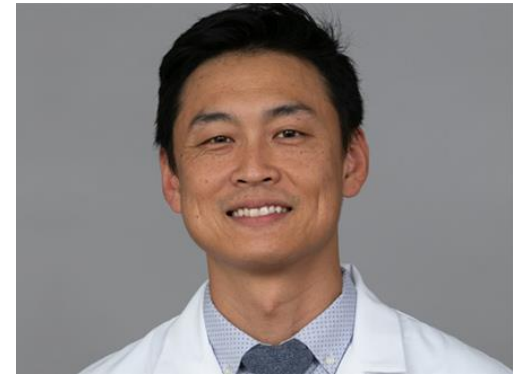


New Treatments to Prevent or Treat Graft-versus-Host Disease (GvHD)

**Celebrating a Second Chance at
Life Survivorship Symposium**

May 3-9, 2025



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Treatments on the Horizon to Prevent or Treat Graft-versus-Host Disease

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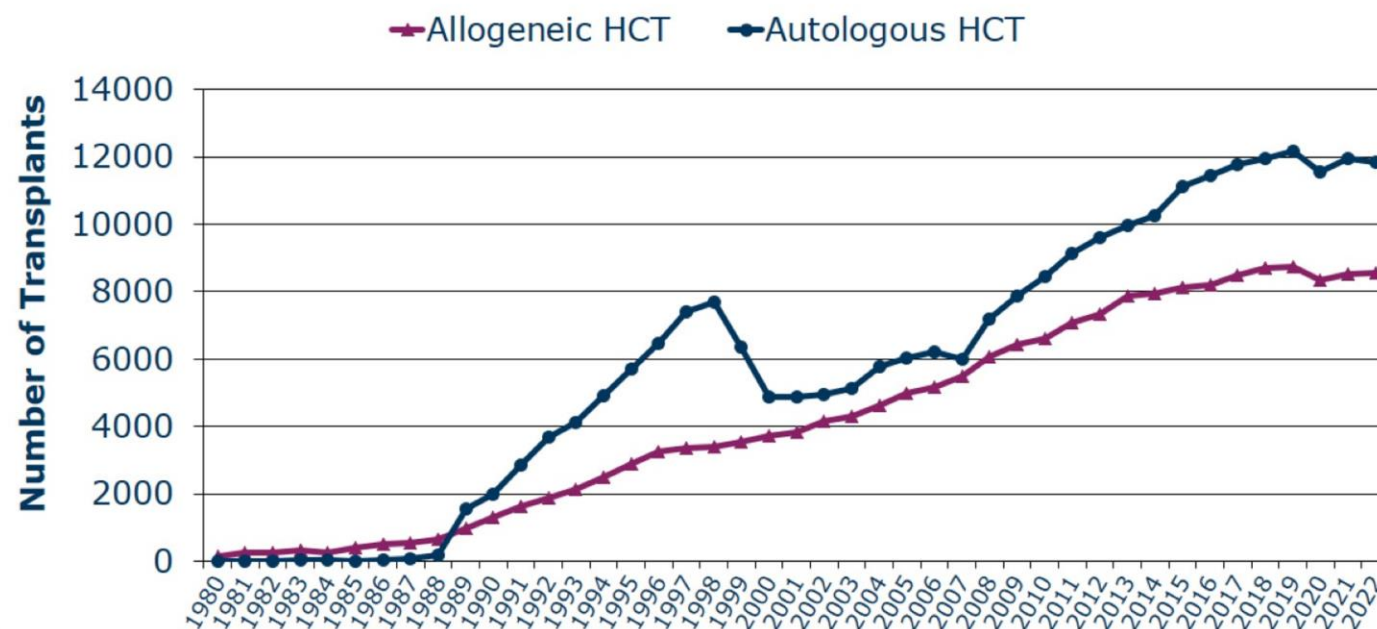
Learning Objectives

- What is GVHD?
- How many patients develop acute and/or chronic GVHD in the modern era? Are the numbers coming down? Who's at risk?
- Recent developments in GVHD treatment that have improved treatment and prevention of GVHD.
- New promising therapies under investigation to prevent and manage GVHD
- How can patients learn about enrolling in a GVHD clinical trial?



What is Hematopoietic Stem Cell Transplantation?

