Search, download and explore ClinicalTrials.gov with R

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R Users Group - 18 November 2022 - LSHTM

Overview

- Project motivation
- What is ClinicalTrials.gov ?
- {rctapi} + {rctexplorer}
  - Search and download
  - Explore and interact
- Features and technical details: live demo
- Limitations and Opportunities

Project motivation

- Health Data Science MSc – Summer project
- Partnered with UCB biopharmaceutical
- Aim: Build a tool that enables R users to interface with CT.gov
- Objectives:
    1. Targeted extraction from database
    2. Interactive exploration of extracted data
    3. Utility for pooled analysis (NMA)

What is Clinicaltrials.gov?

- A free public online database since 2000
- Affected by legislation: Compulsory results since 2008
- Holds 430.000 records
  - RCTs, Observational studies (80/20)
  - Each record has room for 300 data fields
  - Types: Categorical, Free-text, Continuous
  - Often multiple pieces of information are found in the same field

Web-view: NCT02814175

Study Details | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Study Type	Interventional
Study Design	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: None (Open Label); Primary Purpose: Treatment
Condition	**Psoriatic Arthritis**
Interventions	Drug: methotrexate (MTX) Biological: adalimumab (ADA)
Enrollment	246

Participant Flow Go to

Recruitment Details	There were 246 participants randomized; 1 participant did not receive study medication. Upon completion of Part 1, eligible participants continued to Part 2, so no additional participants were enrolled in Part 2.
Pre-assignment Details	Intent-To-Treat Part 1 (ITT Part 1) population comprised all participants randomized and received at least 1 dose of study medication in Part 1. ITT Long Term (ITT LT) population included all participants who continued to Part 2 and received at least 1 dose of Part 2 study medication; no additional participants were enrolled into Part 2.

Arm/Group Title	Part 1: MTX Escalated Dose	Part 1: ADA + MTX	Part 2: MTX Escalated Dose	Part 2: ADA +MTX Escalated Dose	Part 2: ADA	Part 2: ADA ew + MTX
▼ Arm/Group Description	Methotrexate (MTX) escalated to 20 - 25 mg or highest tolerable dose every week (ew)	Adalimumab (ADA) 40 mg every other week (eow) in combination with methotrexate (MTX) 15 mg	Participants achieving minimal disease activity (MDA) at Week 16 on methotrexate (MTX) escalated to 20 -25 mg or	Participants not achieving minimal disease activity (MDA) at Week 16 on methotrexate (MTX) escalated to 20 - 25 mg or	Participants achieving minimal disease activity (MDA) at Week 16 on adalimumab (ADA) 40 mg every other week	Participants not achieving minimal disease activity (MDA) at Week 16 on adalimumab (ADA) 40 mg every other week

rctapi - Interface with clinicaltrials.gov

- Through clinicaltrials.gov official API (2019)
- *get_study_fields(search_expr, fields, max_studies, response_content)*
- Use pseudo-code to build search expression
- Select fields to retrieve (there are 300+)
- The main use returns a dataframe with one row per study
- Toggling *response_content* we get a look at API response metadata

