Poster # 597

Characteristics of Patients and Predictors of Composite Disease Activity Scores for Switching to Monotherapy vs Continuing TNF Inhibitor and Methotrexate Combination Therapy in RA: A Retrospective Analysis of the Brigham and Women's Rheumatoid Arthritis Sequential Study Registry

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INTRODUCTION

- Rheumatoid arthritis (RA) is a systemic, inflammatory, autoimmune disease that causes synovitis and joint damage, negatively impacting the physical health and patient functionality due to pain, swelling, and stiffness[1]
- Biologic disease-modifying antirheumatic drugs in combination with methotrexate (MTX) are being incorporated earlier in RA therapy to prevent long-term damage and maintain patient function[2]
- While some patients transition off combination therapy (tumor necrosis factor inhibitor [TNFi] + MTX) to monotherapy (either TNFi or MTX), differences in patient characteristics and attainment of disease control for the combination and monotherapy groups are unclear

OBJECTIVES

- To describe the rate of change from combination therapy to monotherapy, and the characteristics of these groups at baseline and index date
- To identify baseline, pre-index, and index predictors for disease activity scores, and treatment group at index
- To describe disease activity status two years post-index

METHODS

Data source

- Data were obtained from the Brigham and Women's Rheumatoid Arthritis Sequential Study (BRASS) RA Registry, collected from 2003 to 2016
- BRASS RA Registry has collected data prospectively from over 1,400 patients diagnosed with RA since 2003
  - At baseline visit and annual visits, rheumatologists completed the 28-joint count and overall disease activity score assessments
  - At 6-month intervals, patients completed questionnaires on functional status including but not limited to Multidimensional Health Assessment Questionnaire, EuroQoL-5D, and Rheumatoid Arthritis Disease Activity Index

Eligibility criteria

- Adults (≥ 18 years of age) enrolled in BRASS RA Registry with a minimum of one follow-up visit in addition to a baseline visit
- Evidence of treatment with combination therapy for ≥ 2 follow-up visits

Study design

- The study period was from March 1, 2003 to December 31, 2016
- Patient follow-up period was from baseline through the index date and until the end of available data (censored cases), or patient exit from the registry
- Baseline was defined as date of first recorded use of combination therapy at, or, following enrollment
- Index date was defined as date of conversion from combination to monotherapy
  - For patients who continued on combination therapy until the end of the follow-up period, index date was defined as their baseline date plus the average time taken to switch to a monotherapy

Statistical considerations

- Descriptive analysis was used to describe the rate of change from combination to monotherapy, group characteristics at baseline and index date, and disease activity two years post-index
- Analysis of covariance was used to identify predictors of disease activity scores at index
- Multinomial regression was used to identify predictors of treatment group at index

RESULTS

Table 1. Demographic and Disease Characteristics at Index

	Treatment Pattern at Index			
Characteristic at Index	Continued Combination Therapy (n = 157)[a]	Switched to TNFi Monotherapy (n = 105)	Switched to MTX Monotherapy (n = 79)	*P*-Value[b]
Mean age (SD), years	61.2 (11.8)	59.4 (15.1)	64.9 (12.9)	**0.0256**
Gender, n (%)				0.0831
Female	140 (89.2)	85 (81)	63 (79.7)	
Male	17 (10.8)	20 (19.0)	16 (20.3)	
White, n (%)	144 (87.8)	99 (90.0)	76 (88.4)	0.3099
Disease status by DAS28-CRP-4, n (%)	(n = 123)	(n = 84)	(n = 60)	0.1425
Remission (DAS < 1.6)	39 (31.7)	21 (25.0)	13 (21.6)	
Low (DAS 1.6 to ≤ 2.4)	32 (26.0)	28 (33.3)	15 (25.0)	
Moderate (DAS 2.4 to ≤ 3.7)	29 (23.6)	22 (26.2)	15 (25.0)	
High (DAS > 3.7)	23 (18.7)	13 (15.5)	17 (28.3)	
Biologic initiation era, n (%)				**0.0153**[c]
Late (2012–2016)	32 (20.4)	13 (12.4)	5 (6.3)	
Intermediate (2006–2011)	27 (17.2)	11 (10.5)	13 (16.5)	
Early (2003–2005)	98 (62.4)	81 (77.1)	61 (77.2)	
Mean (SD) time from baseline to switch, months	n/a	23.4 (24.5)	23.5 (22.2)	0.9357
Time from baseline to switch, n (%)				
< 1 year	n/a	56 (53.3)	38 (48.1)	0.0784
1–2 years	n/a	23 (22.0)	13 (16.4)	
2–3 years	n/a	7 (6.6)	16 (20.3)	
3–4 years	n/a	9 (8.6)	4 (5.1)	
> 4 years	n/a	10 (9.5)	8 (10.1)	
Mean (SD) time on TNFi before index, months	28.2 (20.5)	29.7 (28.4)	24.6 (23.2)	0.3350
Mean (SD) time on MTX before index, months	34.3 (25.0)	28.6 (27.1)	35.2 (29.2)	0.1541

