Recent advances in IEI

Jenny Lingman Framme

211111

J Clin Immunol. 2020; 40(1): 24–64.
Published online 2020 Jan 17. doi: 10.1007/s10875-019-00737-x
PMCID: PMC7082301
PMID: 31953710

Human Inborn Errors of Immunity: 2019 Update on the Classification from the International Union of Immunological Societies Expert Committee

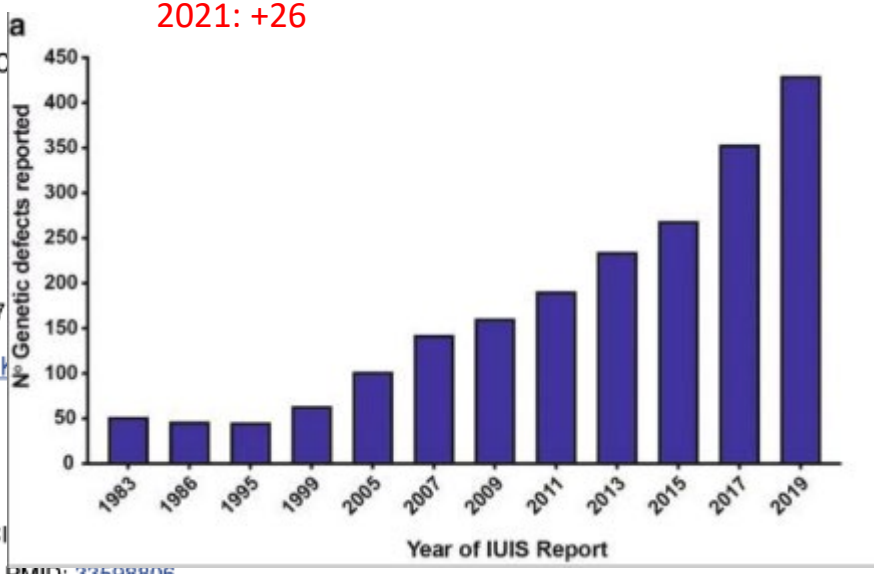
Stuart G. Tangye,[1,2] Waleed Al-Herz,[3] Aziz Bousfiha,[4] Talal Chatila,[5] Charlotte Cunningham-Rundles,[6] Amos Etzioni,[7] Jose Luis Franco,[8] Steven M. Holland,[9] Christoph Klein,[10] Tomohiro Morio,[11] Hans D. Ochs,[12] Eric Oksenhendler,[13] Capucine Picard,[14,15] Jennifer Puck,[16] Troy R. Torgerson,[12] Jean-Laurent Casanova,[17,18,19,20] and Kathleen E. Sullivan[21]

2019: 404 IEI, 430 genetic defects (+64)
2021: +26

J Clin Immunol. 2020; 40(1): 66–81.
Published online 2020 Feb 11. doi: 10.1007/s10875-020-00758-x
PMC

Human Inborn Errors of Immunity: 2019 Update of the IUIS Phenotypical Classification

Aziz Bousfiha,[1,2] Leila Jeddane,[3] Capucine Picard,[4,5] Waleed Al-Herz,[6] Fatima Ailal,[1] Talal Chatila,[7] Charlotte Cunningham-Rundles,[8] Amos Etzioni,[9] Jose Luis Franco,[10] Steven M Holland,[11] Christoph K Tomohiro Morio,[13] Hans D. Ochs,[14] Eric Oksenhendler,[15] Jennifer Puck,[16] Troy R. Torgerson,[14] Jean-Laurent Casanova,[17,18,19,20] Kathleen E. Sullivan,[21] and Stuart G. Tangye[22,23]



J Clin Immunol. 2021; 41(3): 666–679.
Published online 2021 Feb 18. doi: 10.1007/s10875-021-00980-1
PMCI
PMID: 33598806

The Ever-Increasing Array of Novel Inborn Errors of Immunity: an Interim Update by the IUIS Committee

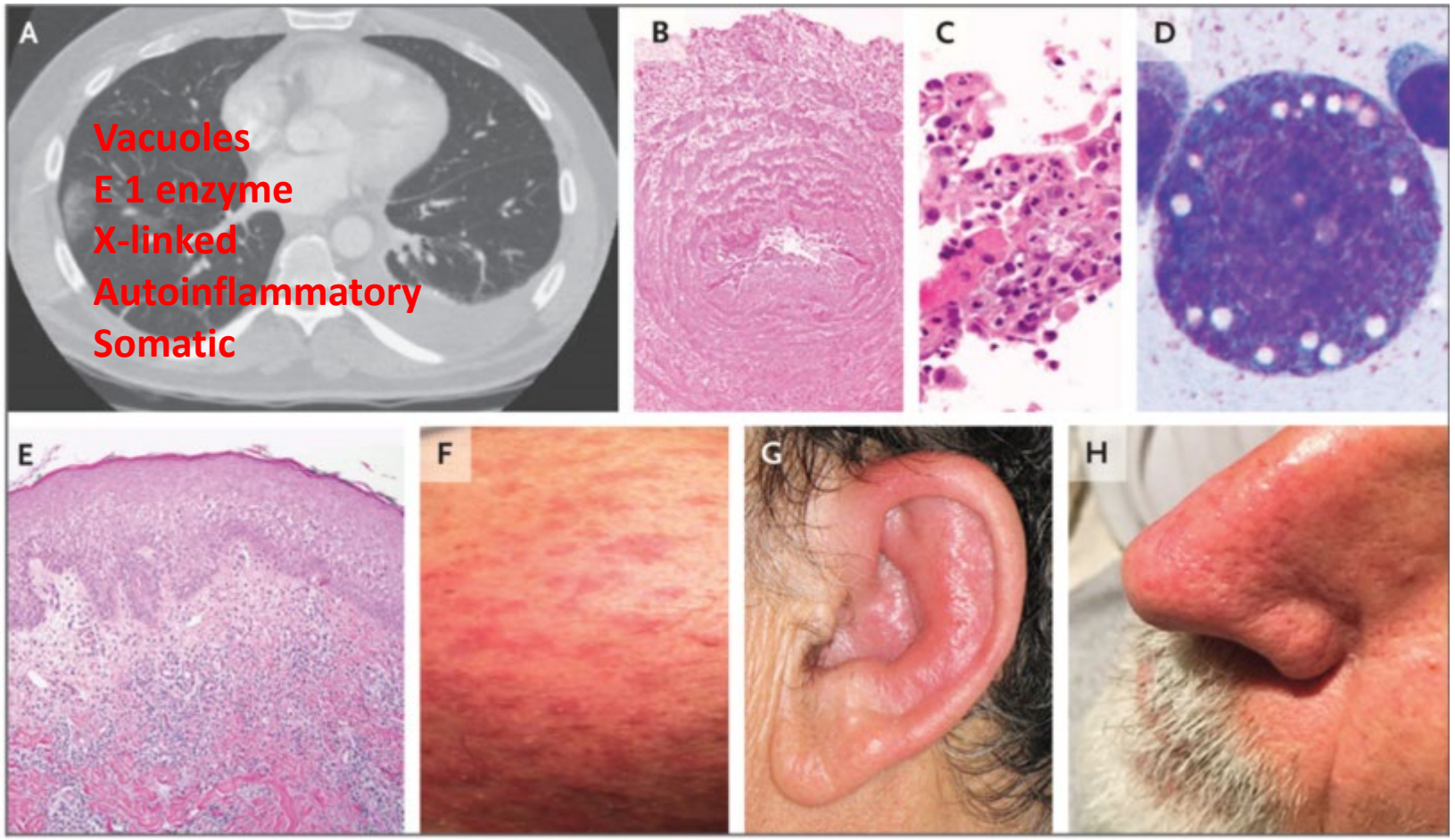
Stuart G. Tangye,[1,2] Waleed Al-Herz,[3] Aziz Bousfiha,[4] Charlotte Cunningham-Rundles,[5] Jose Luis Franco,[6] Steven M Holland,[7] Christoph Klein,[8] Tomohiro Morio,[9] Eric Oksenhendler,[10] Capucine Picard,[11,12] Anne Puel,[13,14] Jennifer Puck,[15] Mikko R. J. Seppänen,[16] Raz Somech,[17] Helen C Su,[7] Kathleen E. Sullivan,[18] Troy R. Torgerson,[19] and Isabelle Meyts[20]

