



Screening for TNF response prior to initiation of biologic therapy for precise targeted therapy

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INTRODUCTION

- RA affects 1.3 million Americans, and around 75% of RA patients are women
- Anti-CCP antibodies seen in early development of disease and show those likely to develop severe and irreversible joint or organ damage
- Treatment modalities: conventional Disease Modifying Antirheumatic Drugs (DMARDs) and Biologic/Targeted Synthetic DMARDs (b/tsDMARDs)
- TNF inhibitors (TNFi) are started first line therapy 90% of the time, but over one third of those patients do not respond to TNFi
- A trial-and error approach to biologic therapy using TNFi is often used to treat patients with anti-CCP RA with moderate to severe disease

Problem: Trial-and-Error Approach to Treatment Selection

- Many treatment modalities with comparable efficacies
- Providers do not recommend one targeted therapy over another
- Therapy selection is usually driven by administrative decisions
- Ineffective predictive biomarkers used to guide RA treatment in the past

PURPOSE

- Ending the trial-and error approach to prescribe b/tsDMARDs in Rheumatoid Arthritis(RA) patients who are anti-CCP positive.
- Identify true non-responders to TNFi therapy best suited for an alternative mechanism of action (MOA).
- Get patients on the right medication for their specific disease biology sooner to improve outcomes and quality of life.
- Improve clinical decision-making process of b/tsDMARD section to lower healthcare costs, slow disease progression, lower mortality rate, decrease pain, improve function and quality of life by helping patient avoid ineffective drugs.

IMPLEMENTATION

Methods

prism/RA
Stop Forward RA
MUSCULAR BIOMARKER TEST

Framework

Lewin's Change Theory

- Unfreeze:** TNFi Not the Answer, Test and learn approach
- Change:** TNFi Response Test, Choose an MOA if indicated
- Refreeze:** Continue to assess by TNFi, and determine if the trial and error pathway

QI Model

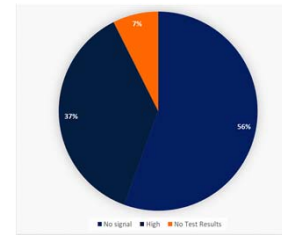
- A 10-day reflective practice log was conducted
- Literature Review on alternative to the trial-and error standard approach to b/tsDMARD selection
 - Potential alternative therapies
 - Precision medicine tools
- Identification of patients meeting the quality improvement project inclusion criteria
- Implementation of the TNFi non-responder tool
- Predicted non-responders were given the choice alternative mechanism of actions or TNFi
- Evaluation of impact of incorporation of the TNFi non-responder tool on patient care

Intervention

prism/RA
Stop Forward RA
MUSCULAR BIOMARKER TEST

RESULTS

- 27 patients meeting criteria screened
- 15 no signal predicted response
- 10 non-responder predicted response
- 2 no test results



- 15 No signal predictors
- 7 went on to TNFi
- 6 on alt-MOA
- 2 cont cDMARDs
- 10 Predicted non-responders
- 8 changed to JAKi
- 2 changed to alt-MOA

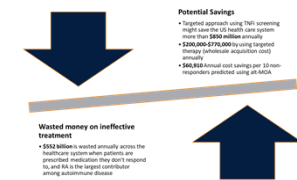
MOA	100 samples produced non-responders	100 predicted non-responders
Ag. Inhib. (n=27)	21 (78%)	21 (78%)
Col. Inhib. (n=2)	0 (0%)	0 (0%)
IL-6 Inhib. (n=8)	2 (25%)	2 (25%)
IL-17 Inhib. (n=2)	0 (0%)	0 (0%)
IL-23 Inhib. (n=2)	0 (0%)	0 (0%)
IL-36 Inhib. (n=2)	0 (0%)	0 (0%)
IL-37 Inhib. (n=2)	0 (0%)	0 (0%)
IL-38 Inhib. (n=2)	0 (0%)	0 (0%)
IL-39 Inhib. (n=2)	0 (0%)	0 (0%)
IL-4 Inhib. (n=2)	0 (0%)	0 (0%)
IL-6 Inhib. (n=2)	0 (0%)	0 (0%)
IL-17 Inhib. (n=2)	0 (0%)	0 (0%)
IL-23 Inhib. (n=2)	0 (0%)	0 (0%)
IL-36 Inhib. (n=2)	0 (0%)	0 (0%)
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Outcomes

- 1 - Surgery
- 1 - Established
- 1 - New Start

DISCUSSION

- Predicted therapy guides treatment, reducing adverse effects and avoid treatments with drugs without positive outcomes
- The screening tool allowed for a targeted approach controlling disease in a matter of weeks compared to what could have taken months to figure an out inadequate response before changing therapies.
- The average period to assess TNFi failure can take 9-12 months



LIMITATIONS/ REFERENCES

- Project timeline. Normally, follow ups are two to three months to assess response to therapy. Full response can take up to 6 months
- JAKi therapy has rapid onset but contraindicated in some conditions
- Patients not keeping follow up appointments. Sufficient data could not be collected, and patients were excluded
- Insurance formularies
- Population sample size

DNP Project & References:

