Lunch & Learn: Hemophagocytic Lymphohistiocytosis (HLH)
IDF MISSION
Improving the diagnosis, treatment, and quality of life of people affected by primary immunodeficiency through fostering a community empowered by advocacy, education, and research.
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- Attendees will not have access to their microphone or webcam throughout the event.
- To see the full slides, you can adjust the settings on the speaker view panel on the top of the Zoom screen and select "side-by-side" in the dropdown option.
- Please submit all questions for the presenter via the Q&A box
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IDF Website: www.primaryimmune.org
To view all HLH Resources and Materials, visit:
https://primaryimmune.org/disease/hemophagocytic-lymphohistiocytosis-hlh
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- **Monthly Lunch & Learns**: medical experts present on various diagnosis-specific topics
- **Get Connected Groups**: share experiences, receive information, and gain support
- **IDF Forums**
- **Ask IDF**
- **Annual PI Conference**

To view a list of all upcoming IDF events, visit: [https://community.primaryimmune.org/s/events?language=en_US](https://community.primaryimmune.org/s/events?language=en_US)
WELCOME!

Rebecca Marsh, MD
Clinical Director, Primary Immune Deficiency Program and HLH Center of Excellence
Cincinnati Children’s Hospital
Outline for Today

• Brief introductory case
• Review HLH terminology
• Discuss why HLH happens and genetic disorders that cause HLH
• Talk about HLH testing
• Go over traditional and newer treatments
Disclosures

• I have no disclosures other than I will be discussing off-label use of several therapeutics
Introductory Case: Sunday Morning in Cincinnati, OH….

- 6 month old male comes to the ER with 5 days of fever, decreased oral intake, less active, no other symptoms
- On exam, febrile, tachycardic, spleen palpable 2cm below the costal margin, petechiae
- Platelets are noted to be 67, ANC 973
- AST 296, ALT 77
- Fibrinogen 137
- Someone checked a ferritin…3,430
- Admitted, started on IVF, broad-spectrum antibiotics, consults to help with work-up for infections and malignancy…
6 month old male comes to the ER with 5 days of fever, decreased oral intake, less active, no other symptoms

On exam, febrile, tachycardic, spleen palpable 2cm below the costal margin, petechiae

Platelets noted to be 67, ANC 973

AST 296, ALT 77

Fibrinogen 137

Someone checked a ferritin…3,430

Admitted, started on IVF, broad-spectrum antibiotics, consults to help with work-up for infections and malignancy...

Introductory Case: Sunday Morning in Cincinnati, OH....
Brief Presentation

• 6 month old male comes to the Emergency Room with 5 days of fever, not eating well, less active

• No other symptoms, had a cold 2 weeks ago

• Exam: Has a fever, heart rate is fast, and doctors can feel an enlarged spleen
Brief Presentation

• Labs:
  • Several blood counts are low:
    • Platelets 47
    • White blood cell count 1.9, Neutrophil count 1137
  • Liver enzymes are elevated (liver seems a little sick)
    • AST 296, ALT 77
  • Fibrinogen is low 137
    • Fibrinogen is a protein made by the liver that helps stop bleeding by helping blood clots to form
  • Ferritin is high 2970
    • Ferritin is a blood protein that contains iron, and ferritin is elevated in inflammation
Course

• Baby was admitted to the hospital, given IV fluids and antibiotics.
• Several specialized doctors were consulted to help determine what was wrong: evaluate for infections or cancer or other problems
  • Bone marrow examination: no cancer
  • CT Scan did not show any concerns for cancer or infection
  • Lots of testing for infections: negative.
  • Specialized blood tests for inflammation were checked and were high:
    • Soluble IL-2Rα 13,234
    • CXCL9 5,783
    • IL-18 987
Does This Patient Have HLH?
Does This Patient Have HLH?

- Yes (We are at an HLH Education Session after all)
Does This Patient Have HLH?

- **Yes** (We are at an HLH Education Session after all)
- **No** (This seems like a trick question since we are at an HLH Education Session!)
HLH: What do we mean?

