7TH International Chronic Graft-versus-Host Disease Symposium

OCTOBER 16-17, 2024 / VANCOUVER, CANADA

Sheraton Vancouver Wall Centre

PROGRAM

PRIME MINISTER · PREMIER MINISTRE

October 16–17, 2024

Dear Friends:

I am pleased to extend my warmest greetings to everyone attending the 7th International Chronic Graft-versus-Host Disease (cGvHD) Symposium.

This annual gathering offers professionals in the field of cGvHD an important platform to learn from and network with their peers. I am certain that the activities planned for the next two days will inspire a great deal of thoughtful discussion.

I would like to thank Cell Therapy Transplant Canada and Krohem for putting together an informative and rewarding program for delegates. You can take pride in your commitment to advancing knowledge and collaboration in cGvHD research.

Please accept my best wishes for an enjoyable and productive meeting in Vancouver.

Sincerely,

The Rt. Hon. Justin P. J. Trudeau, P.C., M.P.
Prime Minister of Canada

PRIME MINISTER · PREMIER MINISTRE

Du 16 au 17 octobre 2024

Chères amies,
Chers amis,

Je suis heureux de présenter mes salutations les plus chaleureuses à toutes les personnes qui participent au 7e symposium international sur la maladie chronique du greffon contre l'hôte.

Cette rencontre annuelle offre aux professionnels du domaine de la maladie chronique du greffon contre l'hôte une plateforme importante pour apprendre de leurs pairs et réseauter avec eux. Je suis convaincu que les activités prévues au cours des deux prochains jours susciteront de nombreuses discussions approfondies.

Je remercie Transplantation et thérapie cellulaire Canada et KroHem de proposer un programme informatif et enrichissant pour les délégués. Vous pouvez tirer fierté de votre engagement à faire progresser les connaissances et la collaboration dans la recherche sur la maladie chronique du greffon contre l'hôte.

Je vous souhaite un symposium des plus agréables et productifs à Vancouver.

Cordialement,

Le très honorable Justin P. J. Trudeau, C.P., député
Premier ministre du Canada

CITY OF VANCOUVER

MAYOR KEN SIM

October 16-17, 2024

A MESSAGE FROM THE MAYOR

On behalf of the residents of Vancouver and my colleagues on City Council, I want to extend my warmest greetings to everyone attending the 7th International Chronic Graft-versus-Host Disease Symposium.

As Mayor, I am excited to welcome this important event to Vancouver, marking the first time this conference is being held in North America. It is an exciting moment to bring together physicians, scientists, and caregivers to share insights, build connections, and lay the groundwork for future collaborations in addressing Chronic graft-versus-host disease (cGvHD).

I want to express my gratitude to Cell Therapy Transplant Canada and KroHem for organizing this crucial event and sparking essential discussions on addressing cGvHD issues and improving outcomes for alloHCT patients.

Best wishes for a successful event!

Sincerely,

Mayor Ken Sim

SYMPOSIUM PROGRAM

7TH International Chronic Graft-versus-Host Disease Symposium

Contents

CTTC
CELL THERAPY TRANSPLANT CANADA
TRANSPLANTATION ET THÉRAPIE CELLULAIRE CANADA

A Message from the CTTC President

Dear Colleagues:

On behalf of Cell Therapy Transplant Canada (CTTC) I am pleased to welcome you to the 7th International chronic Graft-versus-Host Disease (cGvHD) Symposium. This is the first time that this event has been held in North America, and CTTC is proud to advance the science of cGvHD by hosting this important event in beautiful Vancouver, British Columbia.

cGvHD is a significant challenge faced by many patients undergoing allogeneic transplant. Recent innovations in the treatment and prevention of cGvHD make this an exciting time to be part of the transplant field. The symposium planning committee, led by CTTC Past-President Dr. Kirk R. Schultz, has compiled an exciting program of educational sessions, panel discussions, oral and poster abstract presentations, and corporate symposia. Sessions featured over the 2-day meeting will cover basic biology, updates from the NIH Consensus working groups, trial design, alternate assessments and therapies, and patient-reported outcomes. Don't miss the debate on Thursday afternoon, followed by the three top oral abstracts. I look forward to seeing many of you at the Welcome Reception on Wednesday night, where we will engage with poster abstract presenters and other colleagues, and at our social event on Thursday night at the Tap & Barrel (Bridges location).

Finally, I would like to thank our sponsors for their support of this important symposium. Without their support, meetings like this would not be possible. We encourage you to attend the corporate symposia that take place during mealtimes. Please take the time to visit the exhibit hall during breaks, learn about the companies, and find out what's new and exciting in the cGvHD field.

Kylie Lepic, *BSc, MD, FRCPC*
President, Cell Therapy Transplant Canada (CTTC)

KroHem

A Message from the KroHem Organizing Members

Dear friends and colleagues,

We are delighted to welcome you in Vancouver, Canada, for the 7th International Chronic Graft-versus-Host Disease (cGvHD) Symposium, October 16-17, 2024.

This is the first time for this international meeting being held outside of Europe, after being hosted exclusively in Zagreb in Croatia since the first symposium in 2013. Previous six meetings were organized mainly by the Croatian Cooperative Group for Hematologic Diseases KroHem (www.krohem.hr), co-chaired with professor Pavletic from NCI/NIH, Bethesda, US, and with other distinguish international experts in the field of the cGvHD.

This 7th International cGvHD Symposium is being hosted this year by Cell Therapy Transplant Canada (CTTC; www.cttcanada.org) with support from the KroHem as a partner organization.

The next 8th International cGvHD Symposium is planned to be organized again in Croatia in May 2026, aiming to continue alternating between North America and Europe as the leading international event for cGvHD research and clinical practice, bringing together a critical mass of colleagues from different parts of the world.

Warm regards from the Organizing Committee members from KroHem,

Dražen Pulanić (Zagreb, Croatia)
Radovan Vrhovac (Zagreb, Croatia)
Lana Desnica (Zagreb, Croatia)

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General Symposium Information

VENUE

Sheraton Vancouver Wall Centre
1000 Burrard Street, Vancouver
British Columbia, V6Z 2R9
North Tower, Grand Ballroom Level

REGISTRATION

Registration is located on the Lower Lobby level of the North Tower

- From South Tower (Guest rooms), take the 3rd floor concourse bridge to the North Tower, then either 2 escalators (down two levels) or the elevator to the Lower Lobby level
- From outside (ground level), access either from the North Tower entrance and then down one floor (either via the escalator or elevator) OR directly off the Hornby street entrance

REGISTRATION HOURS

- Tuesday, October 15, 14:00 – 19:00
- Wednesday, October 16, 6:00 – 18:00
- Thursday, October 17, 6:00 – 16:30

SPEAKER SERVICES

Speaker Services is located within the Grand Ballroom AB (Plenary Room) at the Tech Table at the back of the room. All speakers are asked to send in their slides in advance, using the Dropbox Link provided by email from the Program Manager.

Visit the Speaker Services Table at least 24 hours before your presentation time (or as soon as you arrive on-site), to ensure your presentation is loaded onto the system and ready for your session start time.

EXHIBIT HALL

The Exhibit Hall is located in Grand Ballroom CD.

EXHIBIT SHOW HOURS ARE AS FOLLOWS:

- Wednesday, October 16, 9:30 – 19:00
- Thursday, October 17, 9:30 – 16:30

POSTER ABSTRACT PRESENTATIONS

The poster presentation is taking place Wednesday, October 16, 17:30 – 19:00 in the Exhibit Hall, as a part of the Welcome Reception. Delegates are invited to network with poster presenters during this time.

- **Poster Installation:**
  Tuesday, October 15, 13:00 – 19:00
- **Poster Take-Down:**
  Thursday, October 17, 15:30 – 18:00

Poster presenters are asked to ensure their poster is put up and taken down during the suggested times. Please note that posters not taken down may be removed and disposed of by the Symposium staff.

SYMPOSIUM PROGRAM

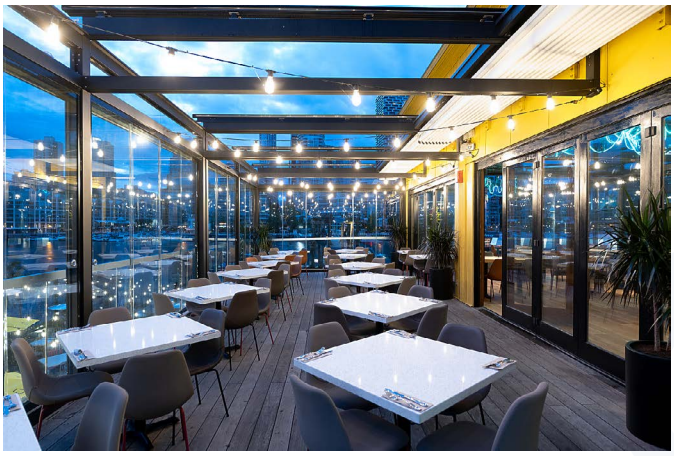
GALA DINNER & SOCIAL EVENT

Thursday, October 17
18:30 – Onwards
(Dinner at 19:00pm, DJ/dancing after dinner)

Tap & Barrel · Bridges
1696 Duranleau St, Vancouver, BC V6H 3S4

Registration: Tickets are $125 for all delegates. Pre-registration is required. Guest tickets may be purchased online or at the registration desk, if tickets are still available. The registration deadline is Thursday, October 17 at noon.

Transportation: Shuttle service has been arranged for delegate transportation to and from the conference venue to the social event venue. Delegates are welcome to take the shuttle or make their own transportation arrangements to get to the venue. Shuttles will begin at 18:15 and begin returning to the Sheraton Wall Centre shortly after dinner. Delegates are asked to meet in the hotel lobby for shuttle service.



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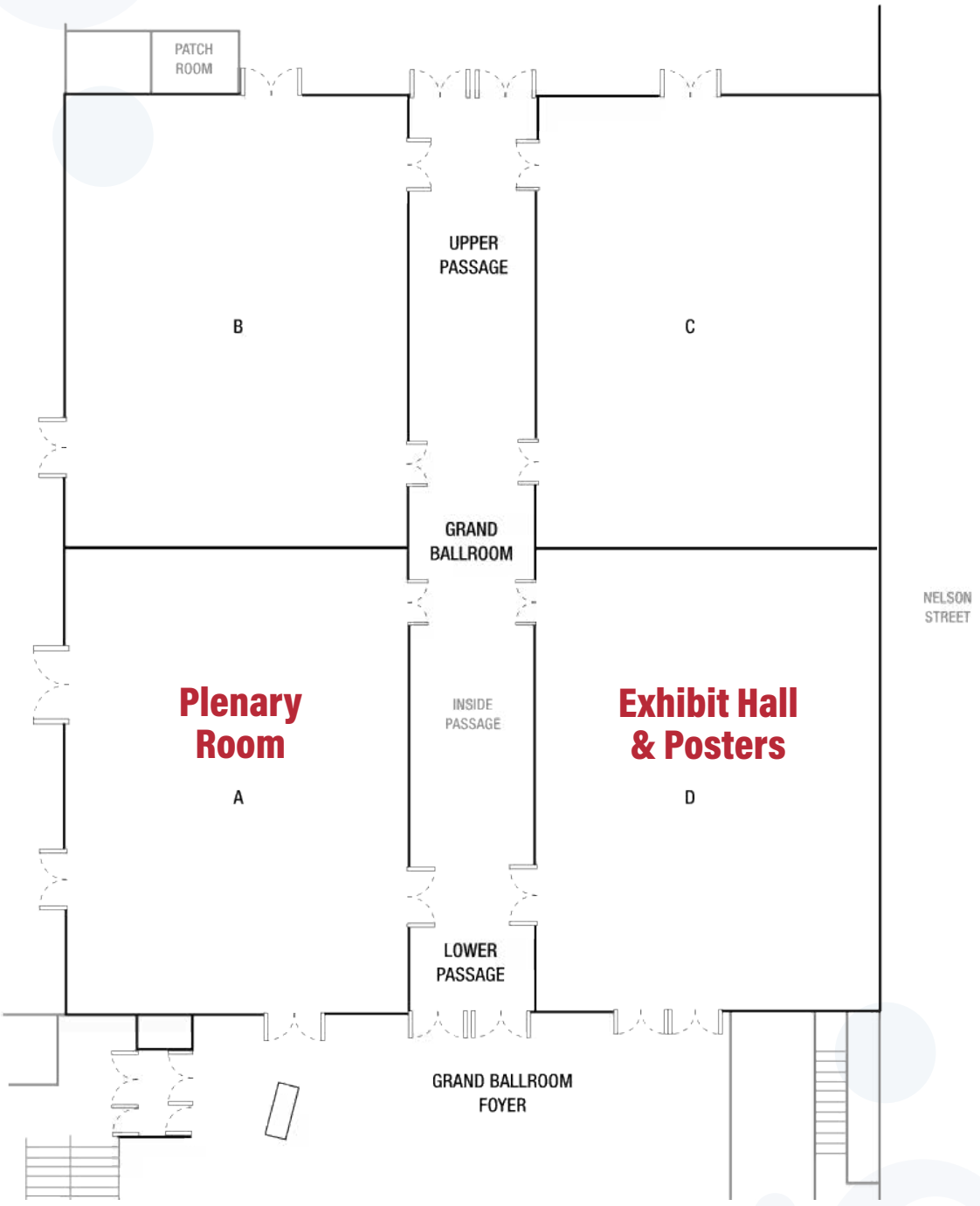
Venue Map


PATCH ROOM
UPPER PASSAGE
B
C
GRAND BALLROOM
NELSON STREET
Plenary Room
A
INSIDE PASSAGE
Exhibit Hall & Posters
D
LOWER PASSAGE
GRAND BALLROOM FOYER

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SYMPOSIUM PROGRAM

7TH International Chronic Graft-versus-Host Disease Symposium

Host Association

Cell Therapy Transplant Canada (CTTC; www.cttcanada.org**)**

CTTC is a member-led, national, multidisciplinary organization providing leadership and promoting excellence in patient care, research and education in the field of hematopoietic stem cell transplant and cell therapy. Our mission is to be a community of excellence, leading national efforts to improve patient lives in hematopoietic cell transplantation and cell therapy, through education, clinical care, research and advocacy, in Canada and worldwide. Our vision is that through national collaboration, CTTC will improve the lives of all patients receiving hematopoietic cell transplantation and cell therapy.

Partner Organization

KroHem, the Croatian Cooperative Group for Hematologic Diseases (www.krohem.hr**)**

KroHem is a non-governmental scientific and professional association that gathers experts in the field of hematology from Croatia and the world. KroHem's members are hematologists, internists, and pediatricians as well as clinical laboratory experts who participate in the diagnosis and treatment of hematological diseases. The goals of the association are the improvement of the treatment of hematological patients and conducting research programs in the field of hematology.

