroshi Ohtsu, Shunya Uchida, Shinya Kaname, Yoshihiro Arakawa, Toshiro Fujita, for the EVALUATE Study Group*



Original Article

jraas

LY3045697: Results from two randomized clinical trials of a novel inhibitor of aldosterone synthase

Journal of the Renin-Angiotensin-Aldosterone System
July-September 2017: 1–14

DOI: 10.1177/1470320317717883
journals.sagepub.com/home/jra
SAGE

Joanne Sloan-Lancaster[1*], Eyas Raddad[1*], Amy Flynt[2], Yan Jin[3], James Voelker[3] and Jeffrey W Miller[4]

IgA Nephropathy

10.3: Corticosteroids

10.3.1: We suggest that patients with persistent proteinuria ≥1 g/d, despite 3–6 months of optimized supportive care (including ACE-I or ARBs and blood pressure control), and GFR >50 ml/min per 1.73 m^2, receive a 6-month course of corticosteroid therapy. (*2C*)

RESEARCH RECOMMENDATION

- Studies using immunosuppressive agents should always include rigorous blood pressure control and antiproteinuric therapy. This is currently being tested in the STOP-IgAN trial.[519] Newer immunosuppressives (alone or in combination) should be compared in RCTs to a "control" group receiving corticosteroids alone.

IgA Nephropathy

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Supportive Care plus Immunosuppression in IgA Nephropathy

Thomas Rauen, M.D., Frank Eitner, M.D., Christina Fitzner, M.Sc., Claudia Sommerer, M.D., Martin Zeier, M.D., Britta Otte, M.D., Ulf Panzer, M.D., Harm Peters, M.D., Urs Benck, M.D., Peter R. Mertens, M.D., Uwe Kuhlmann, M.D., Oliver Witzke, M.D., Oliver Gross, M.D., Volker Vielhauer, M.D., Johannes F.E. Mann, M.D., Ralf-Dieter Hilgers, Ph.D., and Jürgen Floege, M.D., for the STOP-IgAN Investigators*

IgA Nephropathy

The NEW ENGLAND JOURNAL of MEDICINE

CONCLUSIONS

The addition of immunosuppressive therapy to intensive supportive care in patients with high-risk IgA nephropathy did not significantly improve the outcome, and during the 3-year study phase, more adverse effects were observed among the patients who received immunosuppressive therapy, with no change in the rate of decrease in the eGFR. (Funded by the German Federal Ministry of Education and Research; STOP-IgAN ClinicalTrials.gov number, NCT00554502.)

N ENGL J MED 373;23 NEJM.ORG DECEMBER 3, 2015

Uwe Kuhlmann, M.D., Oliver Witzke, M.D., Oliver Gross, M.D.,
Volker Vielhauer, M.D., Johannes F.E. Mann, M.D., Ralf-Dieter Hilgers, Ph.D.,
and Jürgen Floege, M.D., for the STOP-IgAN Investigators*

IgA Nephropathy

Research

JAMA | Original Investigation

Effect of Oral Methylprednisolone on Clinical Outcomes in Patients With IgA Nephropathy
The TESTING Randomized Clinical Trial

Jicheng Lv, MD; Hong Zhang, PhD; Muh Geot Wong, PhD; Meg J. Jardine, PhD; Michelle Hladunewich, MD; Vivek Jha, MD; Helen Monaghan, PhD; Minghui Zhao, MD; Sean Barbour, MD; Heather Reich, MD; Daniel Cattran, MD; Richard Glassock, MD; Adeera Levin, FRCPC; David Wheeler, FRCP; Mark Woodward, PhD; Laurent Billot, MSc; Tak Mao Chan, MD; Zhi-Hong Liu, MD; David W. Johnson, MD; Alan Cass, FRACP; John Feehally, MD; Jürgen Floege, MD; Giuseppe Remuzzi, MD; Yangfeng Wu, MD; Rajiv Agarwal, MD; Hai-Yan Wang, MD; Vlado Perkovic, PhD; for the TESTING Study Group

IMPORTANCE Guidelines recommend corticosteroids in patients with IgA nephropathy and persistent proteinuria, but the effects remain uncertain.

OBJECTIVE To evaluate the efficacy and safety of corticosteroids in patients with IgA nephropathy at risk of progression.

DESIGN, SETTING, AND PARTICIPANTS The Therapeutic Evaluation of Steroids in IgA Nephropathy Global (TESTING) study was a multicenter, double-blind, randomized clinical trial designed to recruit 750 participants with IgA nephropathy (proteinuria greater than 1 g/d and estimated glomerular filtration rate [eGFR] of 20 to 120 mL/min/1.73 m^2 after at least 3 months of blood pressure control with renin-angiotensin system blockade] and to provide follow-up until 335 primary outcomes occurred.

Editorial page 429

Supplemental content

CME Quiz at jamanetwork.com/learning

IgA Nephropathy

Research

JAMA | Original Investigation

Effect of Oral Methylprednisolone on Clinical Outcomes in Patients With IgA Nephropathy

Conclusions and Relevance Among patients with IgA nephropathy and proteinuria of 1 g/d or greater, oral methylprednisolone was associated with an increased risk of serious adverse events, primarily infections. Although the results were consistent with potential renal benefit, definitive conclusions about treatment benefit cannot be made, owing to early termination of the trial.

IMPORTANCE Guidelines recommend corticosteroids in patients with IgA nephropathy and persistent proteinuria, but the effects remain uncertain.

OBJECTIVE To evaluate the efficacy and safety of corticosteroids in patients with IgA nephropathy at risk of progression.

DESIGN, SETTING, AND PARTICIPANTS The Therapeutic Evaluation of Steroids in IgA Nephropathy Global (TESTING) study was a multicenter, double-blind, randomized clinical trial designed to recruit 750 participants with IgA nephropathy (proteinuria greater than 1 g/d and estimated glomerular filtration rate [eGFR] of 20 to 120 mL/min/1.73 m^2 after at least 3 months of blood pressure control with renin-angiotensin system blockade] and to provide follow-up until 335 primary outcomes occurred.

