Landscape Analysis to Identify Effective Drug Repurposing Candidates for the Treatment of Implantation Mycoses: Comparison of World Health Organization Treatment Data and Published Case Reports on CURE ID

Reema Charles1,2, Barbara Milani3, Daniel Argaw Dagne4, Nalini Oliver5, Bisma Ali6, Heather Stone7, Marco Schito2

1 US Food and Drug Administration, 2 CURE Drug Repurposing Collaboratory, 3 World Health Organization

Introduction

Although fungal infections that gain access in a mammalian host through various types of cutaneous or mucosal wounds or by contact are categorized as implantation or inoculation mycoses. These constitute a group of mycoses that, similar to other mycoses, are known to be serious, often life-threatening, and the causative fungi are transfer from their saprophytic or endemic niche to the cutaneous or mucosal tegument. The mycoses described under implantation mycoses are sporotrichosis, chromoblastomycosis, eumycetoma, coccidioidomycosis, and some clinical forms of phaeohyphomycosis are amongst the other fungal diseases that begin at the site of multiple traumatic or transmural traumatic. These are geographically confined mainly to tropical and subtropical areas, and are associated with significant morbidity due to long-term sequelae, incapacity to work and decreased quality of life, mostly associated with severe clinical forms.

Due to the high cost of drugs, long treatment durations, and difficulty in early diagnosis, they can be recalcitrant and very difficult to treat. They are identified as areas of high unmet needs and merit a systematic approach towards identifying cost-effective and efficacious drug candidates.

Materials and Methods

World Health Organization (WHO) in collaboration with the US Food and Drug Administration (US FDA) and CURE Drug Repurposing Collaboratory (CURE) developed a Case Report Form (CRF) in early 2022 to capture treatment data on implantation mycoses from around the world. The survey aimed to collect information on drug development and treatment practices in different settings in various countries on four implantation mycoses: eumycetoma (n=114), chromoblastomycosis (n=597), and cutaneous sporotrichosis (n=510). The global online survey captured real-world data (RWD) on the use of repurposed drugs and non-pharmacological interventions in the treatment of these mycoses. The WHO global online survey collected information from a total of 142 respondents from 41 countries. Majority of the respondents of the survey were clinicians (39%), followed by dual professional profile of laboratory and clinical experts (30%), laboratory technicians/specialists (9%), public health specialists (7%), and pharmacists (4%).

The CURE ID is an internet-based repository developed by the US FDA and the National Center for Advancing Translational Sciences (NCATS), part of the National Institutes of Health (NIH) to gather RWD on the novel use of medicines for the treatment of rare diseases from clinicians, patients and now through Electronic Health Records (EHRs). It can be accessed on the web, smartphone or other mobile devices. The platform enables crowdsourcing of medical information to gather RWD on the off-label use for a new indication, especially for neglected diseases.

The CURE ID sweept the world and pull out all published case reports from PubMed. In total, we did data entry on 658 published implantation mycoses case reports, including sporotrichosis (n=315), chromoblastomycosis (n=148), coccidioidomycosis (n=157), and eumycetoma (n=48). We excluded reports that did not have drug treatment, were not in English, and those that were not full text articles.

Results and Discussion

In the CURE ID database, sixty-four percent of patients are males, and females constitute thirty-five percent of reports on implantation mycoses. (CURE ID) case reports are reported from 40 countries, with majority of cases being reported from Brazil (29%), as highlighted in figure 1. Clinical features/visual inspection (86%) was reported most frequently as a diagnostic tool in the WHO survey. While in CURE ID database, clinical assessment was reported in 52% of published reports, with culture (Bacteriological) being the most reported (81%) diagnostic modality, as is reported in figure 2.

The WHO survey confirms a widespread use of repurposed drugs, with respondents reporting a few medicines that were not included in the survey list. For eumycetoma, chromoblastomycosis and cutaneous sporotrichosis, ketotifen was reported for external use. For chromoblastomycosis, clinical assessment was reported in 52% of published reports, with culture (Bacteriological) being the most reported (81%) diagnostic modality, as is reported in figure 2.

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For cutaneous sporotrichosis, we noted a considerable use of potassium iodide (KI).

