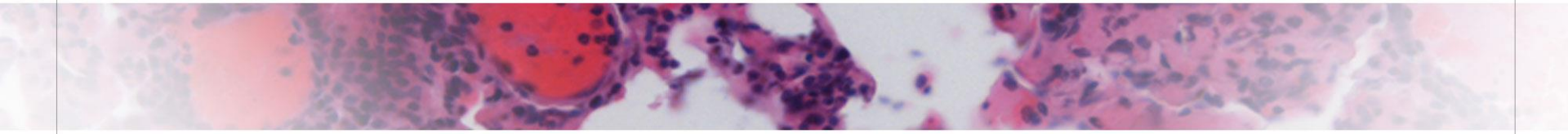
American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



Burden of Idiopathic Multicentric Castleman Disease in the US: A Population-Level Real World Analysis using a Health-Claims Dataset

Ariela Noy[1], Robert Ohgami[2], Nikhil Munshi[3], Imran Siddiqi[4], Kelley C. Dacus[5], Alicia Watson Saltis[5], Francis Shupo[6], Nicole Princic[7], Kristin A. Evans[7], Sudipto Mukherjee[8]

[1]Memorial Sloan Kettering Cancer Center & Weill Cornell Medical College; [2]ARUP Institute for Research & Innovation; [3]Dana-Farber Cancer Institute; [4]University of Southern California, Norris Comprehensive Cancer Center; [5]Recordati Rare Diseases Inc. (USA); [6]Recordati Rare Diseases Ltd. (UK); [7]Merative, Real World Data Research & Analytics; [8]Clevelend Clinic, Dept. of Hematology & Medical Oncology

Background

- Idiopathic Multicentric Castleman Disease (iMCD) is a rare cytokine-driven hematologic disorder characterized by diffuse lymphadenopathy and systemic inflammatory symptoms.
- iMCD is an epidemiologically challenging disease to study due to rarity and diagnostic complexities.
- Administrative claims datasets with extensive geographic coverage provide a valuable resource to study the natural history of rare diseases such as iMCD.
- Introduction of CD specific International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code (D47.Z2) in October 2016 and publication of international diagnostic criteria in 2017 has opened unique opportunities to harness large claims datasets to study iMCD.[1]
- Our group led the first effort to develop a novel claims-based algorithm in 2021 to study the epidemiology of iMCD in the US.
- However, questions regarding accurate ascertainment of iMCD cases and treatment patterns remain.

[1] Fajgenbaum DC, et al. Blood. 2017;129(12):1646-1657, [2] Mukherjee S, et al. Blood Advances. 2022;6(2):359-367.
Abbreviations: CD: Castleman disease, iMCD: Idiopathic Multicentric Castleman Disease, ICD-CM: International Classification of Diseases (Ninth or Tenth Revision) Clinical Modification

Objectives

- To enhance the discriminatory capacity of existing administrative claims-based algorithm using a three-pronged case ascertainment approach to accurately ascertain iMCD cases at the population level.

- To analyze population level trends in the use of siltuximab for iMCD, the sole treatment approved for iMCD by the Food and Drug Administration (FDA) in the US and by European Medicines Agency (EMA) in Europe.[2]