Editorial page 429

Supplemental content

CME Quiz at jamanetwork.com/learning

IgA Nephropathy

10.4: Immunosuppressive agents (cyclophosphamide, azathioprine, MMF, cyclosporine)

10.4.1: We suggest not treating with corticosteroids combined with cyclophosphamide or azathioprine in IgAN patients (unless there is crescentic IgAN with rapidly deteriorating kidney function; see Recommendation 10.6.3). (*2D*)

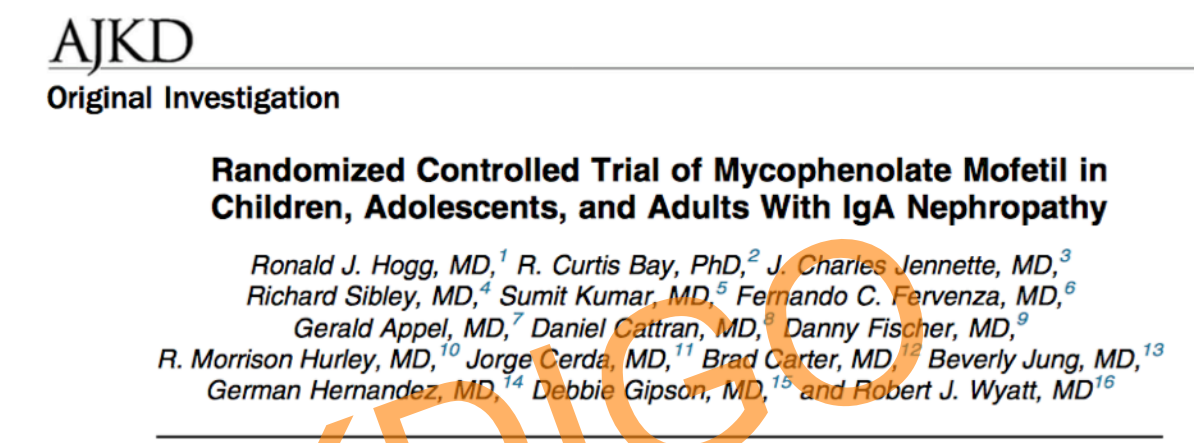
10.4.2: We suggest not using immunosuppressive therapy in patients with GFR < 30 ml/min per 1.73 m^2 unless there is crescentic IgAN with rapidly deteriorating kidney function (see Section 10.6). (*2C*)

10.4.3: We suggest not using MMF in IgAN. (*2C*)

RESEARCH RECOMMENDATIONS

- An RCT is needed comparing MMF and corticosteroids vs. corticosteroids alone in patients receiving optimal antihypertensive and antiproteinuric therapy.
- An RCT is needed to investigate the different efficacy of MMF in Asians vs. Caucasians, including evaluation of drug and metabolite levels.

IgA Nephropathy



AJKD

Original Investigation

Randomized Controlled Trial of Mycophenolate Mofetil in Children, Adolescents, and Adults With IgA Nephropathy

Ronald J. Hogg, MD,[1] R. Curtis Bay, PhD,[2] J. Charles Jennette, MD,[3] Richard Sibley, MD,[4] Sumit Kumar, MD,[5] Fernando C. Fervenza, MD,[6] Gerald Appel, MD,[7] Daniel Cattran, MD,[8] Danny Fischer, MD,[9] R. Morrison Hurley, MD,[10] Jorge Cerda, MD,[11] Brad Carter, MD,[12] Beverly Jung, MD,[13] German Hernandez, MD,[14] Debbie Gipson, MD,[15] and Robert J. Wyatt, MD[16]

AJKD

Original Investigation

Mycophenolate Mofetil Combined With Prednisone Versus Full-Dose Prednisone in IgA Nephropathy With Active Proliferative Lesions: A Randomized Controlled Trial

Jin-Hua Hou, MD,[1,] Wei-Bo Le, PhD,[1,*] Nan Chen, MD,[2] Wei-Ming Wang, PhD,[2] Zhang-Suo Liu, MD,[3] Dong Liu, PhD,[3] Jiang-Hua Chen, MD,[4] Jiong Tian, PhD,[4] Ping Fu, MD, PhD,[5] Zhang-Xue Hu, MD,[5] Cai-Hong Zeng, PhD,[1] Shao-Shan Liang, MD,[1] Min-Lin Zhou, MD,[1] Hai-Tao Zhang, MD,[1] and Zhi-Hong Liu, MD[1]*

IgA Nephropathy

AJKD

Original Investigation

Randomized Controlled Trial of Mycophenolate Mofetil in

Conclusions: MMF did not reduce proteinuria significantly in patients with IgAN who had persistent proteinuria after lisinopril/losartan plus Omacor.

Am J Kidney Dis. 66(5):783-791. © *2015 by the National Kidney Foundation, Inc.*

Gerald Appel, MD,[7] Daniel Cattran, MD,[8] Danny Fischer, MD,[9] R. Morrison Hurley, MD,[10] Jorge Cerda, MD,[11] Brad Carter, MD,[12] Beverly Jung, MD,[13] German Hernandez, MD,[14] Debbie Gipson, MD,[15] and Robert J. Wyatt, MD[16]

AJKD

Original Investigation

Mycophenolate Mofetil Combined With Prednisone Versus Full-Dose Prednisone in IgA Nephropathy With Active

Conclusions: MMF plus prednisone versus full-dose prednisone did not differ in reducing proteinuria, but patients treated with the former had fewer adverse events in patients with IgAN with active proliferative lesions.

Am J Kidney Dis. 69(6):788-795. © *2017 by the National Kidney Foundation, Inc.*

Jiong Tian, PhD,[4] Ping Fu, MD, PhD,[5] Zhang-Xue Hu, MD,[5] Cai-Hong Zeng, PhD,[1] Shao-Shan Liang, MD,[1] Min-Lin Zhou, MD,[1] Hai-Tao Zhang, MD,[1] and Zhi-Hong Liu, MD[1]

IgA Nephropathy

10.5.2: Antiplatelet agents

10.5.2.1: We suggest not using antiplatelet agents to treat IgAN. (*2C*)

RESEARCH RECOMMENDATION

- A multicenter RCT is needed to address the role of antiplatelet therapy in IgAN.

IgA Nephropathy

10.5.3: Tonsillectomy

10.5.3.1: We suggest that tonsillectomy not be performed for IgAN. (*2C*)

RESEARCH RECOMMENDATION

- A multicenter RCT is needed to address the role of tonsillectomy in IgAN.

IgA Nephropathy

Nephrol Dial Transplant (2014) 29: 1546–1553
doi: 10.1093/ndt/gfu020
Advance Access publication 3 March 2014

A multicenter randomized controlled trial of tonsillectomy combined with steroid pulse therapy in patients with immunoglobulin A nephropathy

Tetsuya Kawamura[1], Mitsuhiro Yoshimura[2], Yoichi Miyazaki[1], Hidekazu Okamoto[1], Kenjiro Kimura[3], Keita Hirano[1], Masato Matsushima[4], Yasunori Utsunomiya[1], Makoto Ogura[1], Takashi Yokoo[1], Hideo Okonogi[1], Takeo Ishii[1], Akihiko Hamaguchi[1], Hiroyuki Ueda[1], Akira Furusu[5], Satoshi Horikoshi[6], Yusuke Suzuki[6], Takanori Shibata[7], Takashi Yasuda[3], Sayuri Shirai[3], Toshiyuki Imasawa[8], Koichi Kanozawa[9], Akira Wada[10], Izumi Yamaji[11], Naoto Miura[12], Hirokazu Imai[12], Kenji Kasai[13], Jun Soma[14], Shouichi Fujimoto[15], Seiichi Matsuo[16], and Yasuhiko Tomino[6] and The Special IgA Nephropathy Study Group

