

# Natural history study of idiopathic multicentric Castleman disease identifies effective treatments for a large proportion of patients but treatment-refractory patients remain

Sheila K. Pierson<sup>1</sup>, Yue Ren<sup>1</sup>, Johnson Khor<sup>1</sup>, Eric Haljasmaa<sup>1</sup>, Jasira Ziglar<sup>1</sup>, Katherine Floess<sup>1</sup>, Erin Napier<sup>1</sup>, Faizaan Akhter<sup>1</sup>, Amy Liu<sup>1</sup>, Damilola Gibson<sup>2</sup>, Karan Kanhai<sup>2</sup>, Rabecka Martin<sup>3</sup>, Amy Chadburn<sup>4</sup>, Gordan Srkalovic<sup>5</sup>, Corey Casper<sup>6</sup>, Megan Lim<sup>7</sup>, Thomas S Uldrick<sup>8</sup>, Elaine S. Jaffe<sup>9</sup>, Frits van Rhee<sup>10</sup>, Hongzhe Lee<sup>1</sup>, David Fajgenbaum<sup>1</sup>

<sup>1</sup>University of Pennsylvania, Philadelphia, PA; <sup>2</sup>EUSA Pharma, Hemel Hempstead, UK; <sup>3</sup>EUSA Pharma, Boston, MA; <sup>4</sup>Weill Cornell Medicine, New York, NY; <sup>5</sup>Sparrow Herbert-Herman Cancer Center, Lansing, MI; <sup>6</sup>Infectious Disease Research Institute, Seattle, WA; <sup>7</sup>Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA; <sup>8</sup>Fred Hutchinson Cancer Research Center, Seattle, WA; <sup>9</sup>Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda; <sup>10</sup>Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR



## INTRODUCTION

- Human herpes-virus 8-negative/idiopathic multicentric Castleman disease (iMCD) is a rare inflammatory disorder involving multicentric lymphadenopathy with characteristic histopathology.
- Clinical presentation is heterogeneous and includes cytokine-driven constitutional symptoms, cytopenias, systemic inflammation, and multi-organ dysfunction.
- International consensus treatment guidelines are based on a large cohort of case studies and a few clinical trials, but the available evidence is limited.
- Siltuximab, an anti-IL-6 therapy, is the only FDA-approved treatment for iMCD; 34% of patients achieved durable symptomatic and tumor response in the phase II trial.<sup>1</sup>
- Tocilizumab, an anti-IL-6 receptor therapy, is frequently used off-label.
- The treatment guidelines recommend siltuximab +/- corticosteroids (CS) as first-line therapy for all iMCD patients and tocilizumab as a substitute when siltuximab is not available.
- Rituximab, a CD20 antibody, is recommended as an alternate first-line therapy; however, it has never been systematically evaluated.
- Better understanding of treatment effectiveness is urgently needed.

