Treatment Patterns and Persistency Following the First Biologic DMARD in Patients with Rheumatoid Arthritis: Real-World Analysis of 2012–2016 US Medicare Data

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Background

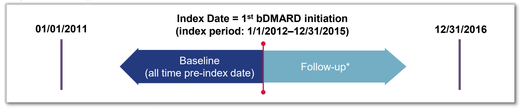
- For rheumatoid arthritis (RA) patients not meeting treat-to-target goals on a biologic disease-modifying antirheumatic drug bDMARD, 2015 ACR guidelines[1] recommend using other targeted immunomodulators (TIM): tumor necrosis factor-α inhibitor (TNFi), non-TNFi bDMARDs, or Janus kinase inhibitor (JAKi)
- Understanding treatment patterns and persistency can help optimize next treatment selection among Medicare recipients who initiated first bDMARD
- This study described treatment patterns, persistency, healthcare costs, and the use of glucocorticoids and opioids in Medicare RA patients on first bDMARD

Objectives

- To characterize RA patients who initiated their first bDMARD, overall and by persistency status of first bDMARD (persisters and non-persisters)
- To describe the type of treatment disruption among non-persisters [restarting, switching, or stopping of any TIMs (bDMARD or JAKi)] and the persistency of the first bDMARD by these cohorts
- To map longitudinal trends in healthcare costs and the use of glucocorticoids and opioids by persistent patients and those who experienced disruptions of their first bDMARD treatment

Methods

Figure 1. Study schema



*followed from index date through 12/31/2016, censored at death or end of Medicare A/B/D coverage
bDMARD, biologic disease modifying antirheumatic drug

Patient selection

- 20% random-sample Medicare fee-for-service administrative database
- Adult patients (≥18 years old) with ≥1 RA diagnosis code initiating their 1st bDMARD (index date) between 1/1/2012 and 12/31/2015 (index period)
  - bDMARDs included TNFi (adalimumab, etanercept, infliximab, golimumab) and non-TNFi bDMARDs (tocilizumab, rituximab, abatacept)
- No prior bDMARD use during the pre-index period (≥ 1 year pre index date)
- No evidence of pregnancy at any time
- No evidence of malignancy or other autoimmune disease during pre-index period and on index date

Measures

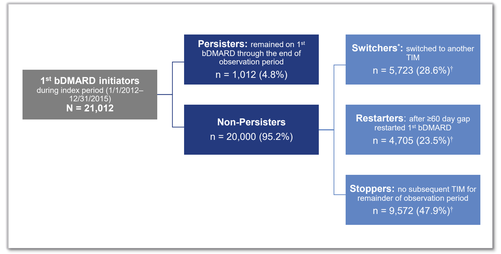
- Patient demographic characteristics [as mean±SD and median [IQR] or counts (%)]
- Time to loss of persistency
- By persistency cohort (persisters, restarters, switchers, stoppers) we described the following in 6-month increment:
  - Healthcare cost (2015 U.S. dollars): DMARD- and non-DMARD-related (total excluding DMARD costs)
  - Glucocorticoid use (prevalence and doses)
    - systemic exposure to glucocorticoids included formulations for oral, intravenous, intramuscular and trigger point, subcutaneous, and intra-articular forms of administration
  - Opioid use (prevalence and doses)

Statistical analysis

- Descriptive statistics—mean±SD, median [IQR], counts (%)—characterized patient demographics and study follow-up
- Unadjusted Kaplan-Meier curves assessed persistency on 1st bDMARD
- Healthcare costs were estimated as mean per patient per month (PPPM) longitudinally in 6-month increments
- Glucocorticoid and opioid use as count (% cohort) were estimated in 6-month increments
- Mean total glucocorticoid dose (prednisone equivalent dose PED)[2] and mean daily opioid dose (morphine milligram equivalent; MME)[3] were estimated in 6-month increments

Results

Figure 2. Patient disposition



*Switchers: 1291 patients switched to another bDMARD/JAKi before completing all prescribed days of their first bDMARD (medication possession), with 762 switching within 30 days prior to end of first bDMARD medication possession (some Switchers had overlap of TIM and some had a gap in TIM therapy)
†Percentages shown are within the 20,000 *Non-Persisters*. The estimates as a percent of N=21,012 first bDMARD initiators: *Switchers* 27.2%, *Restarters* 22.4%, and *Stoppers* 45.6%
bDMARD, biologic disease modifying antirheumatic drug; TIM, targeted immunomodulator