- Allogeneic hematopoietic stem cell transplantation (HCT) relies on an immunotherapy effect to cure hematologic disorders or cancers
- A donor's new bone marrow or stem cells produce blood and immune system cells



Cusatis, et al. TCT 2024



- Age/Genetics
- Comorbidity
- Psychosocial
- Lifestyle factors



Pre-
HCT

- Chemotherapy, biologic, and radiation
- Remission



HCT

- HLA-match
- Conditioning chemotherapy
- Immune Suppression



Post-
HCT

- Graft-versus-Host Disease (GVHD)
- Medications
- Health Maintenance



Improving Outcomes: Post-Transplant Cyclophosphamide

- Prevent/Reduce: Rejection, GVHD, Infections, and Relapse

- Donor Availability

Matched (8/8)

Haploidentical (4/8)

Mismatched (<8/8)

Cord Blood



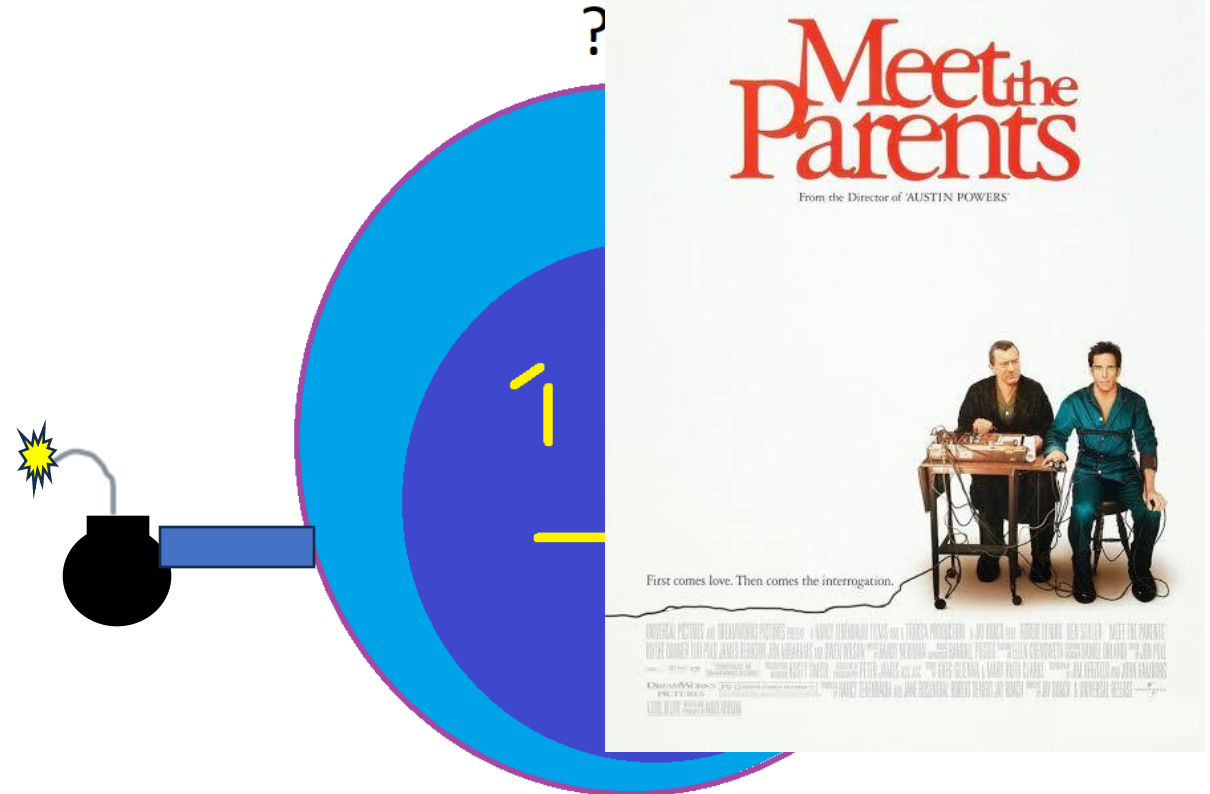
Improving Outcomes: Platforms

- Standard Plus New Agent
 - HCT + **Ruxolitinib**
 - Anti-inflammatory drug approved for treatment of GVHD
 - HCT + **Vedolizumab**
 - Protectant against immune system damage to the gastrointestinal tract
- Graft Engineering
 - Manipulation of stem cells to promote engraftment, reduce GVHD and relapse