NEJM, 2020.

ORIGINAL ARTICLE

Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease

David B. Beck, M.D., Ph.D., Marcela A. Ferrada, M.D., Keith A. Sikora, M.D., Amanda K. Ombrello, M.D., Jason C. Collins, Ph.D., Wuhong Pei, Ph.D., Nicholas Balanda, B.Sc., Daron L. Ross, M.D., Daniela Ospina Cardona, B.Sc., Zhijie Wu, M.D., Ph.D., Bhavisha Patel, M.D., Kalpana Manthiram, M.D., et al.



Mutant *UBA1* and Severe Adult-Onset Autoinflammatory Disease

Acquired X monosomy in bone marrow in females with VEXAS syndrome. Arlet et al. NEJM, 2021

Successful HSCT in 46 yo male with VEXAS syndrome. Diarra et al. NEJM, 2021

LETTER TO BLOOD | JULY 1, 2021

Novel somatic mutations in UBA1 as a cause of VEXAS syndrome

LETTER TO BLOOD | JULY 1, 2021

Vacuolization of hematopoietic precursors: an enigma with multiple etiologies

Carmelo Gurnari, Simona Pagliuca, Lisa Durkin, Laila Terkawi, Hassan Awada, Sunisa Kongkiatkamon, Misam Zawit, Eric D. Hsi,

REGULAR ARTICLE

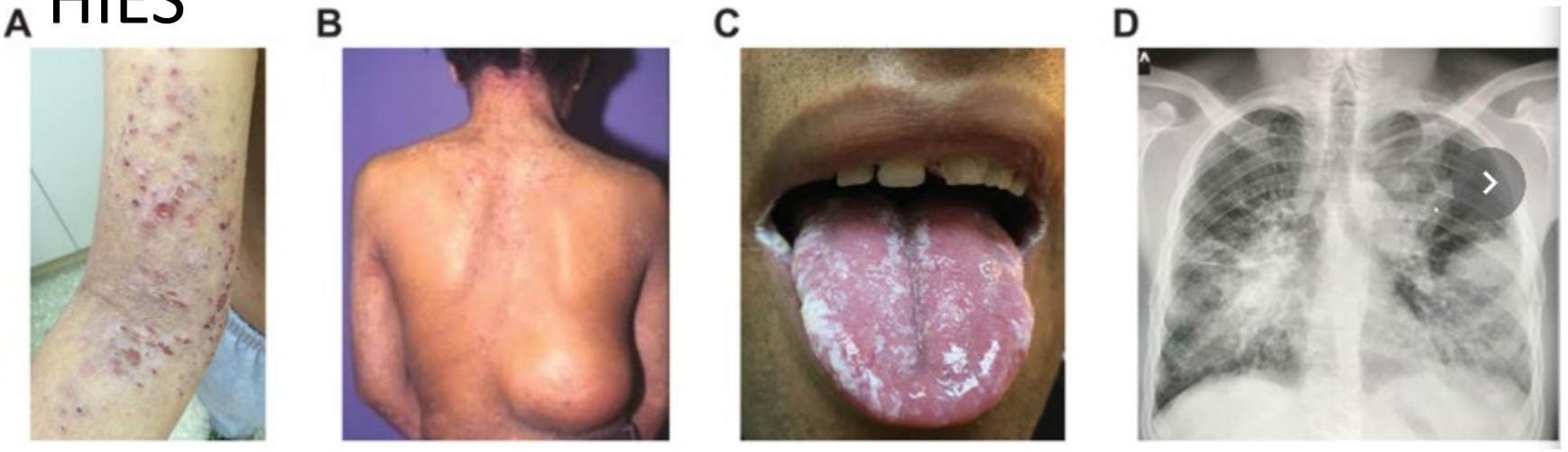
blood advances

Benign and malignant hematologic manifestations in patients with VEXAS syndrome due to somatic mutations in *UBA1*

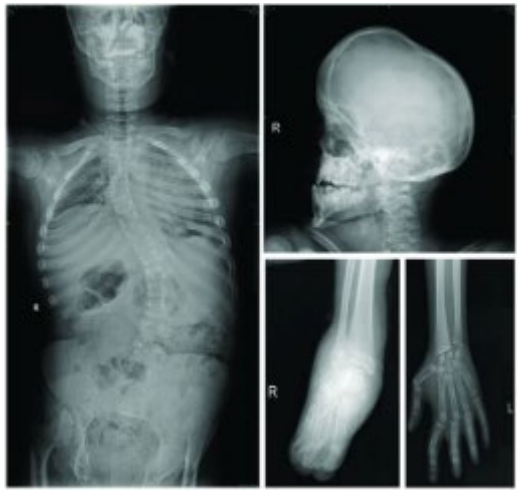
Ifeyinwa Emmanuela Obiorah,[1,2,*] Bhavisha A. Patel,[3,*] Emma M. Groarke,[3,*] Weixin Wang,[2] Megan Trick,[2] Amanda K. Ombrello,[4] Marcela A. Ferrada,[5] Zhijie Wu,[3] Fernanda Gutierrez-Rodrigues,[3] Jennifer Lotter,[3] Lorena Wilson,[4] Patrycja Hoffmann,[4] Daniela Ospina Cardona,[4] Nisha Patel,[2] Alina Dulau-Florea,[2] Daniel L. Kastner,[4] Peter C. Grayson,[5] David B. Beck,[4] Neal S. Young,[3,†] and Katherine R. Calvo[2,†]

Advances in understanding of immunopathogenesis

HIES



Frey-Jakobs et al.
Science Immunology, 2018



Shahin et al.
Haematologica, 2019

Advances in understanding of immunopathogenesis of **HIES**

Loss of the interleukin-6 receptor causes immunodeficiency, atopy, and abnormal inflammatory responses