Organizing Committee

Kirk R. Schultz (Vancouver, Canada)
Dražen Pulanić (Zagreb, Croatia)
Steven Z. Pavletic (Bethesda, USA)
Radovan Vrhovac (Zagreb, Croatia)
Stephanie Lee (Seattle, USA)
Hildegard Greinix (Graz, Austria)
Daniel Wolff (Regensburg, Germany)
Sylvie Lachance (Montréal, Canada)
Lana Desnica (Zagreb, Croatia)
Meredith Cowden (Patient Advocate, USA)

International Faculty

Michelle Bishop (USA)
Peggy Burkhard (USA)
Paul Carpenter (USA)
Guang-Shing Cheng (USA)
Meredith Cowden (USA)
Corey Cutler (USA)
Geoff Cuvelier (Canada)
Andrei, Isabela and Arthur De Almeida (Canada)
Zack DeFilipp (USA)
Daniel Demers (Canada)
Lana Desnica (Croatia)
Hildegard Greinix (Austria)
Randi Gurholt-Seary (Canada)
Nada Hamad (Australia)
Andy Harris (USA)
Geoffrey Hill (USA)
Edwin Horwitz (USA)
Sabine Ivison (Canada)
Dennis Kim (Canada)
Sylvie Lachance (Canada)
Madeline Lauener (USA)
Stephanie Lee (USA)
Alina Markova (USA)
Paul Martin (USA)
Jacqueline Mays (USA)
Iveta Mercep (Croatia)
Yoko Ogawa (Japan)
Sophie Paczesny (USA)
Steven Pavletic (USA)
Joseph Pidala (USA)
Naomi Victoria Pinada (Canada)
Dražen Pulanić (Croatia)
Jonathan Rayment (Canada)
Juliana Roden (Canada)
Rachel Rosenstein (USA)
Natasha Sani (Canada)
Stefanie Sarantopoulos (USA)
Hélène Schoemans (Belgium)
Kirk Schultz (Canada)
Lynne Spina (USA)
Christian Stockmann (Switzerland)
Eric Tkaczyk (USA)
Jennifer White (Canada)
Kirsten Williams (USA)
Daniel Wolff (Germany)
Fabiola Wu Wu (Canada)
Yui Kambara Yamamoto (Japan)

SYMPOSIUM PROGRAM

7TH International Chronic Graft-versus-Host Disease Symposium

cGvHD 2024 Program

Wednesday, October 16, 2024

Grand Ballroom A/B

8:00 – 8:30	Continental Breakfast
8:30 – 8:35	**Welcome** Kirk Schultz (Canada)
8:35 – 10:15	**Session 1 – Biology of cGvHD** Moderators: Daniel Wolff (Germany), Lana Desnica (Croatia)
8:35 – 8:55	Predictive biomarkers – Sophie Paczesny (USA)
8:55 – 9:15	Roadblocks in biomarker development – Hildegard Greinix (Austria)
9:15 – 9:35	Tissue vs. blood biomarker – Jacqueline Mays (USA)
9:35 – 9:55	Application of clinical trials algorithms – Andy Harris (USA)
9:55 – 10:15	Roundtable discussion – The way forward
10:15 – 10:45	Health Break
10:45 – 12:15	**Session 2 – Follow up on NIH Consensus Updates and recommendations by the Chairs** Moderators: Steven Pavletic (USA), Stephanie Lee (USA)
10:45 – 11:15	WG3 – Therapy of cGvHD – Zack DeFilipp (USA) / Hildegard Greinix (Austria)
11:15 – 11:45	WG2a – Clinical implementation and early diagnosis – Corey Cutler (USA) / Carrie Kitko (USA)
11:45 – 12:15	WG2b – Preemptive therapy – Joseph Pidala (USA) / Geoffrey Hill (USA)
12:15 – 13:45	**Lunch Symposium – Supported by SANOFI** **How do you assess and define treatment success in cGvHD clinical care?** Moderators: Sylvie Lachance (Canada), Stephanie Lee (USA)
12:25 – 12:30	Welcome and introduction – Sylvie Lachance (Canada), Stephanie Lee (USA)
12:30 – 12:50	Assessing cGvHD manifestations: Tools for clinical trials and patient care – Paul Carpenter (USA)
12:50 – 13:10	Pulmonary cGvHD: Exploring effective management practices – Guang-Shing Cheng (USA)
13:10 – 13:25	Multidisciplinary approaches for managing atypical cGvHD – Kirk Schultz (Canada)
13:25 – 13:35	Discussion and closing remarks
13:45 – 15:15	**Session 2 – Follow up on NIH Consensus (continued)** Moderators: Steven Pavletic (USA), Stephanie Lee (USA)
13:45 – 14:15	WG1 – Etiology and prevention – Kirsten Williams (USA) / Stefanie Sarantopoulos (USA)
14:15 – 14:45	WG4 – Highly morbid forms – Daniel Wolff (Germany) / Sophie Paczesny (USA)
14:45 – 15:15	Task Force 2020: Atypical Chronic GvHD – Geoff Cuvelier (Canada) / Daniel Wolff (Germany)
15:15 – 15:45	Health Break

SYMPOSIUM PROGRAM

7TH International Chronic Graft-versus-Host Disease Symposium

Wednesday, October 16, 2024

Grand Ballroom A/B

15:45 – 17:30	**Session 3 – Innovative trial design (ASTCT Joint Session)** Moderator: Steven Pavletic (USA)
15:45 – 16:05	Innovative trial design - Front line therapy for cGvHD – Daniel Wolff (Germany)
16:05 – 16:25	Innovative trial design - Beyond front line – Corey Cutler (USA)
16:25 – 16:35	Discussion of FDA Guidance Regarding Trials for Treatment of Chronic GvHD – Paul Martin (USA)
16:35 – 16:45	New clinical trial regulations in Europe – Iveta Mercep (Croatia)
16:45 – 17:30	Panel Discussion
17:30 –19:00	**Welcome Reception & Poster Session**

Thursday, October 17, 2024

Grand Ballroom A/B

6:45 – 8:15	**Breakfast Symposium – Supported by Incyte** **Local management strategies for chronic GvHD** Moderator: Daniel Wolff (Germany)
7:10 – 7:25	Management of ocular cGvHD – Yoko Ogawa (Japan)
7:25 – 7:40	Management of oral cGvHD – Jacqueline Mays (USA)
7:40 – 7:55	Management of skin cGvHD – Alina Markova (USA)
7:55 – 8:15	Discussion
8:30 – 10:10	**Session 4 – Alternative cellular therapies for cGvHD (ISCT Joint Session)** Moderators: Sylvie Lachance (Canada), Edwin M. Horwitz (USA)
8:30 – 8:55	Treg therapy – Sabine Ivison (Canada)
8:55 – 9:20	Vaccine-based immunotherapy for fibrosis – Christian Stockmann (Switzerland)
9:20 – 9:45	NKreg cell therapy for cGvHD – Madeline Lauener (USA)
9:45 – 10:10	MSC therapy for cGvHD – Edwin M. Horwitz (USA)
10:10 – 10:40	Health Break
10:40 – 12:00	**Session 5 – Patient reported outcomes and their impact on care** Moderators: Meredith Cowden (USA), Hélène Schoemans (Belgium)
10:40 – 10:55	Bridging the gap in perspectives between GvHD patients and health care professionals – Meredith Cowden (USA)
10:55 – 11:10	Patient reported outcome (PRO) use in GvHD studies — Hélène Schoemans (Belgium)
11:10 – 11:25	PRO use in cGvHD routine care – Juliana Roden (Canada)
11:25 – 11:40	International aspects of cGvHD – Nada Hamad (Australia)
11:40 – 12:00	Panel discussion - Interactive round table around patient unmet needs in GvHD

SYMPOSIUM PROGRAM

7TH International Chronic Graft-versus-Host Disease Symposium

Thursday, October 17, 2024

Grand Ballroom A/B

12:00 – 13:30	**Lunch Symposium – Supported by the Meredith A. Cowden Foundation GVHD Alliance: Uniting to Raise Awareness of GVHD** Moderator: Meredith Cowden (USA) Speakers: Peggy Burkhard (USA), Lynne Spina (USA), Natasha Sani (Canada), Hélène Schoemans (Belgium)	
13:30 – 15:00	**Session 6a – Alternate methods to assess cGvHD** ***Grand Ballroom A/B*** Moderator: Jennifer White (Canada), Kirk Schultz (Canada)	**Session 6b – Patient/ Family/ Caregiver (PFC) Session – GvHD throughout the ages** ***Port McNeill Room, 4th Floor*** Moderator: Meredith Cowden (USA)
13:30 – 13:50	Gene expression classification in skin cGvHD – Rachel Rosenstein (USA)	Pediatrics –Andrei, Isabela and Arthur De Almeida (Canada)
13:50 – 14:10	AI-based skin cGvHD assessment – Eric Tkaczyk (USA)	Adolescent and young adult
14:10 – 14:30	Assessment of pulmonary cGvHD in patients unable to perform PFTs – Jonathan Rayment (Canada)	Adult+ – Daniel Demers (Canada)
14:30 – 15:00	Panel discussion	Caregivers – Randi Gurholt-Seary (Canada)
15:00 – 15:30	Health Break	
15:30 – 16:30	**Session 7a – Debate – Do we need GvHD for GvL?** Moderators: Drazen Pulanic (Croatia), Kirk Schultz (Canada) Discussants: Stefanie Sarantopoulos (USA), Geoffrey Hill (USA)	**Session 7b – PFC Session – Panel discussion and networking** Moderator: Meredith Cowden (USA) Panelists: Juliana Roden (Canada), Hélène Schoemans (Belgium), Madeline Lauener (USA), Andy Harris (USA), Michelle Bishop (USA)
16:30 – 17:25	**Session 8 – Top abstracts** Moderators: Drazen Pulanic (Croatia), Lana Desnica (Croatia)	
16:30 – 16:45	Oral Inflammation and Microbiome Dysbiosis Impacts on Chronic Graft-versus-host Disease – Yui Kambara Yamamoto (Japan)	
16:45 – 17:00	Different Metabolomic Profiles in Adult Compared to Pediatric Chronic Graft-Versus-Host Disease – Fabiola Wu Wu (Canada)	
17:00 – 17:15	Real-World Experience of Belumosudil Shows an Improvement of Modified Lee Symptom Score in Fibrotic Symptom Burden in Chronic GVHD Treatment – Dennis Kim (Canada)	
17:15 – 17:25	Presentation of travel awards for top poster abstracts	
17:25 – 17:30	**Wrap up** Drazen Pulanic (Croatia), Kirk Schultz (Canada)	
18:30 – 21:00	**Gala Dinner & Social Event** Tap & Barrel Bridges | First bus at 18:15	

An-Sophie Claerbout,
Associate Scientist, Ghent, Belgium
Plateforme de Recherche sur les Nanocorps, Belgique

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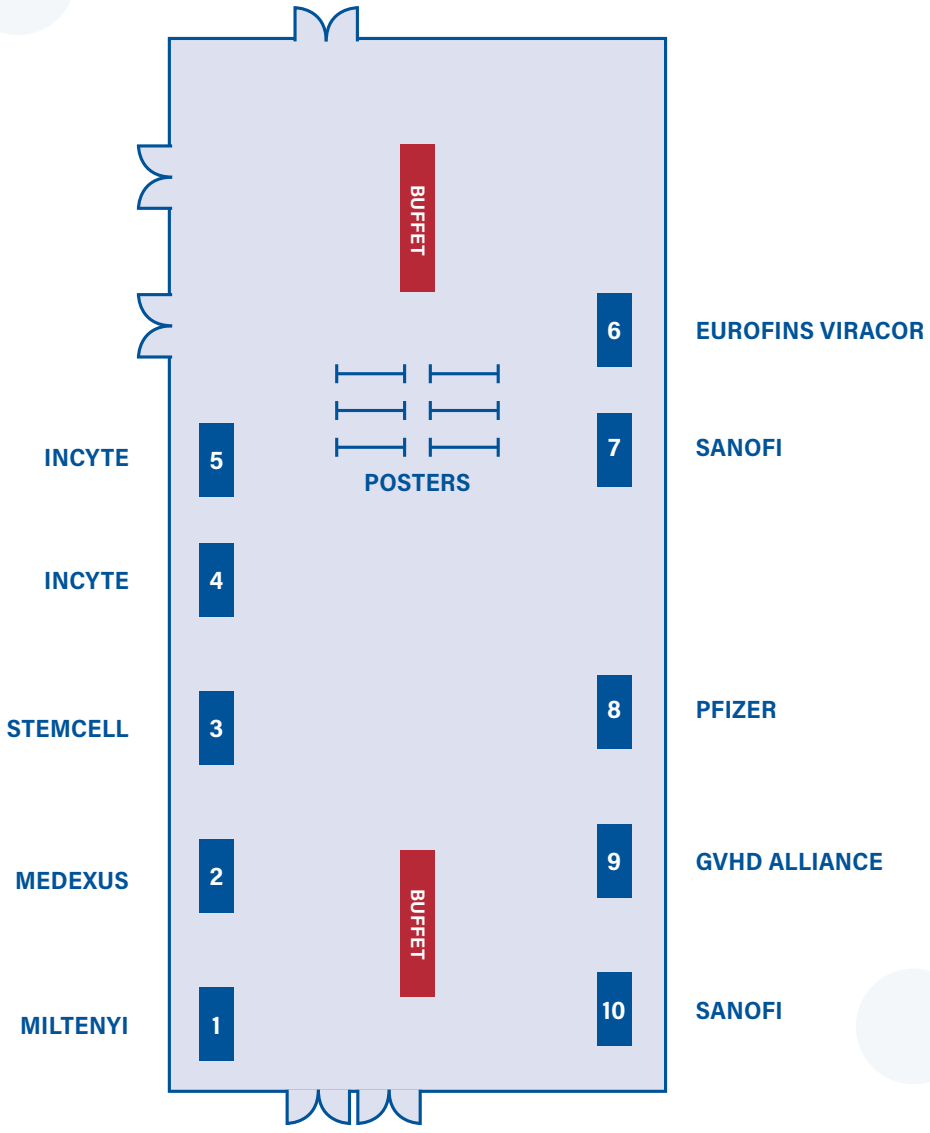
7TH International Chronic Graft-versus-Host Disease Symposium

Exhibitor Floorplan

Grand Ballroom C/D



7TH International Chronic Graft-versus-Host Disease Symposium

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SESSION

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THE UNIVERSITY OF BRITISH COLUMBIA Department of Pediatrics Faculty of Medicine

