Initiation of Biologic Disease-Modifying Antirheumatic Drug Therapy and Associated Changes in Disease Activity Measures in Routine Clinical Practice: Findings From a Next Generation Registry

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Background

- The introduction of biologic disease modifying antirheumatic drugs (DMARD) was a major step forward in the treatment of rheumatoid arthritis (RA)
- Given the marked differences in price between therapeutic options for RA, it is important to evaluate whether the more expensive biologic DMARD (bDMARD) are more effective than the cheaper non-biologic DMARD (nDMARD)
- While many clinical trials provide direct comparisons between a bDMARD and conventional synthetic DMARD, there is a need for additional evidence on the effectiveness of these therapies in routine clinical practice
- Available real world evidence comes from observational studies and registries but these are also prone to selection bias as both providers and patients may choose not to participate in such studies
- We present results from a Next Generation Registry, a novel approach to real world evidence generation. The OM1 platform collects, links, and leverages, structured and unstructured data from electronic medical records and other sources in an ongoing and continuously updating manner
- The Next Generation Registry offers a time- and resource-efficient alternative to traditional real world data collection methods. It also avoids potential selection bias as data from all patients seen by all providers at each practice are included in the analysis

Objectives

To evaluate changes in disease activity measures associated with bDMARD therapy in patients with RA who initiated nDMARD and later switched to or added a second nDMARD or a bDMARD

Methods

- Analyses were conducted using the OM1 RA Next Generation (Next Gen) Registry which includes deep clinical data on a large cohort of patients with RA from rheumatology practices across the US
- From the Next Gen Registry, a cohort was selected that includes >60,000 RA patients on DMARD therapy treated by rheumatologists between January 2013 and June 2016
- This analysis included 4,005 patients who met study criteria:
  - Were treated with nDMARD
  - Had not received prior treatment with bDMARD
  - Either added or switched to another nDMARD or initiated bDMARD during the observation period (date of change in therapy is the index date) and
  - Had at least 2 disease activity measures
- Disease activity measures commonly evaluated by rheumatologists in routine clinical practice included RAPID-3, HAQ-II, CDAI, and DAS28
- Established American College of Rheumatology (ACR) cut points were used to define remission [1]
- Data were censored at 12 months to reduce the impact of subsequent treatment changes
- Survival analyses were conducted to evaluate the time to initial remission
- Log rank tests were used to compare time to initial and sustained remission (defined as 2 consecutive scores denoting remission) in the bDMARD versus nDMARD group
- Since disease activity measures were not collected according to a pre-defined study schedule but rather as part of routine clinical practice, we conducted a sensitivity analysis to account for differences in timing of data collection by matching patients on time to first disease activity measure

Results

- During the 12-month study period, of the 4,005 patients included in this analysis
  - There were ~14,000 disease activity measures
  - None of the patients were in remission (based on the ACR cut points) at index date
  - 2,006 added or switched to a bDMARD
  - 1,999 added or switched to another nDMARD
- Age, gender distribution, race distribution, and disease activity measures, swollen and tender joint counts, and Charlson Comorbidity Index, at baseline, were similar in both groups [Table 1]
- Patients in the bDMARD group had higher mean number of disease activity measures than in the nDMARD group (3.9 versus 3.0) but medians are equal (3 in both groups). The mean number of disease activity measures are more balanced in the matched cohort (2.7 versus 3.0) [Table 1]
- Kaplan Meier plots indicate that time to initial remission was significantly shorter in the bDMARD group compared to the nDMARD group (mean ± SD=5.6 ± 4.4 months versus 6.0 ± 4.4 months, p<0.001) [Figure 1]
- More patients in the bDMARD group achieved initial remission (21% versus 16%; p<0.05) [Table 2] and sustained remission (14% versus 11%, p<0.05) compared to the nDMARD group [Table 3]
- Sensitivity analysis in the cohort matched on time of disease activity measurement also demonstrated shorter time to remission in the bDMARD group (p<0.05)