Sarah Spencer,[1,2,*] Sevgi Köstel Bal,[3,4,*] William Egner,[5,6,*] Hana Lango Allen,[7,8,*] Syed I. Raza,[9,*] Chi A. Ma,[10,**] Meltem Gürel,[11,**] Yuan Zhang,[10,**] Guangping Sun,[10,**] Ruth A. Sabroe,[12] Daniel Greene,[7,8,13] William Rae,[2] Tala Shahin,[3,4] Katarzyna Kania,[11] Rico Chandra Ardy,[3,4] Marini Thian,[3,4,22,23] Emily Staples,[2] Annika Pecchia-Bekkum,[2] William P.M. Worrall,[2] Jonathan Stephens,[7,8,14] Matthew Brown,[7,8,14] Salih Tuna,[7,8,14] Melanie York,[5,6] Fiona Shackley,[5,6] Diarmuid Kerrin,[15] Ravishankar Sargur,[5,6] Alison Condliffe,[5,6] Hamid Nawaz Tipu,[16] Hye Sun Kuehn,[17] Sergio D. Rosenzweig,[17] Ernest Turro,[7,8,13,14] Simon Tavaré,[11,18,19] Adrian J. Thrasher,[20] Duncan Ian Jodrell,[21] Kenneth G.C. Smith,[2] Kaan Boztug,[3,4,22,23,24,***] Joshua D. Milner,[10,***] and James E.D. Thaventhiran[1,2,11,***]

J Exp Med 2019

Dominant-negative mutations in human *IL6ST* underlie hyper-IgE syndrome

Vivien Béziat[1,2,3], Simon J. Tavernier[4,5*], Yin-Huai Chen[6,7*], Cindy S. Ma[8,9*], Marie Materna[1,2], Arian Laurence[6,7], Jens Staal[5], Dominik Aschenbrenner[6,7], Lisa Roels[4], Lisa Worley[8,9], Kathleen Claes[10], Lisa Gartner[6,7], Lisa A. Kohn[11], Marieke De Bruyne[10], Klaus Schmitz-Abe[12,13,14], Louis-Marie Charbonnier[15,16], Sevgi Keles[17], Justine Nammour[1,2], Natasha Vladikine[1,2], Majistor Raj Luxman Maglorius Renkilaraj[1,2], Yoann Seeleuthner[1,2], Mélanie Migaud[1,2], Jérémie Rosain[1,2], Mohamed Jeljeli[18], Bertrand Boisson[1,2,3], Eva Van Braeckel[19], Jill A. Rosenfeld[20], Hongzheng Dai[20], Lindsay C. Burrage[20], David R. Murdock[20], Bart N. Lambrecht[21,22], es Network, Charles R. Esther Jr.[25], Sule Haskologlu[26], Figen Dogu[26], irette[30], Marie-Noëlle Lebras[31], Clément Gauvain[32], Colas Tcherakian[33], [34,35], Bodo Grimbacher[36,37,38,39,40], Louis-Jean Couderc[33,41],], Claire Fieschi[28,42**], Talal A. Chatila[15,16***], Stuart G. Tangye[8,9***], [1,2,3,44,45***], and Anne Puel[1,2,3***]

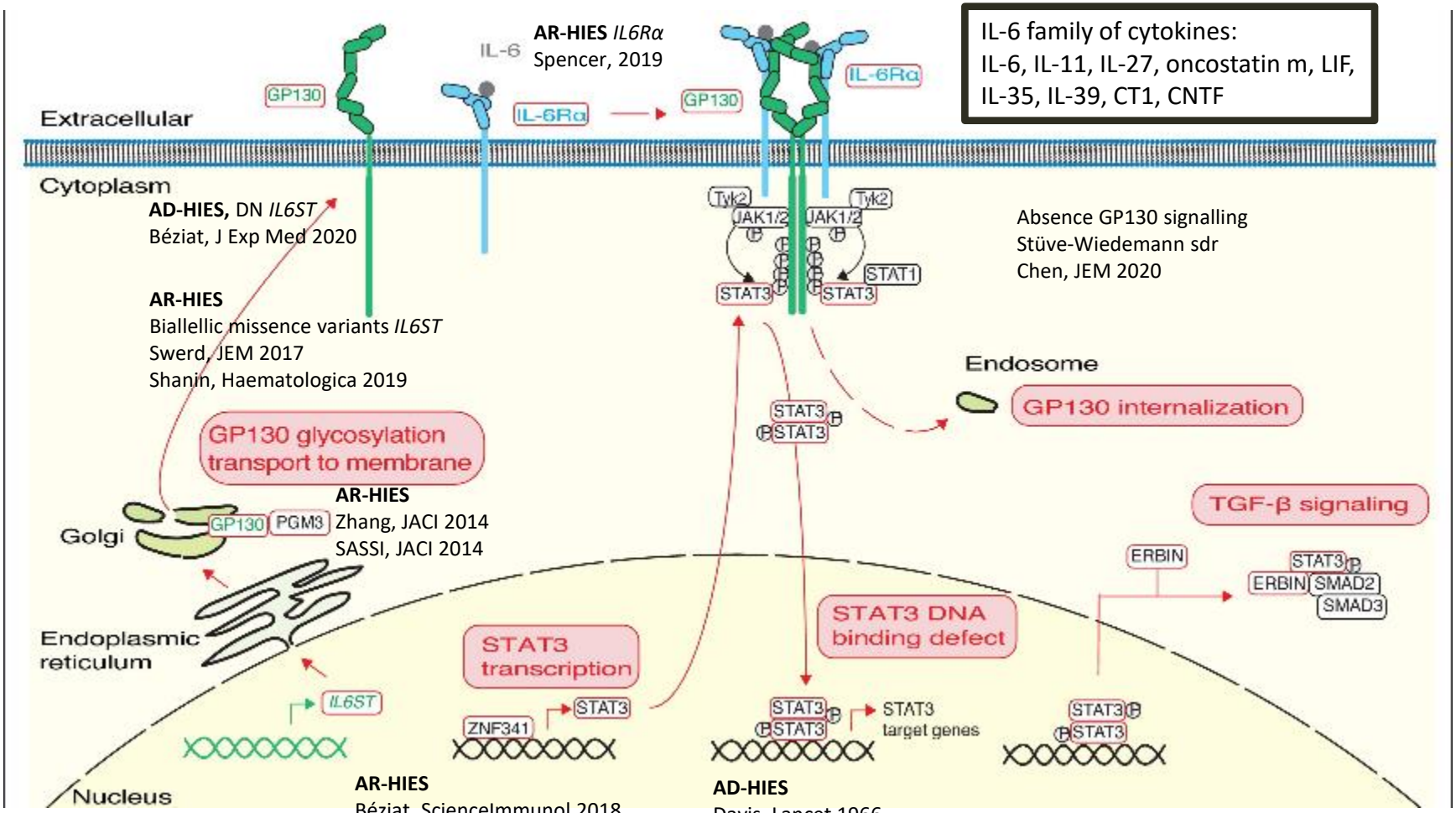
J Exp Med 2020

Selective loss of function variants in *IL6ST* cause Hyper-IgE syndrome with distinct impairments of T-cell phenotype and function

Tala Shahin,[1,2*] Dominik Aschenbrenner,[3*] Deniz Cagdas,[4,5*] Sevgi Köstel Bal,[1,2,6] Cecilia Domínguez Conde,[1,2] Wojciech Garncarz,[1,2] David Medgyesi,[1,2] Tobias Schwerd,[3,7] Betül Karaatmaca,[4] Pınar Gur Cetinkaya,[4] Saliha Esenboga,[4] Stephen R. F. Twigg,[8] Andrew Cant,[9] Andrew O. M. Wilkie,[8] Ilhan Tezcan,[4,5] Holm H. Uhlig[3,10] and Kaan Boztug[1,2,11,12]