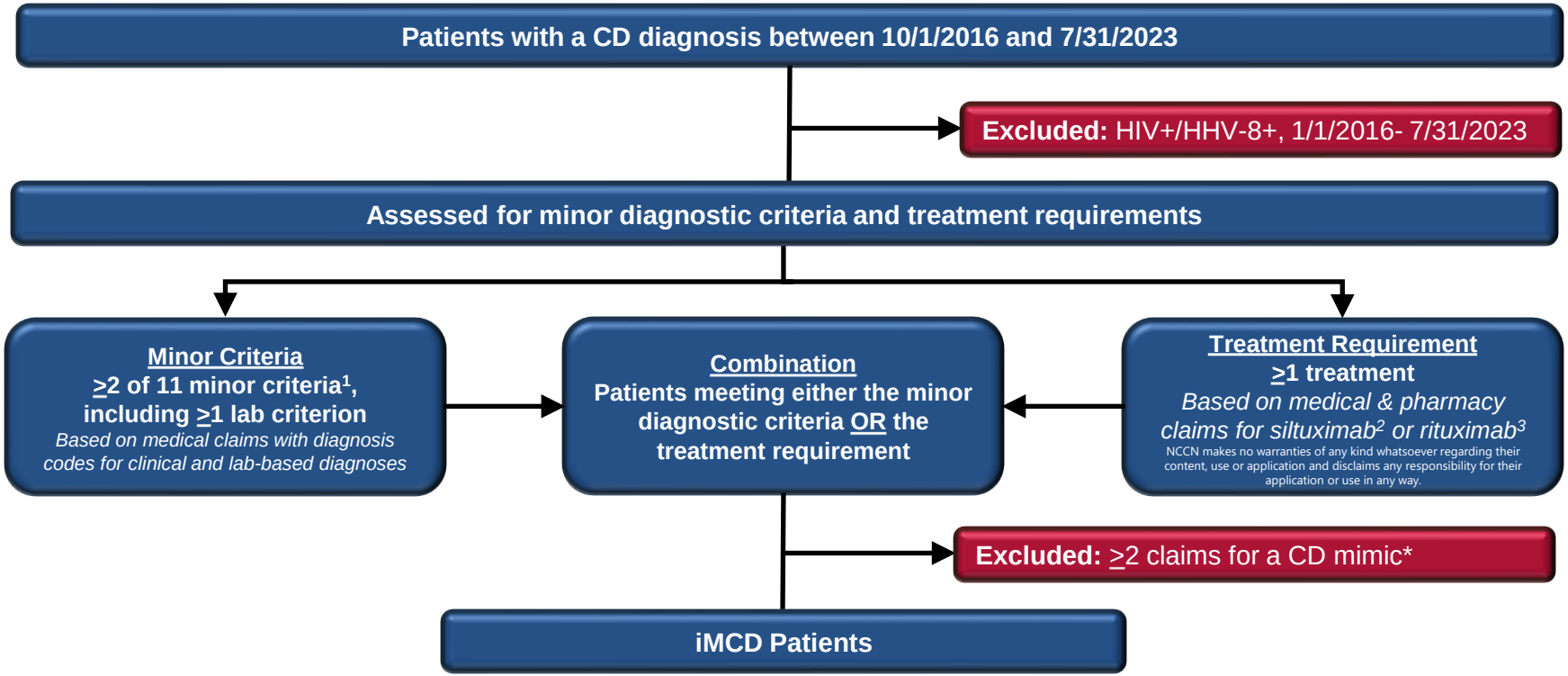
[1] Mukherjee S, et al. Blood Advances. 2022;6(2):359-367, [2] Sylvant [package insert], Bridgewater, NJ: Recordati Rare Diseases Inc. 2024.
Abbreviations: CD: Castleman disease, FDA: Food and Drug Administration, iMCD: Idiopathic Multicentric Castleman Disease, ICD-CM: International Classification of Diseases (Tenth Revision) Clinical Modification

Study Design

- **Study Design:** Retrospective cohort study
- **Study Period:** October 1, 2016 – July 31, 2023
- **Data Source:** US Administrative claims data from Merative™ MarketScan® Commercial and Medicare Databases comprising 66 million unique patients
- **Initial Patient Pool:** Patients with at least one eligible* medical claim with an ICD-10-CM diagnosis of CD (D47.Z2) during the study period

*Ineligible claims include lab tests or other procedures that may be used initially to rule-out a suspected diagnosis. The diagnosis is included on the claim for reimbursement purposes, though the diagnosis may or may not be confirmed by the results of the test/procedure. Only non-rule out claims (i.e., claims NOT for such tests/procedures) are considered eligible and used to identify patients with each diagnosis to ensure that the diagnosis is confirmed rather than just suspected.
Abbreviations: CD: Castleman disease, ICD-CM: International Classification of Diseases (Tenth Revision) Clinical Modification

