DIAGNOSTIC DELAYS AND COMPARABLE RESPONSE RATES TO IMCD-DIRECTED THERAPIES IN PATIENTS WITH AND WITHOUT EXPERT-CONFIRMED IDIOPATHIC MULTICENTRIC CASTLEMAN DISEASE DIAGNOSES

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INTRODUCTION

Idiopathic multicentric Castleman disease (iMCD) is a rare cytokine-driven lymphoproliferative disorder with clinical and histopathologic features that overlap with numerous mimicking conditions, making diagnosis challenging. Delayed or uncertain diagnosis may contribute to increased morbidity and complicate treatment decisions. Although siltuximab, an anti-interleukin-6 monoclonal antibody, is the only FDA-approved therapy for iMCD, treatment strategies for patients with uncertain diagnoses remain poorly defined.

AIM

To compare diagnostic characteristics and treatment outcomes between patients with expert-confirmed iMCD and those with a low likelihood of iMCD within the ACCELERATE international registry.

METHOD

We analyzed patients enrolled in ACCELERATE, the largest international registry of individuals with suspected iMCD. An expert physician panel assigned each case a diagnostic certainty classification (expert-confirmed or low likelihood of iMCD). Treatment regimens were defined as therapies initiated within two weeks of one another, and clinical response was defined as a ≥50% reduction in the proportion of abnormal symptoms and laboratory measures. Diagnostic timelines, biopsy approaches, treatment patterns, and response rates were compared between groups.

CONCLUSIONS

Among patients with suspected iMCD, substantial diagnostic delays were common, particularly in those with a low likelihood of iMCD. Initial core needle biopsy frequently led to subsequent surgical excision, supporting the use of upfront excisional biopsy when feasible. Despite differences in diagnostic certainty, patients received similar iMCD-directed therapies and demonstrated comparable response rates to siltuximab-based regimens, highlighting the need for improved diagnostic pathways while supporting the use of iMCD-directed therapy in selected patients with uncertain diagnoses.

RESULTS

DIAGNOSTIC DELAY & BIOPSY

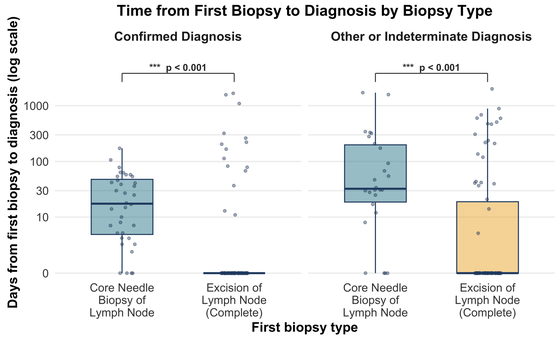

Figure 1. Excisional Biopsy Reaches Diagnosis Faster. Days from first biopsy to the date of iMCD diagnosis (log scale); boxes show median and IQR, points are individual patients. Excisional biopsy reached diagnosis faster in both groups.

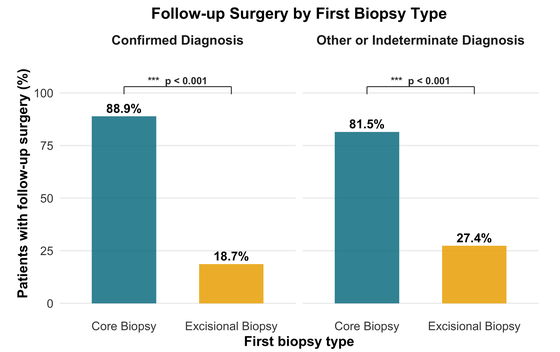

Figure 2. Core Needle Biopsy Often Requires Repeat Surgery. Follow-up surgery by first biopsy type. Overall, core needle biopsy more often required subsequent surgical excision than after upfront excisional biopsy in both expert-confirmed iMCD (**89% vs. 19%**) and other or indeterminate diagnoses (**82% vs. 27%**; Fisher's exact **p<0.001** for both). These findings support consideration of upfront excisional biopsy when feasible.