[a]For each patient who continued combination therapy, the index date was calculated as their baseline date plus 24 months.
[b]*P*-values by analysis of variance for means (F-tests) and Chi-square for frequency counts, significant values (*P* < 0.05) are **bolded**.
[c]*P*-value across all categories.
DAS28-CRP-4, Disease Activity Score 28-joint count with C-reactive Protein; MTX, methotrexate; n/a, not applicable; SD, standard deviation; TNFi, tumor necrosis factor inhibitor.

- Overall, 341 patients with RA and treated with TNFi + MTX combination therapy were identified
  - 157/341 (46%) patients were persistent on combination therapy throughout the study
  - 105/341 (31%) patients switched to TNFi monotherapy
  - 79/341 (23%) patients switched to MTX monotherapy
- Of the 184 patients that switched to monotherapy (either TNFi or MTX), 94 (51%) did so in the first year after baseline
  - Average time to switch of 23.4 months
- Differing patient characteristics at index included:
  - Age (patients who switch to MTX monotherapy were older)
  - Biologic initiation era (fewer patients who initiated late switched to MTX monotherapy)

Table 2. Predictors of Disease Activity Scores at Index

	DAS28-CRP-4 (N = 251)		RAPID3 (N = 211)		SDAI (N = 227)		CDAI (N = 245)		RADAI (N = 113)	
Predictor Variables	Estimate	*P*-Value	Estimate	*P*-Value	Estimate	*P*-Value	Estimate	*P*-Value	Estimate	*P*-Value
Biologic initiation era										
Early	**0.65**	**0.0072**	2.10	0.0941	**6.08**	**0.0112**	**5.58**	**0.0115**	0.65	0.1889
Intermediate	0.26	0.3528	2.01	0.1549	3.30	0.2199	1.60	0.5137	0.67	0.1962
Late	ref		ref		ref		ref		ref	
Disease duration	**0.03**	**< 0.0001**	**0.09**	**0.0063**	**0.30**	**< 0.0001**	**0.30**	**< 0.0001**	0.03	0.1274
Narcotic use										
No	0.47	0.1030	–0.01	0.9902	5.24	0.0707	**5.41**	**0.0361**	–0.08	0.9105
Yes	ref		ref		ref		ref		ref	
Baseline disease activity score	**0.32**	**< 0.0001**	**0.46**	**< 0.0001**	**0.32**	**< 0.0001**	**0.31**	**< 0.0001**	**0.34**	**0.0004**

Analysis of covariance data are presented, significant values (*P* < 0.05) are **bolded**. Positive values are higher/worse disease activity, negative values are lower/better disease activity compared with reference variable. Initiation eras were defined as: late (2012–2016), intermediate (2006–2011), and early (2003–2005).
Treatment pattern, age, gender, college education, marital status, and steroid use did not predict disease activity scores at index.
CDAI, Clinical Disease Activity Index; DAS28-CRP-4, Disease Activity Score 28-joint count with C-reactive Protein; RADAI, Rheumatoid Arthritis Disease Activity Index; RAPID3, Routine Assessment of Patient Data 3; ref, reference group; SDAI, Simplified Disease Activity Index; TNFi, tumor necrosis factor inhibitor.