For antimycotics, several antibiotics from several classes were reported in the WHO survey, suggesting a high level of drug repurposing. Diclofenac (30%), itraconazole (27%), ceftriaxone (21%) and fosfomycin (10%) were amongst the other drugs reported in the WHO survey.

Assessing treatment data from published case reports on CURE ID from 2015 onwards, thioTEPA was the most frequently used drug across all implantation mycoses. It was used in 99% reports on sporotrichosis, while for eumycetoma and chromoblastomycosis, its use was reported at 64% and 50% respectively. Betamethasone has been reported in 76% cases of eumycetoma and 57% for chromoblastomycosis, while it was used sparingly in just 3% of cases of sporotrichosis. While newer generation azoles were reported for chromoblastomycosis and eumycetoma, they were used less frequently (9- 29%) in published reports, as compared to the WHO survey. Use of ketoconazole was reported sparingly (1%) for chromoblastomycosis in case reports published from 2015 onwards, while it is reported more consistently for chromoblastomycosis (14%) and eumycetoma (9%) from all the published reports in CURE ID dating back to the 1990s.

Conclusions

Implantation mycoses affects a significant percentage of the world’s population. Severe clinical forms are associated with significant morbidity due to long-term sequelae and decreased quality of life. This is further complicated by the lack of effective therapies and increased cost and limited availability of medicines.

Analysis of existing data from both the WHO online survey and the CURE ID database identified ketoconazole as the most frequently used drug across the studied implantation mycoses. While thioTEPA is used worldwide as a standard of care in the treatment of implantation mycoses, it is not yet approved by the FDA for use in most of these conditions of interest. This effort should be further facilitated by capturing large volumes of RWD for hypothesis generation and informing clinical trials about efficacy signals to support regulatory decisions, especially for neglected diseases.
Medical Imaging Working Group

PRESENTER: Paul Nagy, Seng Chan You

INTRO:
Medical Imaging play an essential part of medical care in diagnosing and measuring disease as well as the response to medical interventions. The OHDSI medical imaging WG has developed an extension to the Observational Medical Outcomes Partnership (OMOP) common data model (CDM) to support incorporating medical imaging studies as well as measurements derived from medical imaging.

METHODS:
The steps taken to create this extension were:
1. Create use cases of this data model is intended to be able to answer for observational research.
2. Identify the vocabularies needed to support clinical findings. RadLex is employed as a comprehensive vocabulary of radiologic terminology which has been developed and maintained by the RSNA.
3. Create data models required to be able to support the use case questions.

Primary Use Case
The primary use case we created was tracking of pulmonary nodules over time that require treatment. This is a good example as patients can have multiple clinical findings within any given imaging study and each clinical finding can have multiple features that describe that finding.

An imaging study includes a collection of medical images, and each study can have multiple clinical findings (nodule). Each imaging finding can have multiple imaging features (attribute size, composition, location). An example Pulmonary Nodule is a 55-year-old patient that quit smoking 8 years ago. It is able to see the case tables through the QR code in the middle of this poster.

Seng Chan You's email (seng.chan.you@hrl.com) Brian Malek: Kodee Zhao; Tarik Abakar; Pedro Malot; Paul Nagy

Development of the Medical Imaging Extension

We aim to harmonize and standardize information for medical images to overcome current challenges in interoperability and reproducibility in medical image research. From pixels to Phenotypes.
Protocol for finding supplemental oxygen data in electronic health record (EHR) flowsheets for inclusion in the OMOP ETL

**PRESENTER:** Tanner Zhang MD,MS

**INTRO:**
- Incorporating flowsheet data from EHRs into the OMOP ETL has been a challenge due to the high volume of entries and high variability of facility-specific customization.
- We propose a standardized and reproducible protocol to identify the flowsheet elements of interest, map them to their appropriate OMOP concept IDs, and load them into the OMOP Common Data Model (CDM).

**METHODS**

1. **Flowsheet Identification**
   - Wildcard search for candidates
   - Manually identified nonintuitive flowsheet names
   - Manually identify anesthesia records
   - List template and flowsheet measurement identification numbers
   - Extract based on included template, measurement numbers
2. **Semantic Mappings**
   - Semantic mappings were created by clinicians, then reviewed by informaticians, terminologists
   - Proposed custom OMOP concept IDs for BIPAP, CPAP & NIPPV
3. **Utilization of OMOP CDM Tables**
   - Measurement/Observation tables are used for respiratory device settings, and device_exposure table is used for respiratory device information.
   - Linkage is kept by the time stamps. The datasets for analysis could be curated by the analysts’ needs for different use cases.
   - Current plot sites are mainly Epic sites. Thus the scripts and mappings are curated for Epic templates and internal measurement IDs. We welcome other EHR vendor sites to join the forums.
4. We have designed flowsheet-specialized data quality checks and this may potentially be an add-on to the DQD 2.0 version.