HOSPITALIZATION BURDEN

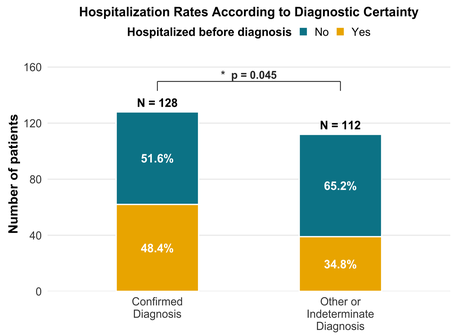

Figure 3. More Expert-Confirmed iMCD Patients Hospitalized Before Diagnosis. Hospitalization at any point before the diagnosis date. Expert-confirmed patients were hospitalized more often (**48% vs. 35%**) and had a higher overall hospitalization rate (**p=0.045**).

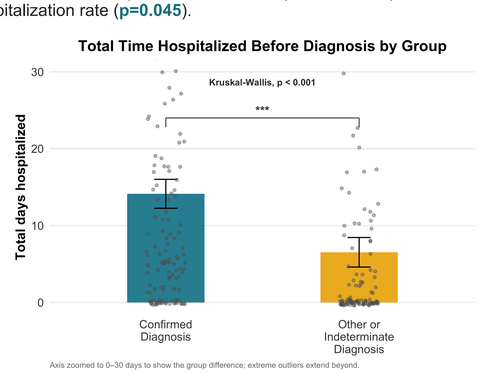

Figure 4. Longer Hospital Stays Before Diagnosis. Total days hospitalized before diagnosis by group (Kruskal-Wallis **p<0.001**; axis zoomed to 0-30 days). Median days hospitalized before diagnosis was **6 vs. 0** for confirmed vs. low-likelihood iMCD.

SYMPTOM ONSET TO DIAGNOSIS

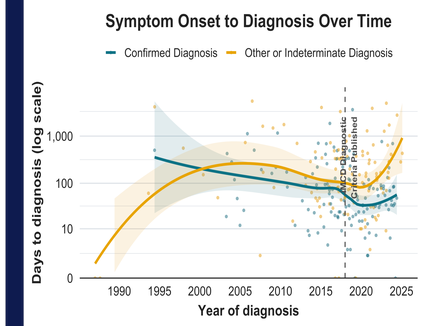

Figure 5. Diagnostic Delays Remain Common Despite Availability of iMCD Diagnostic Criteria. Days to diagnosis by year (log scale). Delay fell in confirmed cases but persists and stays longer in low-likelihood cases.

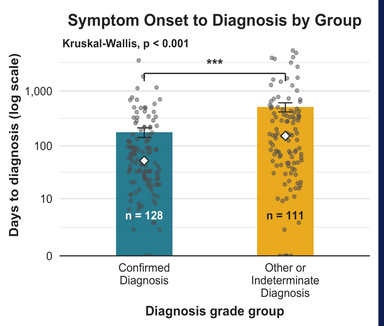

Figure 6. Longer Delay in Low-Likelihood iMCD. Median time from symptom onset to diagnosis was **53 vs. 152 days (p<0.001)**. Bars show mean±SE; diamonds, median.

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CONTACT INFORMATION

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CLINICAL & DURABLE RESPONSE BY DIAGNOSTIC CERTAINTY

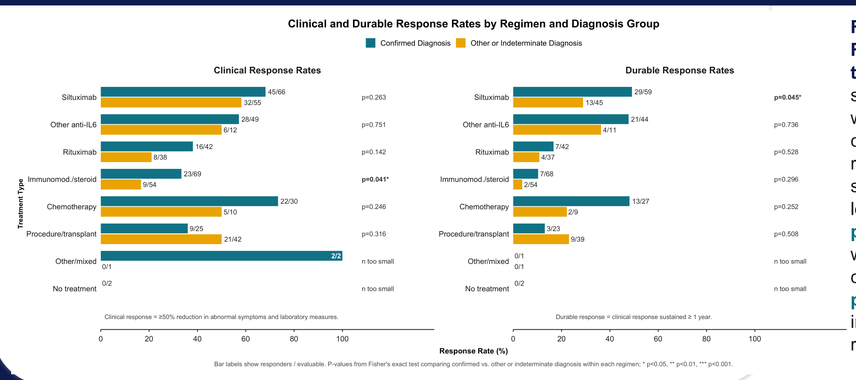

Figure 7. Clinical and Durable Response to iMCD-directed therapy. Treatment patterns were similar across diagnostic groups, with siltuximab-based regimens most common. Siltuximab clinical response rates did not differ significantly between confirmed and low-likelihood cases (**68% vs. 58%; p=0.263**), whereas durable response was significantly higher among confirmed cases (**49% vs. 29%; p=0.045**). Rituximab and other immunomodulators showed lower response rates in both cohorts.