## OBJECTIVES

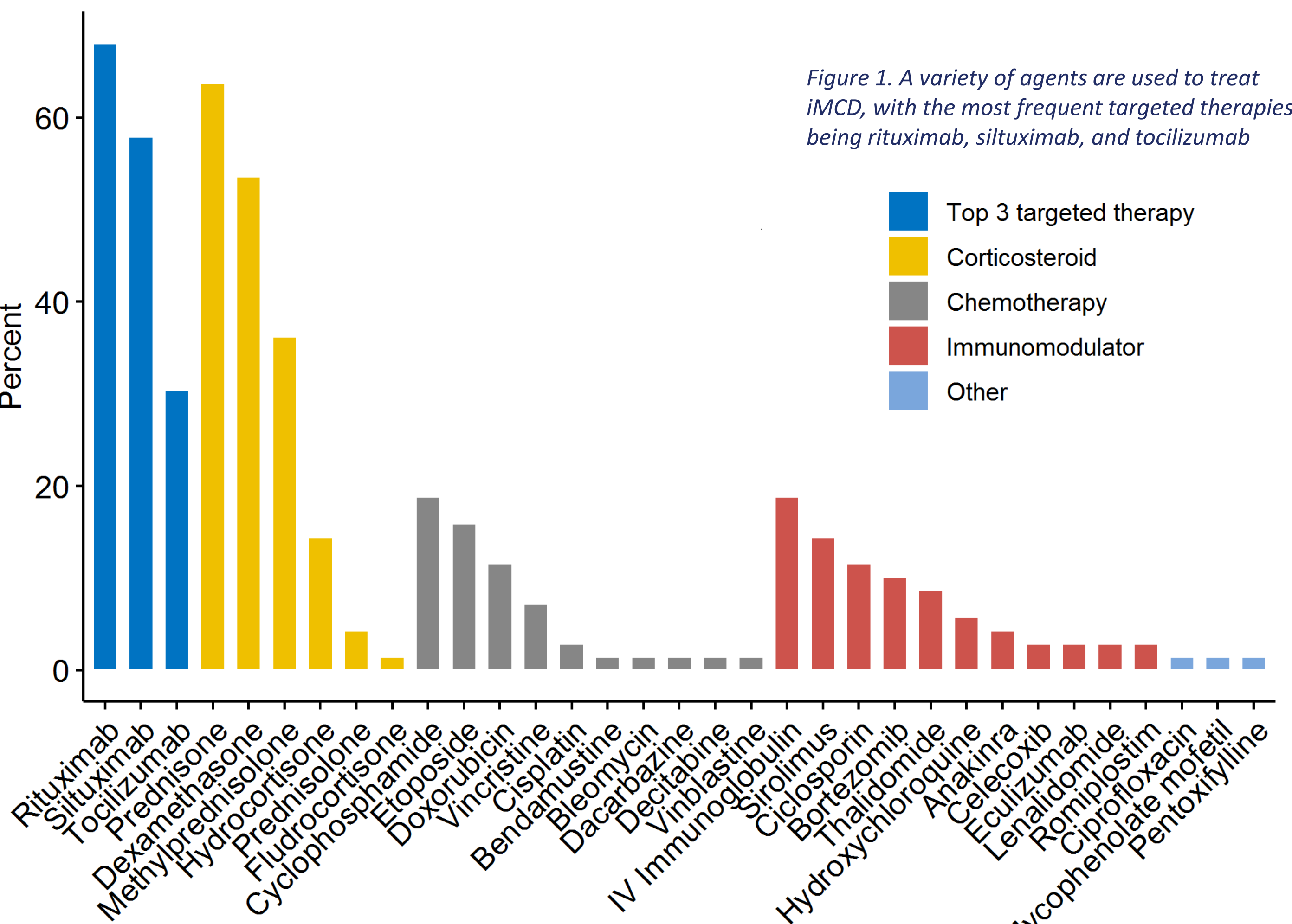
- To describe the most frequently used treatments and response to treatment in a real-world cohort of iMCD patients.