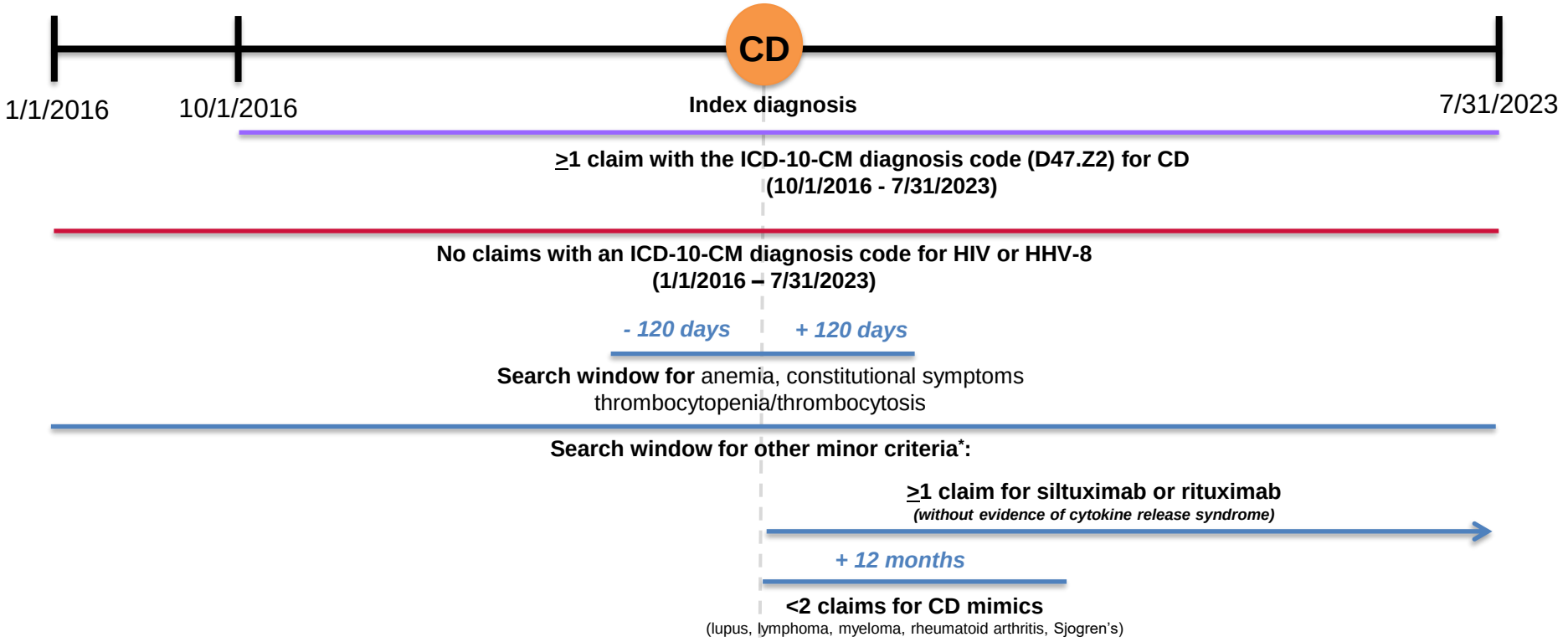
Algorithm Development and Methodological Approach



[1] Fajgenbaum DC, et al. Blood. 2017;129(12):1646-1657, [2] Sylvant [package insert], Bridgewater, NJ: Recordati Rare Diseases Inc. 2024, [3] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Castleman Disease V.1.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed November 13, 2024. To view the most recent and complete version of the guideline, go to NCCN.org. NCCN makes no warranties of any kind regarding their content, use or application and disclaims any responsibility for their application or use in any way.

