Primary Immune Deficiency Treatment Consortium

NEWSLETTER

Spring 2024 | Issue 19

Picture of a jaguar taken by Dr. Elie Haddad when on safari recently

Remembering Vicki Modell

We are deeply saddened to announce that the Jeffrey Modell Foundation's beloved Co-Founder, Vicki Modell, has passed away.

Vicki was a strong, courageous, and empathetic leader, and was the heart of the Foundation for 37 years. She dedicated her life to the Primary Immunodeficiency community and touched the lives of millions of people. Vicki was a passionate advocate for patients and families living with PI worldwide and was dedicated to answering Jeffrey's plea to *Do Something*, always leading with compassion.

Vicki was a friend to so many, and loved attending global workshops and meetings, surrounded by our community. It was her dream to see newborn screening for SCID approved in every country so that more lives would be saved. She was proud to support groundbreaking research, provide educational opportunities for physicians, pursue advocacy and awareness efforts, and encourage patient support programs worldwide. Vicki's dedication and love for patients and their families will be her legacy forever.

We mourn her death and will miss her terribly. We hope you will join us in honoring her memory by committing to *Do Something* and continuing her mission to save as many lives as possible.

Greetings from Drs. Jennifer Puck, Chris Dvorak, and Elie Haddad, Multi-PIs

Dear PIDTC,

We are proud of the heroic efforts by our participating sites and our UCSF staff to push to open the new protocols 6906 PIRD, 6907 SCID and 6908 CGD and enroll new patients into these protocols. Keep up the great work!

We are also very excited about the upcoming Annual PIDTC Workshop and Education Day to be held in Atlanta this April, hosted by our Emory and Children's Healthcare of Atlanta investigators Shan Chandrakasan and Suhag Parikh. They have lined up a stellar scientific program and it will be a great chance to catch up in person with all of you.

See you soon!

Jennifer Puck,
Chris Dvorak and
Elie Haddad

IN THIS ISSUE

New PIDTC Publication

Genotype, oxidase status, and preceding infection or autoinflammation do not affect allogeneic HCT outcomes for CGD

Leiding JW, Arnold DE, Parikh S, Logan B, Marsh RA, Griffith LM, Wu R, Kidd S, Mallhi K, Chellapandian D, Si Lim SJ, Grunebaum E, Falcone EL, Murguia-Favela L, Grossman D, Prasad VK, Heimall JR, Touzot F, Burroughs LM, Bleesing J, Kapoor N, Dara J, Williams O, Kapadia M, Oshrine BR, Bednarski JJ, Rayes A, Chong H, Cuvelier GDE, Forbes Satter LR, Martinez C, Vander Lugt MT, Yu LC, Chandrakasan S, Joshi A, Prockop SE, Dávila Saldaña BJ, Aquino V, Broglie LA, Ebens CL, Madden LM, DeSantes K, Milner J, Rangarajan HG, Shah AJ, Gillio AP, Knutsen AP, Miller HK, Moore TB, Graham P, Bauchat A, Bunin NJ, Teira P, Petrovic A, Chandra S, Abdel-Azim H, Dorsey MJ, Birbrayer O, Cowan MJ, Dvorak CC, Haddad E, Kohn DB, Notarangelo LD, Pai SY, Puck JM, Pulsipher MA, Torgerson TR, Malech HL, Kang EM. Genotype, oxidase status, and preceding infection or autoinflammation do not affect allogeneic HCT outcomes for CGD. Blood. 2023 Dec 14;142(24):2105-2118. doi: 10.1182/blood.2022019586. PMID: 37562003; PMCID: PMC10862239 : https://pubmed.ncbi.nlm.nih.gov/37562003/

Lead Author: Jennifer Leiding, MD

Summary

Chronic granulomatous disease (CGD) is a primary immunodeficiency characterized by life-threatening infections and autoinflammation. Hematopoietic cell transplantation (HCT) is the definitive treatment for CGD, but the effects of patient selection and active disease at the time of transplant on patient outcomes have yet to be fully explored.

In this study, researchers from the Primary Immune Deficiency Treatment Consortium investigated the effects of patient selection and active disease on health outcomes of patients with CGD, focusing on infection density, frequency of disease, and medication use.

HCT patients had higher infection density, higher frequency of noninfectious lung and liver diseases, and more steroid use before undergoing their transplants than conventionally treated patients, but that these issues did not adversely affect HCT survival. Patients displayed improved growth and nutrition, resolved infections and inflammatory disease, and lower rates of antimicrobial prophylaxis or corticosteroid use a three to five years post-transplant compared with both their baselines and those of conventionally treated patients. HCT leads to durable resolution of CGD symptoms and lowers the burden of the disease.