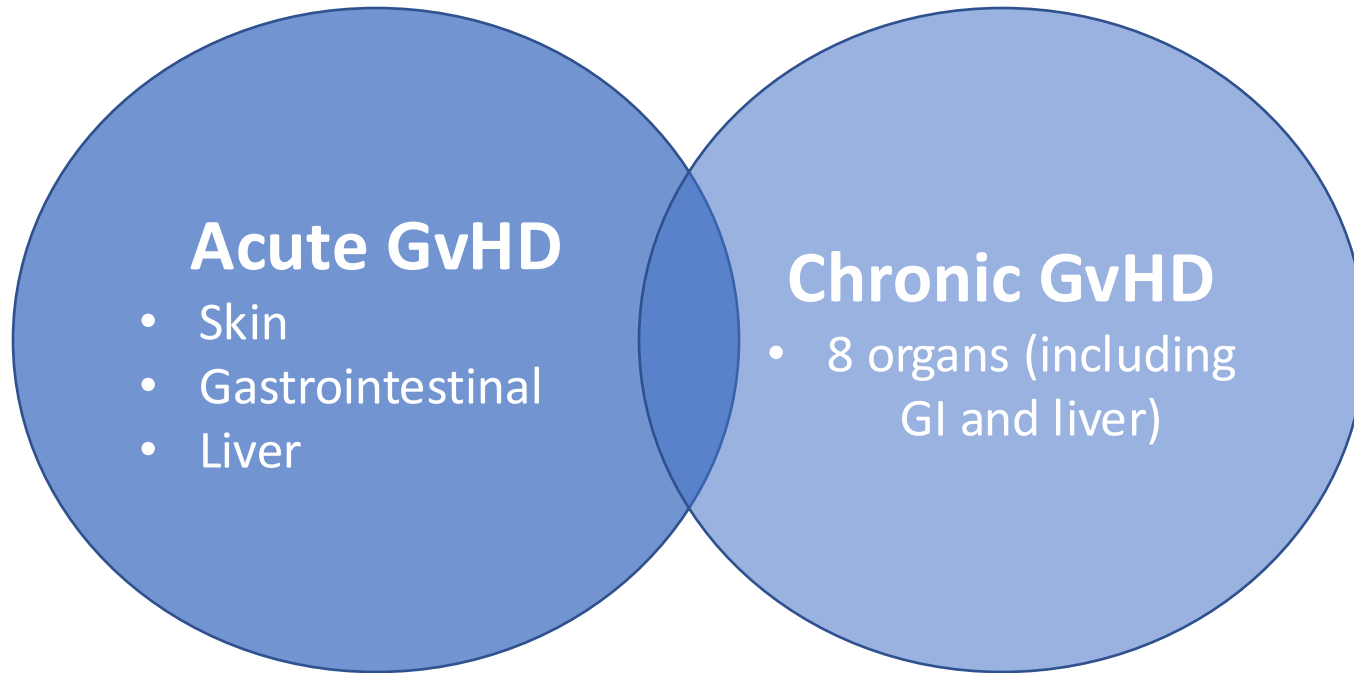
Graft-versus-Host Disease

- HCT relies on the graft-versus-cancer effect
- However, the graft-versus-host disease (GVHD) phenomenon may lead to “friendly fire”
- Leads to tissue damage due to donor immune system cells



