TRIO STUDIO: Study on the Role of Inflammation in Progressive Multifocal Leukoencephalopathy (PML)

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October 24, 2018
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Attendees:
Tharani Jeyaram, UChicago; Jairo Chavez, RUMC; Cynthia Tom Klebba, Loyola; Drew Simon, RUMC; Raj Shah, RUMC; Keiichi Sato, IIT; Nurie Dervishi ITM, UChicago; Kathleen Ferraro, ITM UChicago; and Sherry Robison, ITM UChicago

Summary
Igor Koralnik, M.D., Neuroinfectious Diseases, Rush University Medical Center, introduced Progressive Multifocal Leukoencephalopathy (PML) and the subsequent challenges of enrolling eligible PML subjects at Rush University Medical Center and John H. Stroger, Jr. Hospital of Cook County. Dr. Koralnik gave background information on his study personnel which includes three physicians all at Rush and two who also practice at Stroger. He also has two clinical coordinators in his team. He gave background information on PML which is often a deadly disease of the brain for which there is no cure. It is caused by the reactivation of JC virus, which infects most of the healthy population without causing any disease. If patients are on immunosuppresants, JC virus can destroy brain cells, leading to multifocal demyelination and PML.

The primary aims of the study are to determine the role of inflammation in PML, characterize T cell response against JC virus, define MRI markers of outcome and understand why PML patients develop seizures. Procedures for the study include an office visit at 3, 6 and 12 months which are billed to insurance. Blood samples are drawn to measure cellular immune response to JC virus, a dense array EEG is done, and an MRI at UIC MRI Core Center also is performed. These are all billed to the study.

Dr. Koralnik requested studio audience to ideate solutions for two questions:

1. How to improve recruitment and communication with potential study subjects?

2. How do we improve the number of referrals for this study from across Chicagoland?
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Design Thinking approach was used to solve the problems faced by Dr. Koralnik and his team at Rush University Medical Center, Department of Neuroinfectious Diseases. Many suggestions, based on experiences at different institutions, were made.

Top 3 Actions Proposed by the Studio Participants to Dr. Koralnik:

1. **Social Media Based Solutions**: Create a Facebook and Twitter account to assist in reaching savvy participants. Target support groups through social media to post study information. Create a self-service portal for potential study participants to learn more about study. Create testimonials of study participants and family members as well.

2. **Internet Based Solutions**: Optimize search engines, simplify symptoms so that people can browse and learn. Make symptoms more understandable to patients who have not yet been diagnosed but are looking for a diagnosis, and maybe simplify enough to provide a portal/self-service tool for potential participants to volunteer.

3. **Physical Outreach Through ITM via TRIO**: Use the Trial Innovation Network (TIN) as a potential tool for reaching potential participants. Share IRB approved flyers/advertisements with TRIO so they can distribute to ITM partners and work with ITM Communications to post on the ITM website.
TRIO Studio Problem Description:

The goal is to enroll eligible participants into the Progressive Multifocal Leukoencephalopathy (PML) study at Rush University Medical Center and John H. Stroger, Jr. Hospital of Cook County.

Igor J. Koralnik, M.D. from Rush University Medical Center introduced the problem. PML is a rare disease. Patients may be severely incapacitated which may limit their availability for doctor visits. There are barriers for referrals across hospital networks. Dr. Koralnik has given PML talks at RUMC, NWMH, UIC, UChicago and Loyola. He has sent emails and “Dear Doctor Letters” to various neurologist. In addition, he and his team have done cyber consults with PML patients who contact him over the internet.

Dr. Koralnik’s call to action: “Do you have suggestions for improving recruitment and communication with potential study subjects? How do we improve the number of referrals for this study?”

Figure 1. Dr Koralnik leading the discussion on PML and Recruitment Issues.
Main problem for the studio participants to solve:
Problem context and issues and opportunities were discussed. Here is the visualization of the discussion.