New PIDTC Publication

Allogeneic hematopoietic cell transplantation is effective for p47phox chronic granulomatous disease: A Primary Immune Deficiency Treatment Consortium study

Grunebaum E, Arnold DE, Logan B, Parikh S, Marsh RA, Griffith LM, Mallhi K, Chellapandian D, Lim SS, Deal CL, Kapoor N, Murguía-Favela L, Falcone EL, Prasad VK, Touzot F, Bleesing JJ, Chandrakasan S, Heimall JR, Bednarski JJ, Broglie LA, Chong HJ, Kapadia M, Prockop S, Dávila Saldaña BJ, Schaefer E, Bauchat AL, Teira P, Chandra S, Parta M, Cowan MJ, Dvorak CC, Haddad E, Kohn DB, Notarangelo LD, Pai SY, Puck JM, Pulsipher MA, Torgerson TR, Malech HL, Kang EM, Leiding JW. Allogeneic hematopoietic cell transplantation is effective for p47phox chronic granulomatous disease: A Primary Immune Deficiency Treatment Consortium study. J Allergy Clin Immunol. 2024 Jan 28:S0091-6749(24)00081-2. doi: 10.1016/j.jaci.2024.01.013. Epub ahead of print. PMID: 38290608. https://pubmed.ncbi.nlm.nih.gov/38290608/

Lead Author: Eyal Grunebaum, MD

Summary

Chronic granulomatous disease (CGD) is a primary immunodeficiency characterized by life-threatening infections and autoinflammation. The most common cause of autosomal recessive CGD is p47phox (neutrophil cytosolic factor-1) deficiency. Allogeneic hematopoietic cell transplantation (HCT) for p47phox CGD is not well-described.

Researchers from the Primary Immune Deficiency Treatment Consortium investigated the outcomes of thirty patients with p47phox CGD who underwent allogeneic HCT since 1995, focusing on patients' height and weight, need for nutritional supplementation via tube or total parenteral nutrition, performance status, infections, inflammatory and autoimmune manifestations, organ dysfunction, and surgical resection.

CGD-related infections, frequency of inflammatory bowel disease, and use of steroids decreased significantly after transplantation. The two-year overall and event-free survival rates were 92.3% and 82.1%, respectively, while at 5 years they were 85.7% and 77.0%, respectively.

New PIDTC Publication

Relevance of lymphocyte proliferation to PHA in severe combined immunodeficiency (SCID) and T cell lymphopenia

Abraham RS, Basu A, Heimall JR, Dunn E, Yip A, Kapadia M, Kapoor N, Satter LF, Buckley R, O'Reilly R, Cuvelier GDE, Chandra S, Bednarski J, Chaudhury S, Moore TB, Haines H, Dávila Saldaña BJ, Chellapandian D, Rayes A, Chen K, Caywood E, Chandrakasan S, Lugt MTV, Ebens C, Teira P, Shereck E, Miller H, Aquino V, Eissa H, Yu LC, Gillio A, Madden L, Knutsen A, Shah AJ, DeSantes K, Barnum J, Broglie L, Joshi AY, Kleiner G, Dara J, Prockop S, Martinez C, Mousallem T, Oved J, Burroughs L, Marsh R, Torgerson TR, Leiding JW, Pai SY, Kohn DB, Pulsipher MA, Griffith LM, Notarangelo LD, Cowan MJ, Puck J, Dvorak CC, Haddad E. Relevance of lymphocyte proliferation to PHA in severe combined immunodeficiency (SCID) and T cell lymphopenia. Clin Immunol. 2024 Apr;261:109942. doi: 10.1016/j.clim.2024.109942. Epub 2024 Feb 15. PMID: 38367737. https://pubmed.ncbi.nlm.nih.gov/38367737/

Lead Author: Roshini Abraham, PhD

Summary

Severe combined immunodeficiency (SCID) is a primary immunodeficiency characterized by a severe deficiency in T cell numbers causing high susceptibility to severe infections. T cell proliferation as a response to polyclonal stimulants such as phytohemagglutinin has been used as an indicator of T cell function. The method used to measure PHA-stimulated T cell proliferation can strongly influence the interpretation of the result.

Researchers investigated the impact of utilizing radioactive labels or flow cytometry on the interpretation of PHA proliferation. In patients with CD3+ T cell counts between 51 and 300 cells/µL, there was a higher proliferative response with the PHA flow assay compared to the radioactive assay. Furthermore, many SCID patients with profound T cell lymphopenia were observed to have normal T cell proliferation when assessed by flow cytometry. Such results suggest that the method of analysis influences the resolution and interpretation of PHA results and that the flow cytometry method should only be used as supportive data for SCID diagnosis.