- DAS28-CRP-4 at index was predicted by:
  - Early TNFi initiation era (*P* = 0.0072)
  - Longer disease duration (*P* < 0.0001)
  - Higher baseline DAS score (*P* < 0.0001)
  - But not by treatment pattern at index (continued combination therapy, switch to TNFi monotherapy, or switch to MTX monotherapy)
- Simplified Disease Activity Index and Clinical Disease Activity Index at index were predicted by early TNFi initiation era (*P* = 0.0112 and *P* = 0.0115, respectively)
- Other disease activity measures had similar predictors at index

Table 3. Predictors of Treatment Group at Index

	Switch to MTX vs Persist on Combination Therapy			Switch to TNFi vs Persist on Combination Therapy		
Predictor Variables	Odds Ratio	Chi-Square	*P*-Value	Odds Ratio	Chi-Square	*P*-Value
Early biologic era vs late biologic era (baseline data)	**8.764**	**10.1278**	**0.0015**	**4.456**	**9.2496**	**0.0024**
Months receiving MTX prior to initiating combination therapy	0.988	1.8691	0.1716	**0.972**	**7.3397**	**0.0067**
Months on combination therapy (baseline to index)	**0.967**	**21.1339**	**< 0.0001**	**0.959**	**31.0402**	**< 0.0001**
Low disease activity at index vs high disease activity at index	1.1560	0.0631	0.8017	**3.4540**	**4.7707**	**0.0289**

Multinomial regression analysis data are presented, significant values (*P* < 0.05) are **bolded**.
Biologic initiation era (intermediate), baseline DAS28-CRP-4 value, duration of biologic Rx prior to first combination Rx, and disease activity at index (remission and moderate) did not predict treatment group at index.
DAS28-CRP-4, Disease Activity Score 28-joint count with C-reactive Protein; MTX, methotrexate; Rx, prescription; TNFi, tumor necrosis factor inhibitor.

- Patients who initiated in the early biologic era were estimated to be 4 and 8 times as likely to switch to TNFi or MTX monotherapy, respectively, as those who initiated in the late era
- Patients with longer duration between baseline and index dates were less likely to switch to a monotherapy (MTX or TNFi), than those with a shorter duration between baseline and index date
  - Additionally, patients with longer MTX treatment prior to first combination therapy were less likely to switch to TNFi monotherapy from combination therapy, than those with a shorter MTX treatment

Table 4. Disease Activity Two Years Post-Index

	Disease Status at Two Years Post-Index								Missing Score at Two Years Post-Index
	Remission		Low Activity		Moderate Activity		High Activity		
Disease Status at Index	N	%	N	%	N	%	N	%	N
Remission (n = 67)	40	70.2	10	17.5	5	8.8	2	3.5	10
Low Activity (n = 70)	4	6.2	47	72.3	9	13.9	5	7.7	5
Moderate Activity (n = 63)	3	5.5	9	16.4	39	70.9	4	7.3	8
High Activity (n = 51)	0	0	2	4.3	4	8.5	41	87.2	4

Percentages are based on those with disease activity scores at 2 years post-index. At two years post-index, 6, 5, 5, and 2 patients in the remission, low, moderate, and high disease activity states, respectively, had been lost during the follow-up period.
DAS28-CRP-4, Disease Activity Score 28-joint count with C-reactive Protein.

- Patients tended to remain or stabilize in their index disease activity at two years post-index
- Highest proportion of patients improving during the two years post-index period were in moderate disease activity at index

LIMITATIONS

- Study population may not reflect the general RA population:
  - Majority of patients were recruited during early biologic initiation era (2003–2005)
  - Small number of patients had moderate-to-high disease activity at index
- Key clinical information, including disease and medication history, prior to initiation of combination therapy are unavailable

CONCLUSIONS

- Patients on combination therapy tend to transition to monotherapy about 50% of the time within a year of starting combination with the majority transitioning to TNF monotherapy
- Disease duration and baseline disease activity had the greatest influence on disease activity at the time of medication change
  - Longer the disease duration and the more severe the baseline disease score, the worse/higher the disease score at medication change
- Patients initiating combination therapy in the early biologic era (2003–2005) were more likely to transition to monotherapy with either TNFi or MTX
- Most patients remained or had stabilized in their index disease activity two years post-index

REFERENCES

1. Gibofsky A. *Am J Manag Care*. 2014;20:S128-S35.
2. Singh JA, et al. *Arthritis Rheumatol*. 2016;68:1-26.

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- Tigwa Davis is an employee of Health Analytics, LLC.
- Christopher Young is an employee of Health Analytics, LLC.
- David H. Collier is an employee of and owns stock in Amgen Inc.
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