Confused Lymphocyte

Types of Graft-versus-Host Disease



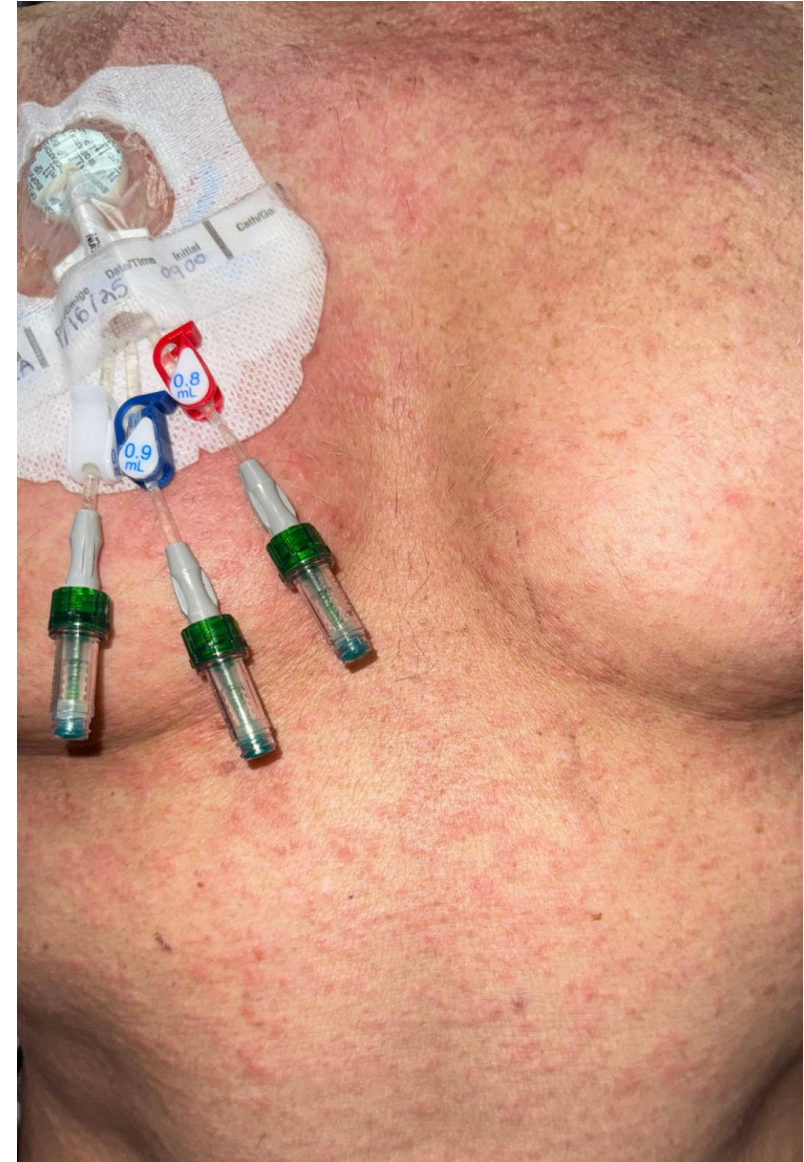
Definitions and Subtypes

- Acute versus chronic GVHD is classically defined in relation to Day + 100
- However, clinical findings now differentiate between the acute or chronic GVHD diagnosis



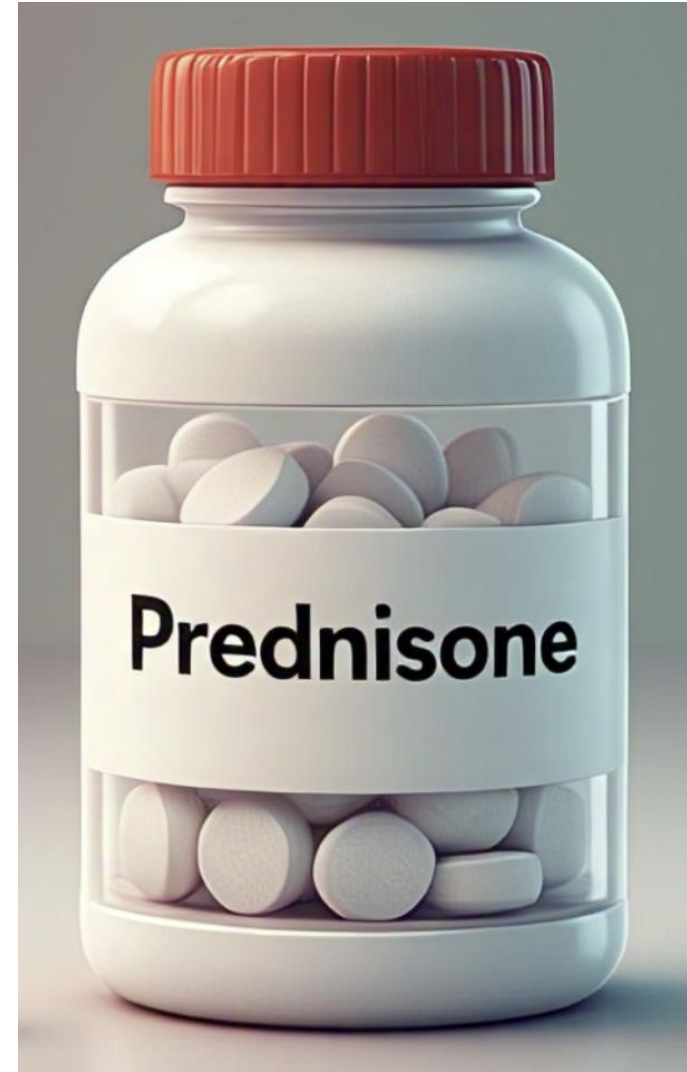
Acute GVHD (aGVHD)

- Usually presents in the first 1-2 months after HCT
- Clinical picture can be confusing as manifestations can be attributed to other causes
 - Rash
 - Poor appetite, nausea, diarrhea
 - Liver enzyme changes