[1]Division of Kidney and Hypertension, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan, [2]Department of Internal Medicine, Kanazawa Medical Centre, Kanazawa, Japan, [3]Division of Kidney and Hypertension, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan, [4]Division of Clinical Epidemiology, Research Center for Medical Science, Jikei University School of Medicine, Tokyo, Japan, [5]Second Department of Internal Medicine, Nagasaki University Hospital of Medicine and Dentistry, Nagasaki, Japan, [6]Division of Nephrology, Department of Internal Medicine, Juntendo University School of Medicine, Tokyo, Japan,

IgA Nephropathy

Nephrol Dial Transplant (2014) 29: 1546–1553
doi: 10.1093/ndt/gfu020
Advance Access publication 3 March 2014

A multicenter randomized controlled trial of tonsillectomy combined with steroid pulse therapy in patients with im

Conclusions. The results indicate tonsillectomy combined with steroid pulse therapy has no beneficial effect over steroid pulses alone to attenuate hematuria and to increase the incidence of clinical remission. Although the antiproteinuric effect was significantly greater in combined therapy, the difference was marginal, and its impact on the renal functional outcome remains to be clarified.

Tet[illegible][3],
Kei[illegible]
Hic[illegible]shi[6],
Yus[illegible]ozawa[9],
Aki[illegible]
Sho[illegible]dy

Group

[1]Division of Kidney and Hypertension, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan, [2]Department of Internal Medicine, Kanazawa Medical Centre, Kanazawa, Japan, [3]Division of Kidney and Hypertension, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan, [4]Division of Clinical Epidemiology, Research Center for Medical Science, Jikei University School of Medicine, Tokyo, Japan, [5]Second Department of Internal Medicine, Nagasaki University Hospital of Medicine and Dentistry, Nagasaki, Japan, [6]Division of Nephrology, Department of Internal Medicine, Juntendo University School of Medicine, Tokyo, Japan,

IgA Nephropathy

Nephrol Dial Transplant (2014) 29: 1546–1553
doi: 10.1093/ndt/gfu020
Advance Access publication 3 March 2014

Clin Exp Nephrol (2016) 20:244–252
DOI 10.1007/s10157-015-1159-2

CrossMark

ORIGINAL ARTICLE

Pathological sub-analysis of a multicenter randomized controlled trial of tonsillectomy combined with steroid pulse therapy versus steroid pulse monotherapy in patients with immunoglobulin A nephropathy

Ritsuko Katafuchi[1] · Tetsuya Kawamura[2] · Kensuke Joh[3] · Akinori Hashiguchi[4] · Satoshi Hisano[5] · Akira Shimizu[6] · Yoichi Miyazaki[2] · Masaharu Nagata[7] · Seiichi Matsuo[8] · The IgA nephropathy Study Group in Japan

[1]Division of Kidney and Hypertension, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan, [2]Department of Internal Medicine, Kanazawa Medical Centre, Kanazawa, Japan, [3]Division of Kidney and Hypertension, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan, [4]Division of Clinical Epidemiology, Research Center for Medical Science, Jikei University School of Medicine, Tokyo, Japan, [5]Second Department of Internal Medicine, Nagasaki University Hospital of Medicine and Dentistry, Nagasaki, Japan, [6]Division of Nephrology, Department of Internal Medicine, Juntendo University School of Medicine, Tokyo, Japan,

IgA Nephropathy

10.6: Atypical forms of IgAN

10.6.1: MCD with mesangial IgA deposits

10.6.1.1: We recommend treatment as for MCD (see Chapter 5) in nephrotic patients showing pathological findings of MCD with mesangial IgA deposits on kidney biopsy. (*2B*)

10.6.2: AKI associated with macroscopic hematuria

10.6.2.1: Perform a repeat kidney biopsy in IgAN patients with AKI associated with macroscopic hematuria if, after 5 days from the onset of kidney function worsening, there is no improvement. (*Not Graded*)

10.6.2.2: We suggest general supportive care for AKI in IgAN, with a kidney biopsy performed during an episode of macroscopic hematuria showing only ATN and intratubular erythrocyte casts. (*2C*)

IgA Nephropathy

10.6.3: Crescentic IgAN

10.6.3.1: Define crescentic IgAN as IgAN with crescents in more than 50% of glomeruli in the renal biopsy with rapidly progressive renal deterioration. (*Not Graded*)

10.6.3.2: We suggest the use of steroids and cyclophosphamide in patients with IgAN and rapidly progressive crescentic IgAN, analogous to the treatment of ANCA vasculitis (see Chapter 13). (*2D*)

RESEARCH RECOMMENDATION

- RCTs are needed to investigate the benefits of cyclophosphamide, MMF, and azathioprine in crescentic IgAN.

IgA Vasculitis

Chapter 11: Henoch-Schönlein purpura nephritis

11.1: Treatment of HSP nephritis in children

11.1.1: We suggest that children with HSP nephritis and persistent proteinuria, >0.5–1 g/d per 1.73 m^2, are treated with ACE-I or ARBs. (*2D*)

11.1.2: We suggest that children with persistent proteinuria, >1 g/d per 1.73 m^2, after a trial of ACE-I or ARBs, and GFR >50 ml/min per 1.73 m^2, be treated the same as for IgAN with a 6-month course of corticosteroid therapy (see Chapter 10). (*2D*)

11.2: Treatment of crescentic HSP nephritis in children

11.2.1: We suggest that children with crescentic HSP with nephrotic syndrome and/or deteriorating kidney function are treated the same as for crescentic IgAN (see Recommendation 10.6.3). (*2D*)

11.3: Prevention of HSP nephritis in children

11.3.1: We recommend not using corticosteroids to prevent HSP nephritis. (*1B*)

11.4: HSP nephritis in adults

11.4.1: We suggest that HSP nephritis in adults be treated the same as in children. (*2D*)

IgA Vasculitis

RESEARCH RECOMMENDATIONS

- An RCT comparing a 6- to 12-month course of corticosteroids to shorter-duration corticosteroids (28 days) should be performed in children with moderately severe HSP nephritis (acute nephritic syndrome or nephrotic syndrome with normal kidney function and <50% crescents or sclerosing lesions on biopsy).
- RCTs are required to determine whether immunosuppressive agents (cyclosporine, azathioprine, MMF) and corticosteroids are effective in treating children with severe HSP nephritis (acute nephritic syndrome, nephrotic syndrome with or without reduced kidney function with >50% crescents or sclerosing lesions on biopsy).