**RESULTS**

- The semantic mappings for respiratory devices and the associated settings were designed by a group of clinicians and reviewed by informaticians and terminologists.
- In addition to the custom codes proposed by NSC, we have proposed three more to complete the respiratory device mapping. See below.
- We are working with OHDSI to finalize the related vocabulary table changes (in concept and in concept_relationship and etc.).

**Features:**

1. Measurement/Observation tables are used for respiratory device settings, and device_exposure table is used for respiratory device information.
2. Linkage is kept by the time stamps. The datasets for analysis could be curated by the analysts’ needs for different use cases.
3. Current plot sites are mainly Epic sites. Thus the scripts and mappings are curated for Epic templates and internal measurement IDs. We welcome other EHR vendor sites to join the forums.
4. We have designed flowsheet-specialized data quality checks and this may potentially be an add-on to the DQD 2.0 version.

**Semantic mappings for flowsheet data, and statistics among patients hospitalized with COVID-19 at JHU**

<table>
<thead>
<tr>
<th>Measurement/Observation table</th>
<th>Device_exposure table</th>
</tr>
</thead>
<tbody>
<tr>
<td>O2 Device</td>
<td>O2 Device</td>
</tr>
<tr>
<td>O2 Flow Rate (L/min)</td>
<td>O2 Flow Rate (L/min)</td>
</tr>
<tr>
<td>Vent FiO2 (%)</td>
<td>Vent FiO2 (%)</td>
</tr>
<tr>
<td>High flow nasal cannula</td>
<td>High flow nasal cannula</td>
</tr>
<tr>
<td>Nasal cannula</td>
<td>Nasal cannula</td>
</tr>
<tr>
<td>10/6/19 12:12 AM</td>
<td>10/6/19 12:12 AM</td>
</tr>
</tbody>
</table>

**Take a picture to download the full paper**

Tanner Zhang, Steven Miller, Michael Cook, Alan Coltri, Zachary Wang, Paul Nagy, Justin M Rucci, Galina Lozinski, Matthew Robinson
**INTRODUCTION**

Goal: To systematically collect anecdotal data of how clinicians use existing drugs in new ways to treat diseases with limited or no treatment options.

Aim: To simplify ETL process and create pathway for real-world data to be made available in CURE ID

Method: Data harmonization using OMOP CDM

Impact: Secure deidentified data elements for assessing the effectiveness of repurposed treatments for diseases of high unmet clinical need.

**METHODS**

With funding from HHS Assistant Secretary for Planning and Evaluation:

1. Developed tools and resources to disseminate harmonization methods developed by Johns Hopkins University
2. Expand CURE ID from physician entered reports to automated EHR data collection
3. Promote conversion of non-common data model EHR systems to OMOP standards
4. Developed minimal dataset for drug repurposing research in COVID-19 as a use case

**RESULTS**

- Possible to lower OMOP ETL barrier
  - Default configuration transformations
  - Support and feedback from experienced site
  - Project continues with site implementing OMOP using Perseus

**CONCLUSION**

It is feasible to reduce the ETL implementation time by providing default configuration transformations along with assistance and feedback on the process. Further reduction in the person-hours required to perform an OMOP ETL will be evaluated with the Perseus web-based OHDSI ETL project and cloud provider deployments of Atlas and the DQD. Our goal is to increase the adoption of OMOP in sites with fewer resources and enable wider participation in high-quality clinical registries with sufficient patient numbers and data variables to perform appropriate observational research techniques to control for potential confounders (e.g., propensity score matching).