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Oral Abstract Index

S8.01 – Oral Inflammation and Microbiome Dysbiosis Impacts on Chronic Graft-versus-host Disease

Dr. Yui Kambara Yamamoto[1], Dr. Hideaki Fujiwara[2], Dr. Akira Yamamoto[2], Dr Kazuyoshi Gotoh[3], Dr. Mari Kunihiro[4], Dr. Tadashi Oyama[4], Dr. Toshiki Terao[4], Dr. Ayame Sato[5], Dr. Takehiro Tanaka[6], Dr. Daniel Peltier[7], Dr. Keisuke Seike[2], Dr. Hisakazu Nishimori[2], Dr. Noboru Asada[2], Dr. Daisuke Ennishi[8], Dr. Keiko Fujii[9], Dr. Nobuharu Fujii[10], Dr. Ken-ichi Matsuoka[2,4], Dr. Yoshihiko Soga[5], Dr. Pavan Reddy[11], Dr. Yoshinobu Maeda[2,4]

[1]*Department of Hematology, Oncology and Respiratory Medicine, Okayama University Medical School, Okayama, Japan, Okayama, Japan,* [2]*Department of Hematology and Oncology, Okayama University Hospital, Okayama, Japan,* [3]*Department of Medical Laboratory Science, Okayama University, Graduate School of Health Sciences, Okayama, Japan,* [4]*Department of Hematology, Oncology and Respiratory Medicine, Okayama University School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan,* [5]*Division of Hospital Dentistry, Okayama University Hospital, Okayama, Japan,* [6]*Department of Pathology and Oncology, Okayama University School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan,* [7]*Division of Pediatric Hematology, Oncology, and Stem Cell Transplantation, Department of Pediatrics, Herman B. Wells Center for Pediatric Research, Simon Cancer Center, Indiana University School of Medicine, Indianapolis, USA,* [8]*Center for Comprehensive Genomic Medicine, Okayama University Hospital, Okayama, Japan,* [9]*Department of Clinical Laboratory, Okayama University Hospital, Okayama, Japan,* [10]*Division of Blood Transfusion, Okayama University Hospital, Okayama, Japan,* [11]*Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine, Houston, USA*

Background: Advancements in allogeneic hematopoietic cell transplantation (allo-HCT) have improved long-term survival rates; however, the incidence of chronic graft-versus-host disease (cGVHD) has been increasing. Although new therapeutic agents such as JAK2 inhibitors have reduced the burden of cGVHD, the use of immunosuppressants carries risks of infection and relapse, thereby compromising long-term outcomes post-transplantation. Therefore, developing strategies to prevent or mitigate cGVHD without relying on immunosuppressants is an urgent priority.

Recent studies have revealed that gut dysbiosis is associated with poor long-term outcomes, including acute GVHD. However, due to individual variability and the complex influence of antibiotics, therapeutic interventions targeting gut microbiota are challenging. The oral cavity, which harbors a large bacterial load and is connected to the gastrointestinal tract, is thought to significantly impact gut microbiota. Although oral dysbiosis has been linked to various systemic diseases, reports on the relationship between oral microbiota and GVHD are limited.

Purpose: The purpose of this study is to elucidate the impact of the oral microbiota on cGVHD.

Methods and Results: Given that oral dysbiosis is associated with oral mucosal damage during the transplantation period, we retrospectively analyzed the severity of oral mucosal damage and the incidence of GVHD in allo-HCT patients at Okayama University Hospital (2010-2022, N=344). In both HLA-matched transplants and PTCy-combined haploidentical transplants, patients with severe oral mucosal damage had a significantly higher incidence of cGVHD, regardless of immunosuppressant use or preconditioning regimen. Analysis of buccal

mucosal microbiota of patients underwent HCT (2019-2020, N=17) showed a decrease in diversity in the cGVHD group post-transplantation, strongly suggesting a relationship between oral dysbiosis and cGVHD.

Next, to elucidate the mechanisms by which oral dysbiosis induces or exacerbates cGVHD, we conducted transplantation experiments using a murine model with induced oral dysbiosis via oral ligature placement (OLP). In a cGVHD mouse model (B10.D2 → BALB/c), the OLP group exhibited oral dysbiosis and exacerbated both the cGVHD scores and overall survival compared to the control group. The injury scores in the target organs of cGVHD, as well as cytokine levels in the spleen and lymph nodes, were also significantly increased. The OLP group showed an increase in the total bacterial load in both the oral cavity and feces throughout the transplantation period, with Enterococcaceae significantly increasing in both the oral cavity and feces. Based on these results, we hypothesize that pathogenic bacteria increased in the oral cavity due to OLP might not only exacerbate local inflammation but also enhance systemic inflammation post-transplantation. Additionally, these bacteria might translocate to the gut and form ectopic colonies, further amplifying systemic inflammation.

Conclusions: Our study suggests that dysbiosis of the oral microbiota may exacerbate cGVHD in both humans and mice. Improving oral dysbiosis through oral care requires no special equipment and is minimally burdensome for patients, making it easily applicable in clinical practice. Ultimately, this research aims to establish new GVHD prevention and treatment methods by recovering the oral microbiota independent of immunosuppressants, thereby enabling safer hematopoietic cell transplantation.

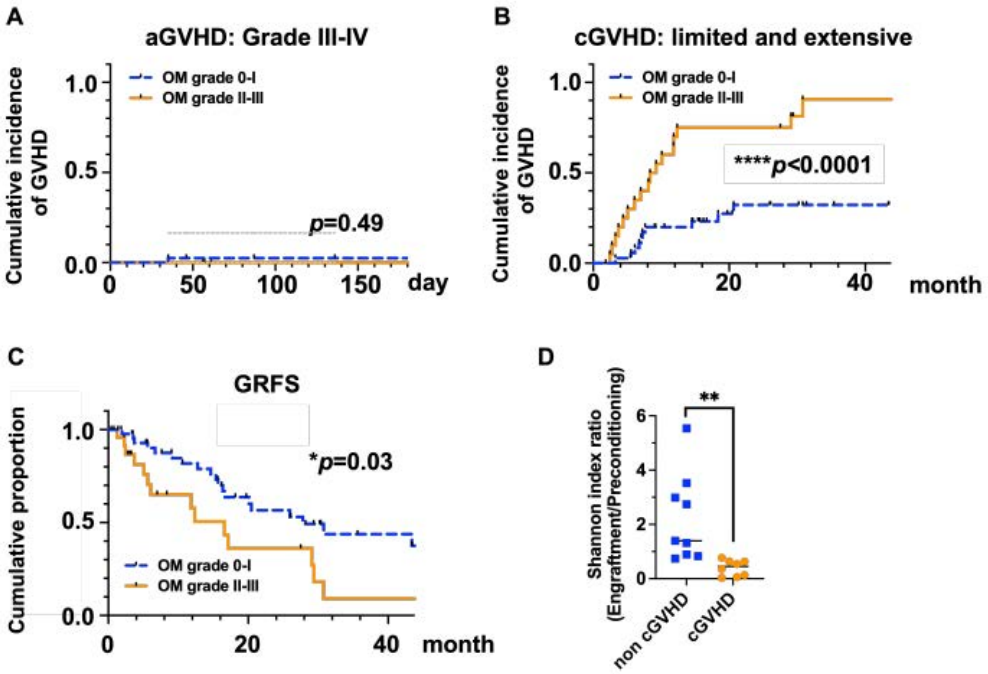

Figure 1. Oral mucositis (OM) and dysbiosis correlated with chronic GVHD in allogeneic HCT recipients. The retrospective cohort of patients receiving a haplo-identical HCT using post-transplant cyclophosphamide (Haplo-PTCy) is shown. Outcomes for patients with (grades II-III) or without moderate-severe OM are depicted. Statistical significance in panels (A) and (B) was assessed using Gray's test for competing risks.(A) Cumulative incidence of aGVHD (Grade III-IV) at 180 days post Haplo-PTCy. (B) Cumulative incidence of cGVHD (limited and extensive) at 36 months post Haplo-PTCy. (C) Cumulative proportion of GRFS at 36 months post Haplo-PTCy, with significance assessed via the log-rank test considering aGVHD (grade III-IV), cGVHD (extensive), relapse, and death as events.(D) Changes in alpha diversity (Shannon index) of buccal mucosa microbiota prior to conditioning and at engraftment for each group are shown. Shannon index ratio = Shannon index at engraftment/Shannon index prior to conditioning. Statistical significance between those with (n = 8) and without (n = 9) cGVHD was determined using the Mann-Whitney U test (**p < 0.01). Error bars represent the mean ± SD.

S8.02 – Different Metabolomic Profiles in Adult Compared to Pediatric Chronic Graft-Versus-Host Disease

Miss Fabiola Wu Wu[1,3], Tashi Rastogi[1], Bernard Ng[2], Liam Johnston[3], Sayeh Abdossamadi[1], Amina Karimina[1], Madeline Lauener[1,3], Elena Ostroumov[1], Barnaby Malong[1], Dong Jun Zheng[1], Dr. Kirk R. Schultz[1]

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Background: Chronic graft-versus-host disease (cGvHD) is the leading cause of morbidity following allogeneic hematopoietic stem cell transplantation (HSCT). In a previous large pediatric study (ABLE1.0, PBMTC1202), we (Subburaj et al., 2022) identified significant metabolomic differences associated with cGvHD. Specifically, we observed a significant elevation of α-ketoglutarate (a-KG), kynurenine, and glutamic acid, along with a decrease in C8 levels.

Purpose: 1) To validate the metabolomic changes seen in ABLE1.0 with another pediatric cohort, ASCT0031. 2) To characterize the metabolomic patterns in adult cohort and determine the distinction between adults and pediatric. 3) To identify biomarkers that correlate with a-KG.

Methods: The validation pediatric cohort came from the COG ASCT0031 cGvHD therapeutic trial, with 63 patient samples available, including 38 with cGvHD onset and 25 with no cGvHD. From the adult cGvHD biomarker study, 133 patients were enrolled, including 18 patients with cGvHD onset samples between 100 – 365 days post-HSCT, compared to 115 non-GvHD patients obtained at 3, 6, and 12 months post-HSCT. Plasma was separated from whole blood and examined using direct injection mass spectrometry with reverse-phase LC-MS/MS for ~142 metabolites. The non-GvHD controls only included those who had primary tolerance with no aGvHD or cGvHD. Differences in metabolite levels between cGvHD and non-cGvHD patients were compared using multiple regression and considered significant if a metabolite met all three of the following criteria: (1) p-value < 0.05; (2) effect ratio of ≥1.3 or ≤0.75; and (3) receiver operator characteristic AUC ≥0.60. We also performed correlative studies on the ABLE 1.0 cohort between a-KG or sCD13, two major markers previously found, for the closest associations with other cellular and cytokine/chemokine markers.

Results: In a mixed analysis, time-matching cGvHD onset samples compared to those who did not develop cGvHD, we validated the previous observations from the pediatric ABLE1.0 pediatric cohort in the pediatric ASCT0031 cohort with elevated a-KG, methionine-sulfoxide, and glutamic acid. In contrast, we could not validate the pediatric findings in the adult cohort. Instead, we found a significant decrease in trimethylamine N-oxide and 3-(3-hydroxyphenyl)-3-hydroxypropionic acid (HPHPA) at cGvHD onset in adults. (Table 1)

Analysis of the ABLE1.0 cohort found a strong correlation between a-KG and sCD13. Additional analysis of the cGvHD onset group identified strong positive correlations for a-KG with CD56dimCD69+_CD56+, CD27- NK cells ($t = 5.13$; $p = 6.0 \times 10\text{-}5$), CD45RA+_CD8+ T cells ($t = 6.72$, $p = 7.4 \times 10\text{-}7$), and CXCL11 ($t = 6.05$, $p = 6.5 \times 10\text{-}6$) at the onset of cGvHD.

Conclusion: We validated the previously identified metabolomic changes in the ASCT0031 pediatric validation cohort. Interestingly, we observed a different metabolomic pattern in adults with a decrease in trimethylamine N-oxide and HPHPA compared to the pediatric pattern. Despite the completely different patterns observed in adults, they may still affect similar pathways since kynurenine and indole acetic acid can signal through the aryl hydrocarbon receptor (AhR). The a-KG correlation analysis suggests that a-KG may play a role in natural killer (NK) cell activation or maturation as part of cGvHD development.

Metabolite	Effect Ratio (≥1.3 or ≤0.75)	P-value (≤ 0.05)	AUC (≥ 0.60)	ASCT0031 (status at onset)	ABLE1.0 (status at onset)	Adult (status at onset)
Methionine-Sulfoxide	1.48	5.26×10^{-4}	0.69	Increased	Increased	-
LYSOC26:1	1.30	1.35×10^{-2}	0.63	Increased	Increased	-
Glutamic Acid	1.44	2.62×10^{-2}	0.61	Increased	Increased	-
α-Ketoglutaric acid	2.64	1.42×10^{-6}	0.74	Increased	Increased	-
Kynurenine	1.42	3.93×10^{-2}	0.59	Increased	Increased	-
Trimethylamine N-oxide	0.66	1.43×10^{-2}	0.78	-	-	Decreased
HPHPA	0.49	1.85×10^{-2}	0.73	-	-	Decreased

S8.03 – Real-World Experience of Belumosudil Shows an Improvement of Modified Lee Symptom Score in Fibrotic Symptom Burden in Chronic GVHD Treatment

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Background: The modified Lee Symptom Score (mLSS) is a measure to reflect symptom burden in cGvHD patients with fibrotic manifestation. Belumosudil (BEL), a selective Rho-associated coiled-coil kinase 2 (ROCK2) inhibitor, is effective in chronic graft-versus-host disease (cGvHD) treatment, reversing fibrotic component. Its compassionate program has been available in Canada since March 2023. Herein, we present a preliminary result of serial changes in mLSS, response rates, and failure-free survival (FFS) following BEL treatment.

Methods and patients: This retrospective study evaluated the efficacy of BEL in 37 patients enrolled in the compassionate program from 4 Canadian centers.

The 7-day mLSS was serially captured in 28 patients at baseline and every 3 months. The summary score, sum of 7 domains and the fibrotic sum score (FSS; defined as the sum of the score for limited joint movement, difficulty swallowing solids and liquids, and thickened skin) were calculated and compared with the baseline score using a repeated measure based on general linear model (GLM).

Clinically meaningful improvement in mLSS was defined as reduction ≥ 7 points in overall mLSS, ≥2 reduction of sum of a domain mLSS, and ≥2 reduction of the FSS. Failure-free Survival (FFS) was defined as the time from starting BEL to the addition of new GVHD therapy, relapse, or death.