- HLH=Hemophagocytic Lymphohistiocytosis
  - Same # of syllables as: Supercalifragilisticexpialidocious!
HLH: What do we mean?

- HLH = Hemophagocytic Lymphohistiocytosis
  - Same # of syllables as: Supercalifragilisticexpialidocious!
- Name stems from the pathologic findings observed in patients
  - Hemophagocytic
    - hem = blood
    - phagocytic = of a cell that eats
  - Lymphocytosis = expansion of lymphocytes
  - Histiocytosis = expansion of tissue macrophages
HLH: What do we mean?

• HLH=Hemophagocytic Lymphohistiocytosis
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• Name stems from the pathologic findings observed in patients
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  • Lymphocytosis = expansion of lymphocytes
  • Histiocytosis = expansion of tissue macrophages

• HLH= a severe hyperinflammatory syndrome:
  • a recognizable pattern of clinical, laboratory, and microscopic findings caused by inflammation
What does this syndrome look like?

• Many doctors use the HLH-1994/2004 “criteria”
  • Developed for the Histiocyte Society treatment studies
  • Caveat 1: patients may lack 5/8
  • Caveat 2: patients with 5/8 may have something else

• Other manifestations can include:
  • Liver problems or liver failure
  • Brain/Spine Disease (sometimes isolated)
  • Other labs may be abnormal
    • LDH, D-Dimer

Caution: Not very accurate
Other Tools to Diagnose HLH or MAS

- The HScore (Fardet et al, 2014)
  - Developed in adults with primarily malignancy or infection-associated HLH

- The MAS-2016 criteria (Ravelli et al, 2016)
  - Developed to classify MAS in patients with systemic JIA

### Questions

1. **Known underlying immunosuppression?**
   - No

2. **Temperature?**
   - 38.4-39.4 °C

3. **Organomegaly?**
   - Hepatomegaly or splenomegaly

4. **Number of cytopenias?**
   - 2 lineages

5. **Ferritin?**
   - 2,000-6,000 ng/mL

6. **Triglyceride level?**
   - ≤2.5 g/L

7. **Fibrinogen?**
   - ≥30 U/L

8. **AST?**
   - No

9. **Hemophagocytosis features on bone marrow aspirate?**
   - No

### Results

- **H Score**
  - 208

- **Probability of Hemophagocytic syndrome**
  - 88-93%

A febrile patient with known or suspected systemic juvenile idiopathic arthritis is classified as having macrophage activation syndrome if the following criteria are met:

- Ferritin > 684 ng/mL
- Platelet count ≤ 181 x 10⁹/liter
- Aspartate aminotransferase > 48 units/liter
- Triglycerides > 156 mg/dl
- Fibrinogen ≤ 360 mg/dl

*and* any 2 of the following:
Who develops the syndrome of HLH?

- And what is primary versus secondary HLH?
Primary Versus Secondary HLH

- **Primary (or Genetic) HLH**: Inherited genetic immune deficiencies/immune dysregulation disorders that cause HLH
  - Genetic problems lead to immune systems that are broken in 1 of 2 ways:
    - 1: Immune system cells can’t kill infected or cancerous cells
    - 2: Immune system is making too many inflammation proteins
Primary Versus Secondary HLH

- **Secondary HLH**: HLH that occurs in “normal” people because of a *strong immune stimulus*: Cancer, Infection, Metabolic or Rheumatologic Disease
NACHO Conceptualization

Secondary HLH

Primary HLH

Genetic/Primary HLH = PRF1, UNC13D, STXB2, STX11

Other Genetic HLH

Other IEI

Secondary HLH

Genetic/Primary HLH

Other Genetic HLH

Other IEI
Why does the HLH happen?

• Let’s start with the syndrome of HLH in the genetic HLH disorder setting
Genetic HLH Disorders

- Inborn errors of immunity which have a high risk of developing HLH and HLH is a main problem of the disorder.