Haematologica 2019

Advances in understanding of immunopathogenesis of **HIES**



Chen et al, Curr opin Immunol 2021

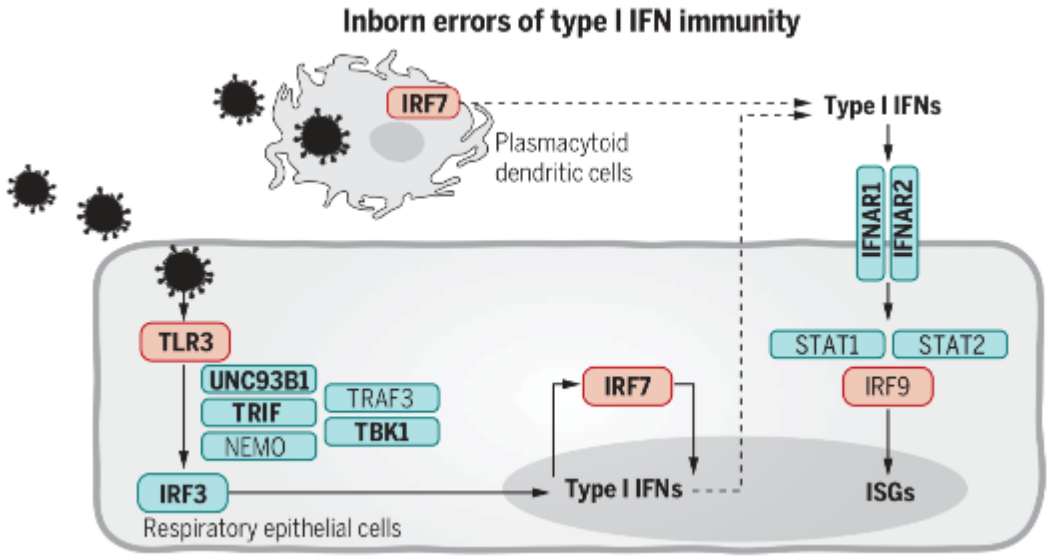
CORONAVIRUS

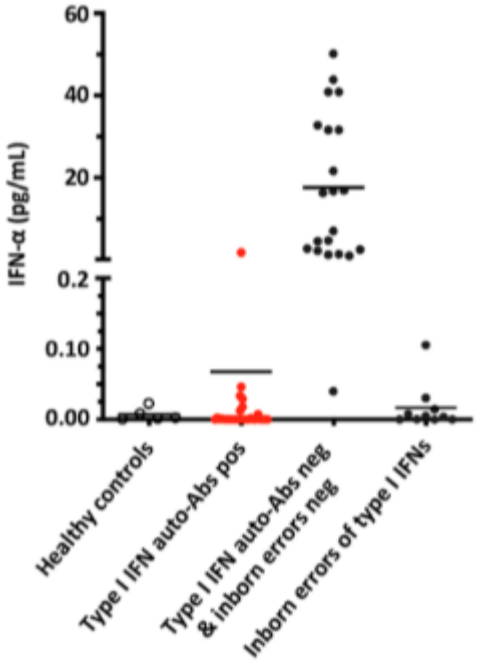
Inborn errors of type I IFN immunity in patients with life-threatening COVID-19

Qian Zhang *et al.* Science, 2020.

Cite as: P. Bastard *et al.*, *Science* 10.1126/science.abd4585 (2020).

Auto-antibodies against type I IFNs in patients with life-threatening COVID-19





Neutralizing Autoantibodies to Type I IFNs in >10% of Patients with Severe COVID-19 Pneumonia Hospitalized in Madrid, Spain

Jesús Troya[1] · Paul Bastard[2,3,4] · Laura Planas-Serra[5] · Pablo Ryan[1] · Montse Ruiz[5] · María de Carranza[1] · Juan Torres[1] · Amalia Martínez[6] · Laurent Abel[2,3,7] · Jean-Laurent Casanova[2,3,4,7] · Aurora Pujol[5,8,9]

JoCI, 2021

Autoantibodies against type I interferons are associated with multi-organ failure in COVID-19 patients

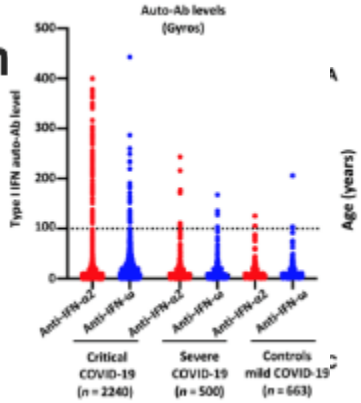
Rutger Koning,[1] Paul Bastard,[2,3,4] Jean-Laurent Casanova,[2,3,4,5] Matthijs C. Brouwer,[1] Diederik van de Beek,[1] and with the Amsterdam U.M.C. COVID-19 Biobank Investigators

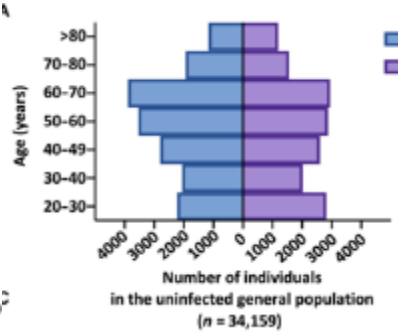
Intensive Care Med, 2021

Autoantibodies neutralizing type I IFNs are present in ~4% of uninfected individuals over 70 years old and account for ~20% of COVID-19 deaths

PAUL BASTARD, ADRIAN GERVAIS, TOM LE VOYER, JÉRÉMIE ROSAIN, QUENTIN PHILIPPOT, JÉRÉMY MANRY, ELEFTHERIOS MICHAILIDIS, HANS-HEINRICH HOFFMANN, SHOHEI ETO, [...] JEAN-LAURENT CASANOVA

Intensive Care Med, 2021





Type I interferon autoantibodies are associated with systemic immune alterations in patients with COVID-19

MONIQUE G. P. VAN DER WIJST, SARA E. VAZQUEZ, GEORGE C. HARTOULAROS, PAUL BASTARD, TIANNA GRANT, RAYMUND BUENO, DAVID S. LEE, JOHN R. GREENLAND, YANG SUN, [...] ON BEHALF OF THE UCSF COMET CONSORTIUM

