Poster Number 157

Drug Treatment Pathways 2 Years Following Clinical Diagnosis of Nontuberculous Mycobacterial Lung Disease in a Large US Managed Care Population

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BACKGROUND

- Nontuberculous mycobacterial lung disease (NTMLD) is increasingly common, with recent evidence indicating a growing prevalence and incidence in the United States[1]
- NTMLD is a chronically progressive and potentially debilitating disease that can lead to an impaired quality of life[2] and increased risk of mortality[3]
  - *Mycobacterium avium* complex (MAC) is the most commonly isolated pathogen in NTMLD in the United States[4]
- Current guidelines from the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) recommend initial treatment of NTMLD due to MAC with a multidrug regimen consisting of a macrolide, rifamycin, and ethambutol, with or without aminoglycosides based on initial presentation (eg, cavitary disease) and disease severity[5]
- Literature suggests that adherence to the ATS/IDSA guidelines is limited
  - In a study of 349 US physicians who were treating patients with NTMLD, 56% of regimens did not include a macrolide and 30% used regimens associated with the development of macrolide resistance[6]
- Patients who require treatment modification due to disease progression have limited options,[7] and completing treatment is often difficult due to side effects and duration[2]
- Macrolide monotherapy is known to be a key driver of the development of resistant MAC strains, yet antibiotic regimens associated with the development of macrolide resistance are frequently prescribed[6]
- The choice of treatment regimen and when to initiate therapy largely depend on the goals for the specific patient and involve multiple considerations, including patient comorbidities, disease severity and progression, nontuberculous mycobacterium (NTM) species, and the patient's willingness to engage in therapy[5,8]
- Despite the growing prevalence of NTMLD, data characterizing its associated treatment pathways at the national level are limited

OBJECTIVE

- To understand and describe drug treatment patterns 2 years following the first clinical diagnosis of NTMLD

METHODS

- A national managed care insurance database was searched for physician claims for NTMLD (*International Classification of Diseases, Ninth Revision* [*ICD-9*] code 031.0 or *Tenth Revision* [*ICD-10*] code A31.0) on ≥2 separate occasions ≥30 days apart between 2007 and 2016 to identify definitive NTMLD patients (N=9476)
- A patient cohort (N=1039) was selected by including those who were insured continuously over 36 months, beginning 12 months (baseline) before the first diagnostic claim of NTMLD and continuing 24 months after the claim
- Baseline health conditions were identified using *ICD-9* or *ICD-10* codes, and use of immunosuppressive drug agents was identified through pharmacy dispensing claims
- A minimum of 30 days of drug supply was required to qualify as a drug therapy for NTMLD treatment
- Drug therapies used in clinical practices for NTMLD were classified into 2 categories (**Table 1**)

Table 1. Treatment Categories

Category name	Drugs
Guidelines-based therapy (GBT) consistent with the ATS/IDSA guidelines	Macrolide + ethambutol + rifamycin, with or without other drugs
Other	Any drug(s) from the NTMLD medication list (**Table 2**) other than GBT regimen

- Time to GBT was evaluated using COX regression to see which patient characteristics were associated with use of GBT

Table 2. NTMLD Medication List

Class	Drug name
Macrolide	Azithromycin, clarithromycin
Ethambutol	Ethambutol
Rifamycin	Rifampin, rifabutin
Aminoglycoside	Amikacin, streptomycin
Fluoroquinolone	Ciprofloxacin, moxifloxacin, levofloxacin
Carbapenem	Imipenem, meropenem
Oxazolidinone	Linezolid, tedizolid
Glycylcycline	Tigecycline
Cephalosporin antibiotic	Cefoxitin
Tetracycline	Doxycycline
Diarylquinoline	Bedaquiline
	Clofazimine

RESULTS

- A total of 1039 patients were included in the analysis

Baseline Demographics and Patient Characteristics

- The mean age of the patient cohort was 68 years, and 67% of all patients were female
- At baseline, the mean Charlson comorbidity index score was 2.0 (±2.16)
  - Approximately 50% of patients had COPD. Other comorbidities included bronchiectasis (37%), asthma (21%), coronary artery disease (18%), cancer (17%), mental disorder (16%), diabetes (15%), HIV infection (2%), organ transplant (1%), and tobacco use (9%)
  - Approximately 56% of patients used an immunosuppressive agent