Results: Thirty-seven patients were treated with BEL, and 27 were evaluated for response with a minimum follow-up of 3 months. At the time of starting BEL, 25 (67.5%) patients had severe grade cGvHD, with a median of 4 (1-4) affected organs, and had received a median of 5 (2-10) prior lines of therapy. The median duration from cGvHD onset to BEL was 41 months (9-150).

With a median follow-up of 10.1 months (2–17), the overall response rate (ORR) at 3 and 6 months was 55.0% (n=15/27) and 69% (n=11/16). The 6-month FFS was 71.9%. Five patients discontinued treatment (n=2 for intolerance; n=2, GvHD progression requiring additional treatment; n=1, mortality due to pre-existing infection).

The mLSS score showed a statistically significant reduction over time (p=0.04): 28.7±2.4 (mean±S.E.), 22.9±2.9,

and 20.9±4.2 at baseline, 3, and 6 months. When compared to baseline, the mLSS was reduced by 6.6±1.3, 7.8±1.8, 11.4±5.0, and 15.8±4.5 at 3, 6, 9, and 12 months. The proportions of patients showing clinically meaningful improvement of the mLSS (≥7 points) were 59%, 75%, 60% and 100% at 3, 6, 9, and 12 months. Over 30% of patients showed clinically meaningful improvement (≥2 points) in skin, eyes/mouth, breathing, and joint/muscle domains.

In terms of the FSS, it showed a statistically significant reduction over time (p=0.002). In comparison to the FSS from baseline, the FSS was reduced by 1.4±0.5, 1.6±0.8, 3.8±0.6 and 3.2±0.6 at 3, 6, 9 and 12 months.

Conclusion: Our study showed a significant improvement in symptom burden based on the mLSS, particularly on fibrotic symptom burder with respect to the FSS over time. The importance of longitudinal monitoring of the mLSS are highlighted as a follow-up tool for cGvHD treatment.

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PP01.01 – Clinical determinants that impact regulatory natural killer cell frequency in healthy donor peripheral blood

Miss Tracy Ngo[1], Dr. Madeline Lauener[2], Dr. Sayeh Abdossamadi[1], Dr. Teesha Baker[1], Dr. Elena Ostroumov[1], Dr. Kirk Schultz[1]

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the infusion of a donor's stem cells into a recipient, to regenerate a healthy immune system. Unfortunately, in roughly one-third of pediatric and two-thirds of adult cases, donor immune cells attack the recipient's tissues. This results in chronic graft-versus-host disease (cGvHD), the leading non-relapse cause of diminished quality of life and has a 10-25% mortality rate.

Our lab identified that regulatory natural killer (NKreg) cells are strongly associated with the absence of cGvHD. Thus, large NKreg populations may prevent cGvHD. One approach to increase NKreg numbers is to adoptively transfer NKreg cells after transplantation, an approach that has already worked for Treg cells.

Purpose: To evaluate for clinical associations (age and sex) of [1] recipient and donor NKreg cells on the development of cGvHD, and [2] NKreg cell frequency in healthy donor peripheral blood, to identify optimal donors for clinical treatment.

Methods: Retrospective data was extracted from our ABLE study cohort. Blood samples collected 100 days post-transplant (117 pediatric patients) were analyzed for NKreg and cytotoxic NK (NKcyt) cells, and correlated with donor sex and recipient age (pre- and post-puberty).

NKregs and NKcyts are isolated from 20 buffy coat samples, from the Canadian Blood Services. Peripheral blood mononuclear cell, NK cell, and NKreg and NKcyt cell counts were recorded. NKregs and NKcyts were sorted using FACS.

T-tests/Mann-Whitney U tests were used for statistical analyses.

Results: Retrospective Analysis – Mean NKreg:NKcyt cell ratios were compared for the impact of recipient puberty and sex as well as the impact of donor sex. For recipients, comparisons between females < 10.9 to ≥ 10.9 and cGvHD males < 12.4 to ≥ 12.4 showed no significant differences ($p > 0.05$). The comparison between no GvHD males < 12.4 to ≥ 12.4 showed a significant decrease in post-puberty males ($p < 0.05$). There was no significant difference in NKreg cell frequency between recipient sex. There was a significant decrease in NKreg cell frequency in cGvHD males and females, compared to those who did not develop GvHD. For donors, there was no significant difference between recipients, when comparing male to female donors.

Prospective Analysis – Comparison of mean NKreg:NKcyt cell ratios between males > 35 (n=4), males < 35 (n=4), females > 35 (n=4), and females < 35 (n=8) showed no significant differences.

Conclusions: Donor age and sex do not significantly impact NKreg frequency, suggesting that these factors do not restrict donor selection. Future studies should explore genetic correlations such as polymorphisms (SNPs) to further explore NKreg variability found in healthy donors.

PP02.01 – Reproducibility of new Myoton users to measure sclerotic cutaneous chronic Graft versus Host Disease

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[1]Sarah Cannon Transplant and Cellular Therapy At Methodist, San Antonio, United States, [2]National Cancer Institute, NIH, Bethesda, United States, [3]Oak Ridge National Laboratory, , United States, [4]Vanderbilt University Medical Center, Nashville, United States , [5]Fred Hutchinson Cancer Center,, Seattle, United States

Background: Sensitive and reproducible quantitative measures of sclerotic cutaneous chronic graft-versus-host disease (scGVHD) remain an urgent unmet need. Currently sclerotic changes are described in qualitative terms related to thickening, pliability, color, and adherence to underlying tissues using the 2014 NIH consensus criteria. The current qualitative skin grading system is poorly suited to detect responses in established sclerosis. Therefore, validation of novel tools for better measurement and documentation of change in skin sclerosis is an area of urgent need. The Myoton (MyotonPRO) is a non-invasive handheld device that has been clinically validated as a reliable measure of soft tissue biomechanical parameters by delivering a mechanical impulse. Preliminary data support the use of the Myoton for quantitative assessment of scGVHD severity.

Purpose: In this study, we aimed to examine the interobserver reproducibility of the Myoton for measuring skin biomechanics and quantifying skin sclerosis.

Methods: 31 adults (≥ 18 years of age) with scGVHD after allogeneic hematopoietic cell transplantation (HCT) were studied. The Myoton was used to measure five biomechanical and viscoelastic properties of soft tissues at 7 bilateral sites (14 anatomic sites in total). After reviewing a written standard operating procedure (SOP) manual and practicing on each other, two study personnel independently performed Myoton measurements on patients in the supine position. The locations measured were marked for the second assessor in the first nine participants but not in subsequent patients. For each participant, averages of an observer's measurement across all anatomical sites were calculated and compared between observers. We focused on oscillation frequency and mechanical relaxation time. The mean pairwise difference (MPD) U-statistics were used to measure the mean disagreement among the two observers.

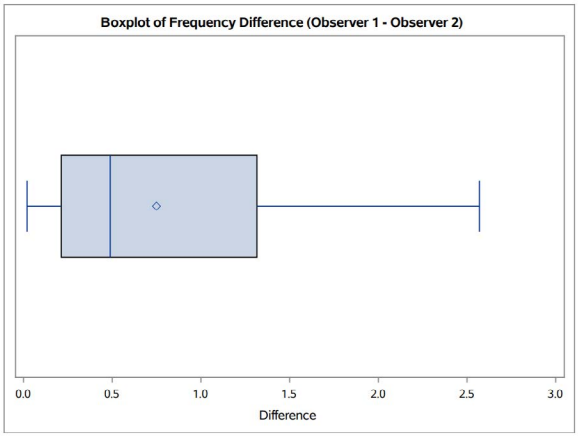
Results: The median age of the study population was 62 years (range 30-70) and 58% were men. The median time from HCT was 6.4 years (range 1.7-18.5). Patients were heavily pretreated with a median of 4 prior lines of therapy (range 1–14). The interobserver MPD were less than 10% of the average overall values for both Myoton parameters. The mean relaxation time for the 2 observers was 18.85 (STD 3.04) and 18.80 (STD 3.01) milliseconds. The overall interobserver MPD for relaxation time was 0.75 (STD 0.69, range [0.02 – 2.57]) milliseconds. The mean frequency was 20.26 (STD 3.01) and 20.29 (STD 3.14) Hertz. The overall interobserver MPD for frequency was 0.53 (SD 0.48, range [0.01– 1.57]) Hertz. Marking the area of interest did not have an impact on interobserver MPD.

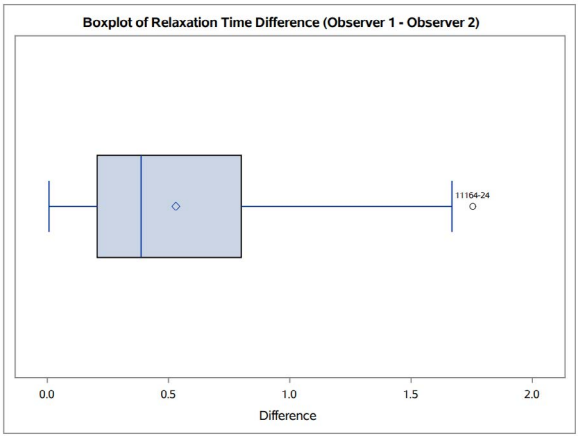
Conclusion: In this study, the Myoton exhibited high interobserver reproducibility in measuring 2 different biomechanical parameters, frequency and relaxation time, characterizing scGVHD. Further prospective longitudinal study is underway to assess the Myoton's ability to measure change in scGVHD.

Table 1: Interobserver reproducibility of Myoton measurements across two observers in patients with skin sclerotic chronic GVHD

	Overall (n = 31)						
	N	Mean	SD	Min	P25	P75	Max
Observer 1 - Frequency (Hz)	31	20.26	3.01	14.80	18.42	21.34	28.53
Observer 2 - Frequency (Hz)	31	20.29	3.14	15.11	18.61	20.95	29.08
Frequency Absolute Difference (Observer 1 - Observer 2)	31	0.75	0.69	0.02	0.21	1.32	2.57
Observer 1 - Relax Time (ms)	31	18.85	3.04	11.98	17.20	20.50	25.21
Observer 2 - Relax Time (ms)	31	18.80	3.01	11.60	17.72	20.07	24.51
Relaxation Time Absolute Difference (Observer 1 - Observer 2)	31	0.53	0.48	0.01	0.21	0.80	1.75

Figure 1. Box-and-whisker plot of interobserver mean pairwise difference (MPD) in skin frequency and relaxation time measurements using MyotonPRO.





PP02.02 – Erosive tarsal conjunctival inflammation leads to fibrosis in the early development of ocular graft-vs-host disease

Marcus Kohnstam[1], Dr. Pier Luigi Surico[1,2], **Dr. Zhonghui Luo**[1]
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Background: Ocular Graft-vs-Host disease (oGVHD) affects more than half of patients following allogeneic stem cell transplantation (allo-HSCT). The disease onset and the pathogenesis of oGVHD are not well understood.

Purpose: Taking advantage of the large number of clinical encounters with post-allo-HSCT patients in our clinic, we hoped to identify triggers and explore clinical signs and symptoms of early oGVHD development, to allow earlier detection of this devastating disease.

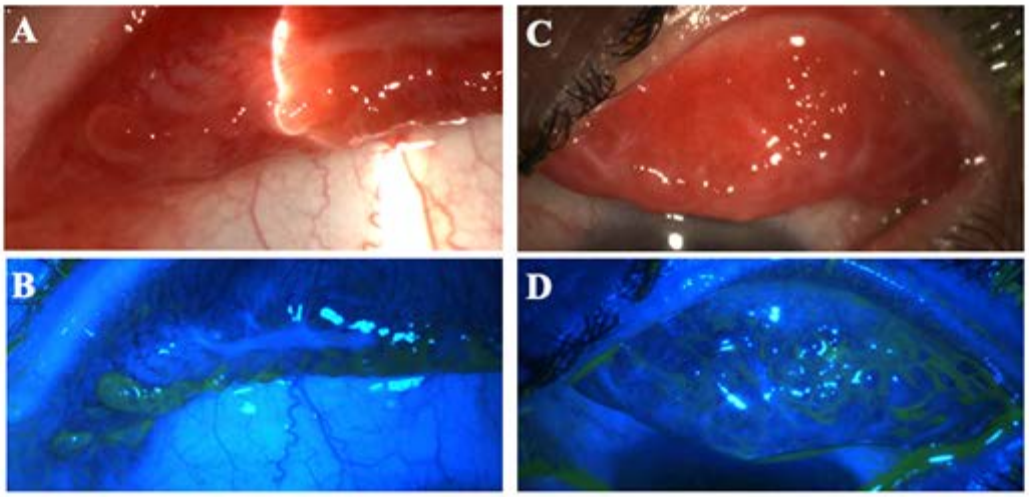
Methods: The records of post-HSCT patients seen consecutively in a 1-year span in a single provider clinic were reviewed. The history, symptoms, and clinical findings of the patients with distinctive erosive tarsal conjunctival inflammation (ETCI) were analyzed.

Results: Out of 228 patients screened, 19 had clinically witnessed ETCI in at least 1 eye during the period.

Twelve (63%) patients had a never-before-described nodular erosions on the subtarsal conjunctiva; 7 (37%) had previously reported pseudomembranous erosions. The ocular symptom onset was within 1 month after immunosuppression (IS) taper or vaccination or donor lymphocytes infusion (DLI) in 16 of the 19 patients. While 16 (84%) patients reported painless mucous discharge, only 9 (47%) reported dryness as the initial symptom. Within 6 months, only 4 (21%) had discharges but 15 (82%) patients endorsed dryness. Subepithelial conjunctival fibrosis followed ETCI immediately at the same location. Corneal punctate staining and dry eye sensation increased with time, while tear production decreased.

Conclusion: The ETCI described is likely one of the earliest detectable findings of oGVHD and triggered by certain immunogenic events. Ocular symptoms of wet mucous discharge should be considered a warning sign for oGVHD activation, particularly so when it occurs shortly after IS taper, DLI and vaccination.

Fig.1



PP02.03 – Early Changes in Marrow Microenvironment after Hematopoietic Stem Cell Transplant in Pediatric Acute Lymphoblastic Leukemia Associated with cGvHD and Relapse

Dr. Catherine Njeru[1], Bernard Ng[1], Vaishnavi Parthasarathy[1], Sayeh Abdossamadi[1], Dr. Chia Huan Ng[1], Dr. Kirk R Schultz[1]

[1]*University of British Columbia, Vancouver, Canada*

Background: Hematopoietic stem cell transplant (HSCT) is a well-established therapy for inducing graft versus leukemia (GvL) effects to attain durable remissions in ALL patients. However, the success of HSCT is limited by chronic graft versus host disease (cGvHD), an off-target complication with multisystem effects that can cause major disability and increased mortality. A better understanding of immune changes in the marrow microenvironment can help guide therapies in reducing the burden of cGvHD and potentially enhancing the GvL effect.