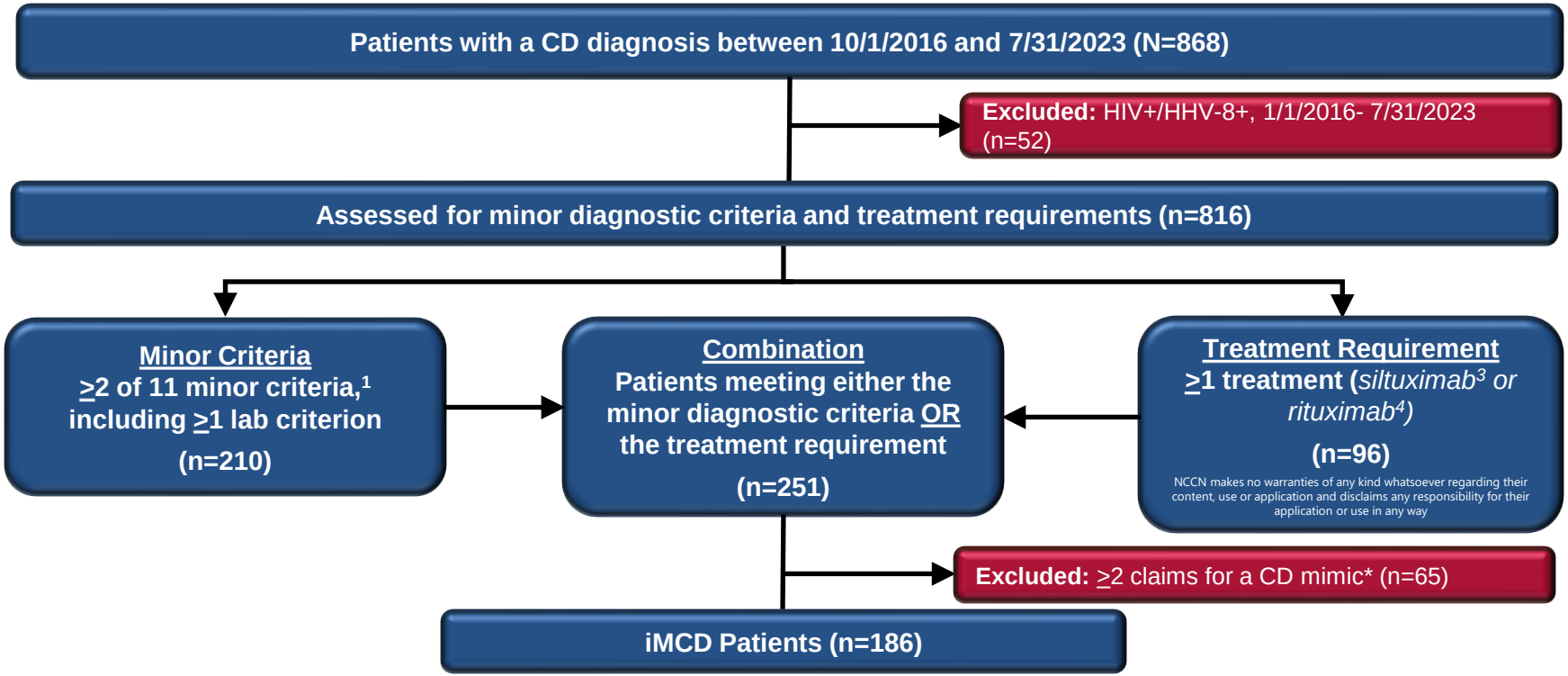
* Lupus, lymphoma, myeloma, rheumatoid arthritis, Sjogren's syndrome. Abbreviations: CD: Castleman disease, HHV-8: herpesvirus-8, HIV: human immunodeficiency virus, iMCD: Idiopathic Multicentric Castleman Disease

Stepwise Selection of Study Cohort



*Elevated CRP/ESR, fluid accumulation, hemangiomatosis, hypoalbuminemia, large liver and/or spleen, lymphocytic interstitial pneumonitis, polyclonal hypergammaglobulinemia, renal dysfunction/proteinuria
Abbreviations: CD: Castleman Disease, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, ICD-CM: International Classification of Diseases (Tenth Revision) Clinical Modification