Two–Year Treatment Pathways

Figure 1. Proportion of Patients Treated With Any Therapy During the 2 Years Following NTMLD Diagnosis

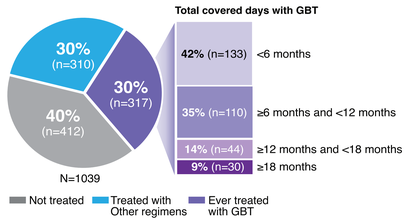
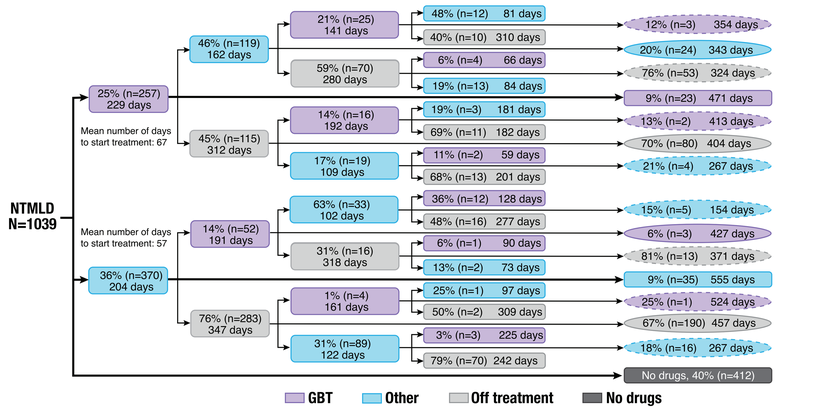


Figure 2. Treatment Pathways Following NTMLD Diagnosis



Note: Days labeled inside each box indicate the average duration of the drug regimen for patients in the box.

Medication Adherence Measured by Proportion of Days Covered (PDC*) to NTMLD Drug Treatment During Year 1

- During the first year following NTMLD diagnosis
  - 57% (592/1039) of patients received NTMLD drug therapy
  - PDC was 54% for both the GBT and Other groups

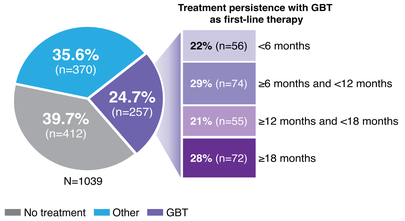
*PDC=days of drug supply/(365 days-days of hospital stay).

Two–Year Persistence and Discontinuation of Drug Therapy in Treated Patients with NTMLD

- The average covered days of therapy was 323 (median=291 days; Q1-Q3: 140-494 days) for the 627 patients ever treated
- Mean treatment persistence for first-line GBT patients (n=257) was 383 days (median=361 days; Q1-Q3: 211-563 days)
  - Total days with GBT drug coverage was 263 (median=235 days; Q1-Q3: 115-360 days) over 2 years
  - 55% (142/257) of these patients also used Other drug therapies within the 2-year period, with a total of 185 days (median=123 days; Q1-Q3, 57-250 days) covered by Other therapies
- Mean treatment persistence for first-line Other patients (n=370) was 306 days (median=254 days; Q1-Q3: 93-483 days)
  - 16% (60/370) of these patients used GBT with an average GBT drug coverage of 224 days (median=188 days; Q1-Q3: 79-320 days) and 199 days (median=148 days; Q1-Q3: 87-287 days) of Other drug coverage

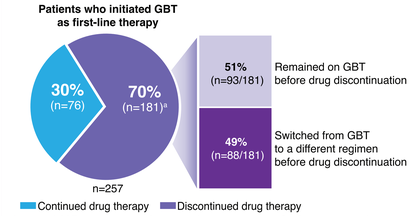
Note: Treatment persistence defined as the time from drug initiation to discontinuation of any drug therapy. Drug discontinuation defined as interruption of drug therapy for ≥90 consecutive days.