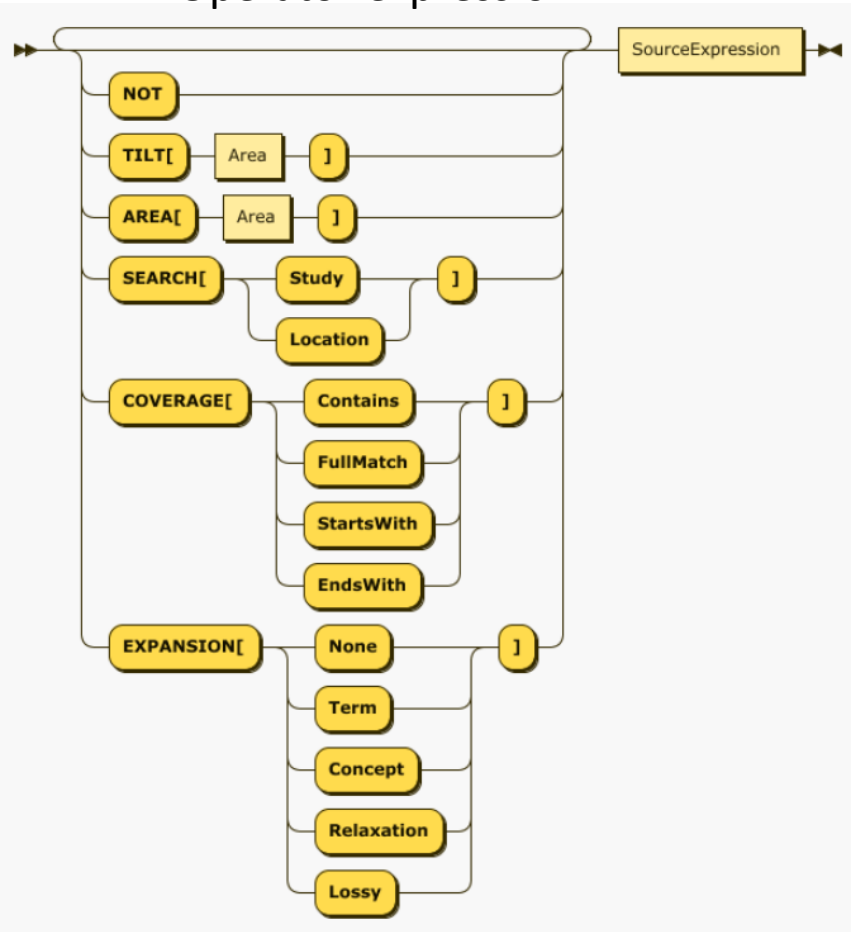
1. Targeted Extraction

- Preserve advanced search functionality
- Allow user to define complex query
- Allow field targeting
- {rctapi} main function:

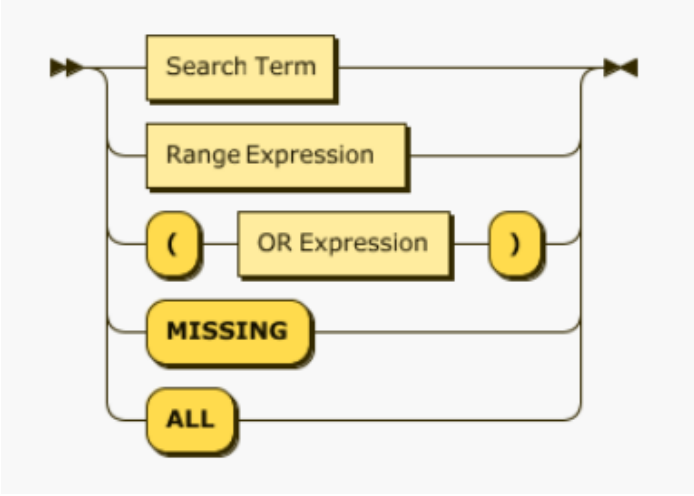
```
get_study_fields(search_expr = “psoriasis OR psoriatic arthritis”,
                 fields = c(“NCTId”,“StudyType”,“OverallStatus”),
                 max_studies = 800)
```

API Search Syntax

"Operator expression"



"Source expression"



rctexplorer – Explore the data

- R Shiny data dashboard optimized for use with *rctapi*
- *set_app_input(search_expr, fields, max_studies) ; launch_explorer(df)*
- Optimized for *fields = for_explorer* but attempts to work with any list.
- *all_fields, registration_fields, results_fields, for_netmeta …*

2. Interactive Exploration + 3. NMA and selection tools

- Data table filtering
- Plotting options
- Missing data fields
- Treatment arms table
- Treatment network

Figure 1: Title page of Mease et al., (2021)