- **Familial HLH:** Defective lymphocyte granule mediated cytotoxicity
  - *PRF1, UNC13D, STXBP2, STX11, RHOG*

- **Pigmentary Disorders Associated with HLH:** Defective lymphocyte granule mediated cytotoxicity
  - *AP3B1, LYST, RAB27A*

Genetic HLH Disorders

- Inborn errors of immunity which convey a high risk of developing HLH and feature HLH as a main manifestation of the disease.

- **Familial HLH:** Defective lymphocyte granule mediated cytotoxicity
  - *PRF1, UNC13D, STXBP2, STX11, RHOG*

- **Pigmentary Disorders Associated with HLH:** Defective lymphocyte granule mediated cytotoxicity
  - *AP3B1, LYST, RAB27A*

> These broken genes mean the immune system can’t kill infected or cancerous cells

> That makes the immune system angry and it gets all fired up!
Normal Cytotoxic Response

De Saint Basile, Nature Rev Imm, 2010
Crippled Cytotoxic Response

1. Can’t Kill Target
2. Expanded Lymphocytes Won’t Die

De Saint Basile, Nature Rev Imm, 2010
Genetic HLH Disorders

- Inborn errors of immunity which convey a high risk of developing HLH and feature HLH as a principal manifestation of the disease.

- Familial HLH: Defective lymphocyte granule mediated cytotoxicity
  - PRF1, UNC13D, STXBP2, STX11, RHOG

- Pigmentary Disorders: Defective lymphocyte granule mediated cytotoxicity
  - AP3B1, LYST, RAB27A

- XLP-1: Defective SLAM-receptor mediated cytotoxicity & other
  - SH2D1A

Nichols and Marsh
Genetic HLH Disorders

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- XLP-1: Defective SLAM-receptor mediated cytotoxicity & other
  - SHD2D1A

- XLP-2: Dysregulated TNF-R and NLRP3 Inflammasome function & other
  - XIAP

- NLR4: GOF/Constitutively Active NLRC4 Inflammasome Function

- CDC42: GOF variants in the C-terminal region of CDC42 lead to increased Pyrin Inflammasone Function (Nishitani-Isa et al)

Constitutively Active Due to Pathogenic GOF Variants

TLR/NLR agonist

HLH

IFNg

(IL-12)

IL-1B

IL-18

IL-1B

IL-18

IL-1B

IL-18

IL-1B

IL-18

NLRP3

inflammasome

XIAP

Ros

Pro-IL-1β

NLRP3

Inflammasome

Zhang et al, 2015

Chiang et al, 2022
Genetic HLH Disorders

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• **XLP-1:** Defective SLAM-receptor mediated cytotoxicity & other
  •  *SHD2D1A*

• **XLP-2:** Dysregulated TNF-R and NLRP3 inflammasome function & other
  •  *XIAP*

• **NLCR4:** Constitutively Active NLRC4 Inflammasome Function

• **CDC42:** Defective Formation of Actin-Based Structures; Defective Proliferation, Migration, and Cytotoxicity; Increased Inflammasome Function; IL-1beta and IL-18 Production

• **EBV Susceptibility Disorders:** *MAGT1, ITK, CD27, CD70, CTPS1, RASGRP1*: Complex but many have specific *cytotoxicity defect*
Pathways to HLH/MAS

**Cytotoxic defect**
(Perforin Deficiency, Degranulation Defect; SAP deficiency, MAGT1, CD27, CD70, etc)

Lack of Target Cell Kill

Uncontrolled, Persistent Activation of Lymphocytes and Macrophages

IL-6, IL-10, IL-1β, IL-18, TNF-α

IFN-γ

IFN-γ
Pathways to HLH/MAS

Cytotoxic defect
(Perforin Deficiency, Degranulation Defect; SAP deficiency, MAGT1, CD27, CD70, etc)

Inflammasome Dysregulation
(XIAP, NLRC4, CDC42?)

