Initiation of Biologic Disease Modifying Antirheumatic Drug Therapy and Associated Changes in Disease Activity Measures in Routine Clinical Practice: Findings from a Large Contemporaneous Real World Cohort

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Background

While many clinical trials provide direct comparisons between biologic disease modifying antirheumatic drugs (bDMARD) and nonbiologic DMARD (nDMARD), there is a need for additional evidence on the effectiveness of these therapies in routine clinical practice. We evaluated changes in disease activity measures associated with bDMARD therapy, in a large cohort of patients with RA, under conditions of routine clinical practice.

Methods

The OM1 platform collects, links, and leverages structured and unstructured data from electronic medical records (EMR) and other sources in an ongoing and continuously updating manner. The OM1 RA Cohort includes data on >95,000 patients treated by rheumatologists. This analysis included patients who were treated with nDMARD between January 2013 and April 2017, had not received prior treatment with bDMARD, and either added or switched to another nDMARD or initiated bDMARD during the observation period (date of change in therapy is the index date). Established American College of Rheumatology cutpoints for standard disease activity measures (RAPID-3, CDAI, DAS28) were used to define remission, low, moderate and high disease activity categories. Advanced natural language processing was used to derive missing disease activity categories. Drug eras were defined using Observational Medical Outcomes Partnership (OMOP) definitions.

The primary analysis was time to initial remission, and a secondary analysis was time to confirmed remission defined as 2 consecutive scores denoting remission. To reduce the impact of subsequent treatment changes, data were censored at 12 months. To reduce the bias that more frequent disease activity measures may be associated with shorter time to remission, we matched the two groups on average number of disease activity measures per patient.

Methods (Continued)

The following analyses were performed:

1. Intent-to-treat (ITT) analysis; non-biologic group includes patients who switched to biologic DMARDs within 6 months after the index date (**Figure 1**).
2. As-treated (AT) analysis; non-biologic group excludes patients who switched to biologic DMARDs within 6 months after the index date (**Figure 2**).
3. Subgroup analysis; the comparator group (nb-biologic shown in the figure) are patients who switched/ added non-biologic DMARDs but switched to biologic DMARDs within 6 months after the index date (**Figure 3**).
4. ITT analysis of time to confirmed remission; note if the last disease activity measure is remission and there are no future data available, this single remission outcome is considered as a remission in this analysis (**Figure 4**).

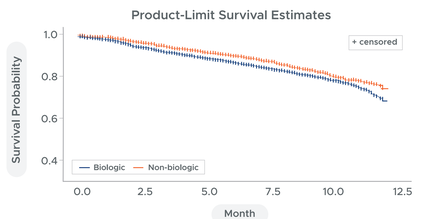
Results

The analysis cohort included 4,957 patients who met study inclusion criteria, none of whom were in remission at index date; 1,334 added or switched to another nDMARD and 3,623 added or switched to a bDMARD. There were an average of 4.2 disease activity measures per patient and a total of 20,605 disease activity measures during the 12 month study period. Age, gender, baseline disease activity measures, and Charlson Comorbidity Index, were similar in both groups [**Table 1**]. In the primary ITT survival analysis, a larger proportion of patients in the bDMARD group achieved remission (p=0.013) within 12 months post the index date [**Figure 1**]. Time to remission was significantly shorter in the bDMARD group (mean±SD=5.2±3.4 months) compared to the nDMARD group (5.7±3.2 months, p<0.05). This finding is supported by the AT analysis (p=0.040) [**Figure 2**]. In the subgroup analysis that compared patients who switched or added bDMARD immediately at the index date versus switching deferred by up to 6 months, the former group showed marginally significant shorter time to remission (p=0.095) [**Figure 3**]. In the secondary ITT survival analysis, a larger proportion of patients in the bDMARD group achieved confirmed remission (p=0.003) compared to the nDMARD group [**Figure 4**].

Table 1. Patient characteristics at the time of change in DMARD therapy (index date), stratified by DMARD class

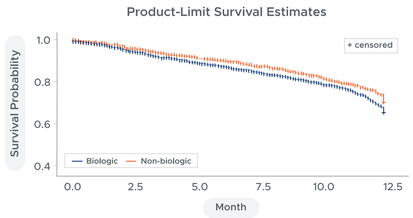
Characteristics		DMARD CLASS bDMARD N=3,623	nDMARD N=1,334	Total N=4,957
Female gender	n (%)	2,919 (81%)	1,110 (83%)	4,029 (81%)
Age (years) at index date	Mean (SD)	58 (13)	57 (13)	58 (13)
Charlson comorbidity index at index date	Mean (SD)	1.5 (1)	1.4 (1)	1.4 (1)
Baseline high disease activity	n(%)	1,530 (42%)	550 (41%)	2,080 (42%)
Number of disease activity measures	Mean (SD)	4.1 (2.5)	4.4 (2.6)	4.2 (2.5)
TJC at index date	Mean (SD)	5.775 (6.36)	5.15 (5.80)	5.644 (6.257)
Extra-articular manifestations	n(%)	882 (18%)	334 (7%)	1,216 (25%)

Figure 1. Initiating biologic DMARDs is associated with shorter time to remission in ITT analysis (Analysis #1; p=0.013)



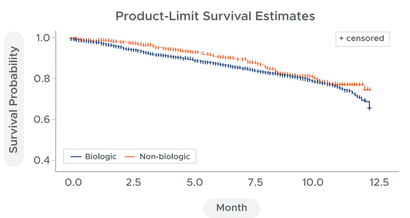
Summary of the Number of Censored and Uncensored Values					
Stratum	Class	Total	Failed	Censored	% Censored
1	Biologic	3623	661	2962	81.76
2	Non-biologic	1334	219	1115	83.58
Total		4957	880	4077	82.25

Figure 2. Initiating biologic DMARDs is associated with shorter time to remission in AT analysis (Analysis #2; p=0.040)



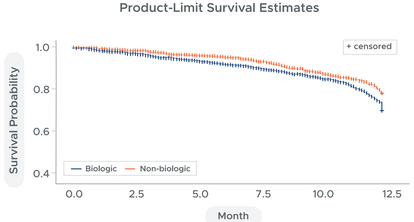
Summary of the Number of Censored and Uncensored Values					
Stratum	Class	Total	Failed	Censored	% Censored
1	Biologic	3623	661	2962	81.76
2	Non-biologic	834	142	692	82.97
Total		4457	803	3654	81.98

Figure 3. Initiating biologic DMARDs is marginally associated with shorter time to remission in a subgroup analysis (Analysis #3; p=0.095)



Summary of the Number of Censored and Uncensored Values					
Stratum	Class	Total	Failed	Censored	% Censored
1	Biologic	3623	661	2962	81.76
2	Non-biologic	500	77	423	84.60
Total		4123	738	3385	82.10

Figure 4. Initiating biologic DMARDs is associated with shorter time to sustained remission defined as the first of two consecutive remission disease activities (Analysis #4; p=0.003)



Summary of the Number of Censored and Uncensored Values					
Stratum	Class	Total	Failed	Censored	% Censored
1	Biologic	3623	486	3137	86.59
2	Non-biologic	1334	149	1185	88.83
Total		4957	635	4322	87.19

Conclusions

Disease activity improved with changes in DMARD therapy; however, the addition of bDMARDs were associated with significantly shorter time to remission. This study uses novel data collection techniques to replicate findings from prior observational studies in a much larger and contemporaneous cohort of patients under conditions of routine clinical practice.