Algorithm for Three Different Case Ascertainment Approaches



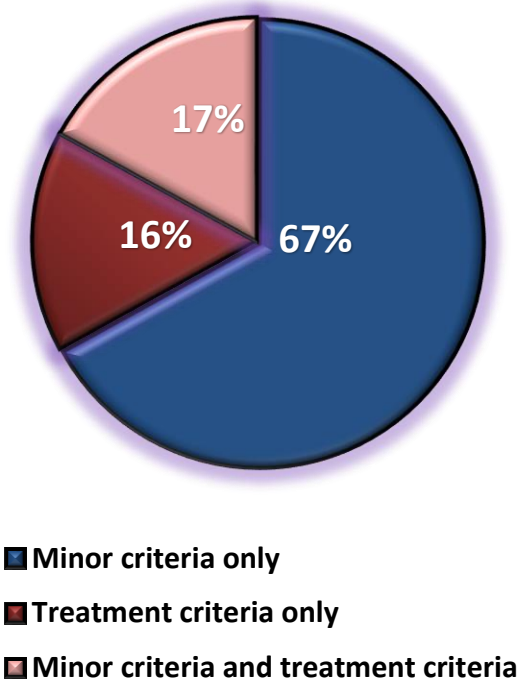
[1] Fajgenbaum DC, et al. Blood. 2017;129(12):1646-1657, [3] Sylvant [package insert], Bridgewater, NJ: Recordati Rare Diseases Inc. 2024, [4] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Castleman Disease V.1.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed November 13, 2024. To view the most recent and complete version of the guideline, go to NCCN.org. NCCN makes no warranties of any kind regarding their content, use or application and disclaims any responsibility for their application or use in any way.

* Lupus, lymphoma, myeloma, rheumatoid arthritis, Sjogren's syndrome; Abbreviations: CD: Castleman disease, HHV-8: herpesvirus-8, HIV: human immunodeficiency virus, iMCD: Idiopathic Multicentric Castleman Disease

Use of Different Search Criteria Algorithms to Identify iMCD Patients

iMCD case numbers differ based on criteria (n=186):

- 124 (66.7%) were identified via the **minor criteria only** (did not meet the treatment requirement)
- 30 (16.1%) were identified via the **treatment criteria only** (did not meet the minor criteria)
- 32 (17.2%) met **both the minor and treatment criteria**



