Lung GVHD. Current Challenges and Future Hope.

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“We are all working so hard to be self-fulfilled, individually successful, and personally healthy...that we have forgotten the real purpose and path to health and healing is to make joyful connections.”
- Francis Peabody MD, 1927
Quotes from patients with Lung GVH

“I need to breathe to live, but I also need to live to breathe.”

“I’m alive, but I’ve had so much loss.”

“If I had known I would get lung disease like this, I would have rather have died from my AML.”

c/o Guang-Shing Cheng MD
Fred Hutchinson Cancer Center
How do we define Lung GVHD

• The lung manifestation of chronic GVHD.
• An “obstructive” airway disease that occurs ~ 1-year post-transplant. Air can get in. It can’t get back out. The air you breathe gets trapped, then stagnant in your lungs.
• Symptoms: Shortness of breadth, chronic cough.
• Develops in 10-20% of all patients with chronic GVHD
• Medical term: Bronchiolitis Obliterans Syndrome (BOS)
Lung GVHD Knowledge Growth in past decade

- Your support
- Novel Clinical Trials
- New Diagnostic Techniques
- Collaborative Teams
- Predictive Biomarkers
Primer: Pathology of Lung GVHD

Air Sac (Alveolus)

Small Airway (Bronchiole)

Normal lungs

Lung GVHD (Bronchiolitis Obliterans Syndrome)
Risk Factors for Lung GVHD.
University of Michigan Data Base (n=1016 patients)

Those at highest risk for Lung GVHD include:
• Patients with a history of severe acute Graft Versus Host Disease.
• Patients who developed viral infections and/or Pneumonia within the first 100 days post-transplant.
• Patients who had very low PFT values either prior to transplant or at Day 100 post-transplant.
How is Lung GVHD Diagnosed?
NIH Criteria for Diagnosing Lung GVHD\textsuperscript{1,2}

- Requires Pulmonary Function Testing.
- The main criteria is an FEV1 < 75% predicted for age and size.
- The FEV1 must have declined $\geq$ 10% from prior measurements.
- No active infection.
- What does all this mean, in English?

\textsuperscript{1} Filipovich AH BBMT 2005, \textsuperscript{2} Jagasia M BBMT 2015
Pulmonary function tests are a group of tests that help healthcare providers to know the efficiency of your lungs.
PFT’s: The main parameter we (MD) look at:

**FEV1**: Forced Expiratory Volume in 1 second

The volume of air you can **forcibly exhale** in 1 sec.
Pulmonary Function Tests: Primer

Residual volume (RV)

Tidal volume

Forced Vital Capacity (FVC)

Normal Breathing

FEV1

Residual volume (RV)
Pulmonary Function Tests: Primer

- Residual volume (RV)
- Tidal volume
- Forced Vital Capacity (FVC)
- Normal Breathing
- FEV1

PFT
Early Diagnosis is Critical.
Survival by FEV1 at “Time of Initial Diagnosis” of Lung GVHD

Median FEV1 = 57% at diagnosis of Lung GVHD
The problem is that we start treating here

Normal lungs

Lung GVHD (Bronchiolitis Obliterans Syndrome)
We need to be treating here

Normal lungs → Lung GVHD
(Bronchiolitis Obliterans Syndrome)
We need to recognize who’s at risk here

Normal lungs  \rightarrow  Lung GVHD
(Bronchiolitis Obliterans Syndrome)
The patient perspective on early detection

- 54 patient surveys administered via email at 3 sites (FHCC, Stanford, Geneva)
- 30 respondents (55% response rate)

5. What aspects of BOS and lung complications after stem cell transplant should researchers focus on? rank in order of importance (1 to 6; 1 being of highest priority)

1. Early diagnosis and prevention
2. Treatment
3. Biological mechanisms
4. Patient and clinician education
5. Quality of life
6. Other - write in next question
Recommendation for monitoring PFT

“85% of success is just showing up”
- Woody Allen, 1987

Just get PFT’s done
How often should PFT be performed?

2020 NIH Consensus Development Project (Kitko TCT 2021)

Recommended: Obtain PFT every 3 months for 1\textsuperscript{st} year after BMT.
Once chronic GVHD is diagnosed: Obtain PFT every 3 months.
Issue: Are there alternatives to standard PFT’s?
PFT testing in your hands

• NIH funded study. Guang-Shing Cheng MD (Seattle)
• Patients perform PFT’s weekly, at home.
• Wireless Bluetooth-enabled device.
• Readings sync with patient’s smart phone. Patient’s can see their FEV1.
• Readings transmitted electronically to MD
• Large, four center study now in progress.
New CT scan technology: Called PRM
Color codes the lungs to see areas of lung damage

1 year post-BMT
Mild lung symptoms.
PFT and CT both normal

2 years post-BMT
Lung GVH is diagnosed

5 years post-BMT
Severe symptoms
Therapy for Lung GVHD

• Few Randomized Clinical Trials
• Two trials that have impacted care:
  a. Inhaled Steroids (Bergeron A, Am J Respir Crit Care Med. 2015)
  b. FAM Therapy (Williams KM, BBMT 2016), n=36 patients
     F = Inhaled Fluticasone (steroid)
     A = Azithromycin (antibiotic and anti-inflammatory agent)
     M = Montelukast (Singular) (anti-inflammatory agent)
Trials for Lung GVHD (BOS) on ClinicalTrials.gov

Belumosudil

Avelestat (NCT02669251)

Itacitinib (NCT02669251)

Ruxolitinib
NCT03315741, NCT04908375

Nintedanib (NCT03805477)

Liposomal CSA (NCT04107675)

Pirfenidone (NCT03315741)
Therapy: The power of exercise

PFT report: 50 year old male with chronic GVH

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<th>LUNG MECHANICS</th>
<th>Actual</th>
<th>Pred</th>
<th>%Pred</th>
<th>Ac</th>
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<tbody>
<tr>
<td>FVC (liters)</td>
<td>3.54</td>
<td>4.47</td>
<td>79%</td>
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<tr>
<td>FEV1 (liters)</td>
<td>1.71</td>
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<td>FEV1/FVC (%)</td>
<td>48%</td>
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<td>FEV6 (liters)</td>
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<td>FET (sec)</td>
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<td>FEF50 (l/sec)</td>
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<td>100%</td>
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<td>MVV (l)</td>
<td>3.54</td>
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<tr>
<th>LUNG VOLUMES</th>
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<td>ERV (liters)</td>
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<td>DLCO (ml/min/mmHg)</td>
<td>22.20</td>
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<td>IVC (liters)</td>
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<td>VA (liters)</td>
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<td>DLCO/VA (ml/mHg/l)</td>
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<td>107%</td>
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<td>Hgb</td>
<td>12.0</td>
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Patient effort appeared good. Heart rate: 80 bpm. RTD

Lung function:
Pre-bike riding stage:
FEV1 = 58%, DLCO = 77%

After years of bike riding
FEV1 = 52%, DLCO = 107%

DLCO measures your ability to transport air into the blood stream.
“what is the bravest thing you’ve ever said?” asked the boy.

“Help,” said the horse.

From: “The Boy, the Mole, the Fox and the Horse” (C. Mackesy)
Thank you everyone.

• To nbmtLINK.
• To the patients we serve.
• To the medical teams we work with.
• To all of you.

“Happy are those who dream dreams, and have paid the price to make them come true.” - L.J. Suenens