Figure 3. First–Line Drug Use and Persistence During the 2 Years Following NTMLD Diagnosis



- Of patients who used GBT as first-line therapy
  - 70% (181/257) discontinued during the 2-year period
  - 28% (50/181) of those who discontinued during the 2-year period went off treatment for good within 6 months (180 days)

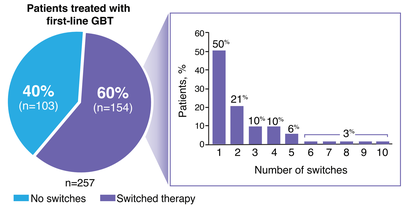
Figure 4. Discontinuation of GBT During the 2–Year Observation Period



aAfter a total GBT drug coverage of 213 days (median=189 days; Q1-Q3=90-301 days)

Switches of Therapy

Figure 5. Switches of Therapy Among Patients Who Used GBT as First–line Therapy



- 26% (27/103) of patients did not switch therapy and went off for good within 6 months

Factors Associated With Use of GBT

- At year 1 after diagnosis of NTMLD
  - Younger patients were more likely to use GBT
  - Patients with preexisting diabetes and pneumonia before NTMLD diagnosis were more likely to use GBT
  - Patients with preexisting aspergillosis, hyperlipidemia, and rheumatoid disease were less likely to use GBT
  - Patients using inhaled corticosteroids at baseline were more likely to use GBT

Table 3. Factors Associated With Use of GBT at Year 1 After Diagnosis of NTMLD

Parameter	Hazard ratio (95% CI)	*P* value
Age	0.99 (0.98. 0.99)	<.0001
Aspergillosis	0.50 (0.23, 1.07)	0.0731
Cystic fibrosis	0.25 (0.10, 0.66)	0.0052
Diabetes	1.38 (1.03, 1.84)	0.0309
Hyperlipidemia	0.79 (0.63, 0.98)	0.0321
Inhaled corticosteroids	1.44 (1.16, 1.77)	0.0008
Pneumonia	1.40 (1.14, 1.72)	0.0013
Rheumatoid disease	0.59 (0.36, 0.97)	0.0388

Macrolide Monotherapy

- 188 patients received macrolide monotherapy during the 2-year period
- Macrolide monotherapy was used by 14% of patients (146/1039) during the first year following NTMLD diagnosis, with a mean of 110 days covered by dispensed drugs
- Of patients who received macrolide monotherapy as a first-line regimen, the vast majority (95/98) received this treatment during the first year following diagnosis

Table 4. Use of Macrolide Monotherapy Following NTMLD Diagnosis

	Year 1	Year 2	Total 2-year period
Patients treated with macrolide therapy			
n	146	100	188
Average days of drug supply*	110 (61, 32-159)	119 (62, 37-150)	127 (60, 33-145)
Patients treated with macrolide monotherapy as first-line regimen			
n	95	3	98
Average days of drug supply*	191 (112, 55-250)	111 (139, 54-140)	188 (112, 55-240)

*Data in parentheses include median and Q1-Q3 range.

LIMITATIONS

- Limitations of this study include the following:
  - The claims database provided information only on days of supply; actual usage of drugs was only inferred

CONCLUSIONS

- During the 24-month postdiagnosis observation period in our sample of commercially insured and Medicare Advantage plan patients
  - 51% of patients who ever received drugs for NTMLD were treated with GBT
  - 41% of all treated patients initiated GBT as first-line treatment for NTLMD
- 40% of the diagnosed patients (n=1039) with NTMLD never received antibiotics treatment 2 years following NTMLD diagnosis
- 70% of patients who used GBT as first-line therapy for NTMLD discontinued therapy within 2 years of diagnosis, and 28% of these patients stopped treatment for good
- 9% (98/1039) of patients received macrolide monotherapy as first-line therapy
- Specific factors, such as younger age, prior pneumonia, immunosuppressant use, and diabetes, were associated with a higher likelihood of using GBT regimen

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