Purpose: The purpose of this study was to investigate early transcriptome changes in day 60 - 100 post HSCT marrow microenvironment that are associated with cGvHD and GvL.

Methods: Post HSCT pediatric ALL patients' day 60-100 bone marrow samples archived in the British Columbia Children's Hospital (BCCH) BioBank were evaluated. Comprehensive clinical data was acquired

through Cerner Power chart, which was used to determine cGvHD or relapse status after day 100. Immune profiling of marrow aspirates was done using BDTM single-cell multiplexing kit and BDTM AbSeq Ab-Oligos for 14 patients. Single cells were captured using the BD RhapsodyTM single-cell analysis system. Single cell RNA (scRNA) libraries were sequenced using illumina NovaSeq. We clustered the scRNA data into 26 cell types and generated pseudobulk estimates of their expression levels for each patient. We then contrasted the pseudobulk expression of cGvHD with non-cGvHD patients, as well as examined the effects of relapse. Significance was declared at an α of 0.05 with false discover rate (FDR) correction.

Results: Among the differentially expression genes (DEG), PI3Kinase (p= 4.16e-05) in CD4+ T cells showed the strongest positive association with cGvHD after day 100 (Figure 1). Other DEGs positively associated with cGvHD included GAPDH (p= 0.00151), IFITM3 (p= 0.000285), and XBP1 (p=0.000755) in plasma cells; and S100A9, or calprotectin, a monocyte associated inflammatory marker (p=0.000320). DEGs negatively associated with cGvHD included FAM129C (p=0.00136), IGKC (p= 0.00452), IRF4 (p=0.00240), ITGAE (p=0.00744), and LYN ((p=0.00248) in plasma cells; IGHM-membrane (p=0.00102), LYN (p=0.000551), IGHG-secreted (p=0.000562), and IGHG2-secreted (p=0.000118) in mature B cells; and CD79A (p=0.000567) in CD16+ monocytes. ALL relapse after day 100 was associated with decrease in a T cell function marker, TRBC2 (p= 0.000247); B cell function markers, MS4A1 (p= 0.000503), IGKC (p=0.000445), and LYN (p= 0.000361); and a gene involved with CD20 expression, SLC7A7 (p= 0.000566).

Conclusion: This discovery phase study has identified differential expression of specific cell populations in the early (day 60 – 100) post HSCT marrow of pediatric ALL patients that are associated with cGvHD and GvL. While the found DEGs suggested activation and inflammatory responses in T and B cells as expected in cGvHD, there also appears to be an aberration in BCR signaling (decreased LYN, CD79A) and B cell homeostasis resulting in decreased IgG and IgM production (decreased IgHM. IgHG1, IgHG2). Common in both cGvHD and relapse was a negative association with DEGs involved in B cell function and maturation (LYN, IgKC). The over expression of PI3Kinase in cGvHD suggested a novel target that should be pursued further in treatment of cGvHD.

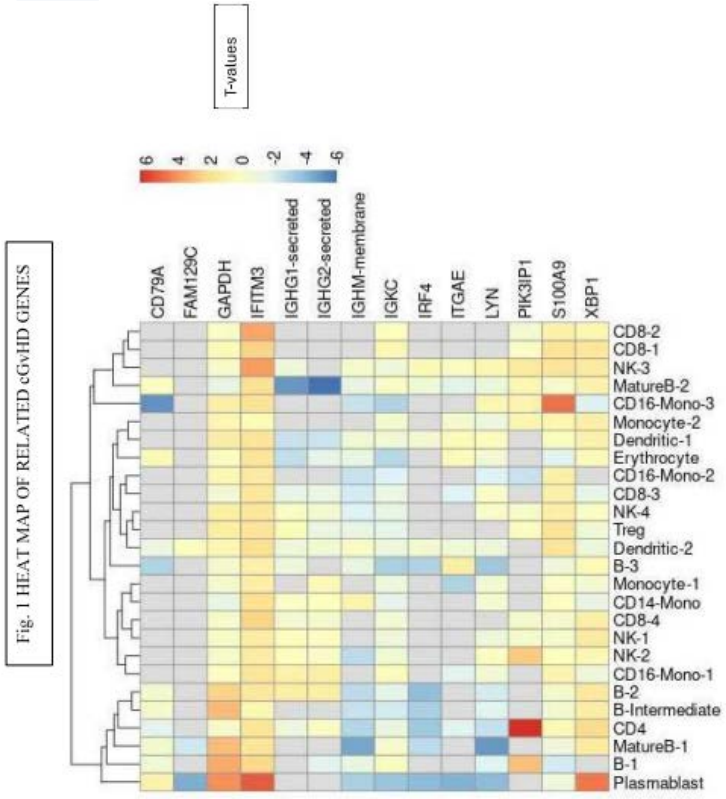


Fig. 1 HEAT MAP OF RELATED cGvHD GENES

PP02.04 – Description of patients and management of cGVHD in France based on natural language processing (NLP) from hospital electronic medical files

Dr Sandrine Colas[1], Dr Véronique Gilles[1], Dr Sylvain Chantepie[2], Dr Etienne Daguindau[3], Dr Anne Huynh[4], Dr Michael Loschi[5], Dr Marie Robin[6], Mrs Nicole Raus[6], Mrs Carole Requillard[7], Ms Lisa Chuttoo[7], Ms Aliette Poplu[7], Dr. Noemie Allali[1], Dr Darko Kiprijanovski[1], Mr Franck Le Ouay[7], Mrs Viviane Jeanbat[8], Mr Justin Kirion[8], Ms Juliette Cottin[8], Dr Nimrod Buchbinder[9], Dr Sylvie François[10], Dr Alban Villate[11], Dr Stephane Bouee[8]

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Backgound: Chronic Graft Versus Host Disease (cGVHD) is the most common and serious complication following allogenic hematopoietic stem-cell transplantation (allo-HSCT). In Europe, there is no agreed-upon standard of care or preferred therapeutic agents for patients who have failed second line of systemic therapy (LOT).

Purpose: The main objective of this study was to describe patient characteristics and their cGVHD treatment patterns by LOT, by using an innovative approach based on an artificial intelligence natural language processing (AI-NLP) method to structure data.

Methods: A cohort of cGVHD patients was identified from the medical records as follows: the AI-NLP scanned all electronic medical records of patients who had received an allo-HSCT, identified patients with a cGVHD diagnosis and at least 12 months follow-up after onset of cGVHD (eligibility criteria) and used relevant information to derive and infer the variables.

To ensure completeness and accuracy of the NLP derived data, a three-step quality check was performed: 1) review by clinical research associate (CRA) 2) comparison with the European Bone Marrow Transplant (SFGM-TC) registry 3) validation by investigator experts.

Results: Among 306 screened allo-HSCT patients' medical files, 20 met the eligibility criteria, whose data were extracted with NLP. In the cohort, 60.0% were men; mean age at allo-HSCT was 49.6 years.

Reasons for allo-HSCT were acute myeloid leukaemia (50.0%), non-Hodgkin's lymphoma (27.8%), acute lymphoblastic leukaemia (11.1%).

Median delay between allo-HSCT and cGVHD was 128 days (mean: 245.1 days).

Eight patients had severe cGVHD (unknown severity for 9 patients).

Organs involved were: skin (65%), mouth (40%), gastrointestinal (40%), liver (15%), lung (10%), eye (5%).

Agents used were:

- LOT-1: corticosteroids (41.2%), ruxolitinib (29.4%), cyclosporine (11.8%), mycophenolate (11.8%), sirolimus (5.9%);
- LOT-2: ruxolitinib (60.0%), vedolizumab (20.0%), methotrexate (10.0%), mycophenolate (10.0%);
- LOT-3: Belumosudil (57.1%), infliximab (14.3%), methotrexate (14.3%), ruxolitinib (14.3%).

Eight patients received at least 3 LOTs at the time of analysis.

The completeness of data varied according to nature of the variables: sociodemographic characteristics and cGVHD treatments (100%), graft characteristics (>75%), mostly depending on the information documented in the medical records.

The review by CRA did not lead to discordance except for the cGVHD treatments, for which some adjustments were needed.

The comparison with SFGM-TC registry showed high concordance rates with the NLP derived data: stem cell source, donor gender and type (100%), allo-HSCT indication (94%) and date (89%), CMV positivity (87%), conditioning and prophylactic treatment of cGVHD (78%).

Validation by the experts is still ongoing.

Conclusion: This study, using an innovative AI-NLP process, provides a first insight into the real-world management of cGVHD in France.

PP02.05 – Evaluation of clinical trial efficacy endpoints in chronic graft-versus-host disease (cGVHD)

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Background: Overall response rate (ORR) within 6 months of treatment has been an endpoint accepted by regulatory agencies to determine the clinical benefit of new therapies for the treatment of chronic graft-versus-host disease (cGVHD). However, due to the number of approved therapies for cGVHD, this endpoint does not help differentiate the efficacy of existing and new therapies. An endpoint that includes clinically relevant assessments and the durability of those responses is important. Assessment at 1 year

of failure-free survival (FFS) with or without complete or partial response are examples of composite endpoints for cGVHD that have been shown to be good approaches to determining both clinical benefit and response durability. However, composite endpoints can be difficult to interpret, and heterogeneity in the clinical definitions among various clinical trials can complicate the assessment of therapeutic benefit. Thus, there is a need for further review of acceptable endpoints and the timing of these assessments in cGVHD studies.

Purpose: To identify the breadth and characteristics of clinical trial efficacy endpoints in pivotal cGVHD studies and compare them with efficacy assessments for regulatory approval.

Methods: Primary publications of pivotal clinical trials for novel cGVHD treatments were identified. The patient population as well as primary and other (ie, secondary or exploratory) endpoints from each study were extracted and compared with regulatory endpoints included in the US prescribing information.

Results: Efficacy endpoints from AGAVE-201 (randomized phase 2 study for axatilimab), ROCKstar (randomized phase 2 study for belumosudil), REACH3 (randomized phase 3 study for ruxolitinib), and a phase 1b/2 study for ibrutinib are summarized in the Table. FFS was included as a composite endpoint in most trials; event-free survival was infrequently used. Notably, cGVHD studies did not typically include central review assessments of ORR, which may result in inconsistent assessment of patient responses.

Conclusions: The infrequent use of event-free survival as a composite endpoint in cGVHD studies may be attributable to challenges in selecting a definition that is clinically meaningful for cGVHD. Additionally, the optimal timing for endpoint assessment is unknown. Although shorter lengths of time may be sufficient for the assessment of anti-inflammatory activity, longer assessments of ≥1 year may be needed to assess antifibrotic activity. Expert evaluation and additional discussion of completed cGVHD studies are needed to inform the design of future clinical trials for cGVHD.

Table. Study population and efficacy endpoints included in pivotal cGVHD studies

Drug (Study)	Prior Systemic cGVHD Therapies	Primary Endpoint of Study	Endpoints for US Regulatory Approval (year)*	Other Efficacy Endpoints
Axatilimab (AGAVE-201)1	≥2	ORR through Cycle 7 Day 1†	—	mLSS‡; DOR; FFS; OS; organ-specific responses†; TTR; CS dose reductions
Belumosudil (ROCKstar)2	2–5	Best ORR at any time†	ORR through Cycle 7 Day 1 (2021)	mLSS‡; DOR; FFS; OS; organ-specific responses†; TTR; CS dose reductions
Ruxolitinib (REACH3)3	1	ORR at Week 24†	ORR through Cycle 7 Day 1 (2021)	mLSS‡; DOR; FFS; ORR up to Week 24*; OS; organ-specific responses†; change in CS dose over time
Ibrutinib (Phase 1b/2 study [NCT02195869])4	≥1	Best ORR at any time†	Best ORR at any time; SRR at any time (2017)	LSS‡; SRR ≥20 weeks; change in CS dose over time

cGVHD, chronic graft-versus-host disease; CS, corticosteroid; DOR, duration of response; FFS, failure-free survival; LSS, Lee Symptom Scale; mLSS, modified Lee Symptom Scale; NIH, National Institutes of Health; ORR, overall response rate; OS, overall survival; SRR, sustained response rate; TTR, time to response.

1. Wolff D, et al. *Blood*. 2023;142(Suppl_1):1. 2. Cutler C, et al. *Blood*. 2021;138(22):2278-2289. 3. Zeiser R, et al. N *Engl J Med*. 2021;385(3):228-238. 4. Miklos D, et al. *Blood*. 2017;130(21):2243-2250.

Composite endpoints are underlined.

* Efficacy endpoints included in the US prescribing information for approved products and year of first cGVHD approval.
† Partial or complete response by NIH 2014 cGVHD consensus criteria.
‡ ≥7-point improvement from baseline.

PP02.06 – Treatment of steroid-refractory Graft-versus-Host Disease is associated with Significant Decline in Hemoglobin Level but Only in Non-Responders Patients

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Background/Purpose: Graft-versus-host disease (GVHD) is a common complication after allogeneic hematopoietic cell transplant (allo-HCT). Ruxolitinib (a JAK 1/2 inhibitor) has become the standard of care for the treatment of steroid refractory acute GVHD (SR-aGVHD). However, cytopenias are a frequent adverse event (AE), as JAKs are necessary for hematopoietic growth factor signaling. Furthermore, GVHD itself is also associated with bone marrow suppression. Little is known about hematologic trends in GVHD patients who achieve response to JAK1/2 inhibitor therapy.

Methods: We conducted a retrospective study evaluating 57 allo-HCT patients with steroid-dependent (SD) or steroid-refractory (SR)-GVHD who were treated with ruxolitinib from 02/2017 to 05/2023. Patients were classified clinically as standard or high-risk acute GVHD, and counts were assessed pre-treatment and at

day 28. Complete blood counts (CBCs) at baseline and day 28, along with change in CBC from baseline, were compared across groups using either a t-test or a paired t-test. Significance was defined as a p-value <0.05.

Results: Most patients received a peripheral blood stem cell graft with calcineurin inhibitor-based GVHD prophylaxis for the treatment of hematologic malignancies (Table). At the time of ruxolitinib initiation, 30 patients (53%) had standard-risk, and 27 patients (47%) had high-risk aGVHD. Counts were first assessed at baseline, prior to ruxolitinib initiation. While high-risk patients had a lower median hemoglobin (hgb) at baseline (10.3 vs. 8.8, p= 0.011), median platelet (plt) counts were similar between the two cohorts (120,000 vs. 87,000, p= 0.14). WBC, ANC, and ALC did not differ between high-risk and standard-risk patients. We next assessed counts 28 days after ruxolitinib initiation and found that standard-risk patients maintained stable hgb counts (p= 0.95, Fig. 1A), while high-risk patients exhibited a significant decline (p= 0.034, Fig. 1B). Both standard and high-risk patients had overall decreases in their plt counts (standard-risk p= 0.001; high-risk p= 0.009). Finally, we analyzed count trends in patients stratified by response to ruxolitinib therapy. Baseline hgb and plt counts were not significantly different between complete and non-responders; however, non-responders showed an average drop in hgb at day 28 (average delta hgb -0.60), while complete responders showed an average increase (average delta hgb 0.60) (p= 0.011, Fig. 1C). Both complete and non-responders showed an average drop in platelet count (-12 vs. -82, p= 0.13).