Uncontrolled, Persistent Activation of Lymphocytes and Macrophages

Lack of Target Cell Kill

IFN-γ

Overactive Monocytes and Macrophages

IL-18

Excessive Antigen Stimulation Due to Overwhelming Infection, Malignancy, Other

Rheumatologic Conditions (sJIA etc)

IFN-γ

IL-1β

IL-6, IL-10, IL-1β, IL-18, TNF-α

IL-12

IL-18

(IL-12)
Pathways to HLH/MAS

**Cytotoxic defect**
(Perforin Deficiency, Degranulation Defect; SAP deficiency, MAGT1, CD27, CD70, etc)

- Lack of Target Cell Kill
  - IFN-γ

**Inflammasome Dysregulation**
(XIAP, NLRC4, CDC42?)

- IL-18
- Overactive Monocytes and Macrophages

**Uncontrolled, Persistent Activation of Lymphocytes and Macrophages**

- IFN-γ
- IL-6, IL-10, IL-1β, IL-18, TNF-α

**Secondary HLH**
Excessive Antigen Stimulation Due to Overwhelming Infection, Malignancy, Other

**Rheumatologic Conditions**
(sJIA etc)

- IL-18
- (IL-12)
Cytokine Storm

Scott Canna & Randy Cron
Blood tests that help diagnosis a syndrome of HLH and monitor activity: Biomarkers

- Ferritin
- Soluble IL-2 Receptor
- HLA-DR
- CXCL9
- IL-18
- Others
Ferritin

- Ferritin stores iron
- Ferritin increases during inflammation
- Easy to check at most hospitals
- Some degree of ferritin elevation is essentially required for the diagnosis of HLH.
  - A level greater than 500 µg/L is very sensitive
  - A level greater than 2000 µg/L can better differentiate HLH
Soluble IL-2R

- Activated T cells (immune system cells) upregulate the IL-2 receptor, which is cleaved by proteases released by activated mononuclear phagocytes.
- High levels indicate high levels of T cell activation - it’s a good barometer of T cell activation.
HLA-DR

- Some centers use T cell HLA-DR expression (a marker of T cell activation) in place of or in addition to measurements of sIL-2R

Amman et al
Newer Tests: CXCL9 and IL-18

- **CXCL9**: Good marker of IFNg pathway activity
  - CXCL9 is secreted by monocytes, endothelial cells, fibroblasts in response to IFN-γ which is a critical inflammatory cytokine in HLH

- **IL-18**: Good marker of Inflammasome Activity
  - The immature forms of IL-18 and IL-1beta are activated by inflammasomes, and high levels indicate that inflammasomes are abnormally active
How do we use these tests?

• Elevations in any or all of these tests help make a diagnosis of the syndrome of HLH
• We can also watch the levels rise and fall as HLH is more or less active
Example: Ferritin
How Do You Diagnose Genetic HLH Disorders?

- Genetic Testing
- Screening Tests
Do All HLH Patients Need Genetic Testing?

- All “young” patients need testing
- Some “old” patients need testing

- It is important to know if there is a genetic disease that caused the HLH
  - Genetic = risk of recurrent HLH
  - Genetic = many (not all) will need a bone marrow transplant
Types of Genetic Tests

• HLH or Immune Deficiency Panels
  • Panels look at many HLH and/or Immune Deficiency genes all at once

• Whole Exome/Whole Genome Sequencing
  • This testing looks at HLH and Immune Deficiency genes along with genes outside of the immune system

• Single Gene Sequencing
  • This is used when the family is already known to have a genetic disease.
    • If one child has HLH due to pathogenic variants in PRF1, then the other siblings can just be tested for variants in PRF1
Screening tests come back quicker than most genetic tests.

These are blood tests that look for protein deficiencies or abnormal immune system cell function.
• Familial HLH
  – PRF1
    • Perforin Expression
  – UNC13D, STXBP2, STX11, RAB27A
    • CD107a

• XLP1
  – SAP Expression

• XLP2
  – XIAP Expression
  – Functional Assay

• Griscelli Syndrome
  – CD107a

• Chediak Higashi
  – CD107a

Selected Screening Tests
Example: Perforin Deficiency

NK cells

Normal Adult

Patient
Inheritance of Genetic HLH Disorders
Autosomal Recessive

**PRF1, UNC13D, STXBP2, STX11**

25% of children are sick (male or female)
X-linked

**XIAP, SH2D1A**

50% of males are sick

50% of females are carriers
Autosomal Dominant

**NLRC4**

50% of children are sick
(male or female)
How Do We Treat HLH/MAS?
How Do We Treat HLH/MAS?