RHEUMATOLOGY

Rheumatology 2021;60:2109–2121
doi:10.1093/rheumatology/keab119

Systematic review and meta analysis

Comparative effectiveness of guselkumab in psoriatic arthritis: results from systematic literature review and network meta-analysis

Philip J. Mease [1], Iain B. McInnes[2], Lai-Shan Tam [3], Kiefer Eaton [4], Steve Peterson[5], Agata Schubert[6], Soumya D. Chakravarty [7,8], Anna Parackal[4], Chetan S. Karyekar[5], Sandhya Nair[9], Wolf-Henning Boehncke[10] and Christopher Ritchlin[11]

Abstract

Objective. The efficacy of the novel interleukin (IL)-23p19 inhibitor guselkumab for psoriatic arthritis (PsA) has recently been demonstrated in two phase 3 trials (DISCOVER-1 & -2) but has not been evaluated *vs* other targeted therapies for PsA. The objective was to compare guselkumab to targeted therapies for PsA for safety and joint and skin efficacy through network meta-analysis (NMA).

Methods. A systematic literature review was conducted in January 2020 to identify randomized controlled trials. Bayesian NMAs were performed to compare treatments on American College of Rheumatology (ACR) 20/50/70 response, mean change from baseline in van der Heijde-Sharp (vdH-S) score, Psoriasis Area Severity Index (PASI) 75/90/100 response, adverse events (AEs) and serious adverse events (SAEs).

Results. Twenty-six phase 3 studies evaluating 13 targeted therapies for PsA were included. For ACR 20 response, guselkumab 100 mg every 8 weeks (Q8W) was comparable to IL-17A inhibitors and subcutaneous tumor necrosis factor (TNF) inhibitors. Similar findings were observed for ACR 50 and 70. For vdH-S score, guselkumab Q8W was comparable to other agents except intravenous TNF therapies. Results for PASI 75 and PASI 90 response suggested guselkumab Q8W was better than most other agents. For PASI 100, guselkumab Q8W was comparable to other active agents. For AEs and SAEs, guselkumab Q8W ranked highly but comparative conclusions were uncertain. Similar results were observed for all outcomes for guselkumab 100 mg every four weeks.

Conclusions. In this NMA, guselkumab demonstrated favorable arthritis efficacy comparable to IL-17A and subcutaneous TNF inhibitors while offering better PASI response relative to many other treatments.

Key words: guselkumab, psoriatic arthritis, interleukin, TNF, biologics, NMA, SLR, ACR, PASI

Rheumatology key messages

- Guselkumab provides better PASI responses than many other agents available in PsA.
- Guselkumab offers joint efficacy comparable to IL-17A and subcutaneous TNF inhibitors available in PsA.

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CLINICAL SCIENCE

Table 1: Studies included in the Network Meta-analysis. Adapted from Mease et al., (2021)

Author, Publication Date	Trial Name	NCTId
Nash 2018	ACTIVE	NCT01925768
Mease 2005	ADEPT	NCT00195689
McInnes 2015	FUTURE 2	NCT01752634
Nash 2018	FUTURE 3	NCT01989468
Kivitz 2019	FUTURE 4	NCT02294227
Mease 2018	FUTURE 5	NCT02404350
Kavanaugh 2009	GO-REVEAL	NCT00265096
Kavanaugh 2017	GO-VIBRANT	NCT02181673
Antoni 2005	IMPACT 2	NCT00051623
Genovese 2007	NA	NA
Gladman 2017	OPAL-BEYOND	NCT01882439
Mease 2017	OPAL-BROADEN	NCT01877668
Kavanaugh 2014	PALACE 1	NCT01172938
Cutolo 2016	PALACE 2	NCT01212757
Edwards 2016	PALACE 3	NCT01212770
Wells 2018	PALACE 4	NCT01307423
McInnes 2013	PSUMMIT 1	NCT01009086
Ritchlin 2014	PSUMMIT 2	NCT01077362
Mease 2013	RAPID-PSA	NCT01087788
Mease 2017	SPIRIT-P1	NCT01695239
Nash 2017	SPIRIT-P2	NCT02349295
Mease 2019	SPIRIT-H2H	NCT03151551
Mease 2017	ASTRAEA	NCT01860976
Mease 2004	NA	NA
Janssen 2019	DISCOVER 1	NCT03162796
Janssen 2019	DISCOVER 2	NCT03158285