## METHODS

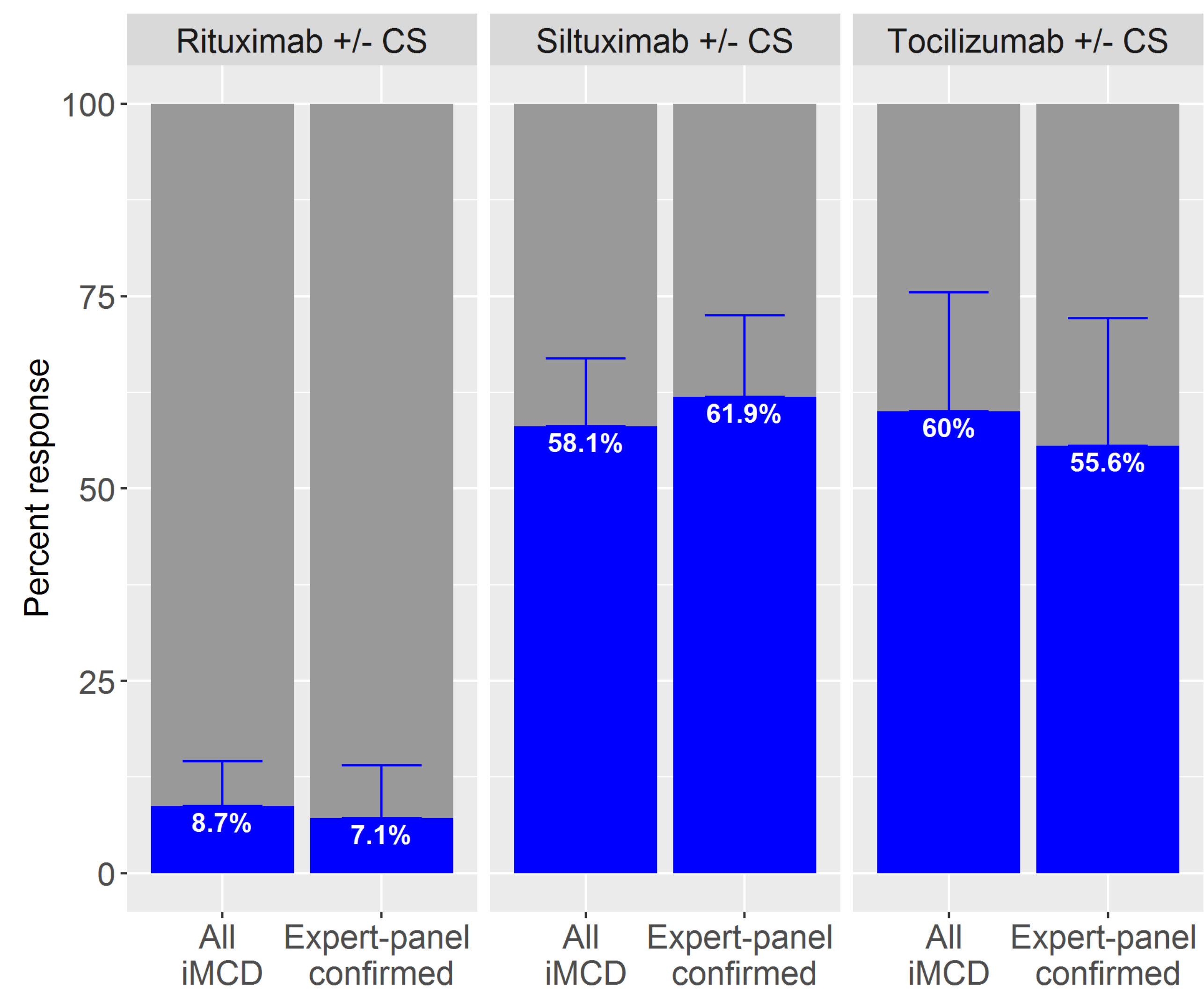
- Data were collected and abstracted for 90 patients enrolled in an on-going IRB-approved natural history study of Castleman disease.
- Diagnosis is graded by an expert panel of clinicians and pathologists on an on-going basis; patients unlikely to have iMCD were excluded from analysis (N=21).
- Of the 69 patients included, 43 (62.3%) are expert panel-confirmed and 26 (37.7%) are awaiting confirmation.
- Durable response is defined as achieving ≥50% improvement in the proportion of abnormal iMCD minor clinical and laboratory diagnostic criteria sustained for ≥1 year.
- The best response was selected for patients with more than one response outcome to a given regimen.

## RESULTS

- Median age at diagnosis is 37 years (range: 1-67 years). The cohort is 44.9% female, 63.8% white, and 4 (5.8%) patients died.
- 33 unique drugs have been administered across the 69 patients.