PIDTC Education Day & Annual Scientific Workshop

April 8 – April 11, 2024

The Atlanta Skyline from Buckhead

The PIDTC is excited to hold our Annual Workshop in the beautiful city of Atlanta, Georgia! We will hold our Education Day on April 8 - 9, where we will once again explore interesting and special aspects of the diagnosis and management of primary immunodeficiencies with leaders in the field, followed by our Scientific Workshop from April 9 - 11.

It has been a year full of achievements for the Consortium and advancements in primary immune deficiency research, and we look forward to discussing the progress we have made and our plans for the future.

Welcome Lisa Lim

Lisa Lim, our new Senior Program Manager, comes to us as a seasoned UCSF research staff member. Prior to joining PIDTC, she was a senior clinical research coordinator in the Cardiology Division, working on several projects from eHealth utilizing smart technologies to genetic research on mitral valve prolapse. She holds a Master of Science in Health Policy and Law from UCSF/UC Law. As a first generation child of refugees, she became passionate about the healthcare system at an early age while navigating medical care for her family. She attained her Bachelor of Arts in Legal Studies and minor in Public Policy from UC Berkeley. While at Cal, she worked as a research assistant, conducting studies on acupuncture in the ICU at the Alameda Highland Hospital. She also volunteered as a patient navigator at UCSF Benioff Children's Hospital Oakland, gaining appreciation for the root causes of health inequities and thinking about preventive approaches to advancing population health.

In her spare time, she sings in two choirs, volunteers as a crisis counselor for survivors of sexual violence and enjoys exploring hiking trails throughout the San Francisco Bay Area with Liam, her miniature pinscher.

Welcome Rafael Ricon

Rafael Ricon is the PIDTC's new Program Coordinator. He was born in the Philippines and grew up in the Bay Area before graduating from UC Davis in June 2023 with a Bachelor's of Science in Global Disease Biology. Rafael interned with the UCDMC Department of Surgery's RESURG Program as a clinical research assistant and later a member of the RESURG administrative team, where he assisted with various studies in vascular surgery, palliative care, and acute care surgery. He also worked as a peer advisor for his major. Rafael is interested in learning how to interact with patients who have complex conditions and diseases, as well as with their families. He particularly enjoys the time he can spend with the PIDTC study participants. Outside of the office and clinic, Rafael loves arranging orchestral music, playing volleyball, and visiting museums and aquariums!

PAG Updates

Jeffrey Modell Foundation

New JMF Public Service Announcements

A new campaign of PSAs was launched this year. PSAs were aired at multiple NFL games including two NFL Playoff games and Super Bowl LVIII!

Rare Disease Day: February 29, 2024

Check out the Jeffrey Modell Foundation's social media pages for infographics and a video celebrating Rare Disease Week and our wonderful patients!

Facebook, Instagram, X/Twitter, and TikTok: @info4pi
LinkedIn: Jeffrey Modell Foundation

For more information about JMF click here: https://www.info4pi.org/

SCID Angels for Life Foundation

SCID Angels Kids Day: April 7th

SCID Angels is collaborating with Johns Hopkins All Children's Hospital in Florida to plan a Kids Day event on Sunday, April 7th which will be sponsored by JMF.

IDF Conference Scholarships

The SCID Angels Foundation is offering travel scholarships to SCID families attending the IDF Conference in June. Eligible applicants must apply on the SCID Angels website at https://www.scidangelsforlife.com/2023/11/travel-scholarship-for-idf-2024/

For more information about SCID Angels for Life click here: http://www.scidangelsforlife.com/

CGD Association of America

CGDAA at the Immune Deficiency Foundation PI Conference

Felicia Morton and the CGD Association of America (CGDAA) will have a strong presence at the Immune Deficiency Foundation (IDF) PI Conference on June 20 - June 22 in Chicago. At the conference, Felicia will be introducing Dr. Harry Malech's talk. Come and learn the potential clinical implications of recent studies and/or date pertaining to chronic granulomatous disease (CGD) diagnostics and treatment. Learn how and why CGD may be included in future newborn screening and gain an awareness of additional CGD research opportunities!

CGDAA Scholarships to attend IDF PI Conference

The CGD Association of America is pleased to offer the CGD community scholarships to attend the IDF PI Conference, thanks to the generosity of an anonymous donor. Patients can fill out the scholarship application link and state their diagnosis is Chronic Granulomatous Disease. The link to apply is here: https://web.cvent.com/event/5cc2fa51-6168-400e-aaed-8c48361ad5b6/summary

CGDAA x J.McLaughlin Fashion Fundraiser

The CGDAA is excited to partner with J.McLaughlin to host a special fashion fundraising event in Palm Beach County to benefit the CGDAA on March 27th. For anyone in South Florida, we hope you can attend!