IgA Vasculitis

Original article

Randomised, double-blind, placebo-controlled trial to determine whether steroids reduce the incidence and severity of nephropathy in Henoch-Schönlein Purpura (HSP)

Jan Dudley,[1] Graham Smith,[2] Anne Llewelyn-Edwards,[3] Kate Bayliss,[4] Katie Pike,[4] Jane Tizard[1]

Arthritis & Rheumatology

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Brief Report

Rituximab for the treatment of adult-onset IgA vasculitis (Henoch-Schönlein purpura)

Federica Maritati, Roberta Fenoglio, Evangeline Pillebout, Giacomo Emmi, Maria L. Urban, Rossana Rocco, Maria Nicastro, Monia Incerti, Matteo Goldoni, Giorgio Trivioli, Elena Silvestri, Aladdin J. Mohammad, David Jayne, Per Eriksson, Mårten Segelmark, Pavel Novikov, Helen Harris, Dario Roccatello, Augusto Vaglio

Accepted manuscript online: 3 October 2017 Full publication history

DOI: 10.1002/art.40339 View/save citation

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Accepted Articles

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What is already known on this topic

- The long-term prognosis of Henoch-Schönlein Purpura (HSP) is predominantly determined by the extent of renal involvement.
- There has been a long debate over the role of steroids in the prevention and management of HSP nephritis.

What this study adds

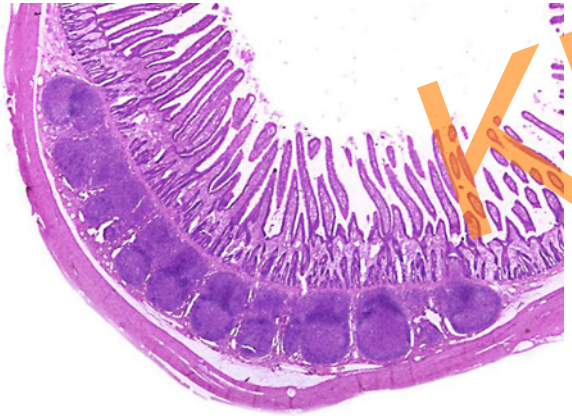
- Our data do not support the routine use of prednisolone in early Henoch-Schönlein Purpura (HSP).
- Further multicentre studies are required to assess the subgroup that develops more severe established HSP nephritis.

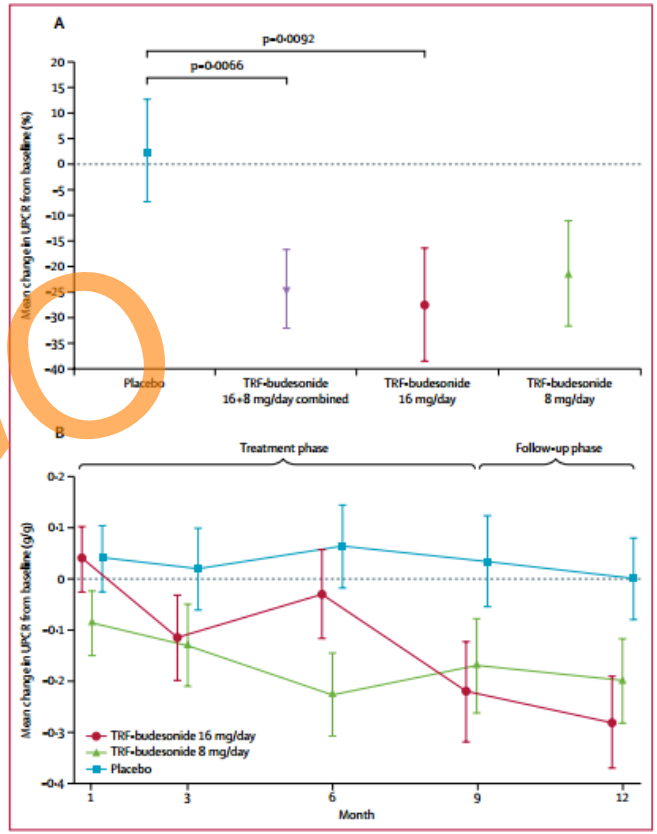
IgA Nephropathy

Articles

Targeted-release budesonide versus placebo in patients with IgA nephropathy (NEFIGAN): a double-blind, randomised, placebo-controlled phase 2b trial

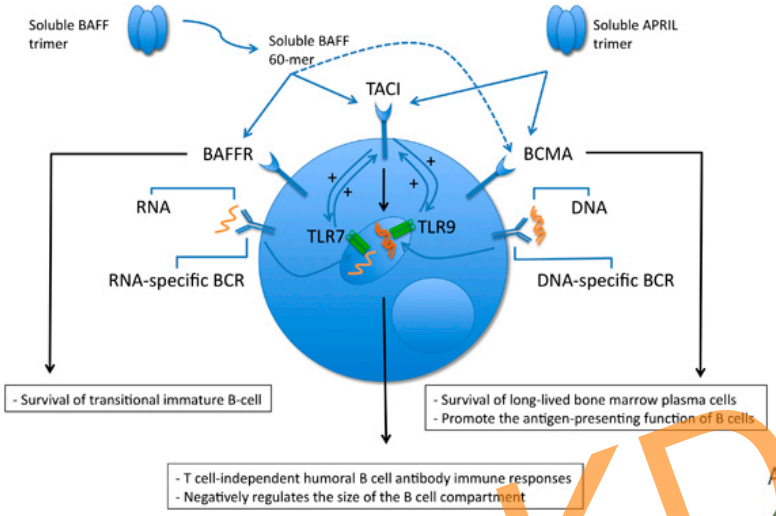
Bengt C Fellström, Jonathan Barratt, Heather Cook, Rosanna Coppo, John Feehally, Johan W de Fijter, Jürgen Floege, Gerd Hetzel, Alan G Jardine, Francesco Locatelli, Bart D Maes, Alex Mercer, Fernanda Ortiz, Manuel Praga, Søren S Sørensen, Vladimir Tesar, Lucia Del Vecchio, for the NEFIGAN Trial Investigators

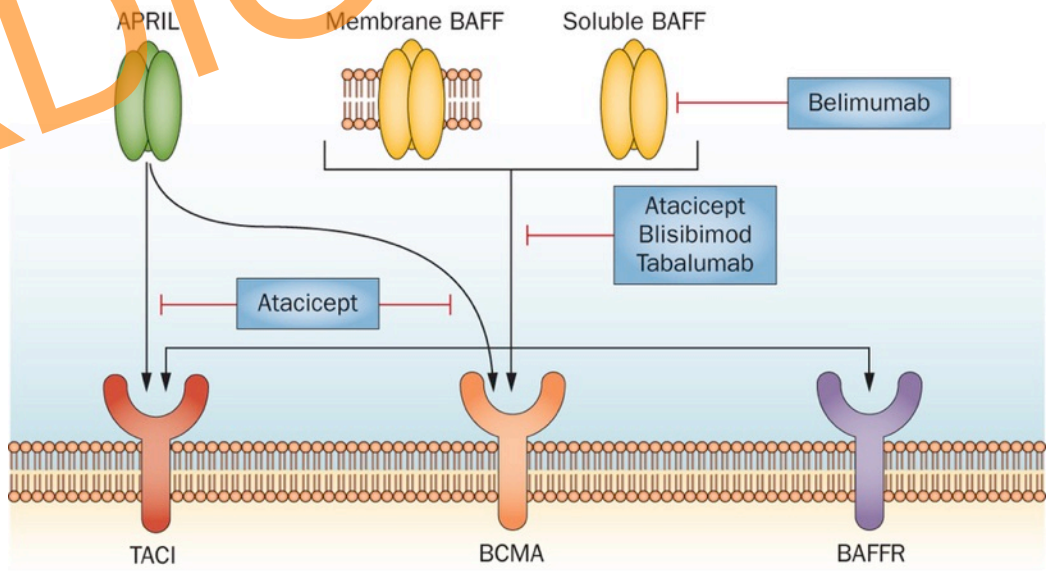




Interpretation TRF-budesonide 16 mg/day, added to optimised RAS blockade, reduced proteinuria in patients with IgA nephropathy. This effect is indicative of a reduced risk of future progression to end-stage renal disease. TRF-budesonide could become the first specific treatment for IgA nephropathy targeting intestinal mucosal immunity upstream of disease manifestation.