Treatment for Acute GVHD

- Corticosteroids (Prednisone)
 - Used to dampen the immune system
 - Can be used at high doses with a gradual dose reduction
- Supportive Therapies
 - Creams/lotions/ointments



The Dark Side of Corticosteroids

- They work by weakening the immune system → Need to monitor for infections
- Symptoms may recur or worsen if corticosteroids are reduced



Side Effects:

- Fatigue
- Elevated blood sugars
- Muscle weakness
- Joint/bone issues
- Skin thinning
- Bruising
- Weight gain
- Appetite changes
- Vision changes
- Heartburn/Ulcers
- Infection
- Insomnia
- Irritability
- Psychosis
- Depression
- Adherence
- Withdrawal
- ..and more



Life after Corticosteroids



Improvement:

- Taper corticosteroids
- Watch for infections
- Watch for recurrent or worsening GVHD

No Improvement, then Second Line:

- Ruxolitinib
- Alternative Immune Suppressants

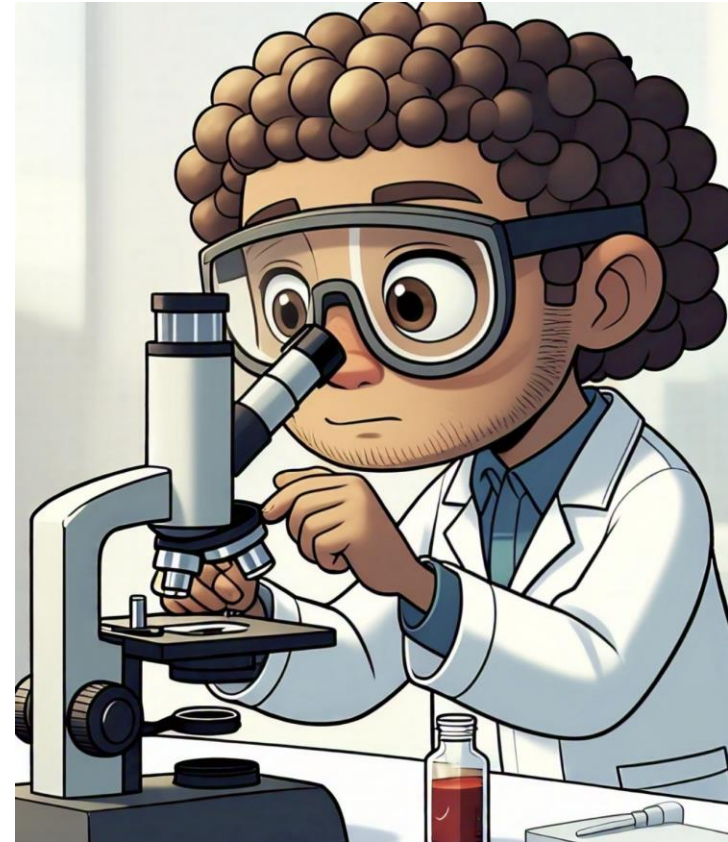
Supportive Therapies

- Antidiarrheals
- Topical therapies



Exciting Updates for Acute GVHD - Risk

- Earlier identification of aGVHD (IL1RL1)
- Blood biomarkers (labs) before symptoms are evident
- Raises potential to intervene before significant organ damage is realized



Exciting Updates for Acute GVHD: Initial Treatment

- **Alpha-1-Antitrypsin** added to Steroids for High-Risk aGVHD
 - The addition of this protein showed a reduced likelihood of needing additional therapy in a large double-blind clinical trial
- Ruxolitinib with **uhCG/EGF** and Steroids de-escalation for lower gastrointestinal GVHD
 - Addition of hormone to help rebalance the immune system, ruxolitinib, and lower doses of corticosteroids to reduce toxicity

(Tandem Meeting 2025 - BMT CTN 1705)

Exciting Updates for Acute GVHD: 2nd Line Therapy

- **Apraglutide** injection added to ruxolitinib in second line
 - Glucagon-like peptide 2 repairs intestinal cells (STARGAZE Trial)
- **Fecal transplantation** to restore microbiome
 - Enema
 - Pills



Chronic GVHD

- Most common long-term complication of HCT
- Affects 30-50% of recipients
- Frequency and manifestations are changing!
- Is a major cause of problems after HCT



The Approach to Chronic GVHD

- Do Nothing (**Observe**)
- Do Something (**Treat**)
 - Treatment a local area (**Topical**)
 - Treat the entire body (**Systemic**)