**Lowering the OMOP ETL Barrier for Clinical Registries**

**PRESENTER:** Smith Heavner

Pilot site implemented OMOP in less than 200 hours

<table>
<thead>
<tr>
<th>Verification</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pass</td>
<td>Fail</td>
</tr>
<tr>
<td>1982</td>
<td>31</td>
</tr>
<tr>
<td>656</td>
<td>23</td>
</tr>
<tr>
<td>301</td>
<td>5</td>
</tr>
</tbody>
</table>

Total: 3019 | 59 | 3078 | 98% | 402 | 4 | 406 | 99% | 3421 | 63 | 3484 | 98%
One institution’s approach to empowering researchers to learn and conduct observational research

**JH OHDSI adoption strategy**

**ORGANIZATIONAL ABILITY**
- Data: Up-to-date EHR data available
- Tools: OHDSI tools
- Tools: R/Python/SQL
- Support: Clinical research core data service team

**TEAM ABILITY**
- Team science: Teams channel with interdisciplinary group
- Networking: Partner with OHDSI institutions
- Registry creation: OMOP sub-setting

**ORGANIZATIONAL MOTIVATION**
- Awareness: Institutional website
- Leadership: Support for OHDSI
- Support: Grant letters of support
- IRB: Enable easier process

**TEAM MOTIVATION**
- Peer Mentoring: Weekly calls
- Networking: Participation in OHDSI working groups
- Data Science: Graduate student project partnering

**INDIVIDUAL ABILITY**
- Online training: EHDA Academy, office hours
- Graduate courses: Observational research, data science

**INDIVIDUAL MOTIVATION**
- Data: Get data faster
- Publications: Produce robust, reproducible publications
- Grants: Grant template library
- Data: Get multi-institutional data

We aim to accelerate the use of OHDSI by creating value for our researchers and our organization. This framework can be adopted to support clinicians and researchers as they incorporate OHDSI into their research efforts.
Historically, pregnant patients have been excluded from conventional clinical trials due to safety and ethical concerns. As a result, very little is known about the efficacy of drugs used off-label for conditions affecting pregnant individuals. FDA and NCATS/NIH built a mobile application and website called CURE ID to capture the experiences of clinicians around the globe, prescribing FDA-approved drugs for new indications to treat infectious diseases, emerging threats, and multidrug-resistant organisms.

The purpose of this project was to expand CURE ID to collect data on drugs used during pregnancy. We collected 174 case reports from the published literature and simulators on drugs used to treat Trichomoniasis (6), Listeriosis (5), Group B Streptococci (15), Toxoplasmosis (20), Gonorrhea (13), Cytomegalovirus (19), and COVID-19 (94) in pregnant patients. We also added a new case report form to collect treatment information for pregnant patients in CURE ID. For drug repurposing to be successful for pregnant patients, data collection on off-label drug use is one of the first steps in showing candidate drugs that can be later studied in a formal setting.

We identified seven high-impact infectious diseases that lack FDA-approved drugs in the pregnant population, namely, Trichomoniasis, Listeriosis, Group B Streptococcus, Toxoplasmosis, Gonorrhea, Cytomegalovirus (CMV), and COVID-19. A group of maternal health experts from within and outside FDA convened to consult on this topic. We updated the case report form in CURE ID to include additional data points to gather information on pregnancy-related details, such as, gestational age at the time of treatment and delivery, and pregnancy outcome. Published literature reviews were conducted to retrieve case reports of the above-mentioned diseases, where the patient was pregnant and was treated with a drug that is not approved for that indication (or for use in pregnancy). We included articles pulled from PubMed using pregnancy and disease-specific keywords and Medical Subject Headings (MeSH) terms. One hundred and seventy-four cases were included after applying the exclusion criteria (Figure 1). After aggregating the data, we looked at the drug labels of the drugs used most frequently for the treatment of each disease to review the pregnancy-related information.

Materials and Methods

The mean gestational age at the time of treatment across all diseases in the Pregnancy Repository was 27 weeks (range: 6 – 39 weeks). More than 75% of cases of Trichomoniasis, Group B Streptococci, Gonorrhea, and COVID-19 were treated with a combination of drugs. More than 80% of CMV cases were treated with a single drug. Fifty percent of cases of Trichomoniasis and 55% cases of Toxoplasmosis were treated with monotherapy. Eighty-seven percent of patients were reported to improve after the treatment in our Repository. The high number of cases with a positive outcome may be attributed to a reporting bias.

