Using OHDSI tools to conduct clinical trial feasibility

Rupa Makadia, MS[1,2], Jamie B. Forlenza[1], PharmD, MS[1], Frank J. DeFalco[1,2], Chris Knoll[1,2], Patrick B. Ryan, PhD[1,2,3]

[1]Janssen Research & Development, LLC, Titusville, NJ [2]OHDSI collaborators, Observational Health Data Sciences and Informatics (OHDSI), New York, NY [3]Columbia University, New York, NY

ABSTRACT

Background: Observational data has been used in support of various epidemiological studies including safety surveillance, cohort characterization and outcomes research. A novel use of observational data that is enabled through the use of OHDSI tools in assessing clinical trial feasibility.

Methods: Using the tools from the OHDSI network we are able to apply standard methods to effectively assess inclusion criteria for a potential clinical trial population. A case study example has been executed to illustrate feasibility.

Results: The result of using observational data has provided efficiencies in protocol design, the ability to address operational questions and possibly avoid protocol amendments. The case study illustrates the ability to adequately simulate 7 out of 9 criteria and provide insights around selected criteria.

Conclusion: Insights gained by protocol simulation can be adapted to enhance how clinical trials are designed and conducted. By using the common data model, standard vocabularies and OHDSI tools we are able to deliver results in a standard, concise, timely and reproducible manner.

BACKGROUND

- The use of observational data in retrospective analyses have been thoroughly explored and studied. Applying this data in the use of clinical trial feasibility has been a new application of the data[1].
- By utilizing the OMOP common data model (OMOP CDM) and the current OHDSI tools, the ability to utilize the data in clinical trial feasibility is possible and can address operational questions, provide insight in overall population eligibility, impact protocol design, and possibly avoid protocol amendments for a clinical trial.

METHODS

- Typical clinical trial feasibility lifecycle (Figure 1.)

  1.) Eligible protocols are identified in therapeutic areas that are of interest to the organization throughout the clinical trial lifecycle from trial design through active trials facing recruitment challenges. Additionally, review of inclusion/exclusion criteria that can be addressed through the data elements available in the CDM data.

  2.) Creation of concept sets and/or utilization of concept sets from standard vocabularies in ATLAS to describe the criteria set.

  3.) Each criteria of interest is applied to the index population (or inclusion criteria) in ATLAS.

  4.) The individual match percentages for each criteria and overall match criteria are evaluated for each protocol.

  5.) Results are shared with clinical team.
- A case study for a major depressive disorder (MDD) protocol has been entered through the process and results generated and evaluated; Inclusion and exclusion criteria are shown in Figure 2 from clinicaltrials.gov.
- The index population was defined as people having a condition occurrence of a primary condition of MDD in the 2014 calendar year between the ages of 21 and 64 and with least 180 days prior. All people matching those criteria must also have no diagnosis of hypothyroidism between 90 days before and including the index. The latest event of MDD for each patient is the index date used in evaluation.

Figure 1. Lifecycle of clinical trial feasibility

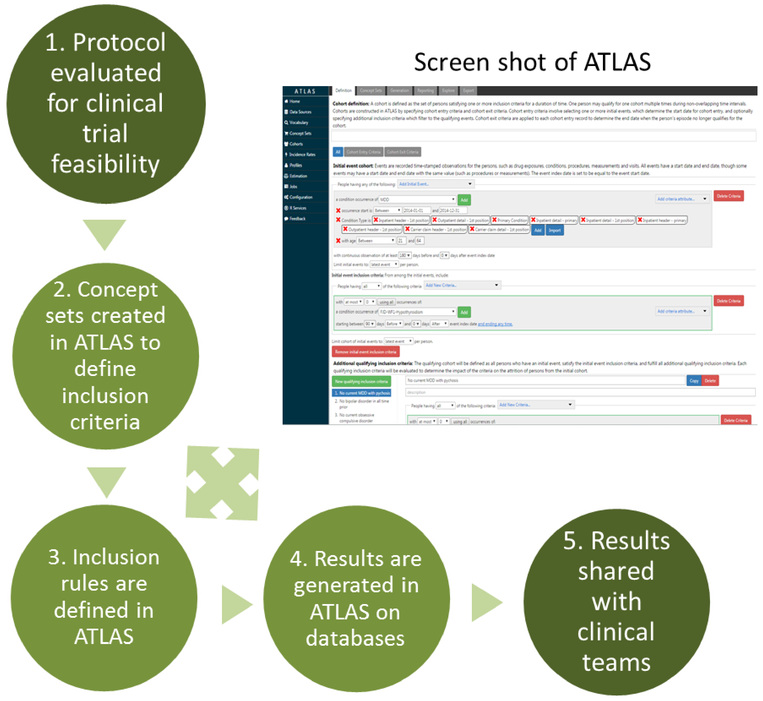

Figure 2. MDD protocol from clinicaltrials.gov[3]

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"
Search for studies: Search
Advanced Search | Help | Studies by Topic | Glossary

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

An Efficacy and Safety Study of Sirukumab in Participants With Major Depressive Disorder

This study is currently recruiting participants. (see Contacts and Locations)
Verified August 2016 by Janssen Research & Development, LLC