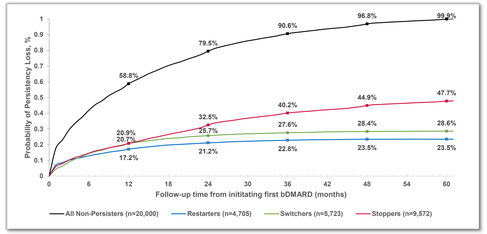
- 21,012 RA patients initiated a first bDMARD (52% intravenous, 48% subcutaneous) during a follow-up time of 60 months (mean 32 months)

Table. Patient demographics and study follow-up

Characteristic	Overall bDMARD initiators	Persisters	Non-Persisters
N (row %)	21,012 (100%)	1,012 (4.8%)	20,000 (95.2%)
Age, years, mean±SD; median [IQR]	66.0±10.9 66.1 [61.6,72.1]	67.2±8.1 66.4 [65.0, 71.1]	65.9±11.0 66.0 [61.3, 72.2]
Female, n (%)	16,673 (79.4%)	727 (71.8%)	15,949 (79.8%)
Race/ethnicity, n (%)			
White	16,945 (80.6%)	855 (84.5%)	16,090 (80.5%)
Black	2,242 (10.7%)	100 (9.9%)	2,142 (10.7%)
Others	1,825 (8.7%)	57 (5.6%)	1,768 (8.8%)
Payer Type, n (%)			
Medicare only	16,348 (77.8%)	918 (90.7%)	15,430 (77.2%)
Medicare/Medicaid dual	4,664 (22.2%)	94 (9.3%)	4,570 (22.9%)
Follow-up duration in study, months, mean±SD; median [IQR]	31.8±15.4 30.9 [20.0,45.2]	33.3±14.1 33.1 [20.8, 45.7]	31.8±15.5 30.9 [20.0, 45.2]
Censored follow-up			
Died before 12/31/2016	1,531 (7.3%)	15 (1.5%)	1,516 (7.6%)
Ended fee-for-service enrollment before 12/31/2016	4,021 (19.1%)	55 (5.4%)	3,966 (19.8%)

bDMARD, biologic disease modifying antirheumatic drug; IQR, interquartile range; SD, standard deviation

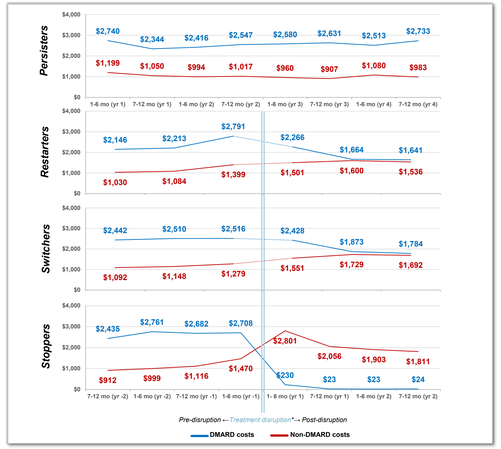
Figure 3. First bDMARD disruptions: restarts, switches, or stops



bDMARD, biologic DMARD.

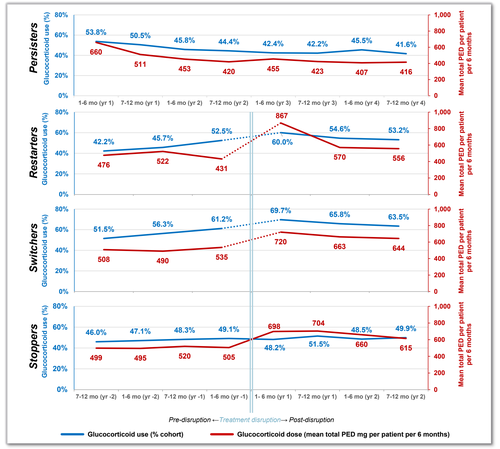
- Disruptions to first bDMARD therapy occurred as a restart after a gap, switch to another TIM, or stop of all TIM use
- Contributions to persistency loss were similar for all cohorts until month 12, after which the rates of restarts and switches plateaued but the rates of TIM discontinuation continued to increase

Figure 4. Unadjusted longitudinal costs (2015 USD, PPPM) by cohorts, in 6-month intervals



