Adult Rheumatoid Arthritis: Evaluating Treatment Effectiveness Among Patients

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Healthcare Studies

Introduction:

CorEvita, LLC - The Company:

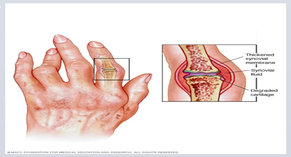
- CorEvitas is a life science health company that supports many registries following patients with autoimmune disease (i.e., rheumatoid arthritis (RA).
- CorEvitas is a biopharma clinical research registry data base organization where their end motive is to provide safety studies and pharmacovigilance reporting activities.

The Clinical Research Internship at CorEvitas included:

- Training on human subject research and epidemiology
- Understanding of the CorEvitas Registry data and its use in clinical research
- Attended research meetings, networking with the teams of biostatistions and epidemiologist
- Administrative tasks to assists in the work being done at CorEvitas

Background – Autoimmune disease and Rheumatoid Arthritis

- An autoimmune disease is an exaggerated immune response involving the existence of autoantibodies and inflammatory reactions. Leads to target organ damage and disabilities.
- Rheumatoid arthritis is a chronic autoimmune disease that can cause unrepairable joint damage and significant disability.
- The diagnosis is based on a combination of clinical and laboratory features.
- Patients typically present in many joints (polyarthritis), specifically the small joints of the hands and feet.
- Any joint lined by a synovial membrane may be involved (e.g. knees, elbows).
- RA may also affect organs such as the skin, heart, lungs, and eyes.



[Janeway CA Jr, Travers P, Walport M, 2001]

- In addition to stiffness, swelling, and inflammation in the joints, RA can be accompanied by morning stiffness, pain in muscles, joints, back, difficulty of every-day life activities, and progressive joint deterioration. **[Ngian GS, 2010]**
- RA occurs in < 1% of the US population
- RA occurs at all ages, yet peaks at about ~ 60 years of age
- Women are twice as likely than men to have RA
- People with lower socioeconomic status may have greater burden of RA **[England, 2021]**
- RA may have both genetic and environmental risk factors (eg, cigarette smoking, infection, or trauma). **[Deane KD, Demoruelle MK, Kelmenson LB, Kuhn KA, Norris JM, and Holers VM, 2017]**
- RA is treated by medications that act on:
  - Pain and inflammation (e.g., NSAIDs (aspirin, ibuprofen) or prescription opioids
  - Prescribed anti-inflammatory drugs (e.g. methotrexate)
  - Treatment that suppress the immune system and prevent joint damage called disease modifying antirheumatic drugs (DMARDs).
- Goal of medications is to help patient's symptoms, reduce disease activity, and slow the progression of disease.

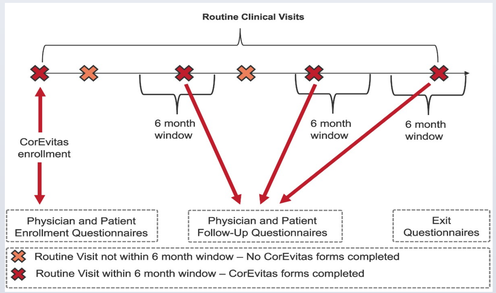
Objectives:

- To provide a basic understanding of Rheumatoid Arthritis and how it is being studied using the CorEvitas RA registry
- To demonstrate the design of an observational cohort study to measure treatment effectiveness in Rheumatoid arthritis.

The RA Registry and Methods for Assessing Disease Status:

CorEvitas RA Registry is:

- Prospective cohort study of adult patients who have been diagnosed with RA by a rheumatologist and who have provided informed consent to be in research studies.
- Patients are recruited from multiple clinical practices across the US
- After enrollment patients are followed prospectively (forward in time) in approximately 6-month intervals



- Data is collected from patient and provider at enrollment and each subsequent patient visit
- These data do not include any patient identifying information and are held in a large database that is used for research.