Conclusion

The aim of the CURE Pregnancy Treatment Repository was to create a digital platform for clinicians across the world to submit information on repurposed drugs used in pregnant individuals who are diagnosed with an infectious disease. The case report form was updated with additional data points for the purpose of this project. The Repository now provides free access to users wishing to view de-identified, aggregated data of pregnant patients and allows reporting of cases involving pregnant patients. All published cases of pregnant patients that met the inclusion criteria were extracted and included in the Repository. Despite our best efforts to collect data directly from clinicians, we did not see much engagement from clinicians in reporting their cases or discussing the forum in the mobile app for queries regarding challenging cases. In both formal and informal discussion with clinicians, we found that there is a hesitation among obstetric care professionals in reporting the use of off-label drugs, especially if the outcome is negative. For drug repurposing to be successful for pregnant patients, collection of large quantities of real-world data (RWD) on off-label drug use is the first stage in discovering therapeutic candidates that can be subsequently examined in a more formal setting.
Deploying the Edge Tool Suite to Extract Real-World Data: an Implementation Science Approach

Maya Younoszai1, Danielle Boyce2,3, Smith Heavenr3,4
1U.S. Food and Drug Administration, 2Johns Hopkins University, 3CURE Drug Repurposing Collaboratory, Critical Path Institute, 4Clemson University

What is EPIS?
- The EPIS framework is an implementation science approach to the implementation of evidence based practices (EBPs)
- The framework is made up of four main phases: exploration, preparation, implementation, and sustainment
- EPS also includes four groups of factors that impact the implementation: inner context, outer context, bridging factors, and innovation factors

Background
- The CURE ID project has developed relationships with over a dozen clinical sites in conjunction with SCCM
- In exchange for a small grant, clinical sites agree to work with OMOP experts to implement the EDGIE tool suite and extract their inpatient COVID cases in the OMOP common data model
- These cases will eventually be sent to SCCM, IDDO, and finally NCATS for inclusion in the CURE ID app
- Guiding sites through the process has been challenging due to time, resource, and regulatory constraints
- This project sought to complete a comprehensive, multi-stakeholder review of site-based implementation
- Although the EPIS framework is often used as a prospective planning tool, we use it here to review an on-going effort and make recommendations for new practices

Introduction to CURE ID:
- Public private partnership between the FDA, National Center for Advancing Translational Sciences, and the Critical Path Institute
- Aims to collect real-world data (RWD) on drug repurposing
- Funded by a grant from HHS ASP's Patient Centered Outcomes Research Trust Fund
- Expanded to build a tool that automates the collection of case reports directly from the electronic health record (EHR)
- The EHR collection project is a collaboration with Johns Hopkins, the Society of Critical Care Medicine, Emory, and the Infectious Disease Data Observatory at Oxford

Methods
- Our team looked at all aspects of the CURE ID project and mapped them to the EPIS framework
- Analyzed stakeholder feedback received in weekly stakeholder meetings held over the two-year project
- Specific stakeholder groups included:
  - Regulators
  - Providers
  - Informatics
  - Data analysts
  - Health researchers
  - Patients/patients advocates
  - Compliance professionals
  - Health care system leaders
- Implementation team engaged in concept mapping activities to organize feedback
- By identifying the inner context, outer context, bridging factors, and individual factors, we are able to find where main roadblocks have developed

Funding Statements
- The CURE ID program was supported by the Office of the Secretary National Institutes of Health, Intramural Research Program, National Institutes of Health, and the Office of the Director, National Institutes of Health, through interagency agreement between the U.S. Department of Energy and FDA

Recommendations, Future Directions:
- Emphasize the benefits of the Edge Tool Suite (the "innovation factor," in the EPS framework) to sites early in the process to encourage engagement and buy-in
- Ensure a complete, thorough, and well-documented technological and regulatory factor review with each site prior to contracting and beginning the EPS process. This should include examining the expertise of the informaticist, the availability of the necessary software and other tools, the informaticist’s access to the data, the ability of a site to get an IRB and DUAs approved, and the availability of resources to initiate the project before contracting with the site is finalized.
- Establish and document a timeline for sites based on the grant timeline. Ensure this timeline is well communicated and able to be met before initiating work with a site.
**Repurposing in RASopathies**

This data was collected from published literature during background research to inform the pilot for the rare disease expansion of the CURE ID app, a joint project between the FDA and NCATS/NIH, but is not a representation of the views of either agency.