Treat HLH/MAS with Chemo/Immuno-Therapy

Secondary HLH

Many (not all) Primary HLH

Figure Out What Is Causing HLH

Treat Underlying Predisposition/Trigger

HCT

Adapted from Mike Jordan
How do we treat HLH? No single answer.

• Treatment modeled on HLH-1994 (steroids, etoposide/VP-16, with or without cyclosporine) is still widely used and recommended, but more treatment approaches are now available, and care is evolving.

• Disclaimer: Individual treatment decisions should be made with the clinical context of the patient in mind, with consideration of local center practices, and in consultation with physicians experienced in the treatment of HLH.
What can we use to treat HLH?

Adapted from Kevin McNerney, ASTCT Cell Therapy Committee: CAR T-cells and HLH Working Group
Dexamethasone & Etoposide +/- Cyclosporine

- Dexamethasone and etoposide usually “modeled” on the HLH 1994 protocol.
Etoposide kills activated immune system cells and reduces inflammation

- Etoposide is a chemotherapy used in various cancer treatments

Johnson et al, 2014

HLH mice: activated T cells

After etoposide treatment!
Recommendations for the Use of Etoposide-Based Therapy and Bone Marrow Transplantation for the Treatment of HLH: Consensus Statements by the HLH Steering Committee of the Histiocyte Society

Stephan Ehl 1, Itziar Astigarraga 2, Tatiana von Bahr Greenwood 3, Melissa Hines 4, AnnaCarin Horne 3, Eiichi Ishii 5, Gritta Janka 6, Michael B Jordan 7, Paul La Rosée 8, Kai Lehmburg 9, Rafal Machowicz 10, Kim E Nichols 11, Elena Sieni 12, Zhao Wang 13, Jan-Inge Henter 14
HLH-94: 2018 consensus recommendations

1. **INITIAL THERAPY**
   - Dexa (mg/m²)
     - Week 1-2: 10 mg/m²
     - Week 3: 5 mg/m²
     - Week 4: 2.5 mg/m²
     - Week 5: 1.25 mg/m²
   - VP-16: 200 mg/m² weekly
   - CSA: 150 mg/m² daily
   - I.T. therapy: 10 mg/m² daily

2. **CONTINUATION THERAPY**
   - Dexa (mg/m²)
     - Week 9: 10 mg/m²
     - Week 10: 10 mg/m²
     - Week 11: 0 mg/m²
     - Week 12: 0 mg/m²
   - VP-16: 150 mg/m²/day
   - CSA: 125 mg/m²/day
   - I.T. therapy: 10 mg/m²/day

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Dexa = Dexamethasone daily with 10 mg/m² for 2 weeks, 5 mg/m² for 2 weeks, 2.5 mg/m² for 2 weeks, 1.25 mg/m² for 1 week and taper and discontinue during 1 week. Then pulses starting every second week with 10 mg/m² for 3 days.

VP-16 = Etoposide 150 mg/m² i.v.

CSA = Cyclosporine A aiming at blood levels of around 200 microgram/L (monoclonal, trough value). Start after 2 weeks with 6 mg/kg daily perorally (divided in 2 daily doses).