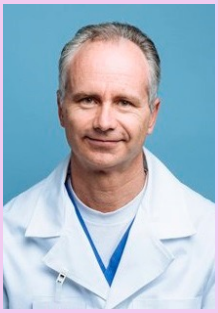
Wiskott-Aldrich Foundation

Planned Paper and Statement
The Wiskott-Aldrich Foundation is working with Dr. Sung-Yun Pai from the PIDTC and Dr. Michael Albert on a paper, "How I Manage WAS", and a position statement on X-Linked Thrombocytopenia.

Wiskott-Aldrich Syndrome Research Symposium November 18, 2024
The fourth international symposium for researchers and clinicians on Wiskott-Aldrich Syndrome is being held in Milan, Italy, and offers access to the latest research and analysis related to this rare disease.

The conference will feature the following keynote speakers:

Luigi Notarangelo, MD



Alessandro Aiuti, MD, PhD

Alessia Cavazza, PhD

Abstract submissions for the conference open on *June 1, 2024*
Symposium Website: https://www.was2024.org/

WAS Foundation Scholarships for IDF Conference
The Wiskott-Aldrich Foundation is providing scholarships to attend the Immune Deficiency Foundation Conference from June 20-22 in Chicago, Illinois! Please contact sumathi.iyengar@wiskott.org for more information.

Immune Deficiency Foundation

IDF PI Conference 2024

The Immune Deficiency Foundation's 2024 PI Conference is happening June 20-22 in Chicago, IL!

Whether you're recently diagnosed, interested in more in-depth scientific medical topics, or want to learn more about the rarest diagnoses, this conference is for you! There will be opportunities for connection with other zebras and the premiere of our feature-length documentary "Compromised: Life Without Immunity". Registration is now open! Questions? Contact events@primaryimmune.org

www.primaryimmune.org/conference

Special thanks to *CGD Association of America, Hyper IgM Foundation, SCID Angels for Life Foundation*, and the *Wiskott-Aldrich Foundation* for their support in the planning of several diagnosis-specific sessions.

For more information about IDF click here: https://primaryimmune.org/

Ongoing Clinical Studies

UCSF Artemis SCID Gene Therapy

In this trial, newly diagnosed or previously treated patients with insufficient immunity due to ART-SCID receive "lentiviral gene transfer," also called "gene therapy." A normal copy of the DCLRE1C gene is inserted into blood-forming stem cells that grow and develop into all blood lineages. The inserted gene provides correct instructions to the defective stem cells so that functioning T and B lymphocytes can develop. So far 10 patients have been treated.

For eligibility or more information about the study, please contact: Mort Cowan, MD (Mort.Cowan@ucsf.edu) or Jennifer Puck, MD (Jennifer.Puck@ucsf.edu).

C-SIDE

The purpose of this trial is to test the efficacy of regimens containing busulfan targeted to 30 mg*h/L vs 60 mg*h/L in patients with X-linked SCID, JAK3 SCID, RAG1/RAG2 SCID. To date 13 IL2RG/JAK3 and 10 RAG1/RAG2 patients have been enrolled. The vast majority of patients have done very well with reconstitution of T cells and varying degrees of humoral immune reconstitution. We encourage all sites to be sure to offer enrollment on CSIDE to every eligible patient. If you have any questions, please email **Sung-Yun Pai, MD** (sung-yun.pai@nih.gov), **Mike Pulsipher** (mpulsipher@chla.usc.edu), and **Janelle Olson** (jolson@nmdp.org).

LAD-I Gene Therapy Trial

This Leukocyte Adhesion Deficiency Type I (LAD-I) gene therapy trial is currently enrolling patients at UCLA (US). Additional treatment centers will include UCL/GOSH (UK) and Hospital Infantil Universitario Niño de Jesús (Spain). The trial is sponsored by Rocket Pharmaceuticals, Inc., and funded by the California Institute of Regenerative Medicine (CIRM). For more information, please visit:

https://clinicaltrials.gov/study/NCT03812263

Viral CTL Consortium (VIRCTLC)

Principal Investigator Mitchell S. Cairo, MD and Study Chairs Julie Talano, MD and Nancy Bunin, MD, are studying (funding by the FDA) the safety, efficacy and biology of viral CTLS derived from related donors by the Cytokine Capture System using the Prodigy device in patients with immunodeficiencies either secondary to HSCT or primary immunodeficiencies with refractory CMV, ADV and/or EBV or intolerant to anti-viral therapy.