Table 1. Patient Characteristics at Time of First Change in DMARD Therapy

	Biologic DMARD (n=2,006)	Non-Biologic DMARD (n=1,999)	Total (n=4,005)
Female (n, %)	1,618 (81%)	1,601 (80%)	3,219 (80%)
Race (n, %)			
Black	224 (11%)	235 (12%)	459 (11%)
White	1,544 (77%)	1467 (73%)	3011 (75%)
Other	238 (12%)	297 (15%)	535 (13%)
Age, Years (mean±SD)	61±13	62±13	62±13
Baseline Disease Activity			
Low (n, %)	380 (19%)	352 (18%)	732 (18%)
Medium (n, %)	633 (32%)	713 (36%)	1,346 (34%)
High (n, %)	993 (50%)	934 (47%)	1,927 (48%)
28-Swollen Joint Count (Mean±SD)	3.6±4.1	3.4±4.0	3.5±4.1
28-Tender Joint Count (Mean±SD)	5.8±6.1	4.9±5.3	5.3±5.7
Charlson Comorbidity Index (Mean±SD)	1.6±1.3	1.7±1.3	1.7±1.3
Time in Months to First Disease Activity Measure after Index Date Median (Q1-Q3) in Full Cohort	2.0 (1.1-3.2)	2.5 (1.4-3.6)	2.2 (1.2-3.4)
Time in Months to First Disease Activity Measure after Index Date in Matched Cohort Median (Q1-Q3)	2.5 (1.4-3.8) (n=2002)	2.5 (1.4-3.6) (v=1999)	2.5 (1.4-3.7)
Number of Disease Activity Measures (Mean±SD; Median) in Full Cohort	3.9±3.0; 3	3.0±2.0; 3	3.4±2.6; 3
Number of Disease Activity Measures (Mean±SD; Median) in Matched Cohort	2.7±1.4; 3	3.0±2.0; 3	2.8±1.8; 3

Figure 1. Biologic DMARD Therapy is Associated with Shorter Time to Initial Remission

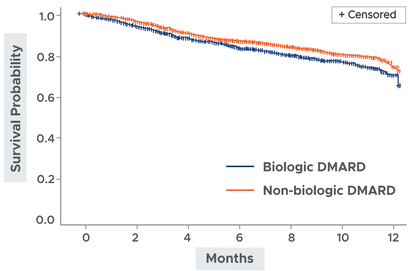

Table 2. More Patients on Biologic DMARD Achieved Initial Remission Compared to Non-Biologic DMARD

Treatment	Total	Remission	Censored	p-value (Log-Rank)
Biologic	2,006	412 (21%)	1,594 (79%)	0.001*
Non-biologic	1,999	325 (16%)	1,674 (84%)	
Total	4005	737 (18%)	3,268 (82%)	

*p=0.044 from the sensitivity analysis in patients matched on time to first PRO measure (see Table 1).

Table 3. More Patients on Biologic DMARD Achieved Sustained Remission Compared to Non-Biologic DMARD

Treatment	Total	Remission	Censored	p-value (Log-Rank)
Biologic	2,006	290 (14%)	1,716 (86%)	0.009
Non-biologic	1,999	225 (11%)	1,774 (89%)	
Total	4005	515 (13%)	3,490 (87%)	

Conclusions

- **Rheumatologists use ACR recommended disease activity measures in routine clinical practice to guide and monitor therapeutic decisions; our data show more frequent assessments in patients on bDMARD**
- **Disease activity improved with changes in DMARD therapy**
- **bDMARD was associated with shorter time to remission and more patients treated with bDMARD achieved initial and sustained remission compared to those on nDMARD**
- **The observed differences were small and may reflect appropriate and optimal matching of patients to DMARD**

Implications

Next Generation Registries are a powerful tool for real world evidence generation and provide the best representation of patient management and clinical decision-making in routine clinical practice.

This RA Next Gen Registry study replicates findings from previous observational studies in a much larger and contemporaneous cohort of patients under conditions of routine clinical practice.

REFERENCES [1] Anderson J, Caplan L, Yazdany J, et al., Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice, Arthritis Care Res (Hoboken). 2012 May; 64(5):640-7