I.T. therapy = Methotrexate doses: <1 year 6 mg, 1-2 years 8 mg, 2-3 years 10 mg, >3 years 12 mg each dose. Maximum 4 doses prior to re-evaluation, but start only if progressive neurological symptoms or if an abnormal CSF has not improved.
Notes Regarding Etoposide Use

- Bone marrow suppression is common. CBC should be monitored.
- Reactions can occur.
- Requires dose adjustment with renal insufficiency.
- Low blood pressure can happen if given too quickly in 1% to 2% of patients. Usually given over 1 hour.
- Other side effects: Generally well tolerated in HLH. Side effects can include hair loss, nausea, vomiting, and inflamed and sore mouth. Small increase in secondary cancer risk, particularly with cumulative dosing of 2.0 g/m² (Pedersen-Bjergaard et al 1991).
- **Lower moderate dosing of 50-100mg/M2 once weekly recently reported by Horne et al 2021**
- **DO NOT USE FOR MONTHS ON END**
- Patients should be on medicines to prevent infections
Notes Regarding Dexamethasone and Other Corticosteroid Use: The List is Long

- Muscle weakness
- High blood sugar
- Difficulty in regulating emotion
- Difficulty in maintaining linear thinking
- Weight gain due to increased appetite
- Corticosteroid-induced lipodystrophy (moon face, central obesity)
- Immune suppression
- Depression, mania, psychosis
- Unusual fatigue or weakness
- Abdominal pain
- Peptic ulcer (Patients should receive prophylaxis)
- Bone thinning/weakness
- Other bone problems
- Stretch marks
- Trouble sleeping
- Severe joint pain
- Cataracts or glaucoma
- Anxiety
- Severe swelling
- Mouth sores or dry mouth
Cyclosporine

9. CSA is not recommended in the first weeks of HLH-94 therapy as this may induce toxicity. In patients with primary HLH who have achieved remission, CSA may be used to potentially prevent disease reactivation. [Strong Consensus]

• Side Effects: unusual hair growth/hirsutism, high blood pressure, abnormal kidney blood tests, kidney toxicity, seizures/posterior reversible encephalopathy syndrome, tremor, gum tissue growth

• Monitor Levels

• Some experts use, some experts don’t.
General Care

- Patients should be on medicines to prevent infections per each institution’s standard of care
- Patients may need varying levels of supportive care and blood transfusion and other support
- May need brain/central nervous system treatment
How Well Do Dexamethasone and Etoposide Work?

• Dexamethasone, Etoposide, -/+ Cyclosporine
  • 25% Remission Rate
  • 50% Remission Rate
  • 75% Remission Rate
  • 100% Remission Rate
How Well Do Dexamethasone and Etoposide Work?

• Dexamethasone, Etoposide, -/+ Cyclosporine
  • 25% Remission Rate
  • 50% Remission Rate
  • 75% Remission Rate
  • 100% Remission Rate
What are some other treatments can we use?

- Rituximab (for EBV- HLH)
- Anakinra
- Emapalumab
- Liposomal Doxorubicin Regimen
- PD-1 Inhibitors? (for EBV- HLH)
- ATG
- Alemtuzumab
- Jak Inhibitors
Rituximab

- Antibody that binds CD20 on B cells
- B cells typically infected with EBV
  - If no more EBV+ B cells, then hopefully no more trigger of HLH

- Will not get rid of other EBV infected cells
Rituximab: Effects in EBV- HLH

Chellapandian et al
Rituximab Notes

• Severe allergic reactions/Infusion Reactions
• Prolonged or permanent destruction of B cells. B cells make antibodies. If B cells are not working, patients need antibody replacement infusions (IVIG).
• Progressive multifocal leukoencephalopathy (PML)
• Hepatitis B reactivation
Anakinra

• Interleukin-1 (IL-1) receptor antagonist: prevents the action of IL-1 which is an inflammatory cytokine

• *Mostly useful in the Rheumatologic setting

• *Data is limited- and most patients also receive other therapies

• However: the rheumatologists can tell you that it works nicely for some patients with rheumatologic HLH/macrophage activation syndrome

Baskar et al, 2016
Anakinra
Notes

• In general, it is safe compared to other agents
  • Increased incidence of serious infections only 2% vs. Placebo < 1% in RA trials
  • Be careful about using it in combination with TNF targeting agents (or other agents) due to increased infection risk
• You may need to increase the dose.
• Give every other day in patients with end-stage renal disease
• Reactions are possible
  • Can cause low neutrophil counts- reduce dose
  • In general- not enough for true HLH.
Emapalumab