IgA Nephropathy





IgA Nephropathy

The Journal of Immunology

Spleen Tyrosine Kinase Is Important in the Production of Proinflammatory Cytokines and Cell Proliferation in Human Mesangial Cells following Stimulation with IgA1 Isolated from IgA Nephropathy Patients

Min Jeong Kim,*,†,‡ John P. McDaid,* Stephen P. McAdoo,* Jonathan Barratt,§ Karen Molyneux,§ Esteban S. Masuda,¶ Charles D. Pusey,* and Frederick W. K. Tam*

Pipeline Overview
Fostamatinib – ITP
Fostamatinib – IgAN
R348 – Dry Eye in GvHD
Partnered Products
Clinical Trials
Publications

sign
Syk Inhibition for GlomeruloNephritis

Fostamatinib

Oral SYK Inhibitor for IgA Nephropathy:

- A major function of the kidneys is to eliminate and dispose of waste products by filtering the blood and producing urine.
- IgA Nephropathy (IgAN) is a chronic autoimmune disease associated with inflammation in the kidneys that diminishes their ability to filter blood.
- IgAN is the most common primary glomerular disease. There are an estimated 82,500 - 165,000 cases in the US, with a higher prevalence in Asia.
- Outside of angiotensin blockade (primarily for blood-pressure control), there are no disease-targeted therapies for IgAN.
- Pre-clinical data show that fostamatinib decreases SYK activation in the kidney, resulting in the reversal of the inflammation in the glomeruli and improvement in kidney function.
- Rigel's oral SYK inhibitor, fostamatinib, is intended to arrest the pathological process of IgAN. Rigel expects results for a Phase 2 study in 2016/17.

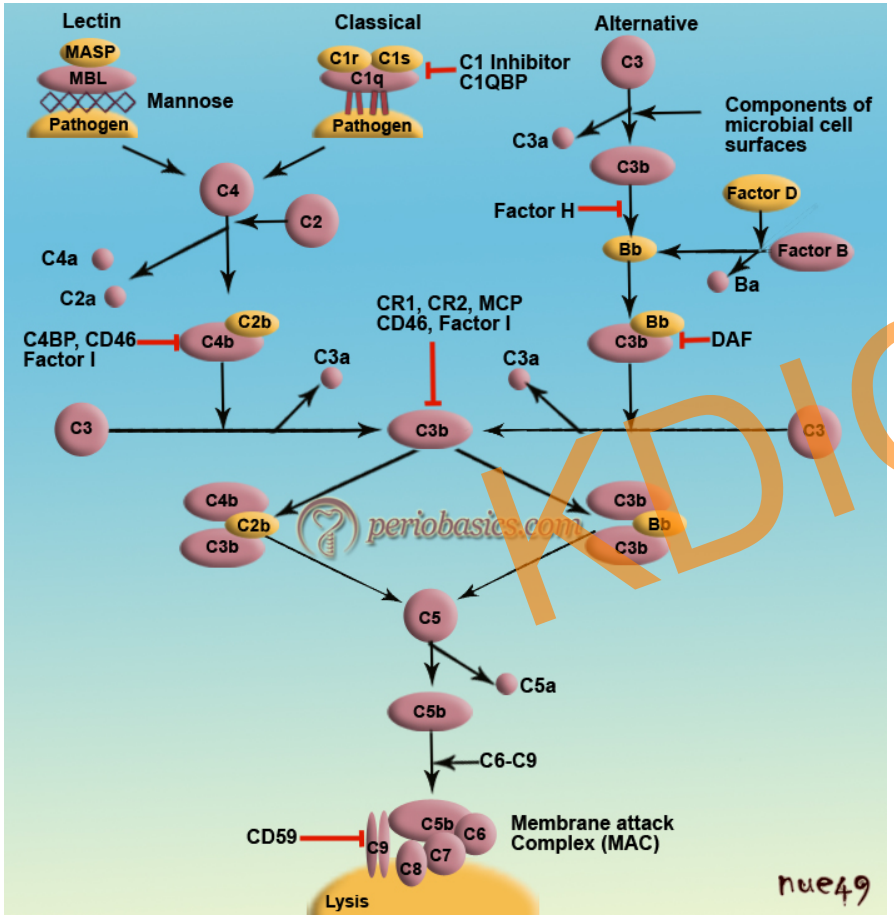
Clinical Trials:

Phase 2 - IgA Nephropathy

MOA Animation:

Fostamatinib – IgA Nephropathy (Ig…

IgA Nephropathy



CLINICAL KIDNEY JOURNAL

ckj OXFORD

Clinical Kidney Journal, 2015, vol. 8, no. 5, 489–491
doi: 10.1093/ckj/sfv076
Advance Access Publication Date: 27 August 2015
Exceptional Case

EXCEPTIONAL CASE

Use of eculizumab in crescentic IgA nephropathy: proof of principle and conundrum?

Troels Ring[1], Birgitte Bang Pedersen[1], Giedrius Salkus[2], and Timothy H.J. Goodship[3]

[1]Department of Nephrology, Aalborg University Hospital, Aalborg, Denmark, [2]Department of Pathology, Aalborg University Hospital, Aalborg, Denmark, and [3]Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, UK