![Diagram](image)

**Figure 2. Problem Context and Definition**

**Studio Methodology**
Design Thinking approach used as part of the studio to solve this problem.

**Design Thinking Method**
We used the Design thinking approach with five steps:

1. Created a free form mind map of the problem and identification of issues – Mind Mapping technique
2. Actionable insights were identified
3. Generated ideas to address issues
4. Synthesized solutions from the smaller ideas – Creative integration of smaller ideas led by Design Thinking Expert facilitator was done using white boards.
5. Solutions were proposed and were rated by the team on implement-ability (0-4 scale)
Design Thinking Based Solutions:

Problem visualized with Insights
The group first discussed the problem and its context yielding the following context diagram as well as the stakeholder map:

Figure 3 Mind Map of Issues and Stakeholders
High level insights:
Following the context discussions, insights were generated as follows:

**Figure 4 Insight into what Rare Disease complication means for recruitment**

- Increased awareness needed
- Risk for developing PML follow sooner
- Patient is severely incapacitated

- People-resources to understand and volunteer
- Physicians-educate and train about PML
- Awareness through Social Media (Twitter)

**Figure 5 Insight into the System Barriers.**

- There are barriers for referrals across hospital network
- Decreased awareness in hospital systems
- Time Pressure

- There’s one referral per month in Boston and Chicago
- There’s one patient every 3 months in Chicago
- No other neuro PML Specialists in Chicago area
- No other PML studies in Chicago
- Need constant recruitment for grants
- Waiting for prescriptions is a barrier

**Solutions Generated by Design Thinking Approach Team:**
Six relatively implementable solutions were created to solve the issues of getting a study started. They are as follows:
1. **Social Media Based Solutions**: Create a Facebook and Twitter account for the study to assist in reaching savvy participants. Target support groups through social media to post study information. Create a self-service portal for potential study participants. Create testimonials of study participants and/or their family members to post on social media.

2. **Internet Based Solutions**: Optimize search engines, simplify symptoms and make them more understandable to patients who have not yet been diagnosis but looking for a diagnosis, and simplify a portal/self-service tool for potential participants.

Figure 6 Solutions as visualized on whiteboards
3. **Physical Outreach Through ITM via TRIO**: Use the Trial Innovation Network (TIN) as a potential tool for reaching potential participants. Share IRB approved flyers/advertisements with TRIO so they can distribute to ITM partners and work with ITM Communications to post on the ITM website.

4. **Grand Rounds**: Conduct Grand Rounds at all ITM institutions (Rush, Advocate, Loyola, Northshore, UChicago). Concentrate on Rare Disease, Infectious Disease, and Primary Care Physicians. Conduct Grand Rounds at Stroger and UIC concentrating on the same departments.

5. **Awareness of Clinicians (Neurologist, Infectious Disease, etc.)**: Establish an awareness campaign through all ITM institutions and departments such as Infectious Disease, Neurology and Primary Care Physicians/Family Medicine.

6. **Speciality Medication Rush Pharmacy Outreach**: Reach out to Rush Pharmacy to determine all patients that are being treated with immunosuppressive drugs with known risk of PML (e.g. Tysabri) Work on specialty pharmacy review of records of patients taking this drug to educate about symptoms of PML and about resources if symptoms noted (including referral to PML Centers of Excellence to reduce diagnostic delays).

<End of Document. Thank you.>
Appendix 1.
Slides used by Igor J. Koralnik, M.D., Rush University Medical Center.

Appendix 2.
Session Pictures
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Appendix 3.
Actual pictures of white board from the studio session.
INSIGHTS:

- Rare Disease
  - Pt. severely incapacitated
  - Barriers for referring across hosp network
    - Referral (1 per month, Boston)
    - 1 pt. every 3 months (Chicago)
- No Neuro PML Spec. in Chicago Area (Closest is at St. Louis)
- No other PML Studies in Chicago
- No competing study in US (so this is not a barrier)
- Need constant recruitment for grant (time pressure)
  - Waiting for dx
  - Risk for developing PML
    - Follow sooner (66 vs 6 per 1000)
  
- Awareness
  - Social media (twitter)
IDEAS

- Increase Geographic Reach outside IL
- Large network of rare disease

Insurance Company

Cost Savings
- Solution to 
- Pharmaceutical Benefits Manager

CTA chain adverts

Social Media brand awareness

Internet adverts

Social Patient Groups

Self Service Portal

Broken down sympathy
Simple to understand
Addendum 1 – 30-Day Follow-Up

Solutions Generated by Design Studio

1. **Social Media Based Solutions**: Create a Facebook and Twitter account for the study to assist in reaching savvy participants. Target support groups through social media to post study information. Create a self-service portal for potential study participants. Create testimonials of study participants and/or their family members to post on social media.