Too much treatment

Infection and drug
related toxicity

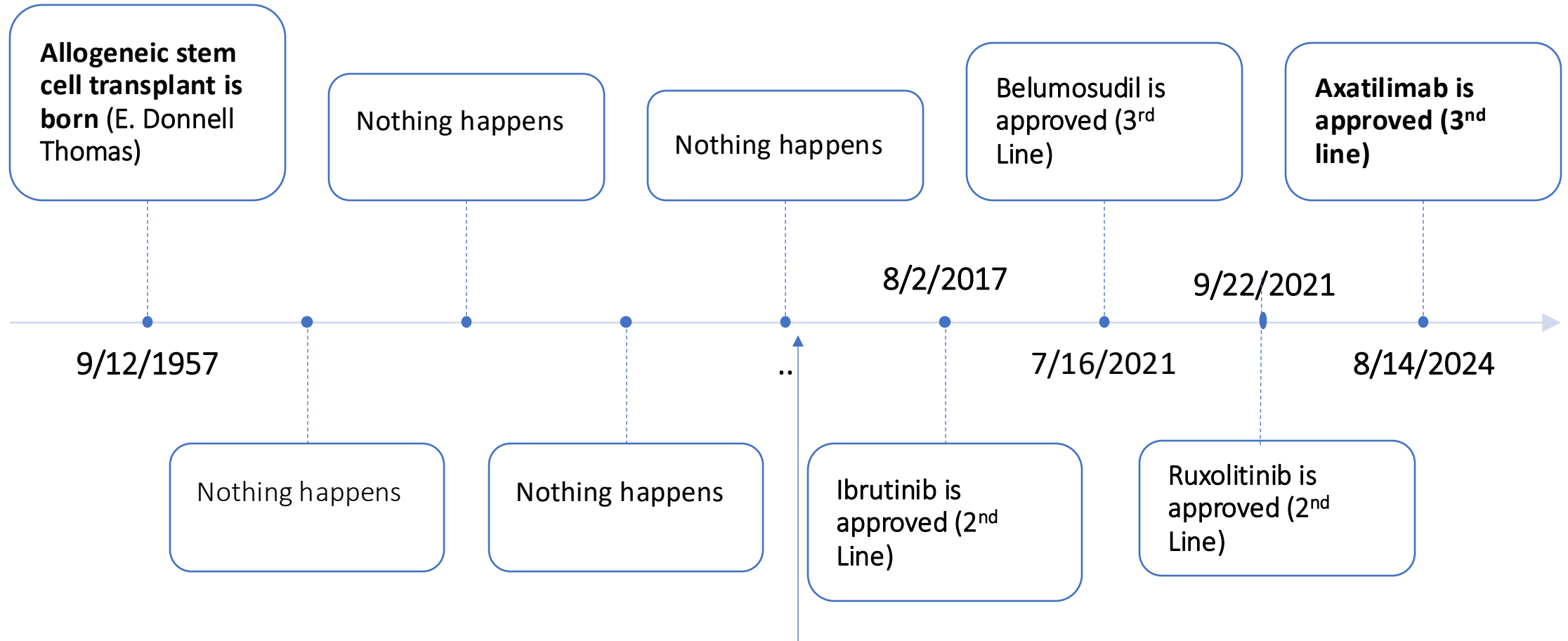


Too little treatment:

Irreversible organ damage,
quality of life impairment



Progress in FDA Approvals for cGVHD



CMS issued Medicare National Coverage Determination that Extracorporeal Photopheresis (ECP) is reasonable and necessary for cGVHD as of 12/19/2006 (without ECP FDA approval)