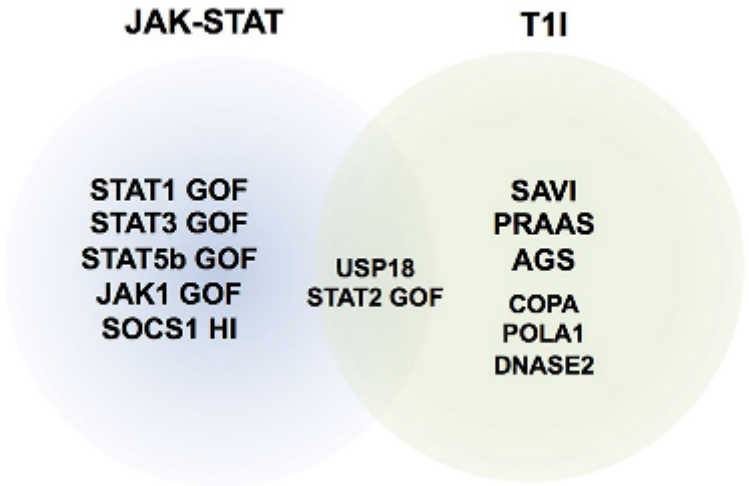
Sci Transl Med, 2021

Emerging Place of JAK Inhibitors in the Treatment of Inborn Errors of Immunity

Frontiers of Immunol, 2021

Jérôme Hadjadj[1,2], *Marie-Louise Frémond*[3,4] *and Bénédicte Neven*[2,3]*

Name	Specificity	Approved indications
Tofacitinib	JAK1/JAK3/(JAK2)	RA, PsA, UC, pA JIA
Baricitinib	JAK1, JAK2	RA
Ruxolitinib	JAK1, JAK2	MPN, acute GVHD
Peficitinib	pan-JAK	RA (Japan)
Fedratinib	JAK2, Flt3	MPN
Upadacitinib	JAK1	RA, PsA
Filgotinib	JAK1	RA (Europe, Japan)



EBMT/ESID inborn errors working party guidelines for hematopoietic stem cell transplantation for inborn errors of immunity

A. C. Lankester[1✉], M. H. Albert[2], C. Booth[3], A. R. Gennery[4], T. Güngör[5], M. Hönig[6], E. C. Morris[7], D. Moshous[8,9,10], B. Neven[8,9,11], A. Schulz[6], M. Slatter[4], P. Veys[3] and on behalf of the Inborn Errors Working Party of the European Society for Blood and Marrow Transplantation and the European Society for Immune Deficiencies, and European Reference Network on Rare Primary Immunodeficiency Autoinflammatory Autoimmune diseases (RITA)

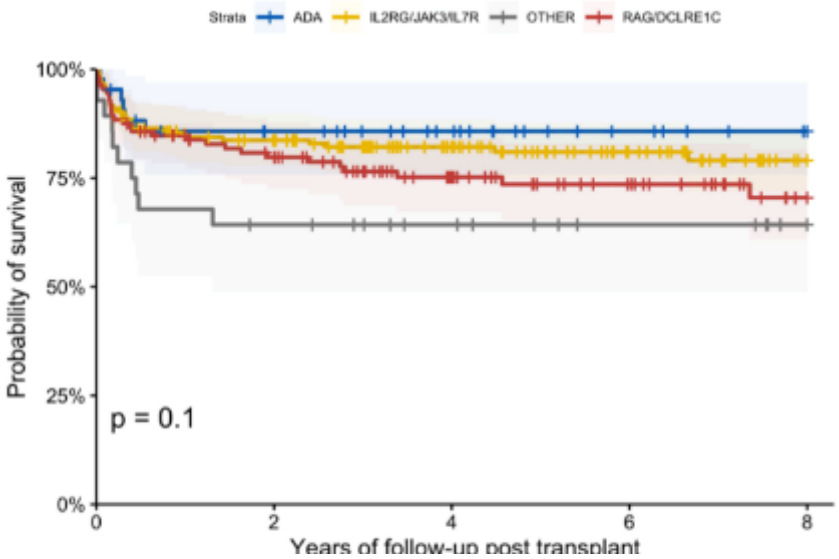
Bone Marrow Transplantation (2021) 56:2052–2062; https://doi.org/10.1038/s41409-021-01378-8

Table 1. Conditioning regimens.

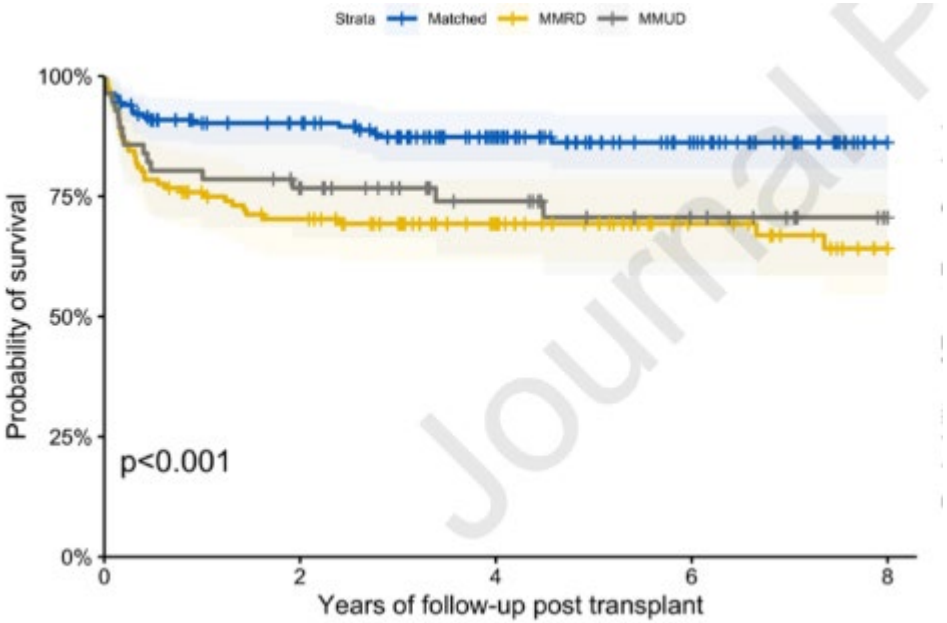
Protocol	Myeloablation		
A			Busulfan i.v (AUC = 85–95 mg*h/L) Fludarabine (160 mg/m^2)
B			Treosulfan (30–42 g/m2) Fludarabine (150–160 mg/m^2) Thiotepa (8–10 mg/kg)
C		Busulfan i.v. (AUC = 60–70 mg*h/L) Fludarabine (160–180 mg/m^2)	
D		Treosulfan (30–42 g/m^2) Fludarabine (150–160 mg/m^2)	
E	Fludarabine (150–160 mg/m^2) Melphalan (140 mg/m^2)		
F	Fludarabine (150 mg/m^2) Cyclophosphamide (20–40 mg/kg)		

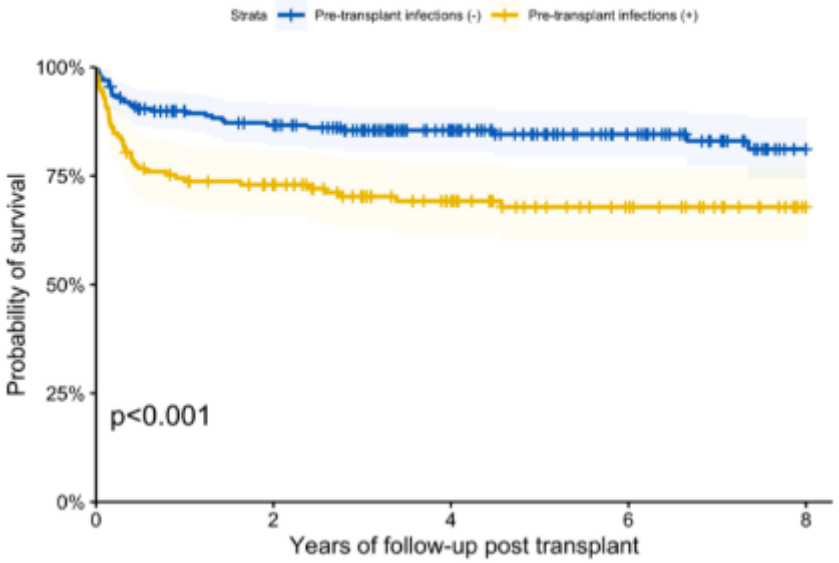
Hematopoietic cell transplantation in severe combined immunodeficiency: the SCETIDE 2006-2014 European cohort

Lankester et al, JACI 2021



A.