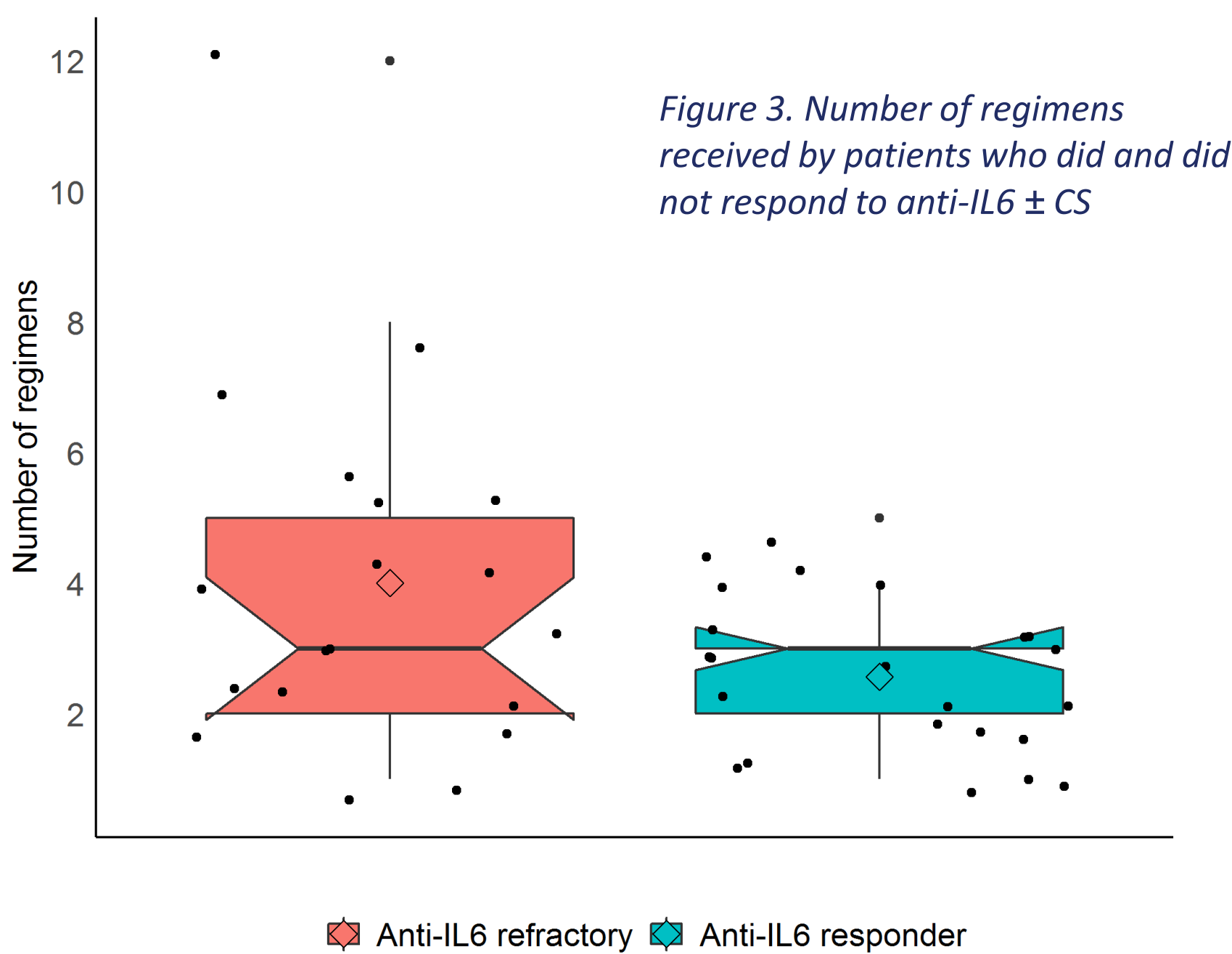


- Rituximab is the most frequent targeted therapy (N=47, 68.1%), followed by siltuximab (N=40, 57.8%) and tocilizumab (N=21, 30.4%).
- Response to siltuximab and tocilizumab is comparable in this cohort.



## RESULTS

- Despite success of anti-IL6 therapies, treatment refractory patients remain.
- 3 of 4 deceased patients received both anti-IL-6 therapy and rituximab and all 4 received chemotherapies and immunomodulators but did not respond to any drug.
- 6 of 19 (31.6%) patients who did not respond to anti-IL6 ± CS received 5 or more treatment regimens, whereas 1 of 23 (4.3%) patients who responded to anti-IL6 ± CS received 5 or more treatment regimens.



## CONCLUSIONS

- These data reveal that despite there being one FDA-approved treatment, iMCD is treated with a variety of agents.
- Among the full cohort, siltuximab ± CS demonstrated a 58% durable response. This may reflect differences in response criteria and/or disease activity of patients in clinical trials versus real world settings.
- Siltuximab and tocilizumab have never been systematically compared; in this cohort they demonstrated similar response.
- Considering the morbidity and mortality of iMCD, additional agents are needed for refractory patients, who have few options and are at risk of death due to disease progression. Further data are needed to compare groups and identify optimal treatment protocols.

## REFERENCES

<sup>1</sup>van Rhee F, Wong RS, Munshi N, Rossi JF, Ke XY, Fosså A, Simpson D, Capra M, Liu T, Hsieh RK, Goh YT. Siltuximab for multicentric Castleman's disease: a randomised, double-blind, placebo-controlled trial. *Lancet Oncol.* 2014 Aug 1;15(9):966-74.

## CONTACT INFORMATION

Sheila Pierson, MS  
University of Pennsylvania  
Sheila.Pierson@pennmedicine.upenn.edu  
1-215-349-5713