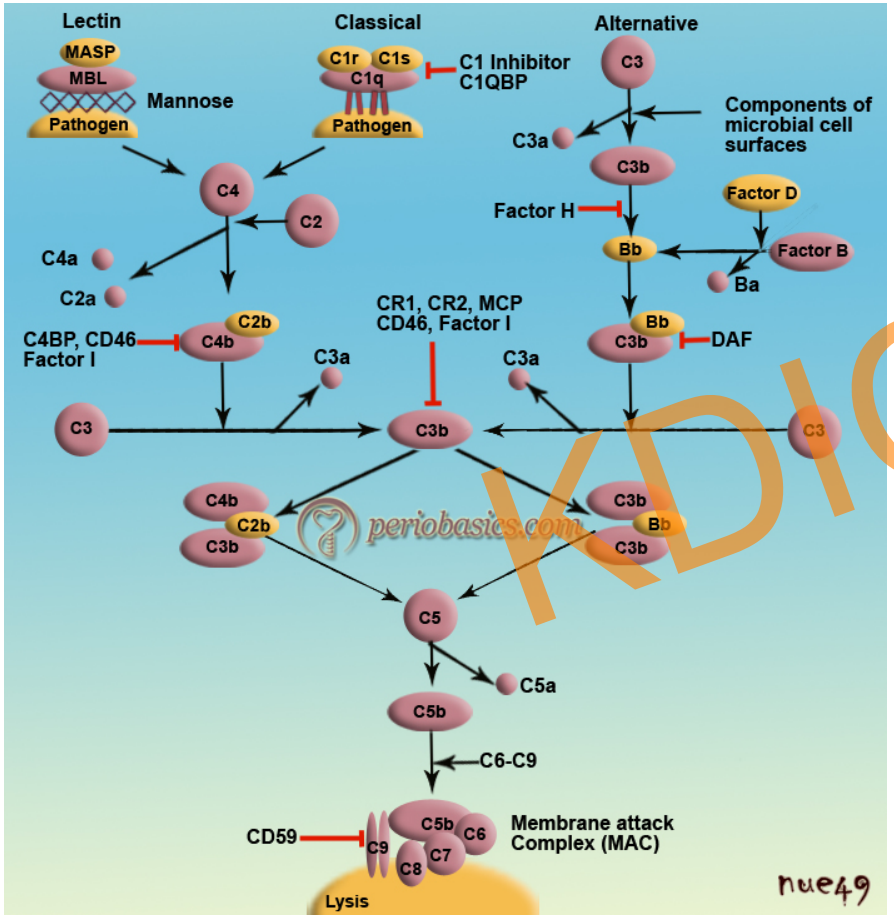
Pediatr Nephrol (2014) 29:2225–2228
DOI 10.1007/s00467-014-2863-y

BRIEF REPORT

Eculizumab treatment for rescue of renal function in IgA nephropathy

Therese Rosenblad · Johan Rebetz · Martin Johansson · Zivile Békássy · Lisa Sartz · Diana Karpman

IgA Nephropathy



Human IgA Activates the Complement System Via the Mannan-Binding Lectin Pathway[1]

Anja Roos,[2]* Lee H. Bouwman,* Daniëlle J. van Gijlswijk-Janssen,* Maria C. Faber-Krol,* Gregory L. Stahl,† and Mohamed R. Daha*

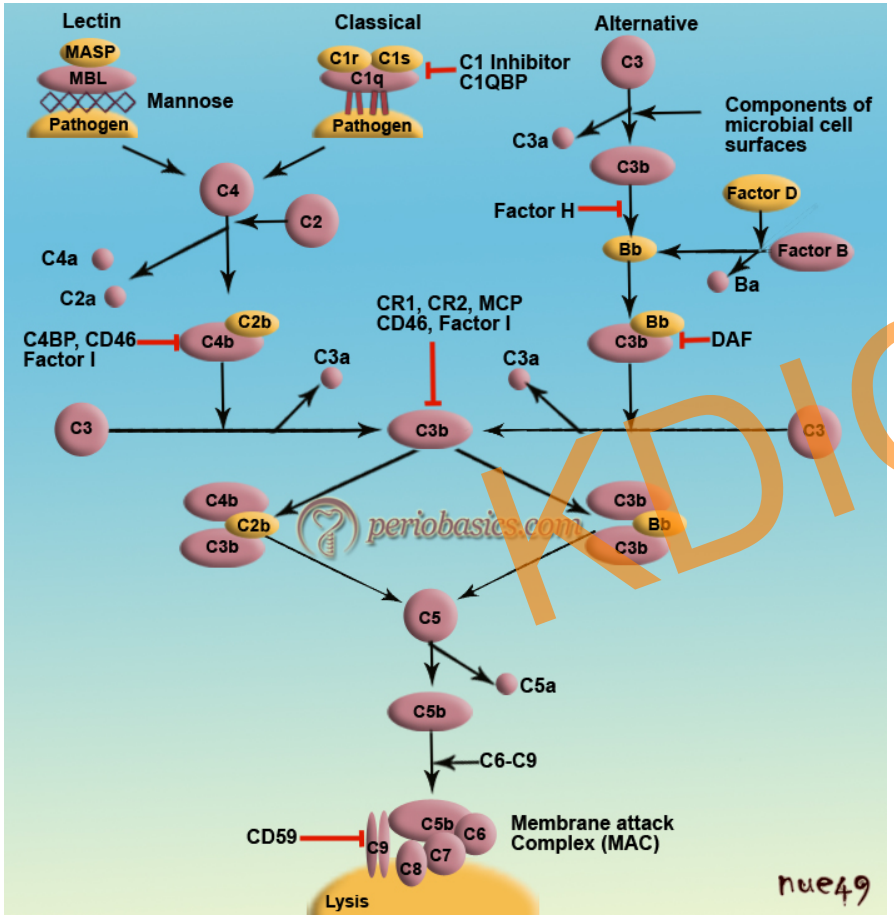
Glomerular Activation of the Lectin Pathway of Complement in IgA Nephropathy Is Associated with More Severe Renal Disease

Anja Roos,* Maria Pia Rastaldi,† Novella Calvaresi,† Beatrijs D. Oortwijn,* Nicole Schlagwein,* Danielle J. van Gijlswijk-Janssen,* Gregory L. Stahl,‡ Misao Matsushita,§ Teizo Fujita,‖ Cees van Kooten,* and Mohamed R. Daha*

*Department of Nephrology, Leiden University Medical Center, Leiden, the Netherlands; †Renal Immunopathology Laboratory, Fondazione D'Amico per la Ricerca sulle Malattie Renali, Associazione Nuova Nefrologia, San Carlo Borromeo Hospital, Milano, Italy; ‡Center for Experimental Therapeutics and Reperfusion Injury, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; §Institute of Glycotechnology and Department of Applied Biochemistry, Tokai University, Hiratsuka, Japan; and ‖Department of Immunology, Fukushima Medical University, Fukushima, Japan

FDA Grants Breakthrough Therapy Designation to Omeros' MASP-2 Inhibitor OMS721 for the Treatment of IgA Nephropathy

IgA Nephropathy



CLINICAL RESEARCH www.jasn.org

Fine Mapping Implicates a Deletion of *CFHR1* and *CFHR3* in Protection from IgA Nephropathy in Han Chinese

Jingyuan Xie,*† Krzysztof Kiryluk,† Yifu Li,† Nikol Mladkova,† Li Zhu,‡ Ping Hou,‡ Hong Ren,* Weiming Wang,* Hong Zhang,‡ Nan Chen,* and Ali G. Gharavi†