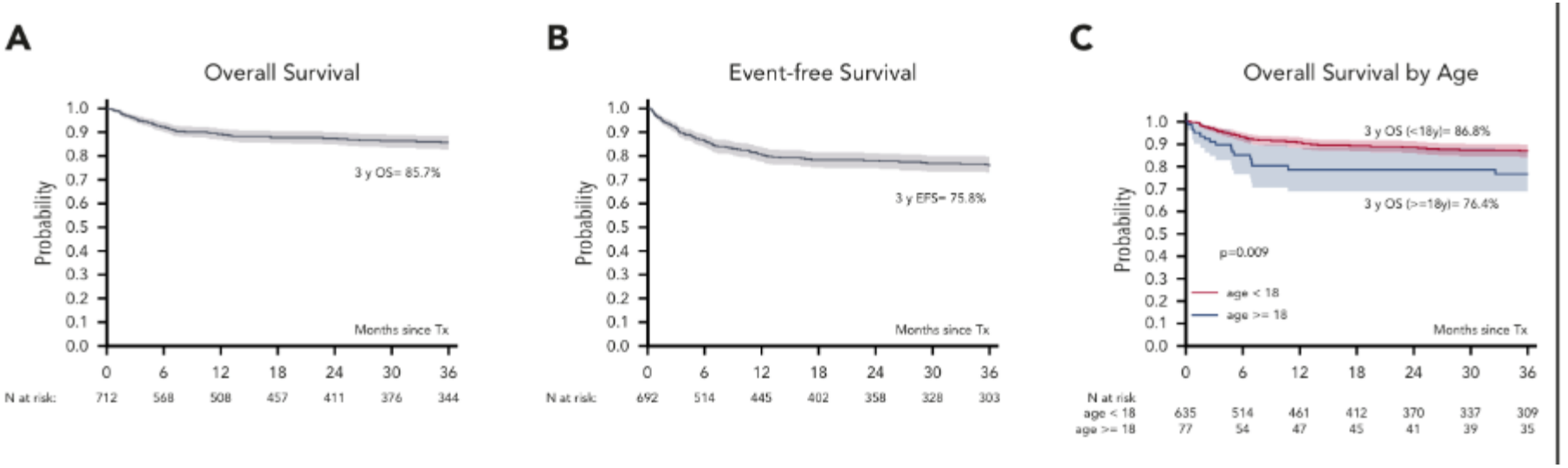


blood®
Regular Article

TRANSPLANTATION

Hematopoietic cell transplantation in chronic granulomatous disease: a study of 712 children and adults

Robert Chiesa,[1] Junfeng Wang,[2,3] Henric-Jan Blok,[2] Sheree Hazelaar,[2] Benedicte Neven,[4] Despina Moshous,[4] Ansgar Schulz,[5] Manfred Hoenig,[5] Fabian Hauck,[6] Amal Al Seraihy,[7] Jolanta Gozdzik,[8] Per Ljungman,[9] Caroline A. Lindemans,[10,11] Juliana F. Fernandes,[12,13] Krzysztof Kalwak,[14] Brigitte Strahm,[15] Urs Schanz,[16] Petr Sedlacek,[17] Karl-Walter Sykora,[18] Serap Aksoylar,[19] Franco Locatelli,[20] Polina Stepensky,[21] Robert Wynn,[22] Su Han Lum,[23,24] Marco Zecca,[25] Fulvio Porta,[26] Mervi Taskinen,[27] Brenda Gibson,[28] Susanne Matthes,[29] Musa Karakukcu,[30] Mathias Hauri-Hohl,[31] Paul Veys,[1] Andrew R. Gennery,[23,32] Giovanna Lucchini,[1] Matthias Felber,[31] Michael H. Albert,[6] Dmitry Balashov,[33] Arjan Lankester,[24] Tayfun Güngör,[31,*] and Mary A. Slatter,[23,32,*] for the EBMT Inborn Errors Working Party



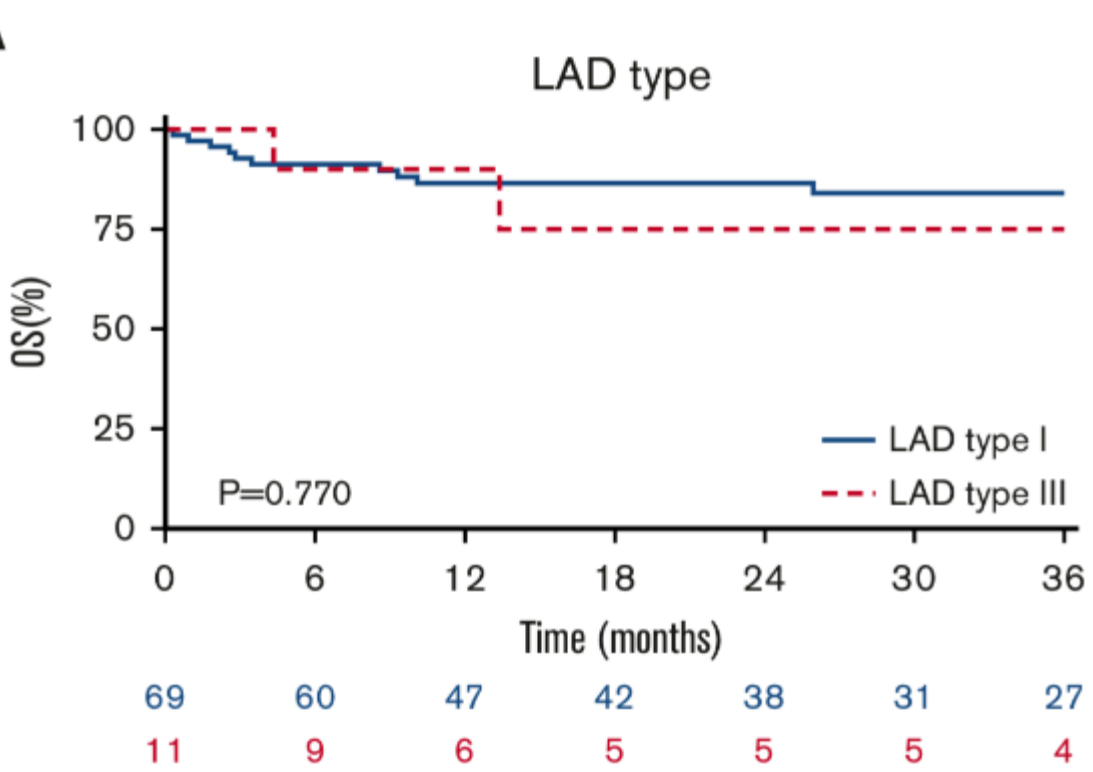
blood advances

Blood Adv. 2021 Jan 12; 5(1): 262–273.
Published online 2021 Jan 11. doi: 10.1182/bloodadvances.2020002185