Conclusion: Patients with SD- or SR-aGVHD often have cytopenias prior to treatment with ruxolitinib. Our results show that standard-risk patients tend to maintain stable hgb during ruxolitinib therapy, while high-risk patients show significant declines in their hgb level. When patients were stratified by response (rather than risk), this effect was primarily seen in non-responders. Both standard and high-risk patients are at risk for worsening thrombocytopenia, regardless of response. Worsening hemoglobin level may therefore serve as a biomarker for treatment failure. Further prospective studies and cellular/molecular analyses are needed to better elucidate the complex interaction between JAK1/2 inhibitor therapy and bone marrow suppression in GVHD.

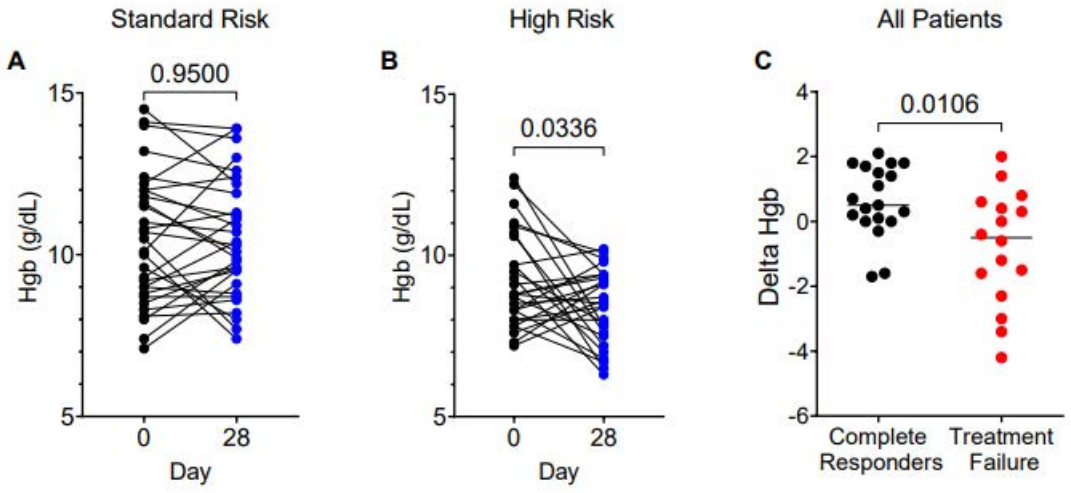

Figure 1: A, B - Hgb trend between day 0 and day 28 after ruxolitinib initiation for standard (A) and high risk (B) patients (paired two-tailed t-test). **C -** Comparison of delta hgb (day 28 - day 0) between complete responders and treatment failure (mixed response, no response, progression) (unpaired two-tailed Welch's t-test).

Table 1: Patient Characteristics

HCT Date	2017-2022
Median day of GVHD diagnosis	30 (14-90)
Median age at HCT	58 (25-74)
Race, n (%)	
Asian	2 (4)
Black	6 (10)
White	45 (79)
Unknown	4 (7)
Sex, n (%)	
Male	40 (70)
Indication for HCT, n (%)	
Acute Leukemia	27 (47)
Lymphoma	14 (25)
MDS/MPN	12 (21)
Multiple Myeloma	4 (7)
Graft Source, n (%)	
BM	4 (7)
PBSC	45 (79)
Double cord blood	8 (14)
Donor Type, n (%)	
Related identical	9 (16)
Related haploidentical	4 (7)
Related nonidentical	3 (5)
Unrelated identical	26 (46)
Unrelated nonidentical	15 (26)
Conditioning Regimen, n (%)	
Myeloablative	14 (25)
Reduced intensity	43 (75)
GVHD Prophylaxis, n (%)	
CNI/MTX +/- other*	32 (56)
CNI/MMF +/- tocilizumab	10 (18)
Cyclophosphamide-based	11 (19)
T-cell depletion	4 (7)

*Other: 3 sirolimus, 1 abatacept, 1 MMF

PP02.07 – Vitamins B12 and folate deficiencies in gastrointestinal chronic graft-versus-host disease

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Background: Since human organisms cannot synthesize vitamin B12 and folic acid, they must be supplemented with oral intake. Gut lesions caused by gastrointestinal chronic graft-versus-host disease (GI cGvHD) may affect vitamin absorption, while active inflammation leads to a higher demand. Moreover, patients with GI cGvHD often avoid vitamin-rich products for fear of worsening symptoms following consumption and dietary restriction.

Purpose: The study aimed to assess the prevalence of vitamin B12 and folate deficiencies in patients with GI cGvHD.

Methods: A retrospective, single-center analysis of allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients, who were transplanted in 2014-2022 for haematological malignancies and have been under outpatient care. All patients with GI cGvHD were diagnosed during the first year after transplantation, and they had been receiving immunosuppressive treatment at the point of evaluation.

Vitamin B12 and folic acid levels were assessed at one year after transplantation.

Levels of vitamin B12 were referred to the National Health and Nutrition Examination Survey and defined in two cut-offs: low level below 200pg/ml and marginal<300pg/ml. Folate deficiency was defined as a serum level below 3.9ng/mL. Diagnosis of anemia were defined according to World Health Organization criteria. The severity of cGVHD was determined according to the National Institutes of Health criteria2014.

Results: Eighty-one patients, 44(54%) males, with a median age at allo-HSCT of 45.6 years (range 18- 69) transplanted from HLA-identical siblings (N=30(37%), matched unrelated donors (N=38(47%), mismatched unrelated donors (N=9(11%), and haploidentical related donors (N=4(5%). There were 50(63%) patients, who received myeloablative conditioning(MAC), 21(26%) reduced-intensity conditioning(RIC), and 4(5%) non-myeloablative conditioning(NMA).

In this group, 42 patients suffered from GI cGVHD, including 12(28%) with moderate and 30(72%) severe global severity cGvHD score (GI tract severity: score 1- 25(59%), score 2- 12(29%) and score 3-5(12%) patients. Diagnosis of GI cGVHD was established by histopathology in 15 patients(likely- 9, possible-6).

The control group included 39 patients, including 13(33%) with no cGvHD and 26(67%) with cGvHD (14-mild, 5-moderate, 7-severe) involving other organs (no GI tract).

More than 95% of patients with cGvHD had been treated with CNI and GCS (local or systemic), and two have been receiving methotrexate additionally. Among GI patients, 23 had gastrointestinal colonization with multidrug-resistant bacteria, including 6 with Clostridioides difficile.

A low level of B12 deficiency was detected in 6/42(14%) patients in the GIcGvHD group and in 0/39 control group. The marginal level of B12 deficiency was observed in 25/42(59%) of GIcGVHD group and in 6/39(15%) control patients.

A low level of folic acid, requiring supplementation, was confirmed in 37/42(88%) GIcGvHD patients and 19/39(48%) patients in the control group.

Anemia was diagnosed in 22/42(52%) GIcGvHD patients, which was mostly macrocytic(77%). While most had iron overload, 4 patients with GIcGVHD had iron deficiency.

Conclusions: Our study revealed that patients with GI cGvHD are at higher risk of B12 and folic deficiencies one year after transplantation and these deficiencies may contribute to anemia frequent in these patients. The current observation warrants further studies and may indicate the need of vitamin level assessment in posttransplant care and supplementation when required.

PP02.08 – Sirolimus as add-on therapy to steroids for moderate-severe chronic graft versus host disease

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Introduction: Chronic graft versus host disease (GVHD) remains the Achilles heel of allogeneic hematopoietic cell transplantation (HCT). The first-line treatment of moderate-severe chronic GVHD involves systemic steroids with/ without calcineurin inhibitors. Around half of these patients will need second-line agents for steroid-refractory/dependent GVHD. We report here our experience using sirolimus as an add-on agent to steroids in moderate-severe chronic GVHD.

Methods: This was a center partial retrospective and prospective study of all consecutive allogeneic cell transplant recipients from 2016-2022. The diagnosis and severity of chronic GVHD were as per the NIH-2014 criteria. Sirolimus was added to a standard steroid taper for moderate to severe chronic GVHD at the physician's discretion. Sirolimus dosing was done per target trough levels of 7-12 ng/ml. The GVHD response was classified as per EBMT-NIH-CIBMTR criteria.

Results: Out of 134 HCT recipients chronic GVHD occurred in 66 (49.2%) recipients during the study. Chronic GVHD was mild in 13 (9.7%) and moderate-severe in 53 (40.2%) recipients. Sirolimus was used in 38/53 (71.6%) patients having moderate-severe chronic GVHD. It was used as primary treatment with steroids in 25 (66%) and as a second-line agent in steroid-dependent/ refractory cases in 13 (34%) recipients. The median age of this cohort was 25.5 years (IQR 21-36). Most patients had malignant conditions and received myeloablative conditioning (60%). There was an equal proportion of matched-related (53%) and haploidentical HCT (47%). All haplo-HCT recipients received post-transplant cyclophosphamide as GVHD prophylaxis. The median time to onset of chronic GVHD was 140 days (IQR 108-182). The onset was de novo in 14 (37%), quiescent in 15 (39%) and progressive in 9 (24%). The GVHD organ severity score of ≥ 2 involved the skin (58%), mouth (55%), and liver/ gastrointestinal tract (40%) of the recipients. Lung GVHD occurred in 13% of recipients. The median duration on sirolimus was 283 days (134-640). Chronic GVHD was controlled in 25 (66%), resolved in 5 (13%), and active in 8 (21%) recipients at 6 months. There were two deaths and relapses each. Two recipients each required another agent for severe adverse events (Thrombotic microangiopathy-acute kidney injury) and steroid-refractory/dependent GVHD. Dyslipidemia was the most typical (73%) adverse event related to sirolimus but was manageable using lipid-lowering therapy. The overall failure-free survival at 3-years was 68%. The 3-year overall survival was 70%.

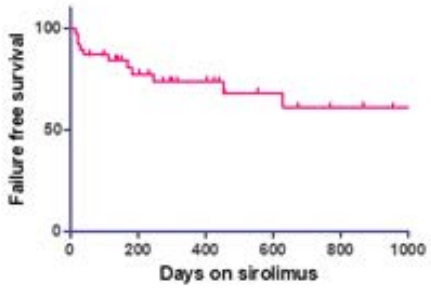
Conclusion: This study demonstrates the safety and efficacy of sirolimus as an add-on agent to systemic steroids in managing moderate-severe chronic GVHD. This strategy has the potential to reduce the burden of steroid-refractory/ dependent chronic GVHD.

Table 1. Sirolimus for moderate-severe chronic GVHD

Characteristics		N=38
Age	Median (IQR) years	25.5 (21-36)
Sex	Males	29 (76%)
	females	9 (24%)
Diagnosis	Acute myeloid leukemia/ myelodysplasia	15 (39%)
	Acute lymphoid leukemia	13 (34%)
	Others	8 (27%)
Conditioning	Myeloablative	23 (60%)
	Reduced intensity/ non-myeloablative	15 (40%)
Type of HCT	Full matched -related donor	20 (53%)
	Haplo-HCT	18 (47%)
GVHD prophylaxis	Cyclosporine + methotrexate	20 (53%)
	Cyclosporine + mycophenolate+ post-transplant cyclophosphamide	18 (47%)
Acute GVHD	Grade 2-4	15 (40%)
	Response	13/15 (87%)
	Dependent/refractory	2/15 (13%)
Chronic GVHD	Quiescent	15 (39%)
	Progressive	9 (24%)
	De-novo	14 (37%)
Time to onset of cGVHD	Median (IQR) days	140 (108-182)
Organ scores	Skin 2/3	22 (58%)
	Mouth 2/3	21 (55%)
	Lungs 1-3	5 (13%)
	Liver/GI 2/3	15 (40%)
Sirolimus indication	Corticosteroid-dependent/refractory	13 (34%)
	Primary treatment	25 (66%)
Response at 6 months	Resolved	5 (13%)
	Controlled	25 (66%)
	Active	8 (21%)
Adverse events	Dyslipidaemia	22/30 (73%)
	Thrombotic microangiopathy/ renal dysfunction	2 (5%)
Days on sirolimus	Median (IQR)	283 (134-640)
Failure-free survival	3-year	68%
Overall survival	3-year	70%

HCT: hematopoietic cell transplantation, GVHD: graft versus host disease, IQR: interquartile range

Figure 1: Failure-free survival after sirolimus for moderate-severe cGVHD



PP02.09 – Real-world experience study of belumosudil in steroid-refractory chronic graft-versus-host disease (cGVHD) demonstrated high treatment response and preserved immune function

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Background: cGVHD is a frequent complication after allo-HCT. Approximately 50% of patients with steroid-refractory (SR) or -dependent (SD) disease respond to second-line therapies. Belumosudil is an inhibitor of Rho-GTPase-associated coiled-coil kinase 2 (ROCK2), approved after failure of more than 2 lines of therapy in cGVHD. Despite its approval, real-world data about its use is lacking in the literature.

Methods: We conducted a retrospective single-center analysis in a high-volume transplant center in the United States. We evaluated 67 allo-HCT recipients with SR/SD cGVHD treated with belumosudil from 03/2021 to 04/2024. Patients who received combined therapy with belumosudil and ruxolitinib were included in the analysis. Immune function was assessed in a cohort of patients (n= 11) at treatment baseline and subsequent timepoints during therapy.