*Institute of Nephrology, Department of Nephrology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; †Department of Medicine, Division of Nephrology, College of Physicians and Surgeons, Columbia University, New York, New York; and ‡Renal Division, Peking University First Hospital, Peking University Institute of Nephrology, Beijing, China

www.kidney-international.org clinical investigation

Elevated factor H–related protein 1 and factor H pathogenic variants decrease complement regulation in IgA nephropathy

see commentary on page 790

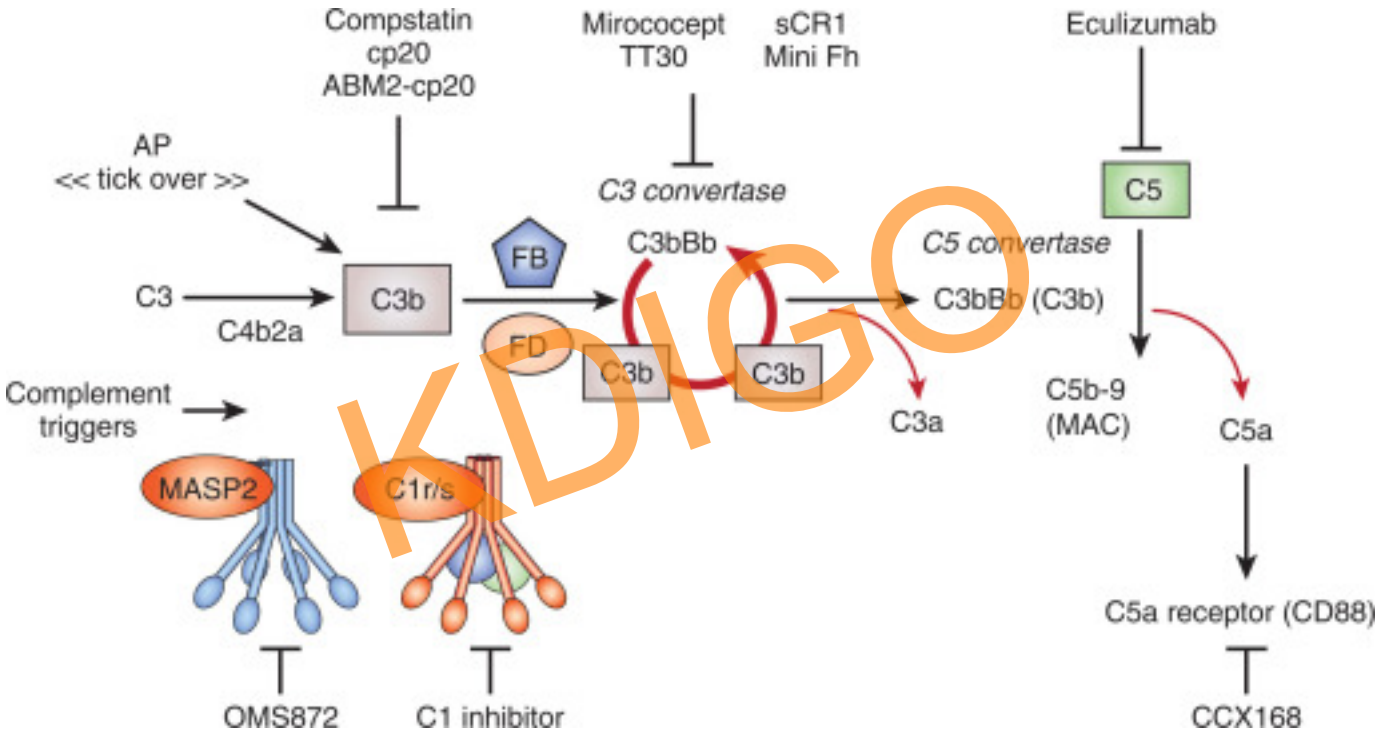
Agustín Tortajada[1,11], Eduardo Gutiérrez[2,11], Elena Goicoechea de Jorge[3,11], Jaouad Anter[1], Alfons Segarra[4], Mario Espinosa[5], Miquel Blasco[6], Elena Roman[7], Helena Marco[8], Luis F. Quintana[6], Josué Gutiérrez[3], Sheila Pinto[1], Margarita Lopez-Trascasa[9], Manuel Praga[2,10] and Santiago Rodriguez de Córdoba[1]

nature chemical biology ARTICLE
PUBLISHED ONLINE: 24 OCTOBER 2016 | DOI: 10.1038/NCHEMBIO.2208

Small-molecule factor D inhibitors targeting the alternative complement pathway

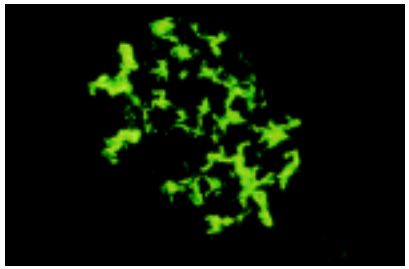
Jürgen Maibaum[1*], Sha-Mei Liao[2], Anna Vulpetti[1], Nils Ostermann[1], Stefan Randl[3], Simon Rüdisser[1], Edwige Lorthiois[1], Paul Erbel[1], Bernd Kinzel[1], Fabrice A Kolb[4], Samuel Barbieri[1], Julia Wagner[1], Corinne Durand[1], Kamal Fettis[1], Solene Dussauge[1], Nicola Hughes[1], Omar Delgado[2], Ulrich Hommel[1], Ty Gould[2], Aengus Mac Sweeney[5], Bernd Gerhartz[1], Frederic Cumin[1], Stefanie Flohr[1], Anna Schubart[1], Bruce Jaffee[2], Richard Harrison[6], Antonio Maria Risitano[7], Jörg Eder[1] & Karen Anderson[2*]

IgA Nephropathy



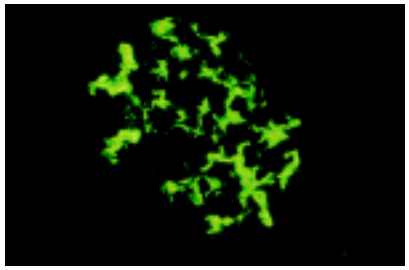
IgA Nephropathy (& IgA Vasculitis?)