PMCID: PMC7805328
PMID: 33570653

Allogeneic hematopoietic stem cell transplantation in leukocyte adhesion deficiency type I and III

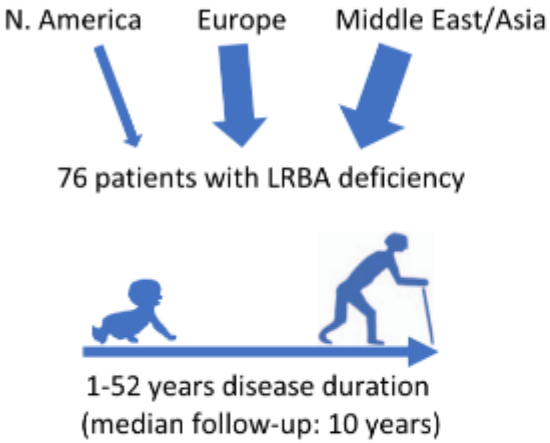
Shahrzad Bakhtiar,[1] Emilia Salzmann-Manrique,[1] Henric-Jan Blok,[2] Dirk-Jan Eikema,[2] Sheree Hazelaar,[2] Mouhab Ayas,[3] Amos Toren,[4] Gal Goldstein,[4] Despina Moshous,[5,6,7] Franco Locatelli,[8] Pietro Merli,[8] Gerard Michel,[9] Gülyüz Öztürk,[10] Ansgar Schulz,[11] Carsten Heilmann,[12] M
Yves Bertrand,[15] Abdelghani Tbakhi,[16] Paul Veys,[17] Musa
Rupert Handgretinger,[21] Emel Unal,[22] Antonio Perez-Marti
Gülsün Karasu,[27] Isabel Badell,[28] Per Ljungman,[29] Elena
Robbert R. G. Bredius,[33] Polina Stepensky,[34] Bella Shadu
Michael H. Albert,[36] Peter Bader,[1,*] and Arjan Lankester[33]
Inborn Errors Working Party of EBMT

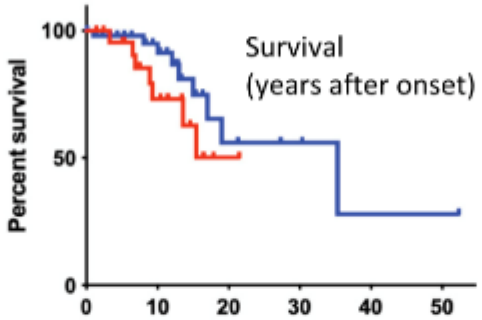


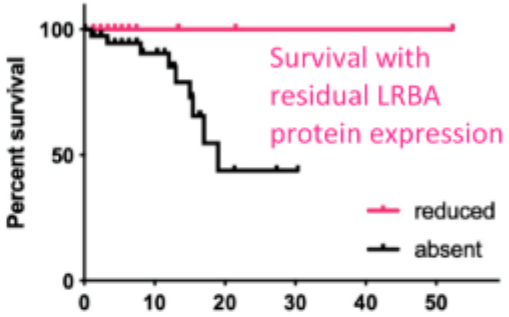
Long-term outcome of LRBA deficiency in 76 patients after various treatment modalities as evaluated by the immune deficiency and dysregulation activity (IDDA) score

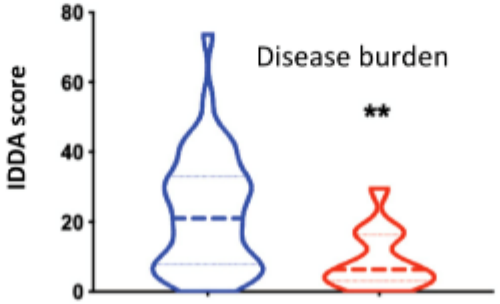
Tesch et al, JACI 2021

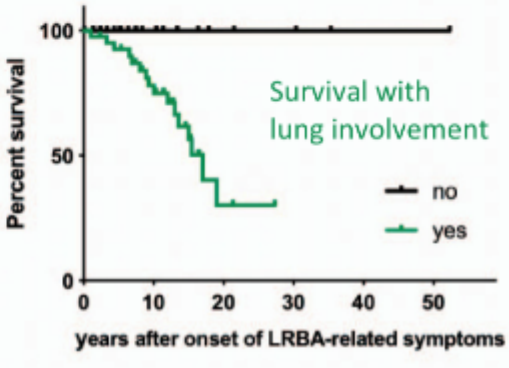
Long-term outcome of LRBA deficiency as evaluated by the immune deficiency and dysregulation activity (IDDA) score