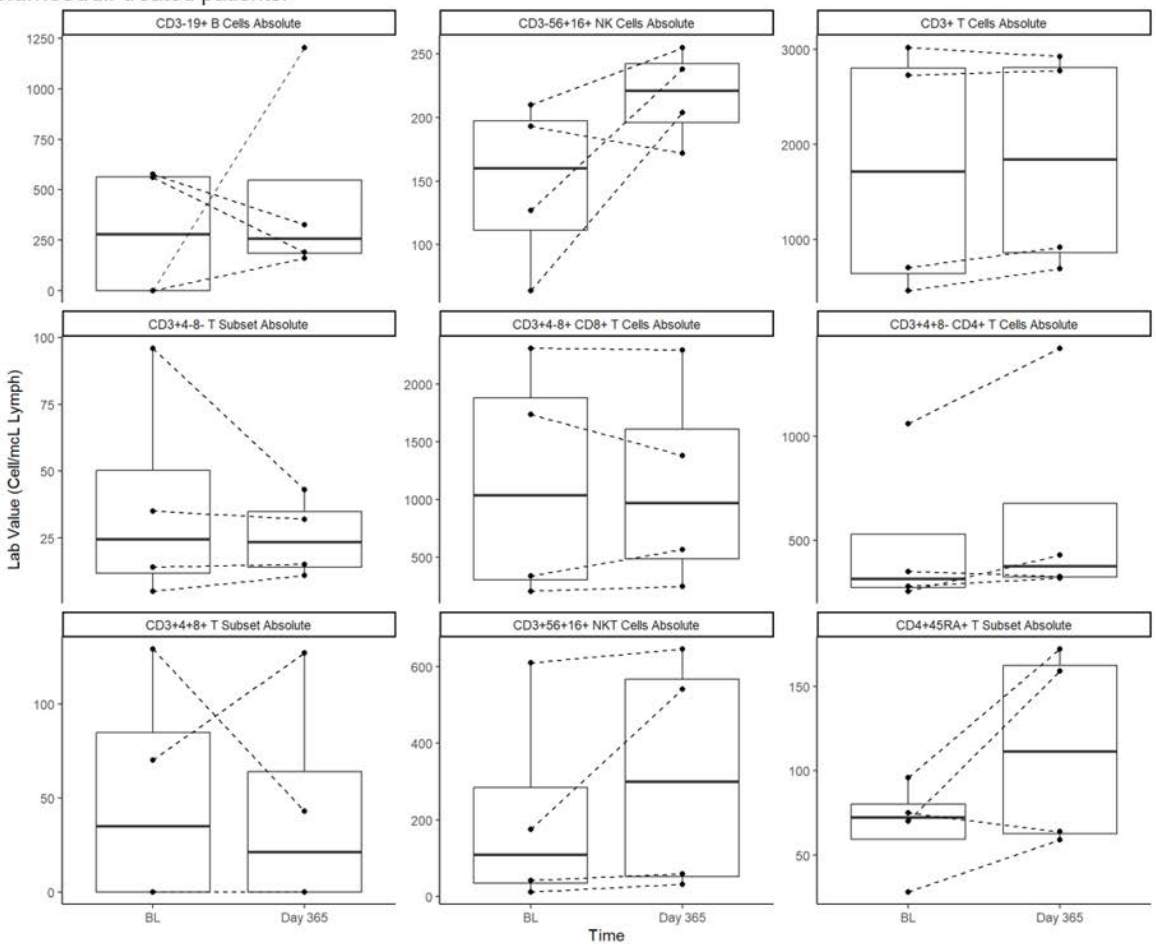
Results: The median age was 57 years (range 44-65) and 47 (70%) were male. Most patients received an unmodified peripheral blood stem cell graft and had calcineurin inhibitor-based GVHD prophylaxis (Table). At baseline, most patients had moderate to severe multi-organ cGVHD involvement, and the most common organ involved was the skin. Forty-eight (72%) patients were previously treated with ruxolitinib. Treatment combination with ruxolitinib occurred in 16 (24%) patients. Among evaluable patients, the 6-month overall response rate (ORR) was 61% (complete response [CR] 4.5%, partial response [PR] 57%) whereas the 12-month ORR was 66% (CR 13%, PR 54%). A subset of patients achieved deeper responses with ongoing therapy at 12 months. With a median follow-up of 16 months, the 6- and 12-month failure-free survival (FFS) was 76% (95%CI: 67-87) and 67% (95%CI: 57-79), respectively. The 6- and 12-month overall survival (OS) was 93% (95%CI: 86-99) and 89% (95% CI: 82-97). Low incidence of drug-related grade >3 toxicities was observed. The most common reason for treatment discontinuation was cGVHD progression, and no patients discontinued due to toxicities. In a small cohort of patients, immune function parameters were analyzed (Figure). It showed stable CD3+ T-cell absolute values at treatment days 100 and 180, and subsequent increase at 1 year. T-cell subsets including CD3+4+8- and CD3+4-8+ demonstrated a similar pattern of stable values followed by an increase of almost double median values at 1 year of treatment. Notably, naïve T-cell subsets (CD4+45RA+) increased their absolute values compared to baseline including timepoints of 6- and 12-months. The B-cell compartment (CD3-19+) demonstrated a gradual increase throughout belumosudil treatment. Notably, none of the patients had a CD19+ median value <150/mm3 at their 1-year treatment assessment. The NK cell compartment including CD3-56+16+ NK cells absolute demonstrated a stable to improved pattern.

Conclusion: Belumosudil was associated with high treatment response and survival outcomes including FFS in patients with advanced cGVHD. Notably, deeper treatment responses were observed with ongoing therapy. Treatment was overall well-tolerated, and toxicity-related therapy discontinuation did not occur. Immune cell populations demonstrated preserved to improved values throughout treatment in a subset of patients. Overall, our real-world study indicates a similar experience to the clinical trial and supports the use of belumosudil in SR/SD cGVHD.

Table.

Characteristic	Patients, n = 67
Median age (range)	57 (44-65)
Male, n (%)	47 (70%)
Diagnosis, n (%)	
Acute leukemia	29 (43%)
MDS/MPN	7 (10%)
NHL/HL	26 (39%)
Multiple myeloma	2 (3%)
Non-malignant disorders	2 (3%)
Intensity of conditioning, n (%)	
Myeloablative	13 (20%)
Reduced intensity	30 (47%)
Nonmyeloablative	21 (33%)
Unknown	3 (4%)
Donor, n (%)	
MRD	16 (24%)
MUD	36 (54%)
MMUD	7 (10%)
Haploidentical	1 (1.5%)
Cord blood	5 (8%)
Cord blood/haploidentical	1 (1.5%)
Unknown	1 (1.5%)
Stem cell source, n (%)	
PBSC	57 (85%)
Bone marrow	4 (6.5%)
Cord blood	6 (9%)
GVHD prophylaxis, n (%)	
CNI-based	58 (87%)
PTCy/CNI/MMF	5 (7.5%)
T-cell depletion	3 (4.5%)
Unknown	1 (1%)
cGVHD severity at baseline, n (%)	
Mild	11 (16%)
Moderate	39 (58%)
Severe	16 (24%)
Severe aGVHD	1 (1.5%)

Figure. Immune reconstitution characteristics (n= 11). Sustained recovery of lymphocytes subsets in belumosudil-treated patients.



PP02.10 – Serositis as a rare manifestation of chronic graft-versus-host disease

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Background: Serositis is a rare and atypical chronic graft-versus host disease (cGvHD) manifestation. (1-3) Published data on its clinical course and management is limited.

Purpose: Herein we report the results of a retrospective review to assess the prevalence risk factors and outcomes in patients with serositis at the time of enrollment in the National Institutes of Health (NIH) cGvHD Natural History study.

Methods: Between April 2002 and August 2023, a total of 518 patients was enrolled in the NIH cross-sectional cGvHD Natural History study (NCT00092235). We performed a retrospective analysis, including review of documentation (baseline data and GvHD assessment forms), imaging reports, laboratory values, and death records.

Results: The overall prevalence of serositis in our population was 3.6% (19 patients), out of which 8 patients

(1.5%) had active serositis at time of evaluation and 11 patients (2.1%) had a history of resolved cGvHD-serositis. All patients with serositis at study enrollment were white males, confirming the previously reported preponderance of male sex in cGVHD serositis (2). At presentation, the median age was 52.5 (range: 27-52) years and the median Karnofsky performance index 70%. All patients presented with severe cGvHD with a median of 6 (range 2-7) organs affected. The median overall survival (OS) from transplant was 78 months (range 55-172). The median OS from cGvHD diagnosis was 83 months (range 28-163). The median time to enrollment was 44 months (range 14-86) after transplant, and 33 months (range 5-74) after cGvHD diagnosis. 6/8 (75%) patients had received myeloablative conditioning, 4/8 (50%) patients had received total body irradiation. Cell source was bone marrow in one patient and peripheral blood in 7/8. The patients had been treated with a median of 6 prior lines of cGvHD therapy (range 4-10). 4/8 patients had been treated with antithymocyte globulin (ATG). 6/8 (75%) patients had a history of cardiovascular diseases. 3 patients had a history of TKI treatment, out of which one had been treated with both imatinib and dasatinib. 6/8 (75%) presented with pleural effusion, 5/8 (62.5%) presented with pericardial effusion and 3/8 (37.5%) presented with ascites. All three areas were involved in 2 patients (25%). One patient had pleural and pericardial effusion due to concurrent cGvHD and nontuberculous mycobacterial pulmonary infection. Serum IgA levels were below normal in all 8, and serum IgG levels below normal in 7/8 patients. Mortality (Figure 1) was significantly higher in the serositis group compared to the rest of the cohort (estimates from unadjusted Cox models - HR=3.79 (95% CI: 1.78, 8.10), p=0.0006). The median survival after serositis diagnosis was 39 months (range 3-158). History of resolved serositis did not significantly affect mortality.

Figure 1. Survival in cGvHD patients with and without serositis, 2004-2023

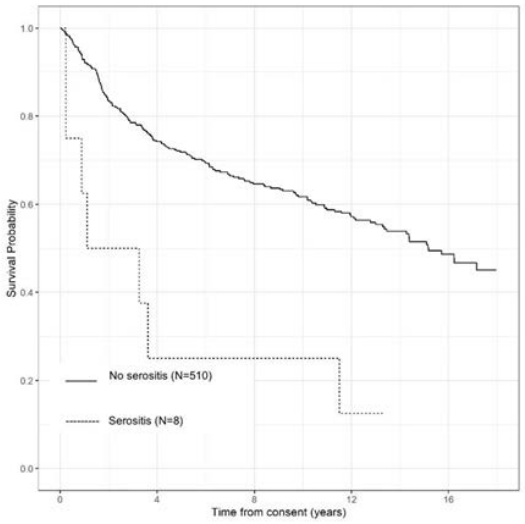

Figure 1. Kaplan-Meier curve showing survival probability for cGvHD patients presenting with serositis (dashed line) and without serositis (full line), at the time of enrolment in the NIH cGvHD Natural History cohort. Mortality was significantly higher in the serositis group compared to the rest of the cohort (HR=3.79 (95% CI: 1.78, 8.10), p=0.0006).

Conclusions: Our results demonstrate that, although often underreported, serositis significantly adds to morbidity and mortality in cGvHD patients. Hence, an increased awareness of this atypical cGvHD manifestation may result in early identification, prompt management and better outcomes.

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PP02.11 – Exposure-response relationships for axatilimab, a humanized monoclonal antibody targeting CSF-1R, in patients with chronic graft-versus-host disease

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Background: Axatilimab, a high-affinity humanized monoclonal antibody against colony-stimulating factor 1 receptor (CSF-1R), is under investigation for the treatment of chronic graft-versus-host disease (cGVHD) and other diseases. A population pharmacokinetic/pharmacodynamic (PK/PD) model for axatilimab was previously developed using pooled data from 4 clinical studies. The structural model consisted of a 2-compartment axatilimab PK model with saturable clearance and turnover models for colony-stimulating factor 1 (CSF-1), nonclassical monocytes, aspartate aminotransferase, and creatine phosphokinase (CPK). Body weight was the only covariate identified that affected axatilimab steady-state exposure by >20%.

Purpose: To describe the exposure-response relationships for efficacy and safety in patients with cGVHD who received axatilimab.

Methods: Exposure-efficacy relationships were assessed in patients treated in the phase 2 AGAVE-201 study (NCT04710576; n=239; axatilimab 0.3 mg/kg every 2 weeks [Q2W], 1.0 mg/kg Q2W, 3.0 mg/kg every 4 weeks [Q4W]). Binary efficacy assessments included the overall response rate (ORR) and ≥7-point improvement in modified Lee Symptom Scale (mLSS response). Duration of response (DOR), a time-to-event endpoint, was assessed among all patients in AGAVE-201 who achieved an overall response. Exposure-safety relationships were assessed in all treated patients with cGVHD (n=278) in AGAVE-201 and a phase 1/2 study (SNDX-6352-0503; NCT03604692; axatilimab 0.15 mg/kg Q2W, 0.5 mg/kg Q2W, 1.0 mg/kg Q2W, 3.0 mg/kg Q2W, 3.0 mg/kg Q4W). Evaluated safety endpoints included 5 general safety assessments (grade ≥3 treatment-emergent adverse events [TEAEs], TEAEs leading to dose modifications, serious TEAEs, treatment-related TEAEs, AEs of special interest) and 6 sets of grouped AE terms (amylase and lipase increases, CPK elevations, liver enzyme elevations, periorbital edema, infections of unspecified etiology [infections not otherwise specified as bacterial, viral, or fungal], infusion-related reactions). For binary or time-to-event endpoints, logistic or Cox regression analyses, respectively, were performed using predicted axatilimab exposure metrics that were derived from the population PK/PD model; axatilimab exposure metrics from the first dose, the first treatment cycle, and a steady-state treatment cycle were evaluated. To further evaluate the effects of body weight with the 0.3 mg/kg Q2W regimen, forward simulations were completed using percentiles of an observed body weight distribution (range, 18.1–151 kg) for each efficacy and safety outcome that was associated with axatilimab exposure in the final model.

Results: For the exposure-efficacy analysis, ORR and mLSS responses were associated with axatilimab exposure, with lower axatilimab exposure increasing the odds of response. Among the 153 patients with a response, DOR did not have a significant association with axatilimab exposure. For the exposure-safety analysis, all safety endpoints except infections of unspecified etiology were associated with axatilimab exposure, with higher axatilimab exposure increasing the odds of TEAEs. In forward simulations evaluating the effect of body weight on the axatilimab 0.3 mg/kg Q2W regimen across 2 efficacy and 10 safety endpoints, the maximum differences in median predicted probabilities between the 10th and 90th percentiles of body weight were <1.4% and <1.7% for efficacy and safety, respectively.

Conclusions: These results support the 0.3 mg/kg Q2W regimen of axatilimab in patients with cGVHD.

PP02.12 – Real-world ruxolitinib and corticosteroid treatment patterns in patients with chronic graft-versus-host disease in the United States

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Background: Ruxolitinib was approved in September 2021 for chronic graft-versus-host disease (cGVHD) after failure of 1–2 lines of systemic therapy in adult and pediatric patients aged ≥12 years. Real-world data describing use of ruxolitinib and how it impacts corticosteroid use in patients with cGVHD following allogeneic hematopoietic stem cell transplantation (alloHSCT) across various practices require further investigation.