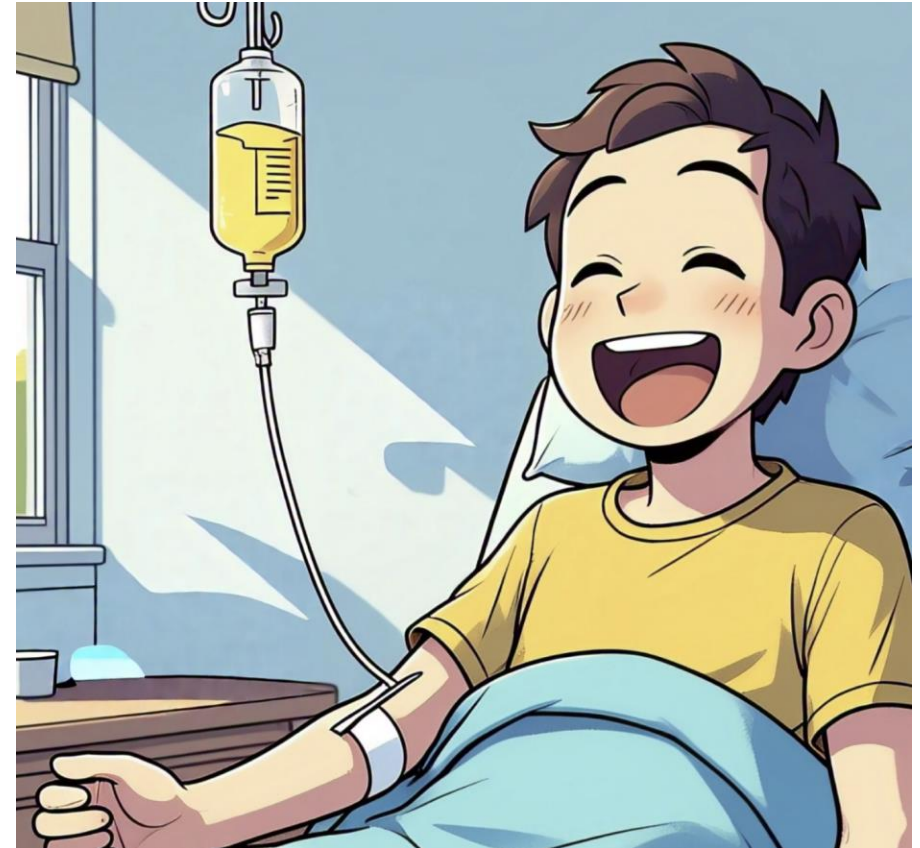
The Three Approved Pills

- **Ibrutinib (Imbruvica®):** Initially FDA approved for chronic lymphocytic leukemia, but approved 8/2/17 for cGVHD after failure of one or more lines of therapy
- **Belumosudil (Rezurock®):** FDA approved 7/16/2021 after failure of 2 or more lines of therapy
- **Ruxolitinib (Jakafi®):** FDA approved 9/22/21 after failure of at least one prior line



Newcomer: Axatilimab (Niktimvo®)

- FDA approved **8/14/24**
- Targets pro-inflammatory and scarring-related immune system monocytes/macrophages
- **Intravenously administered** every 2 weeks
- Works in 74% of patients, including those exposed to newer agents
- Possible Side effects: liver enzyme elevation, eye swelling



Extracorporeal Photopheresis

- Intravenous “blood exchange” treatment that rebalances immune system without significant infection risk
- Cons: Time commitment, catheter
- Possible side effects: fatigue/lightheadedness, catheter/port access site problems, photosensitivity
- Not FDA approved but commonly used (and covered by insurance companies) for treatment of chronic GVHD



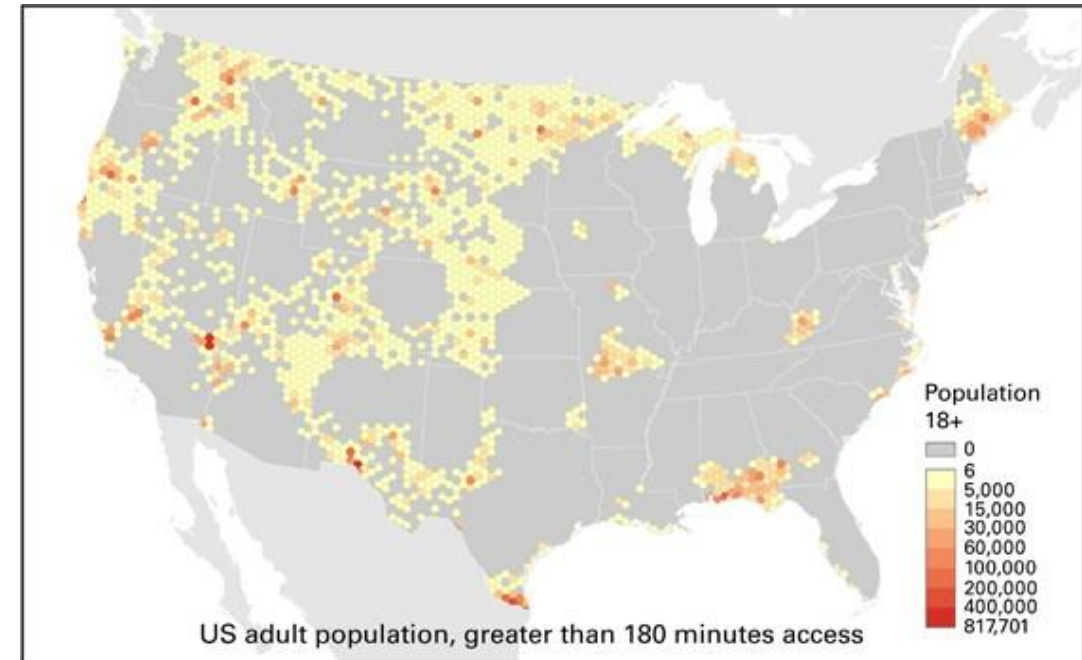
New Treatments, Sequencing, and Combinations