Abbreviations: iMCD: Idiopathic Multicentric Castleman Disease

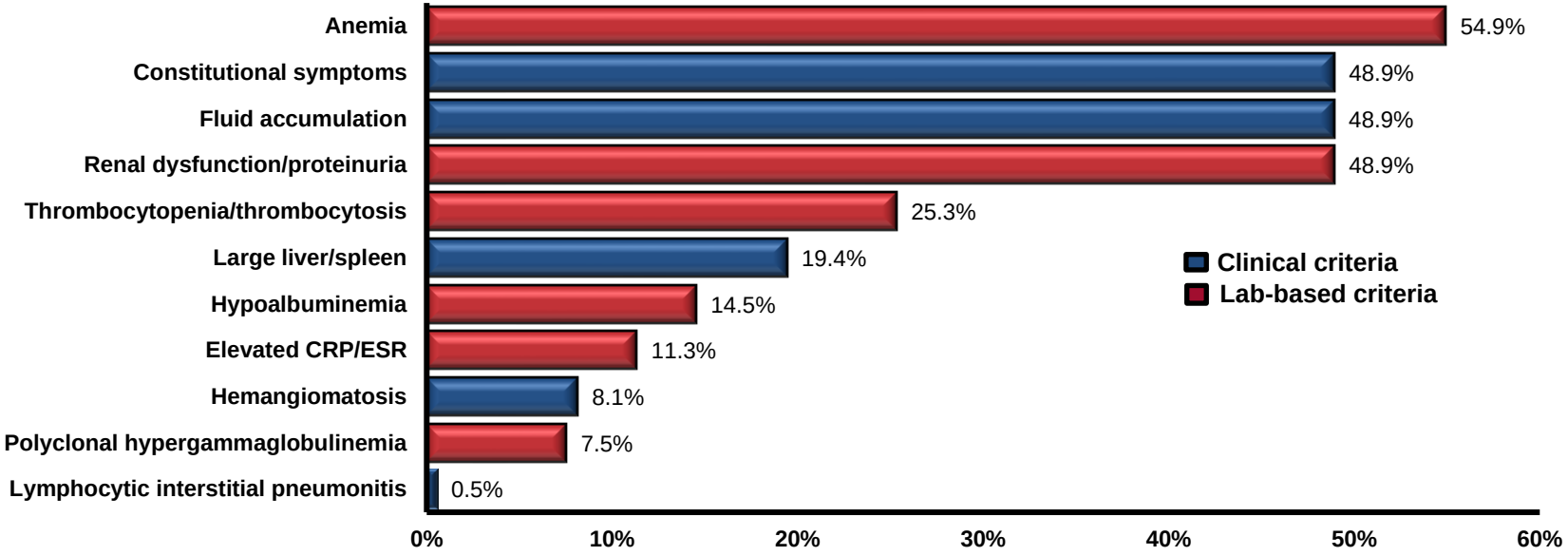
Characteristics of Patients with iMCD

	All iMCD Patients n = 186
Age (n,%)	
<18	12 (6.5%)
18-34	27 (14.5%)
35-64	121 (65.1%)
65+	26 (14.0%)
Mean age (SD)	49 (17.5)
Sex (n,%)	
Male	96 (51.6%)
Female	90 (48.4%)
Payer (n,%)	
Commercial	160 (86.0%)
Medicare Advantage	4 (2.2%)
Medicare Supplemental	22 (11.8%)
Year of CD diagnosis (n, %)	
2016*	5 (2.7%)
2017	42 (22.6%)
2018	43 (23.1%)
2019	29 (15.6%)
2020	21 (11.3%)
2021	19 (10.2%)
2022	17 (9.1%)
2023†	10 (5.4%)
CD diagnosis status (n,%)	
No prior evidence of enlarged lymph nodes‡	91 (48.9%)
With prior evidence of enlarged lymph nodes‡	95 (51.1%)

*The earliest possible diagnosis date was 10/1/2016 (the date the ICD-10-CM code for CD became available); † The latest possible diagnosis date was 7/31/2023; ‡ ICD-10-CM diagnosis code R590, R591, or R599 between 1/1/2016 and the day before the CD diagnosis date.
Abbreviations: CD: Castleman disease, iMCD: Idiopathic Multicentric Castleman Disease, SD: standard deviation

- Of the 186 iMCD patients included in the final sample, mean age was 49 years; 52% were male.
- Most iMCD patients (86%) were commercially insured.
- Nearly half of identified iMCD patients were likely incident cases (i.e., no prior evidence of enlarged lymph nodes).

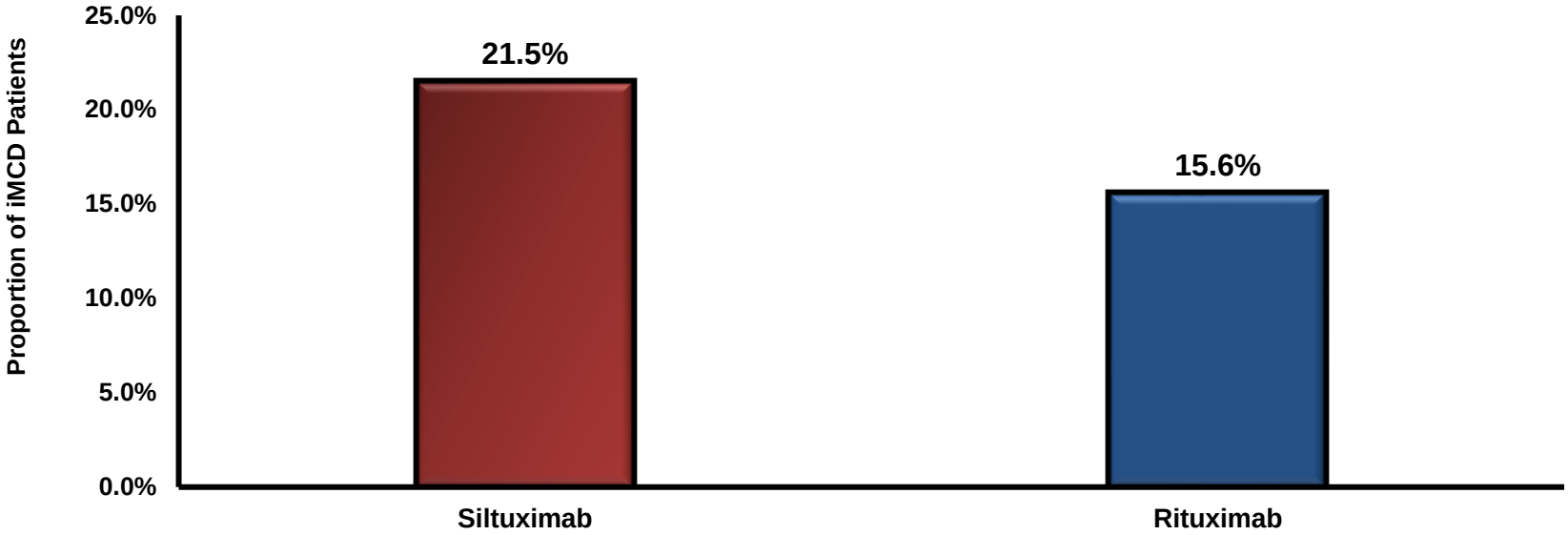
Distribution of Minor Diagnostic Criteria in iMCD patients[1]