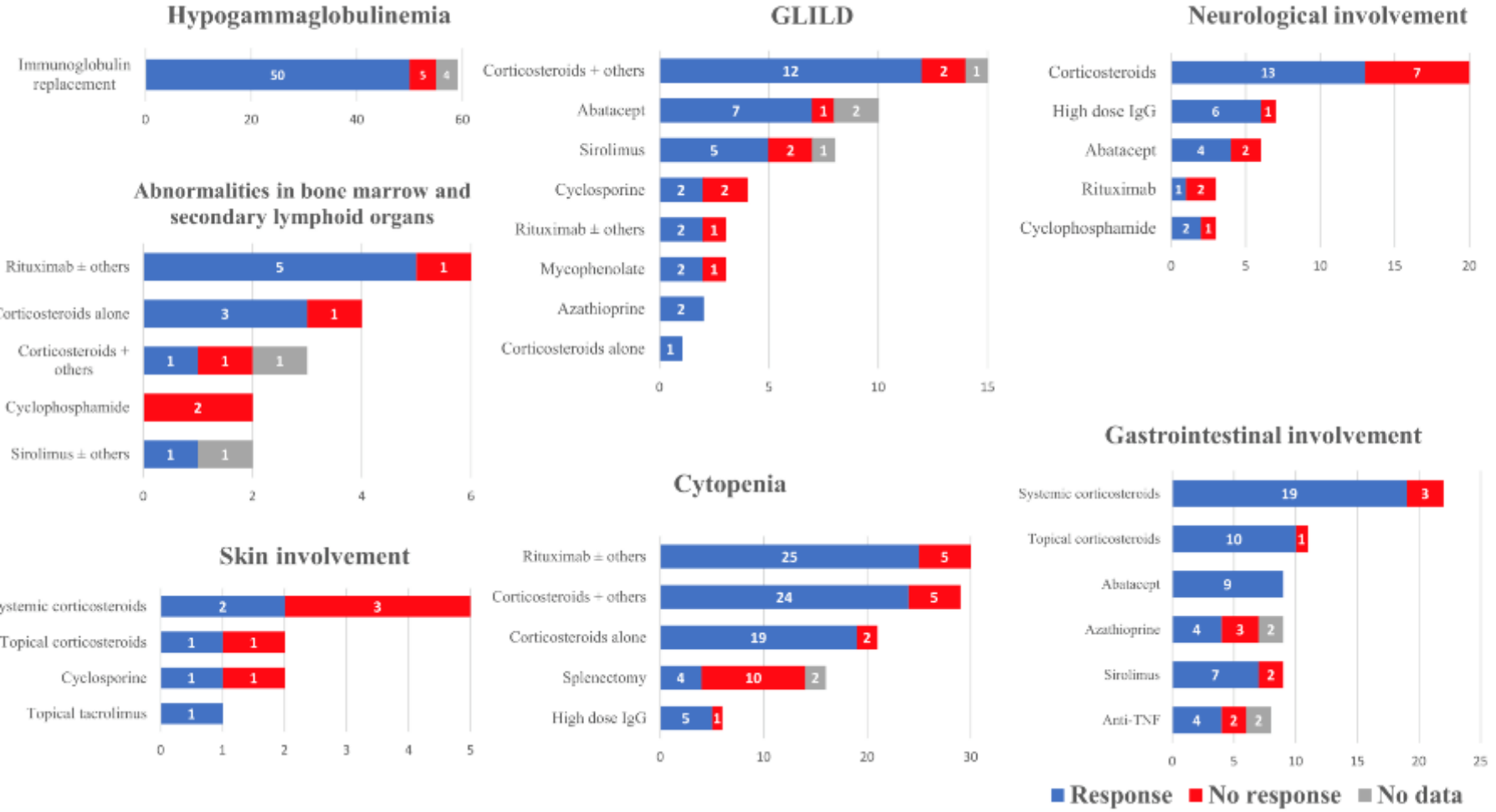




LRBA, lipopolysaccharide-responsive beige-like anchor protein; HSCT, hematopoietic stem cell transplantation

Therapeutic options for CTLA-4 insufficiency

David Egg [a], Ina Caroline Rump MD [a], Noriko Mitsuiki MD, PhD [a], Jessica Rojas-Restrepo [a], Maria-Elena Maccari MD [a, b], Charlotte Schwab MD [a], Annemarie Gabrysch MD [a], Klaus Warnatz MD [a, c], Sigune Goldacker MD [a, c], Virginia Patiño MD [d], Daniel Wolff MD [e], Satoshi Okada MD, PhD [f], Seiichi Hayakawa MD [f], Yoshiaki Shikama MD



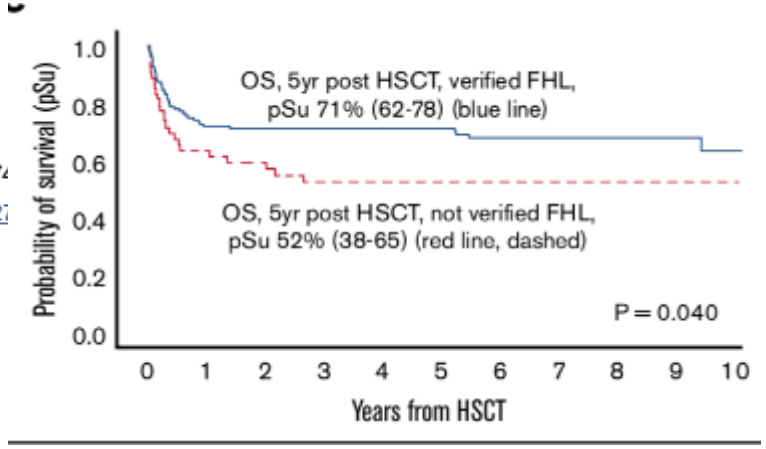
JACI, 2021

blood advances

Blood Adv. 2020 Aug 11; 4(15): 3754–3766. PMCID: PMC74
Published online 2020 Aug 11. doi: 10.1182/bloodadvances.2020002101 PMID: 327

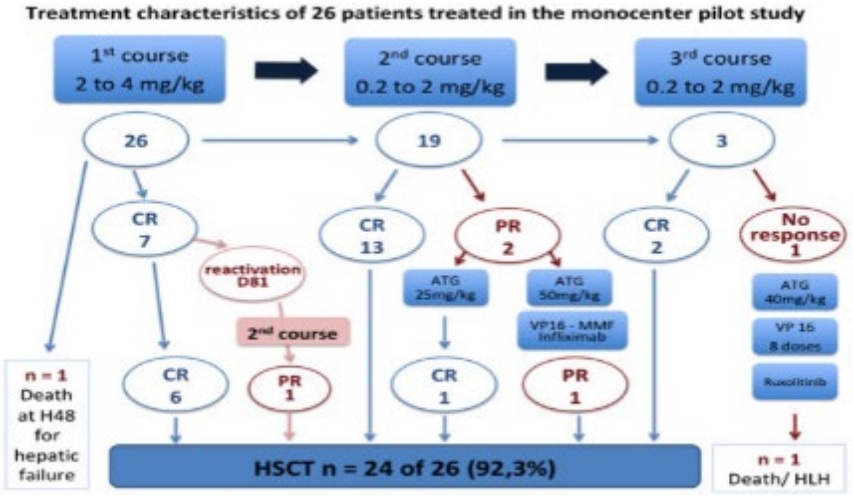
Stem cell transplantation for children with hemophagocytic lymphohistiocytosis: results from the HLH-2004 study

Elisabet Bergsten,[1] AnnaCarin Horne,[1,2] Ida Hed Myrberg,[1] Maurizio Aricó,[3] Itziar Astigarraga,[4] Eiichi Ishii,[5] Gritta Janka,[6] Stephan Ladisch,[7] Kai Lehmberg,[6,8] Kenneth L. McClain,[9] Milen Minkov,[10] Vasanta Nanduri,[11] Diego A. Rosso,[12,13] Elena Sieni,[14] Jacek Winiarski,[2,15] and Jan-Inge Henter[1,2]



Alemtuzumab as First Line Treatment in Children with Familial Lymphohistiocytosis

Despina Moshous, MD PhD, Coralie Briand, MD, Martin Castelle, MD, Laurent Dupic, MD, Guillaume Morelle, MD, Wadih Abou Chahla, MD, Vincent Barlogis, MD PhD, Yves Bertrand, MD, Bénédicte Bruno, MD, Eric Jeziorski, MD PhD, Catherine Paillard, MD PhD, Pierre Simon Rohrlich, MD PhD, Jean Louis Stephan, MD PhD, Caroline Thomas, MD, Stéphanie Chhun, PharmD, PhD, Isabelle Pellier, MD PhD, Aude Marie-Cardine, MD, Mathieu Fusaro, Genevieve de Saint Basile, MD PhD, Capucine Picard, MD PhD, Caroline Elie, MD PhD, Benedicte Neven, MD PhD, Stephane Blanche, MD, Alain Fischer, MD PhD



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ORIGINAL ARTICLE

Emapalumab in Children with Primary Hemophagocytic Lymphohistiocytosis

F. Locatelli, M.B. Jordan, C. Allen, S. Cesaro, C. Rizzari, A. Rao, B. Degar, T.P. Garrington, J. Sevilla, M.-C. Putti, F. Fagioli, M. Ahlmann, J.-L. Dapena Diaz, M. Henry, F. De Benedetti, A. Grom, G. Lapeyre, P. Jacqmin, M. Ballabio, and C. de Min

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COMMENTARY

Is neutralization of IFN-γ sufficient to control inflammation in HLH?

Stephan Ehl, Tatiana von Bahr Greenwood, Elisabet Bergsten, Alain Fischer, Jan-Inge Henter, Melissa Hines, Kai Lehmberg, Gritta Janka, Despina Moshous, Kim E. Nichols

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