Ongoing Clinical Studies Continued...

Clinical Trial at Mayo for LADII Deficiency

A Phase 3 Randomized, Double-blind Crossover Study to Assess the Efficacy and Safety of AVTX-803 in Subjects with Leukocyte Adhesion Deficiency Type II (LAD II; also called SLC35C1-CDG) enrolled the first patient at Clinical Genomics, Mayo Clinic Rochester.
The study enrolls LAD II patients older than 6 months receiving a dietary supplement containing L-Fucose, and randomizes patients in to a two-period study with a withdrawal phase (placebo) and treatment phase (L-Fucose) with crossover. Patients with abnormal sialyl-Lewis antigen and history of recurrent infections are eligible for the study. Please see the link for more information.

Website: https://clinicaltrials.gov/study/NCT05462587

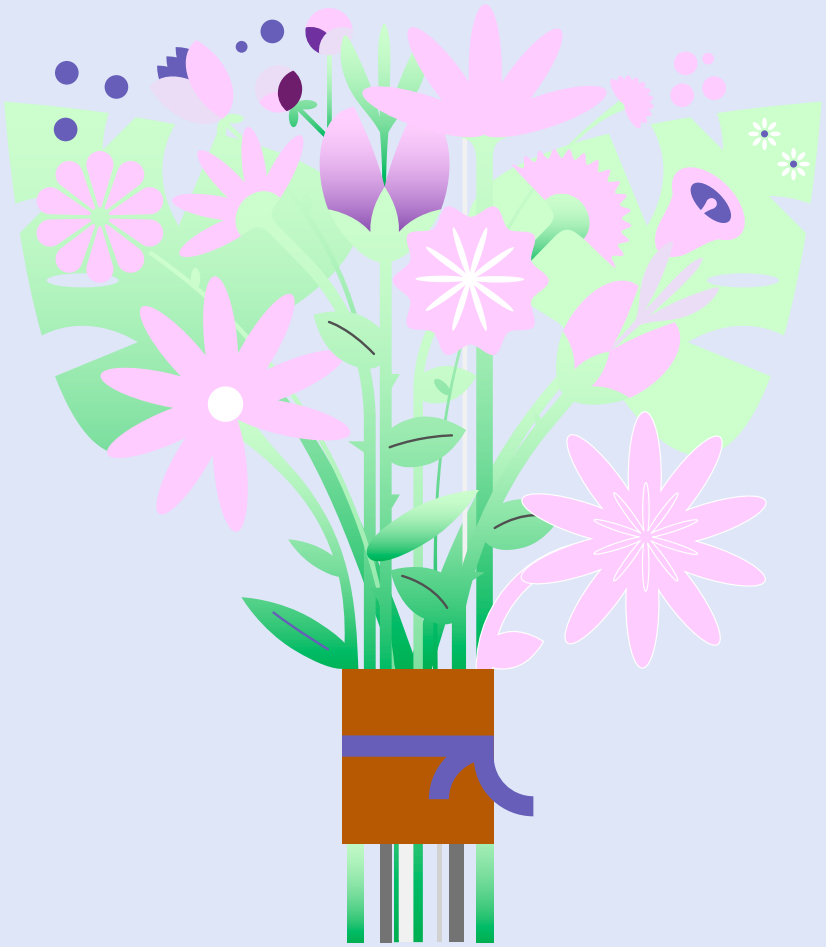
A Study of Mavorixafor in Participants With Severe Congenital Neutropenia and Chronic Neutropenia Disorders

This Phase 1b study will determine the safety and tolerability of mavorixafor in participants with severe chronic idiopathic neutropenia (CIN) and selected congenital neutropenia disorders.

Website: https://www.x4pharma.com/patients/chronic-neutropenia/

Anti-c-KIT (JSP191) Transplant Protocol

This Phase I study is a single arm, open label, dose escalation trial being conducted at multiple PIDTC centers, including: UCSF Benioff Children's Hospital, Lucile Packard Children's Hospital at Stanford and Memorial Sloan Kettering Cancer Center in New York. The study objective is to evaluate the safety and tolerability of allogeneic CD34+ human stem cells (HSC) in patients with Severe Combined Immune Deficiencies (SCID) conditioned for transplantation with JSP191, a monoclonal antibody that targets human CD117.



Newsletter brought to you by the PIDTC Program Management Team. Thank you to our partners at the RDCRN/DMCC!

Got announcements?
Email: rafael.ricon@ucsf.edu