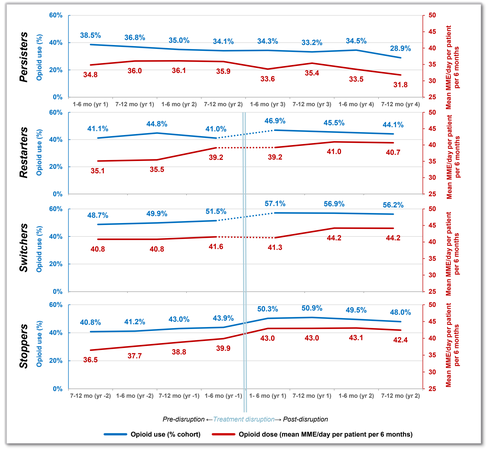
*A treatment gap occurred with Restarters and could have occurred with Switchers. Switchers could have also had overlapping days prescribed between 1st bDMARD and subsequent TIM
bDMARD, biologic disease modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug; PPPM, per patient per month; TIM, targeted immunomodulator; USD, U.S. dollars

Figure 5. Longitudinal prevalence of glucocorticoid use (%) and total PED exposure (mg per patient) by cohort, in 6-month intervals



PED, prednisone equivalent dose accumulated in 6-month intervals

Figure 6. Longitudinal prevalence of opioid use (%) and dose exposure (mean MME per day per patient) by cohorts, in 6-month intervals



MME, morphine milligram equivalent dose

Unadjusted Costs (Figure 4)

Longitudinal trends in healthcare costs varied by persistency status:

- *Persisters* demonstrated a gradual reduction in non-DMARD costs, even though their DMARD costs slightly increased
- Patients with treatment disruptions demonstrated continued increase in non-DMARD healthcare costs
  - *Stoppers* experienced a surge in non-DMARD cost, which partially offset the decrease in total healthcare cost due to DMARD discontinuation

Glucocorticoid use (Figure 5)

- *Persisters* showed a decline in prevalence of glucocorticoid use and in PED exposure longitudinally.
- Cohorts with disruptions (*Switchers, Restarters, Stoppers*) exhibited an increase in glucocorticoids usage and doses after the disruption

Opioid use (Figure 6)

- *Persisters* showed a decline in prevalence of opioid use and unchanged mean daily opioid dose (MME) exposure longitudinally
- Cohorts with disruptions (*Switchers, Restarters, Stoppers*) exhibited increase in the opioid use and daily dose after the disruption

Limitations

- RA patients in the 20% Medicare fee-for-service database may differ from the overall Medicare RA population and reflect a population older than the general RA population in the United States
- Identification of first bDMARD users may not account for possible bDMARD use before the earliest claim date (01/01/2011)
- Changes in DMARD regimen after the end of study observation period could not be captured, which could affect cohort classification
  - Patients who persisted may have eventually stopped therapy
  - Patients who discontinued may have eventually switched or restarted therapy
- This study design did not identify medical nor non-medical reasons for discontinuation, further research on such reasons would support our understanding of treatment disruptions
  - Although the majority of patients used intravenous bDMARDs (which are covered by Medicare Part B), the discontinuations in those who use subcutaneously injected bDMARDs, which are covered by Medicare Part D, may have bene affected by the Medicare "donut hole"
- This study was a descriptive analysis and results were not adjusted for potential confounding—e.g., the influence of Medicare only vs Medicare-and-Medicaid dual coverage in this population

Conclusions

- This longitudinal analysis of rheumatoid arthritis treatment patterns in fee-for-service Medicare beneficiaries initiating a first bDMARD revealed treatment disruptions, suggesting remaining unmet needs despite available treatment options:
  - During the study period (follow-up up to 60 months), only one in twenty patients remained on a first bDMARD. Nearly a quarter of disruptions occurred by 60 days, over half by 1 year, and over 90% by year 3.
  - Patients with bDMARD treatment disruptions experienced increased use of glucocorticoids and opioids and increased healthcare costs (excluding cost of subsequent DMARDs, if any)
- In light of 2015 ACR guidelines suggesting continuous TIM treatment after first bDMARD, the observed treatment patterns suggest opportunities to optimize treatment
  - Among study patients who lost persistency on first bDMARD, nearly half did not proceed to a subsequent TIM within the 60-month observational study period
  - Undertreatment on csDMARDs alone or entire lack of DMARD use may lead to insufficient control of inflammation, leading to further disease progression

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Disclosures

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