Limitations and opportunities

- Not self-contained so could not go on shinyapps.io
- Not on CRAN
- Limit to number of studies retrieved
- Does not deal with actual results
- Does not compute any NMA suitability metrics
- More data-processing before app launch

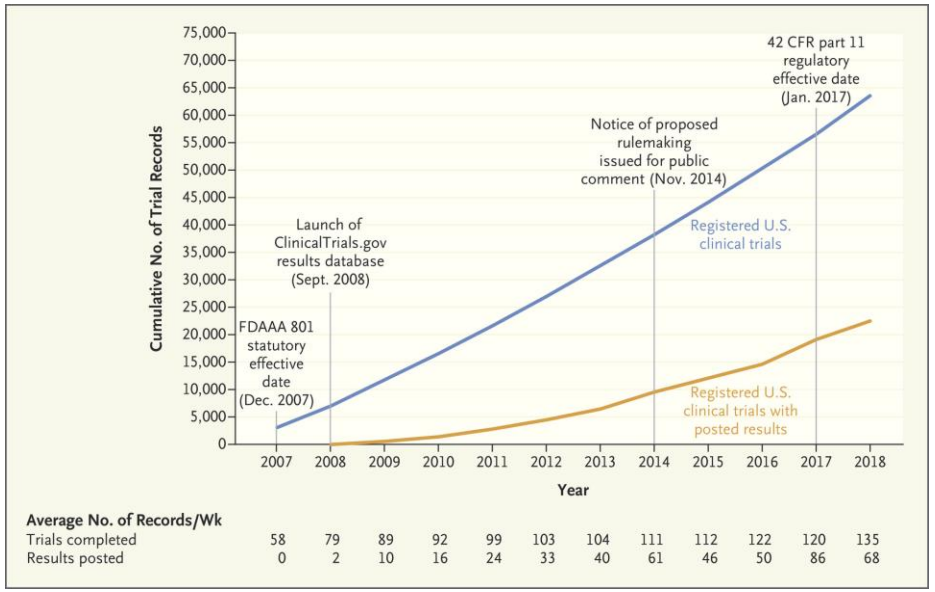
Access

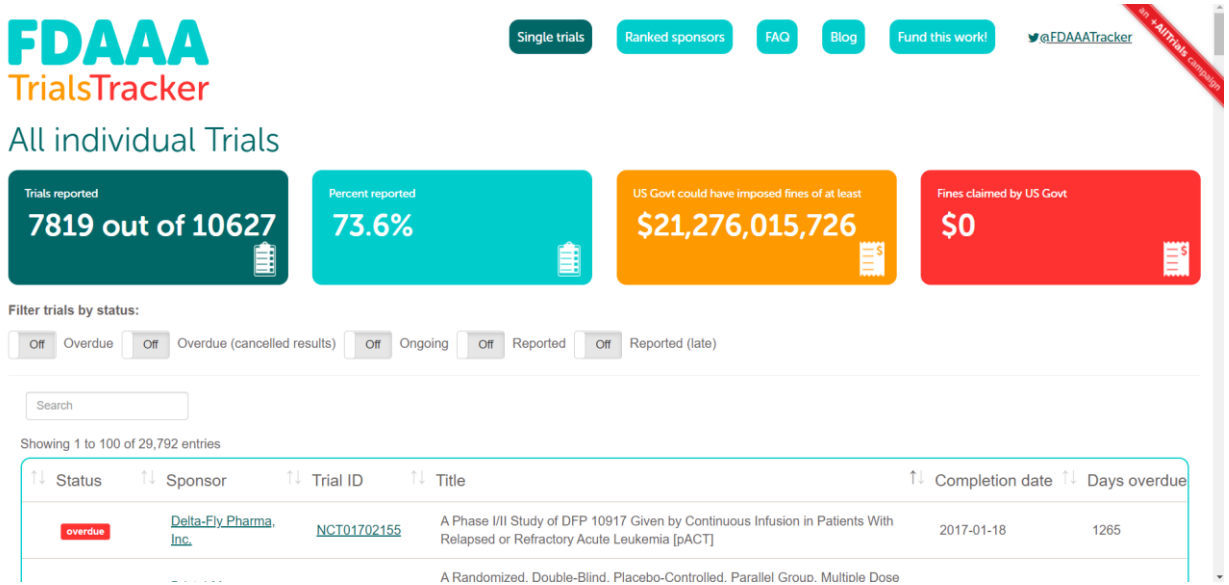
- # install.packages(“librarian”); library(librarian)
- # shelf(devtools)
- devtools::install_github("AdlCruz/rctapi")
- devtools::install_github("AdlCruz/rctexplorer")