**Anemia, constitutional symptoms, thrombocytopenia/thrombocytosis identified in the 120 days before or after CD diagnosis; all other diagnoses identified 1/1/2016 - 7/31/2023; treatments identified anytime on or after CD diagnosis*

[1]] Fajgenbaum DC, et al. Blood. 2017;129(12):1646-1657.
Abbreviations: CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, iMCD: Idiopathic Multicentric Castleman Disease

Treatment Utilization Among Patients with iMCD



Among the 186 patients with iMCD, 21.5% (n=40) had a claim for siltuximab and 15.6% (n=29) had a claim for rituximab at any time following the index CD diagnosis date.

Abbreviations: CD: Castleman disease, iMCD: Idiopathic Multicentric Castleman Disease

Strengths and Limitations

- Largest study to report on the population-level estimates of iMCD prevalence in the US
- Rigorous criteria based on use of the CD-specific ICD-10-CM code combined with international diagnostic criteria and exclusion of CD mimics provides the most accurate population estimates of prevalent iMCD cases.
- Developed claims-based algorithm – a valuable research tool for other researchers studying epidemiology of iMCD using health claims dataset
- Inherent limitations to all administrative claims-based datasets
  - **Misclassification bias** – lack of actual clinical data or lab values or inability to capture minor criteria or treatment criteria if occurring outside the defined period
  - **Underestimation of cases** – lack of qualifying actual lab values or pathology reports or censoring at end of data availability (7/31/2023)
  - **Variations in coding and billing practices** which may lead to inconsistency in diagnoses and procedures between healthcare settings.
- This study was limited to individuals with employer-sponsored commercial or Medicare insurance and results may not be generalizable to patients with other insurance or the uninsured.

Abbreviations: CD: Castleman disease, iMCD: Idiopathic Multicentric Castleman Disease, ICD-CM: International Classification of Diseases (Tenth Revision) Clinical Modification

Conclusions

- Precise identification of iMCD patients in real-world data should rely on a multi-pronged approach, incorporating diagnostic guidelines[1] as well as treatment-based criteria – case numbers will differ based on selected approach.
- CD mimics introduces diagnostic complexities – approximately 25% of patients in this cohort had claims of a CD mimic (different diagnosis) in the year after CD diagnosis.
- High unmet treatment need – use of siltuximab, the only FDA approved therapy for iMCD was dismal at 22%
- Divergence from clinical guidelines in routine clinical practice – use of rituximab, which is not FDA approved for iMCD, was observed in 16%
- Further research to analyze the epidemiology and cost burden among patients with iMCD are planned next steps.

[1]] Fajgenbaum DC, et al. Blood. 2017;129(12):1646-1657.
Abbreviations: CD: Castleman Disease, FDA: Food and Drug Administration, iMCD: Idiopathic Multicentric Castleman Disease

References

1. Fajgenbaum DC, Uldrick TS, Bagg A, et al. International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease. *Blood*. 2017;129(12):1646-1657.
2. Mukherjee S, Martin R, Sande B, et al. Epidemiology and treatment patterns of idiopathic multicentric Castleman disease in the era of IL-6-directed therapy. *Blood Advances*. 2022;6(2):359-367.
3. Sylvant [package insert], Bridgewater, NJ: Recordati Rare Diseases Inc. 2024.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Castleman Disease V.1.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed November 13, 2024. To view the most recent and complete version of the guideline, go to NCCN.org.