Purpose: Describe real-world characteristics and treatment patterns of ruxolitinib and corticosteroids in patients with cGVHD after alloHSCT in the United States.

Methods: This retrospective claims data analysis included commercial, Medicare/Medicare Advantage, and Medicaid plan members with evidence of an alloHSCT, cGVHD diagnosis, ruxolitinib use after cGVHD diagnosis (earliest claim: index date), and health insurance coverage ≥6 months before and ≥6 months after the index date (or less due to death). Patients were followed until the earliest of death, end of continuous plan enrollment, or end of study period. Dosages and treatment length were determined using prescription refills in pharmacy claim records.

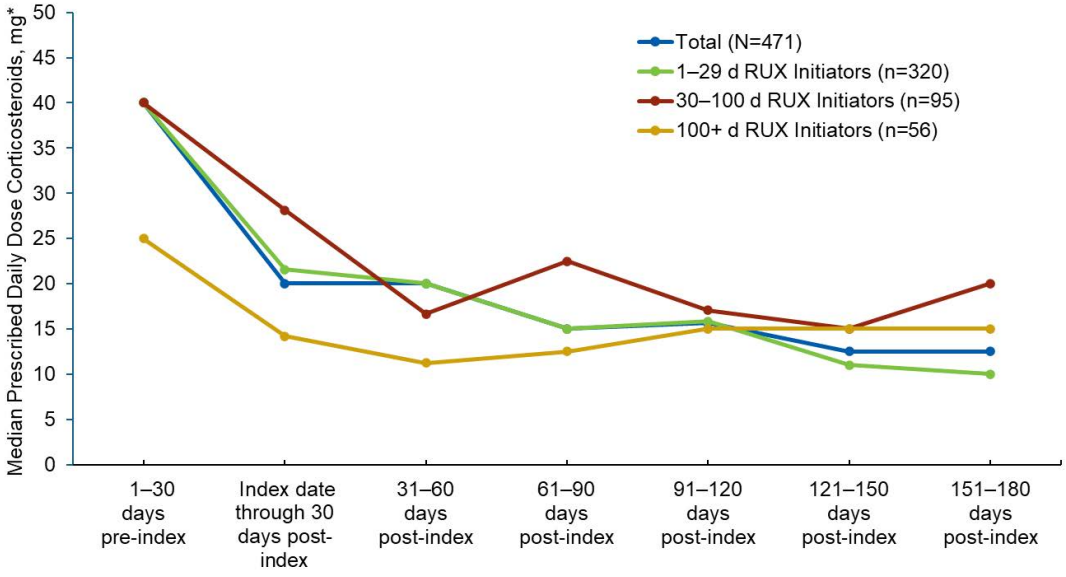
Results: Overall, 471 patients who had cGVHD and started ruxolitinib between July 2019–August 2022 were included. Median (IQR) age was 46 (26–60) years, with 15.3% <18 years. Approximately 60% were male, 59.2% had commercial insurance, 28.0% had Medicaid, and 4.5% had Medicare. Patients were followed for a median (IQR) of 465 (316–694) days from ruxolitinib initiation.

Patients initiated ruxolitinib after a median (IQR) of 116 (26–255) days (pediatric: 83.5 days; adults: 119 days) from cGVHD diagnosis; 45% started ruxolitinib as second-line treatment following corticosteroids. Median ruxolitinib starting dosage was 10 mg/day for pediatric and adult patients (pediatric IQR: 5–10; adult IQR: 10–20). Among patients who had a ruxolitinib refill, 58.4% had a dose change; of those, 55.9% had a dose increase and 44.1% had a dose decrease in their first dose change. Kaplan-Meier analysis showed median length of ruxolitinib treatment across all lines of therapy was 245 days (95% CI: 210–300). At the end of follow-up, 33.1% of patients remained on ruxolitinib treatment for a median of 389 days (IQR: 260–591).

Median corticosteroid dosing decreased 69% from pre-index through 180 days post-index across all patients, with numerically greater reduction in early ruxolitinib initiators (Figure). The number of patients with steroid complication-related healthcare resource utilization (HCRU) ambulatory visits, emergency room visits, and inpatient stays was numerically less after vs before ruxolitinib initiation (Table).

Conclusions: In real-world practice, patients treated with ruxolitinib for cGVHD start at a median dose of 10 mg daily, with most patients receiving dose adjustments as necessary. Patients received ruxolitinib for a median of 8 months, with 33.1% continuing ruxolitinib for a median duration of over 1 year, suggesting long-term safety and ongoing clinical benefit. Patients had a 69% reduction in corticosteroid dosing over the 6 months after initiating ruxolitinib and a decrease in steroid complication-related HCRU, suggesting ongoing clinical benefit of ruxolitinib in reducing steroid dose and related complications.

Figure. Corticosteroid Dosing Over Time



** Prednisone equivalent, among patients with 1+ steroid fill with a known dose during the time period. Fills for dexamethasone were excluded.*

Table. Steroid Complication-Related Healthcare Resource Utilization

	Before Ruxolitinib (N=471)	During Ruxolitinib Treatment (N=471)	Follo wing Ruxolitinib Discontinuation* (n=282)
Healthcare utilization, n (%)			
Ambulatory visit	371 (78.8)	322 (68.4)	183 (64.9)
Office visit	4 (0.9)	9 (1.9)	2 (0.7)
Outpatient visit	371 (78.8)	322 (68.4)	182 (64.5)
Emergency room visit	72 (15.3)	59 (12.5)	30 (10.6)
Inpatient stay	264 (56.1)	175 (37.2)	84 (29.8)
Utilization counts per patient per month, mean (SD)			
Ambulatory visit	1.27 (1.7)	1.25 (1.9)	1.34 (2.7)
Emergency room visit	0.03 (0.1)	0.04 (0.2)	0.15 (1.8)
Inpatient stay	0.19 (0.2)	0.18 (0.3)	0.14 (0.3)
Inpatient days (all patients)	3.89 (6.3)	2.50 (6.7)	2.0 (6.5)

** Among patients with 1 line of therapy after first discontinuation (≥30-day break) of ruxolitinib.*

PP02.13 – Evaluating Molecular Biomarkers in tears of patients with ocular Graft versus Host Disease treated with a Jak Inhibitor

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Background: Ocular graft versus host disease (oGVHD) affects 50% of all patients who undergo an allogenic hematopoietic stem cell transplant (HSCT). Janus Kinase (JAK) is an upstream regulator of cytokine production. A JAK inhibitor, Ruxolitinib, was FDA approved for the treatment of chronic GVHD, but its specific effect on the eye requires further investigation.

Purpose: The goal of this study is to evaluate the protein and cytokine levels in tears of patients who have undergone a HSCT with and without systemic JAK inhibition (Ruxolitinib). We hypothesize that systemic JAK inhibition results in cytokine changes in tears.

Methods: Tears were collected from participants after an ocular surface wash with preservative free artificial tears. The tears were analyzed using multiplex proteomic analysis (OLink (Target-48 Cytokine)) evaluating 45 proteins with 1uL of tear sample per patient.

Results: Six patient's tears were included in the study who underwent HSCT and developed oGVHD based on the International Chronic oGVHD Consensus Group Score. Three patients were prescribed a systemic JAK Inhibitor (Ruxolitnib) by their oncologist. There was a statistically significant decrease in CXCL11, CCL2, MMP12, CXCL9, and HGF in patients who received a JAK inhibitor.

Conclusions: Our data shows a significant change in 5 cytokines in the tears of patients treated with a JAK inhibitor. These results suggest that JAK inhibitors such as ruxolitinib may have an impact on ocular GVHD development. This data suggests that JAK inhibition may change the inflammatory milieu in the ocular surface but further studies are necessary to determine the precise mechanism.

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PP03.01 – Patient perspectives on living with chronic skin graft-versus-host disease

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Background: Cutaneous chronic graft-versus-host disease (GVHD) is independently associated with morbidity and mortality after allogeneic hematopoietic cell transplantation. However, the health-related quality of life (HrQOL) domains that are most important to patients are poorly understood.

Purpose: To perform a concept elicitation study in order to define HrQOL in cutaneous chronic GVHD from the patient perspective and to compare experiences of patients living with epidermal and sclerotic chronic GVHD.

Methods: Single-center qualitative analysis from open-ended, semi-structured interviews and free-listing terms conducted between April – September 2023. Adults ⍺18 years-old with a diagnosis of active cutaneous chronic GVHD were enrolled, purposefully sampled for epidermal and sclerotic disease features,

with ongoing sampling until thematic saturation. HrQOL domains and codes were identified by inductive analysis of semi-structured interviews with patients living with cutaneous chronic GVHD. Smith's Saliency Indices, a measure of saliency for each list term, was calculated from free-listing terms from deidentified patient interviews.

Results: Thirty-one adults with cutaneous chronic GVHD (median [IQR] age 61.1 [52.9-68.7] years; 17 (54.8%) male and 14 (45.2%) female) participated in interviews. Nine (29.0%) had epidermal, 13 (41.9%) sclerotic, and 9 (29.0%) combination disease types. We identified 40 codes of importance grouped within 5 HrQOL domains: skin changes and symptoms, social functioning, psychological and emotional functioning, physical functioning, and general health perceptions. The most frequent symptoms were dry skin (n=20, 65%), tight skin (n=19, 61%), itch (n=15, 48%), and discoloration (n=14, 45%), which were seen in all disease subtypes. Impairment in social functioning was noted by all participants. Psychological and emotional functioning including frustration (Smith's Saliency Index 0.32) and worry / concern (Smith's Saliency Index 0.12) and symptoms including discomfort (Smith's Saliency Index 0.20) were the most salient to patients. Individual and environmental factors such as social comparison, illness comparison to cancer, anatomic location of disease involvement, and disease duration affected the relationship between skin changes and symptoms and functioning and general health perceptions.

Conclusions: This qualitative analysis demonstrates the relationship between cutaneous chronic GVHD and HrQOL domains independent of extra-cutaneous chronic GVHD, and identifies codes not represented in existing GVHD- and dermatology-specific patient-reported outcome measures. These results can guide patient-reported outcome development and instrument selection for clinical trials and improve clinical decision-making.

Table: Health-related quality of life domains and codes from patients with cutaneous chronic GVHD

	Total (n=31)	Epidermal (n=9)	Sclerotic (n=13)	Combination (n=9)
Skin changes and symptoms	31 (100%)	9 (100%)	13 (100%)	9 (100%)
Dry, flaky, scaly skin	20 (65%)	8 (89%)	5 (38%)	7 (78%)
Tight skin	19 (61%)	2 (22%)	11 (85%)	6 (67%)
Itch	15 (48%)	6 (67%)	4 (31%)	5 (56%)
Discoloration	14 (45%)	3 (33%)	3 (23%)	8 (89%)
Painful skin	10 (32%)	4 (44%)	2 (15%)	4 (44%)
Redness	10 (32%)	4 (44%)	3 (23%)	3 (33%)
Rash	10 (32%)	5 (56%)	4 (31%)	1 (11%)
Dimpling, rippling under skin	10 (32%)	1 (11%)	9 (69%)	0 (0%)
Bumpy, rough skin	8 (26%)	3 (33%)	2 (15%)	3 (33%)
Burning Skin	6 (19%)	4 (44%)	0 (0%)	2 (22%)
Sores	6 (19%)	3 (33%)	0 (0%)	3 (33%)
Hard/Thick skin	6 (19%)	2 (22%)	1 (8%)	3 (33%)
Shiny skin	5 (16%)	0 (0%)	3 (23%)	2 (22%)
Fragile/Thin skin	5 (16%)	1 (11%)	3 (23%)	1 (11%)
Difficulty breathing due to skin	5 (16%)	1 (11%)	2 (15%)	2 (22%)
Irritated Skin	2 (6%)	1 (11%)	1 (8%)	0 (0%)
Achy Skin	2 (6%)	0 (0%)	0 (0%)	2 (22%)

	Total (n=31)	Epidermal (n=9)	Sclerotic (n=13)	Combination (n=9)
Thin, fragile fingernails	2 (6%)	1 (11%)	0 (%)	1 (11%)
Hair loss, texture change	2 (6%)	1 (11%)	1 (8%)	0 (0%)
Difficulty sleeping due to skin	2 (6%)	1 (11%)	1 (8%)	0 (0%)
Difficulty speaking due to skin	1 (3%)	1 (11%)	0 (0%)	0 (0%)
Social Functioning	31 (100%)	9 (100%)	13 (100%)	9 (100%)
Adaptations to facilitate social life (e.g. sun protection)	16 (52%)	5 (56%)	7 (54%)	4 (44%)
Self-consciousness, appearance of condition	16 (52%)	5 (56%)	7 (54%)	4 (44%)
Ability to work	9 (26%)	1 (11%)	5 (38%)	2 (22%)
Avoidance of social activities and participation	8 (26%)	2 (22%)	3 (23%)	3 (33%)
Dependency on others	8 (26%)	3 (33%)	3 (23%)	2 (22%)
Sex and intimate relationships	3 (10%)	2 (22%)	1 (8%)	0 (0%)
Psychological / Emotional Functioning	23 (74%)	7 (78%)	8 (62%)	8 (89%)
Frustration (anger, irritation, annoyance)	12 (39%)	6 (67%)	3 (23%)	3 (33%)
Uncertainty/concerns about the future	9 (29%)	3 (33%)	1 (8%)	5 (56%)
Depression (down, unmotivated, sad)	8 (26%)	2 (22%)	2 (15%)	4 (44%)
Anxiety (fear, worry)	7 (23%)	3 (33%)	2 (15%)	2 (22%)
Physical Functioning	18 (58%)	3 (33%)	8 (62%)	7 (78%)
ADLs (walking, dressing, stairs)	12 (39%)	2 (22%)	7 (54%)	3 (33%)
Personal mobility	10 (32%)	0 (0%)	7 (54%)	3 (33%)
Exercise and physical hobbies	5 (16%)	1 (11%)	2 (15%)	2 (22%)
General Health Perceptions	30 (97%)	9 (100%)	12 (92%)	9 (100%)
Good response to treatment	19 (61%)	7 (78%)	6 (46%)	6 (67%)
Poor response to treatment	16 (52%)	4 (44%)	7 (54%)	5 (56%)
Disease knowledge and expectations	10 (32%)	2 (22%)	4 (31%)	4 (44%)
General sense of wellness	6 (19%)	1 (11%)	2 (15%)	3 (33%)
Vulnerability to flares (sun, infections, vaccines)	6 (19%)	3 (33%)	2 (15%)	1 (11%)

First-level codes were mapped to 5 health-related quality of life domains. Second-level codes include specific functions within first-level codes some of which are represented in parentheses in the table.

Abbreviations: ADL, activities of daily living

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