Anti-Interferon gamma monoclonal antibody therapy
Prevents the action of interferon-gamma, an inflammatory cytokine

Response to Emapalumab

• Complete Response: 21-26%
• Partial Response: 30-32%
• Improvement: 7-12%

• FDA approved for second line therapy of patients with HLH 2018

Emapalumab Notes

• The package insert says to start dosing at 1mg/kg: patients usually need more
• CXCL9 monitoring is very useful
  • Are they responding/are we giving enough?
  • Useful to monitor other treatments too
• Patients should be on medicines to prevent infections
Alemtuzumab

• Alemtuzumab is a monoclonal antibody that destroys most immune system cells
• It is very powerful
Alemtuzumab

Notes

• Severe allergic reactions can occur
  • Pre-medications should be given (steroids, diphenhydramine)

• Fever, chills, flushing, dizziness, shortness of breath, nausea, vomiting, or rash/itching

• Patients have a high chance of viral and other infections
  • Patients need to be on medications to prevent infections
  • Patients need to be monitored for EBV, CMV, adenovirus and other viral reactivations which commonly occur

• Usually used in refractory cases or as a bridge to transplant
  • Sometimes used up front, especially if you live in France
JAK Inhibitors: Ruxolitinib

• Several case reports/series

• Blocks signaling of inflammatory cytokines

• Open multi-center trial (Melissa Hines and Kim Nichols: St Jude Research Hospital)
JAK Inhibitors: Ruxolitinib

- Several case reports/series
- Blocks signaling of inflammatory cytokines
- Open multi-center trial (Melissa Hines and Kim Nichols: St Jude Research Hospital)
Ruxolitinib

- Need to be able to take by mouth
- Increased risk of infections
- Can cause anemia, low platelets, and low neutrophil counts - monitor CBC
- Reduce dose if on strong CYP3A4 Inhibitors (azoles)
- Dose adjustment for renal impairment
- Dose adjustment for hepatic impairment
Conclusions

• HLH is a severe life-threatening syndrome of extreme inflammation
• The syndrome can be recognized based on clinical manifestations and laboratory tests
• Some patients with the syndrome of HLH have underlying genetic immune deficiencies
  • A portion of these patients will need a bone marrow transplant
• First line treatments for HLH will not be effective in all patients but treatments are expanding
Resources

- HLH Center of Excellence at CCHMC
  https://www.cincinnatichildrens.org/service/h/hlh/contact

Other Resources:
  https://primaryimmune.org/disease/hemophagocytic-lymphohistiocytosis-hlh
  https://www.matthewandandreww.org/
  https://www.liamslighthousefoundation.org/
  https://histio.org/

Several other major academic centers also have good resources- Google your favorite:
  https://www.chop.edu/conditions-diseases/hemophagocytic-lymphohistiocytosis-hlh
Q&A SESSION:
YOUR QUESTIONS ANSWERED
Additional Resources

- Cincinnati Children’s HLH Center for Excellence: https://www.cincinnatichildrens.org/service/h/hlh

- IDF’s HSCT Resources: https://primaryimmune.org/hematopoietic-stem-cell-transplantation-hsct

- IDF Resource Center: https://primaryimmune.org/resource-center

- IDF Support Services: https://primaryimmune.org/support-services
Have more Questions?

www.Primaryimmune.org/ask-idf

800-296-4433
WE VALUE YOUR FEEDBACK...

Please take a moment to complete our Evaluation Survey after the Program!
Upcoming Events

2022 PI Conference
Thursday October 6-
Saturday, October 8th

IDF Lunch & Learn:
Hyper IgE/ JOB Syndrome
Wednesday, 10/19/22
Alexandra Freeman, MD
2:30 PM ET

For a list of all upcoming IDF Events, visit:
https://community.primaryimmune.org/s/events?language=en_US
THANK YOU!

Rebecca Marsh, MD
Clinical Director, Primary Immune Deficiency Program and HLH Center of Excellence
Cincinnati Children’s Hospital