Inclusion criteria:

- Be at least 18 years of age or older
- Be able and willing to provide written consent for participation in the registry as well as Personally Identifiable Information (PII) that includes Full Name and Date of Birth at a minimum
- Have been diagnosed with rheumatoid arthritis by a rheumatologist
- Complete CorEvitas enrollment patient and provider questionary forms

Exclusion Criteria:

- Unable or unwilling to provide informed consent to participate in the registry
- Currently participating or planning to participate in a clinical trial with a non-marketed or marketed investigational drug
- Death prior to enrollment

Registry Data Collection include:

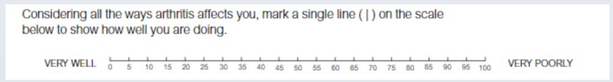
Demographics	Age, Gender, Height, Weight, Education, Body Mass Index (BMI), Work status, Insurance type, Smoking/Alcohol history, Family Hx	Patient Reported
Treatment History	Prior Medication (Biologic and Non-biologic systemics), Current medication and medication changes, Reasons for Start/Change/Discontinuation, Biosimilar drug data capture to begin June 2017	Physician Reported
Disease Characteristics	28 Tender/Swollen Joint Count (TJC/SJC), Physician Global Assessment, ACR Functional Status, Subcutaneous nodules, deformities, sjogren's, Joint Deformity/Secondary Sjogren's Disease, History of comorbidities	Physician Reported
Patient Reported Outcomes	Patient Global Assessment, HAQ; EQ5-D, Patient Pain/Fatigue, Morning Stiffness/Severity	Patient Reported

What are patient recorded outcomes (PROs)?

- In the late 1990's and early 2000's, Pharmaceutical companies recognized the importance of PROs (Patient Reported Outcomes) when measuring health improvements.
- PRO's include items such as patients' healthcare related Quality of Life (QOL), and patient pain
- Repeating these measures over time can help to understand how disease improve or progresses**. [CorEvitas Training materials for RA registry, 2021]**

Patient reported outcomes in the CorEvitas Registry include:

- Patient global assessment

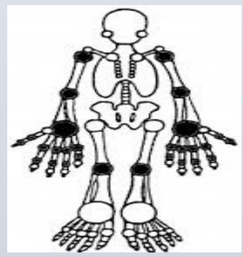


- Patient pain, fatigue, and morning stiffness that are recorded using a VAS scale

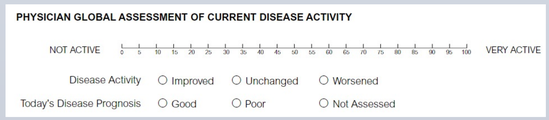
- Patient quality of life, depression, anxiety, and others

Providers assess disease by:

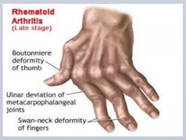
- Counting the number of tender and swollen joints



- Assessing the global status of patients



- As assessing deformity of joints



Disease Activity scores such **as Clinical Disease activity Score (CDAI**) are calculated from these assessments.

The components of CDAI are summed together these are:

- Number of Tender Joints in 28 Joint Counts
- Number of Swollen Joints in 28 Joints Counts
- Value of Physician global assessment / 10
- Value of the Patient global assessment / 10

The score can be grouped into 4 categories remission, low, moderate and high
Or 2 categories low disease activity and high disease activity.

Research Study of Treatment Effectiveness:

Studies of medication in data from real world patients, i.e., registries, aims to measure if drugs are effective when taken by regular patients, who may vary by disease severity, may have different health status, and may or may not take it as prescribed.

Studies plans are outlined in the study protocol that include the following:

- the studies objectives
- the criteria for the study population
- the design
- the start date and follow-up period
- the outcome measure, and
- the analysis plan

Study Design - Cohort studies:

- Prospective cohort studies are a common study design to compare the effectiveness of two drugs in the registry data

- Patients who start a new drug (index date), are followed in time to an endpoint (end date) when the outcomes are measured
- Patients are matched on characteristics such as age and severity of disease to assure that the 2 drug groups are comparable
- Outcomes may include both PRO's or a measure of disease assessed by physician (e.g., CDAI)
- The analysis compare the 2 drug groups with respect to the outcome(s),
  - For eg, the mean change in disease activity (e.g. change in CDAI score from the start of a study to the end of the study); or
  - Measure the proportion of achievement of low disease activity (remission) at the end of the study, the proportion of patients that achieve CDAI ≤ 10 at end date.

Conclusions

- Clinical trials are used to show if a drug is effective under ideal conditions, these are called experimental studies and are done before a drug is licensed.
- After a drug is licensed, observational studies, e.g. cohort studies, aim to determine if the drugs are effective when used by real world patients.

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