**Implementation and Results:**

Since the Design Studio, an amendment has been submitted to the IRB to create a Facebook page to bring awareness to the study. The PI has created an email address for the study so potential
participants can email the study email address. The PI and study team is currently working on the content for a Facebook page.

2. **Internet Based Solutions:** Optimize search engines, simplify symptoms and make them more understandable to patients who have not yet been diagnosis but looking for a diagnosis, and simplify a portal/self-service tool for potential participants.

**Implementation and Results:**

Since the Design Studio, the PI has created a self-service portal and a study email address. The email address is checked daily by the research team.

3. **Physical Outreach Through ITM via TRIO:** Use the Trial Innovation Network (TIN) as a potential tool for reaching potential participants. Share IRB approved flyers/advertisements with TRIO so they can distribute to ITM partners and work with ITM Communications to post on the ITM website.

**Implementation and Results:**

The PI shared his flyer/advertisement with ITM TRIO who has shared it with all ITM institutions. Once the TRIO build is completed on the ITM website, it will be added there.

**Misc:** Prior to Design Studio, there were not any subjects enrolled on the study. Since Design Studio, one subject has consented to the study. The patient was referred by another physician at Rush through Ruth M. Rothstein CORE Center.
Solutions Generated by Design Studio

1. **Social Media Based Solutions**: Create a Facebook and Twitter account for the study to assist in reaching savvy participants. Target support groups through social media to post study information. Create a self-service portal for potential study participants. Create testimonials of study participants and/or their family members to post on social media.

   **Implementation and Results:**
   
   Facebook page has been created and study team is getting a lot of interest through Facebook.

2. **Internet Based Solutions**: Optimize search engines, simplify symptoms and make them more understandable to patients who have not yet been diagnosed but looking for a diagnosis, and simplify a portal/self-service tool for potential participants.

   **Implementation and Results:**
   
   Cyber PML consults will be within the next month.

3. **Physical Outreach Through ITM via TRIO**: Use the Trial Innovation Network (TIN) as a potential tool for reaching potential participants. Share IRB approved flyers/advertisements with TRIO so they can distribute to ITM partners and work with ITM Communications to post on the ITM website.

   **Implementation and Results:**
   
   The study team will send regular emails to TRIO to send to their contact list. Once the website build is completed, the study flyer will be posted on the website.

4. **Grand Rounds**: Conduct Grand Rounds at all ITM institutions (Rush, Advocate, Loyola, Northshore, UChicago). Concentrate on Rare Disease, Infectious Disease, and Primary Care Physicians. Conduct Grand Rounds at Stroger and UIC concentrating on the same departments.

   **Implementation and Results:**
The study team is currently working with Stoger, Cook County Hospital to conduct Grand Rounds and make them aware of the study.

5. **Awareness of Clinicians (Neurologist, Infectious Disease, etc.):** Establish an awareness campaign through all ITM institutions and departments such as Infectious Disease, Neurology and Primary Care Physicians/Family Medicine.

**Implementation and Results:**

The study team will email TRIO regularly about the PML study and TRIO will send email blasts to all TRIO contacts.

6. **Speciality Medication Rush Pharmacy Outreach:** Reach out to Rush Pharmacy to determine all patients that are being treated with immunosuppressive drugs with known risk of PML (e.g. Tysabri) Work on specialty pharmacy review of records of patients taking this drug to educate about symptoms of PML and about resources if symptoms noted (including referral to PML Centers of Excellence to reduce diagnostic delays).

**Implementation and Results:**

The research team has reached out to an EPIC rep. to create searches of the drug and disease groups.

**Misc:** Since the 30-day follow up, they have had 7 patients that were potentially interested in the study. They currently have 6 subjects on study with another 7 interested. The study team is getting a lot of activity through Facebook and will work closely with TRIO to enhance the PML Facebook posts.