- Despite new drug approvals, the optimal sequence and combinations are not clear
- It is common to use more than one treatment at one time
 - Example – prednisone with ruxolitinib, or ruxolitinib with belumosudil
- Study: Steroid-free combination regimens
- Study: Organ-specific treatments



Improving Access to Specialized GVHD Care

- In the modern era, digital healthcare can bridge limited access to GVHD care
- Increase our ability to provide supportive care to patients and caregivers.
- Can guide patients and caregivers through complex survivorship care.
- Provide a patient-centered approach to receiving information at the right pace



Delamater, BMT 2015

Digital Health Interventions Are Being Developed

- Chronic GVHD group intervention and mobile app for improving education, management, and coping
- Sexual health education and coping
- High-risk medication education and adherence



Clinical Trials: Clinicaltrials.gov

- Advances in the field require clinical trial enrollment
- Range of “experimental” therapies from early phase (I, II) to late phase (III)
- Generally, in large cancer centers

The screenshot shows the ClinicalTrials.gov search results page for the query 'gvhd'. The left sidebar contains filters for 'Condition/disease' (gvhd), 'Other terms', 'Intervention/treatment', 'Location', and 'Study Status'. The main results area displays three trials:

- NCT06663722** (Not yet recruiting, New): Axatilimab in Combination With Extracorporeal Photopheresis (ECP) in Chronic Graft-versus-Host Disease. Conditions: Chronic Graft Versus Host Disease, cGVHD. Locations: Miami, Florida, United States.
- NCT04446182** (Terminated, WITH RESULTS): Itacitinib (INCB039110) and Extracorporeal Photopheresis (ECP) for First-Line Treatment in Chronic GVHD. Conditions: Chronic Graft-versus-host-disease. Locations: Salt Lake City, Utah, United States.
- NCT00271869** (Unknown status *): Treatment of Chronic GVHD of Liver or Lungs by ECP. Conditions: (empty).

At the bottom of the sidebar, there are buttons for 'Clear Filters (2)' and 'Apply Filters'.

Clinical Trials: Other Resources

Jason Carter Clinical Trials Search and Support Program

- ctsearchsupport.org



Jason Carter Clinical Trial Search and Support Program

Your one-stop shop: Clinical trials and support for blood cancers and blood disorders

Find personalized clinical trial results in just a few clicks.

Q Disease, treatment, doctor or other keywords

NEXT

LLS Clinical Trials Support Center

- <https://lls.org/treatment/types-treatment/clinical-trials>



DONATE



CLINICAL TRIALS

Taking part in a clinical trial may be the best treatment choice for some blood cancer patients. There are trials for patients at every stage of treatment as well as those in remission. Virtually all of today's standard treatments for cancer are based on previous clinical trials.

Clinical Trial Support Center

Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.

REQUEST CLINICAL TRIAL SUPPORT

For more information or to contact us, [click here](#).



BMT INFONET

2025 SURVIVORSHIP SYMPOSIUM

Summarizing the Key Points: Goals and Achievements – Part 1

- Improve the transplant methodology for all types of donors
 - Different prevention regimens (Post-transplant Cyclophosphamide, vedolizumab, ruxolitinib, graft modifications)
- Diagnose GVHD earlier to allow for earlier intervention (biomarkers)
- Improve the efficiency and toxicity of acute GVHD treatments through new therapies (apraglutide, alpha-1-antitrypsin, uhCG, ruxolitinib)

Summarizing the Key Points: Goals and Achievements – Part 2

- Improve the efficiency and toxicity of chronic GVHD treatments through new therapies (ibrutinib, belumosudil, ruxolitinib, axatilimab)
- Improve access to specialized GVHD care through digital health interventions

Closing Comments

- Watch for new or worsening symptoms and signs of cGVHD, both physical and mental
- Risk of infections
 - Don't Forget: Health maintenance and routine cancer screenings
- New treatment trials focusing on steroid-free regimens, new combinations, and organ-specific treatments
- Also needed: focus on behavioral health and survivorship, implement more digital health platforms

Thank you

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Questions?



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Let Us Know How We Can Help You



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