Sponsor:
Janssen Research & Development, LLC

Information provided by (Responsible Party):
Janssen Research & Development, LLC

ClinicalTrials.gov Identifier:
NCT02473289

First received: June 12, 2015
Last updated: August 17, 2016
Last verified: August 2016
History of Changes

Eligibility Criteria ICMJE	
	Inclusion Criteria: • Participants must have a primary DSM-5 diagnosis of MDD • Must have a HDRS total score greater than or equal to (>=) 18 at screening and predose at Day 1, as recorded by the remote independent rater and must not demonstrate an improvement of > 25 percent (%) on their HDRS total score from the screening to baseline visit • Must be medically stable on the basis of physical examination, medical history, vital signs, clinical laboratory tests and 12-lead ECG performed at screening. If there are abnormalities, the participant may be included only if the investigator judges the abnormalities or deviations from normal to be not clinically significant. This determination must be recorded in the subject's source documents and initialed by the investigator • Participants with hypothyroidism who are on stable treatment for 3 months prior to screening are required to have thyroid stimulating hormone (TSH) and free thyroxine (FT4) obtained. If the TSH value is out of range, but FT4 is normal, such cases should be discussed directly with the medical monitor before the subject is enrolled. If the FT4 value is out of range, the participant is not eligible Exclusion Criteria: • Any other current Axis one psychiatric condition, including, but not limited to, MDD with current psychotic features, bipolar disorder (including lifetime diagnosis), obsessive-compulsive disorder, borderline personality disorder, eating disorder (eg, bulimia, anorexia nervosa), or schizophrenia (lifetime). The MINI will be used to screen for comorbid psychiatric diagnoses. As noted above, subjects with a diagnosis of comorbid GAD, Post-Traumatic Stress Disorder, Persistent Depressive Disorder, ADHD, Social Anxiety Disorder, Panic Disorder with or without agoraphobia or Nicotine/Caffeine Dependence may be included, if the investigator considers MDD to be the primary diagnosis • A history of alcohol or substance use disorder (abuse/dependence) within 6 months prior to screening (nicotine and caffeine dependence are not exclusionary) • A current or recent (within the past year) history of clinically significant suicidal ideation (corresponding to a score of >= 3 for ideation) or any suicidal behavior within the past year, as validated on the C-SSRS at screening or baseline. Subjects with a prior suicide attempt of any sort, or history of prior serious suicidal ideation/plan should be carefully screened for current suicidal ideation and only included at the discretion of the investigator • More than 3 failed antidepressant treatments (of adequate dose and duration) in the current episode of depression (verified by the MGH-ATRQ) • Length of current major depressive episode > 60 months
Gender	Both
Ages	21 Years to 64 Years (Adult)

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RESULTS

- In less than 9 months, the team has used ATLAS to answer over 20+ protocols/programs with regard to various criteria including assessing the impact of individual protocol criteria, operational questions pertaining to cohort selection and population characteristics prior to drafting protocols.
- The types of insights gained by various protocols are: insights of inclusion criteria, assessing impact of changing criteria, and checking for adequate match rates amongst the population found in the retrospective observational data cohort.
- Of the 4 inclusion criteria in the case study, 2 can be adequately be addressed in the tools. Of the 5 exclusion criteria, 5 can be simulated in observational data.
- The overall match rate for this population is 56.60% based on the criteria entered (Table 1) and individual match criteria are displayed in Table 2 for the Truven CCAE database (a large US commercially insured claims database)
- The criteria that have lower than a 90% match rate were: no bipolar disorder in all time prior, no more than 3 previous antidepressants in all time prior.

Table 1. Summary of index population and match percentage

	Match rate	N	Index population
Summary Statistics	56.60%	180,513	318,950

Table 2. Inclusion criteria from MDD protocol simulation

Inclusion Rule	N	% Satisfied	% To-Gain
No current MDD with pychosis	309,510	97.04%	1.31%
No bipolar disorder in all time prior	282,586	88.60%	5.60%
No current obsessive compulsive disorder	318,520	99.87%	0.07%
No current borderline personality disorder	316,888	99.35%	0.19%
No current eating disorder	314,022	98.45%	0.80%
No schizophrenia in all time prior	315,981	99.07%	0.21%
No substance abuse diagnosis 6 months prior to index	302,983	94.99%	2.39%
No diagnosis of suicidal ideation in past 365 days	318,342	99.81%	0.04%
No more than 3 previous antidepressants in all time prior	227,315	71.27%	22.16%
No antidepressant use greater than 1825 days (60 months) all time prior	310,340	97.30%	1.69%

CONCLUSIONS

- The ability to analyze clinical trial feasibility thorough observational data may provide substantial insights in avoiding amendments, recruitment challenges and protocol design.
- By utilizing the common data model across various databases, the analysis to be simulated in different populations and geographies which can be representable of recruitment regions.
- The OHDSI tools can facilitate many assumptions in a protocol for clinical trial feasibility a priori which is a valuable proposition. The tools provide a strong framework to conduct the analysis in a standardized and reproducible manner.

REFERENCES

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CONFLICT OF INTEREST STATEMENT

Rupa Makadia, Jamie Forlenza, Frank DeFalco, Chris Knoll, and Patrick Ryan are full time employees of Janssen Research and Development, a unit of Johnson and Johnson. The work on this study was part of their employment. They also hold pension rights from the company and own stock and stock options.