**Overview**

There are over 7,000 rare diseases with more being discovered everyday. Somewhere between 92-95% of rare disease patients lack FDA approved therapies, leading clinicians and patients to rely on off-label drug usage, also known as “repurposing” for treatment. There is a lack of drug development in the rare disease space due to lack of funding and the challenges that having small patient populations provide for conducting a randomized clinical trial (RCT) along with the ethical implications of doing a controlled study in certain rare diseases with deadly outcomes without medical intervention.

This poster explores repurposing in the group of rare diseases known as the RASopathies as a case study.

**The RASopathies**

The RASopathies are a group of disorders including NF1, Noonan Syndrome, Costello Syndrome, and more that are caused by changes in genes in the Ras/mitogen-activated protein kinase (Ras/MAPK) pathway, which is responsible for a variety of essential bodily functions, including growth and inflammatory responses. No two RASopathy syndromes present in the same, way, however, there are many overlaps including hypertrophic cardiomyopathy (HCM), failure to thrive, lymphatic associated symptoms, and bleeding disorders.(8,9) Because of this, there is not necessarily a “one size fits all” treatment available for the RASopathies, however, therapeutics targeting the underlying pathway has potential to benefit patients unilaterally despite unique presentations.

![Figure 1: RASopathy Pathway (1)](image1)

**Potential of MEKi’s and MTOR Inhibitors**

Pre-clinical data suggested the possible efficacy of mitogen-activated protein kinase inhibitors (MEKi) and drugs that inhibit the mechanistic target of rapamycin (mTOR) in treating the various symptoms of the RASopathies. MEKi’s directly impact the MAPK pathway and are often FDA-approved for cancers that occur as a result of this being deregulated, which accounts from approximately one-third of cancers. Deregulation of the MAPK pathway is also involved in the RASopathies. mTOR inhibitors work by blocking a protein causing cell-division and is also FDA-approved to treat different types of cancers. This is also what makes it potentially effective in treating the RASopathies. (2, 3, 4, 5)

![Figure 2: MEKi Pathway (6)](image2)

**Conclusions**

Clinicians began to use these medications in their practice, based upon the mouse model data that showed decrease and even reversal in HCM. In human patients, clinicians also noted anecdotal improvement in HCM, along with other unexpected outcome measures, such as less need for growth hormones, lessened supplemental nutrition, and even improved cognitive function. Patients and care-partners have been critical in obtaining this data on both unexpected positive and negative effects of these repurposed medications. (2, 3, 4, 5)

![Figure 3: MTOR Inhibitor Pathway (7)](image3)

**References**


**Figure 4: Results from “MAPK and AKT/MTOR Inhibition Improves Childhood RASopathy-Associated Cardiomyopathy” study (5)**

Survival Rate in RASopathy Patients < 6months with HCM

- Use of MEKi's or MTOR inhibitor
- No use of MEKi or MTOR inhibitor

**Figure 5: Repurposing in RASopathies**

- Use of MEKi's or MTOR inhibitor
- No use of MEKi or MTOR inhibitor

- Repurposing in RASopathies

- Potential of MEKi’s and MTOR Inhibitors

- Conclusions

- References
Landscape Analysis of Drug Treatments for PEComa
Jamila Johnson1,2, Dakota Makulec1,2, Reema Charles2, Marco Schito2, and Smith Heavner1,2,3
1 University of South Carolina School of Medicine Greenville, Greenville, SC
2 Critical Path Institute CURE Drug Repurposing Collaboratory, Tucson, AZ
3 Clemson University Department of Public Health Sciences, Clemson, SC

Introduction
Perivascular epithelioid cell neoplasms (PEComas) are rare tumors formed by epithelioid cells. As with other rare cancers, funding, trial recruitment, and other concerns pose a significant barrier to obtaining Food and Drug Administration (FDA) approval for treatments. To date, the FDA has approved only one agent, Nab-Sirolimus, for the treatment of PEComa. However, there is a lack of research that systematically addresses the current landscape of available drug treatments for PEComas.

Aim
Our research aims to identify repurposed pharmacological treatments for PEComas and their associated subtypes.