References

- Zarin, D. A., Fain, K. M., Dobbins, H. D., Tse, T., & Williams, R. J. (2019). 10-Year Update on Study Results Submitted to ClinicalTrials.gov. *New England Journal of Medicine, 381(20), 1966-1974. doi:10.1056/NEJMsr1907644*
- Mease, P. J., McInnes, I. B., Tam, L.-S., Eaton, K., Peterson, S., Schubert, A., . . . Ritchlin, C. (2021). Comparative effectiveness of guselkumab in psoriatic arthritis: results from systematic literature review and network meta-analysis. *Rheumatology, 60(5), 2109-2121. doi:10.1093/rheumatology/keab119*
- *Search Builder Syntax Key: https://clinicaltrials.gov/api/gui/ref/syntax*
- *Web-view:* NCT02814175 *https://clinicaltrials.gov/ct2/show/results/NCT02814175*
- *https://clinicaltrials.gov/api/gui/ref/crosswalks*

Extra stuff





Zarin DA, Fain KM, Dobbins HD, Tse T, Williams RJ. 10-Year Update on Study Results Submitted to ClinicalTrials.gov. New England Journal of Medicine. 2019 Nov 14;381(20):1966–74.

FDAAA tracker - https://fdaaa.trialstracker.net/trials/

{ctrialsgov} vs {rctapi} + {rctexplorer}

https://cran.r-project.org/web/packages/ctrialsgov/index.html

- Pros
  - Expected to be on CRAN soon
  - Pre-processed data through AACT
  - Free-text field analysis (keywords in context, similarity)
- Cons
  - Indirect connection to database (exclusively pre-processed data)
  - One plot type (timeline)
  - No user interface

Other similar projects

- Rclinicaltrials by Michael Sachs (KI)
- Pyclinicaltrials by Joao Vitor Cavalcante
- J&J in 2013 develops Sherlock
- J&J + LASER Analytica in 2016 extends to NMA

More references

- Zarin DA, Fain KM, Dobbins HD, Tse T, Williams RJ. 10-Year Update on Study Results Submitted to ClinicalTrials.gov. New England Journal of Medicine. 2019 Nov 14;381(20):1966–74.
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- Karcher, H., Wiecek, W., Nikodem, M., Voss, E., Sena, A., & Cepeda, S. (2016). PRM111 - A NEW TOOL TO AUTOMATE NETWORK META-ANALYSES OF STUDIES EXTRACTED FROM CLINICALTRIALS.GOV. *Value in Health, 19(3), A91. doi:https://doi.org/10.1016/j.jval.2016.03.1823*
- *https://cran.r-project.org/web/packages/ctrialsgov/index.html*
- FDAAA tracker - https://fdaaa.trialstracker.net/trials/
- Rclinicaltrials - https://rdrr.io/github/sachsmc/rclinicaltrials/
- Pytrials - https://pytrials.readthedocs.io/en/latest/readme.html