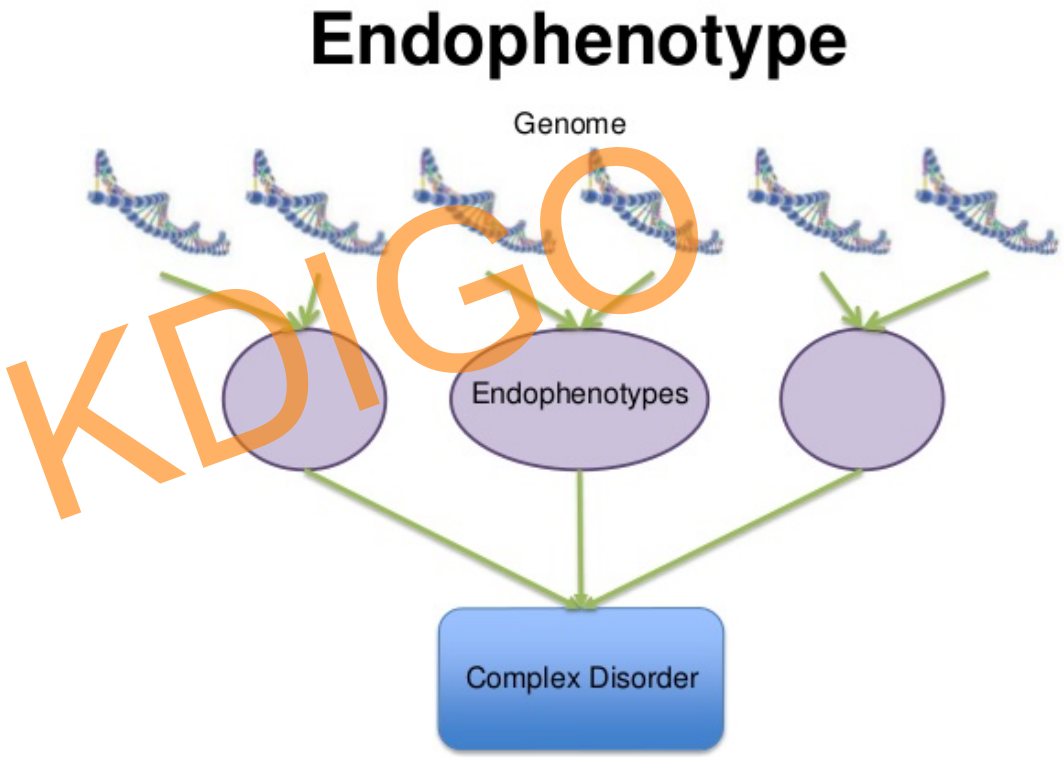
IgA Nephropathy (& IgA Vasculitis?)



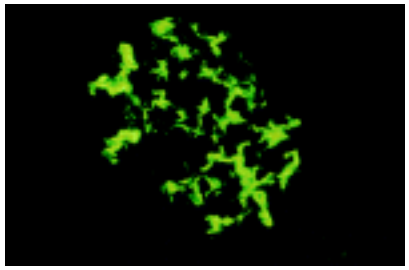
Other risk factors OD or disease	Blood pressure (mmHg) Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP≥180 or DBP≥110
No other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
1–2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
≥3 risk factors, MS or OD	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Immediate drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + Drug treatment			
Established CV or renal disease	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment

IgA Nephropathy (& IgA Vasculitis?)





IgA Nephropathy (& IgA Vasculitis?)



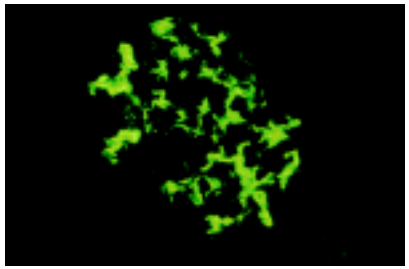
Induction therapies

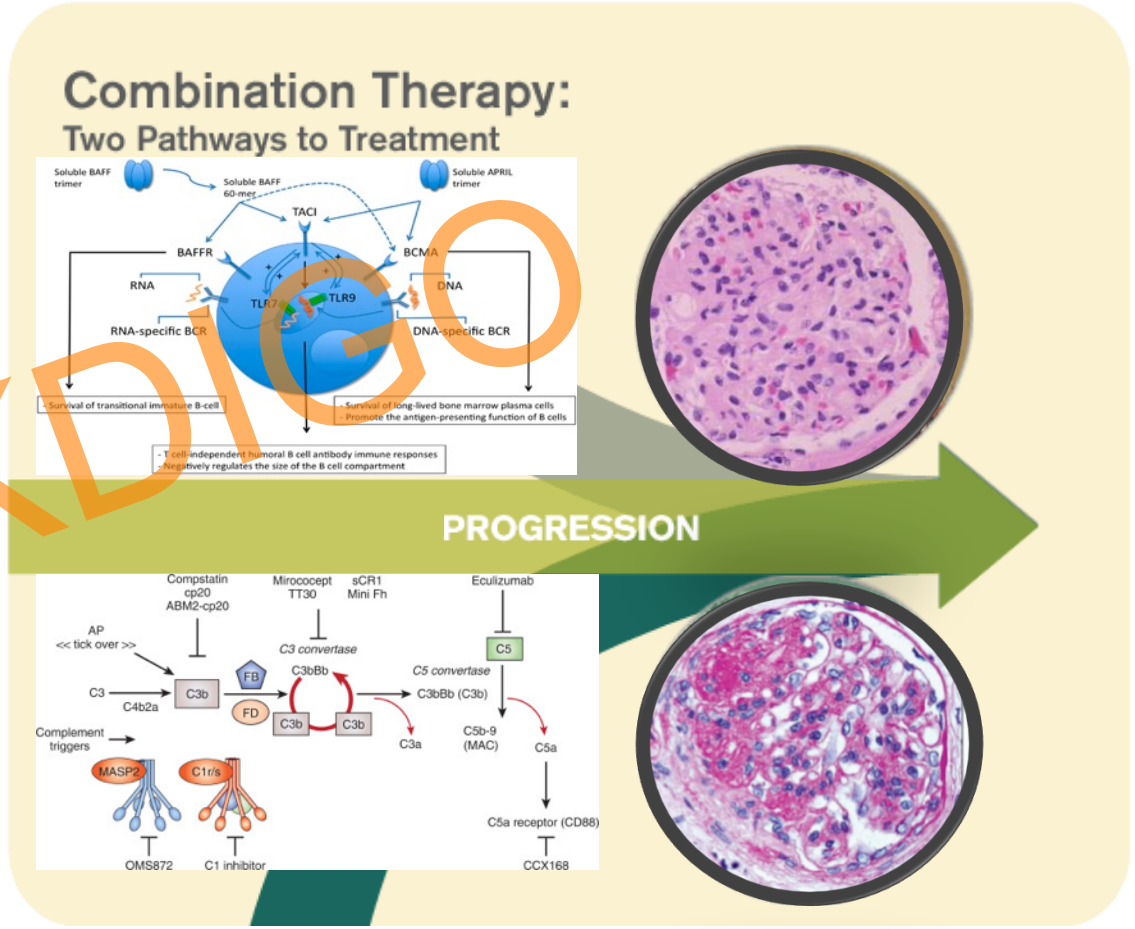
- Short-courses or pulsed therapy
- Very high efficacy
- Irreversible
- Perceived to be higher risk

Maintenance therapies

- Continuous treatment
- Low to very high efficacy
- Reversible
- Perceived to be lower risk

IgA Nephropathy (& IgA Vasculitis?)





IgA Nephropathy

15th International Symposium on IgANephropathy

50th anniversary of IgA Nephropathy

September 27th-29th, 2018

Buenos Aires, Argentina