Methods
- We first conducted a PubMed search with this search string
- In the first pass of our review, we screened the titles and abstracts for inclusion.
- All study types were included.
- Articles that were not in English were excluded.
- Data entry and analysis are still underway using Rayyan software.
- Data entry will be done on Excel workbook containing predefined data variables in the form of a case report form

Results
A total of 1267 articles were retrieved from PubMed and uploaded in Rayyan database for review. After the first pass, a total of 197 articles were included for full-text screening in the second pass. Of these articles, 153 were included in the data entry and analysis. Results show that the majority of research for PEComa treatment focuses on the mTOR inhibitors, with the FDA approved agent, Sirolimus, accounting for 78 articles.

Conclusion
These findings demonstrate the extensive availability of research on PEComa treatment. Our review offers a comprehensive analysis of the current pharmaceutical treatment options for PEComas including FDA approved (i.e., Nab-Sirolimus) and repurposed agents. Our analysis can provide useful information for further research identifying potential targets for repurposed pharmaceutical treatments.
The Landscape of Rare Infectious Diseases – A Proof of Concept with Rare Bacterial Infections

Authors Tahsin Farid, Reema Charles, Keyla Tumas, Heather Stone, Raghav Tirupathi
Location: Cure Drug Repurposing Collaborative (CDRC) Annual Meeting, 2023

Abstract
Here the landscape of rare bacterial infections (RBIs) is reviewed. 22 established RBIs were identified and information regarding their transmission, incidence, and therapy were recorded. Zoonoses was the most common mode of transmission (10), with a worldwide pattern of incidence (6). The observed transmission and incidence patterns are likely influenced by low endemicity, outbreaks in different regions, and socioeconomic, demographic, and/or climate change. Very few RBIs had approved therapy (7). The intentional of this group is to expand the scope of the research to all rare infectious diseases and propose the use of real-world data to better inform therapy.

Introduction
Rare infectious diseases (RIDs) collectively represent a significant source of morbidity and mortality around the world. However, most lack approved medications. Due to their sporadic nature and often, in distribution in limited settings, it has been difficult to perform comprehensive trials on therapeutic efficacy. Additionally, there is little monetary incentive in drug development for these diseases. RBIs therefore remain an area of high unmet medical need. The aim is to review the landscape of RBIs and to highlight those constituting the most urgent medical needs. This poster is a pilot project that focuses on rare bacterial infections (RBIs).

Materials and Methods
A list of bacterial infections was curated by combining reportable infections from health agencies11 with the CURE ID2 database of diseases. This list was independently reviewed by two experts in infectious diseases to identify potential rare bacterial diseases. A literature review was then conducted to identify which of these bacteria met the inclusion criteria of a global incidence of less than or equal to 10,000 cases per year. Table 1 outlines the data that was collected for each RBI that met the inclusion criteria. This data was then analyzed.

Discussion
It was hypothesized that a majority of RBIs occur through zoonoses, while environmental and commensal organisms primarily caused opportunistic infections in immunocompromised patients. Perhaps surprisingly, the majority of zoonoses, had a worldwide distribution. This does not imply higher incidence, rather it may indicate that these RBIs have no sustained endemicity and cause outbreaks in varied geographic areas when animal to human spillover occurs. Transmission patterns may also be related to socioeconomic conditions, climate change, and population growth. The intention of this group is to explore these possibilities and expand the scope to all RBIs. Only a few RBIs had FDA-approved therapies because the paucity of cases makes it difficult to conduct efficacy trials and there is little financial incentive for traditional pharmaceutical development. It is imperative to adopt a new disease approach to those conditions, and to

Results
From the comprehensive list of 183 bacterial infections, 22 met the final inclusion criteria. The workflow process is depicted in Figure 1. The distribution of the RBIs by the World Health Organization (WHO) Region where they have the highest incidence is displayed in Figure 2. The frequency with which each mode of transmission was noted for these RBIs are shown in Figure 3. Table 2 plots the distribution of RBIs that have commonly used standard of care and/or FDA approved therapy. Figure 4 breaks down the transmission mode of infections according to the WHO region where they are most frequent.

Table 2: Standard of care availability plotted against FDA approved therapy availability

Figure 1: Data Flow Diagram

Figure 2: Distribution of RBIs by WHO Region with Highest Incidence

Figure 3: Frequency of transmission modes of RBIs

Figure 4: Plot of transmission mode by WHO region

Table: Standard of care availability plotted against FDA approved therapy availability