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iMCD- in clinical practice

from "watchful waiting" to active treatment

Joint Romania and Greece cohort

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iMCD has a serious and significant impact on patient health and survival:

- **Severe organ damage:** If uncontrolled iMCD can lead to severe organ damage.[1]

- **Increased risk of developing cancer:** In a study of 128 patients with iMCD, the prevalence of cancer was 3-fold higher in patients with iMCD relative to age-matched controls.[2]

- **Poor survival**: 1 in 3 patients die within five years of diagnosis.[1]

References
1. Fajgenbaum DC, Uldrick TS, Bagg A, Frank D, Wu D, Srkalovic G, et al. International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease. Blood. 2017;129(12):1646-57.
2. Liu AY, Nabel CS, Finkelman BS, Ruth JR, Kurzrock R, van Rhee F, et al. Idiopathic multicentric Castleman's disease: a systematic literature review. Lancet Haematol. 2016;3(4):e163-75.

Patients with iMCD often present with a mix of symptoms which can look like an infection, and/or autoimmune/autoinflammatory disease and/or malignancy.

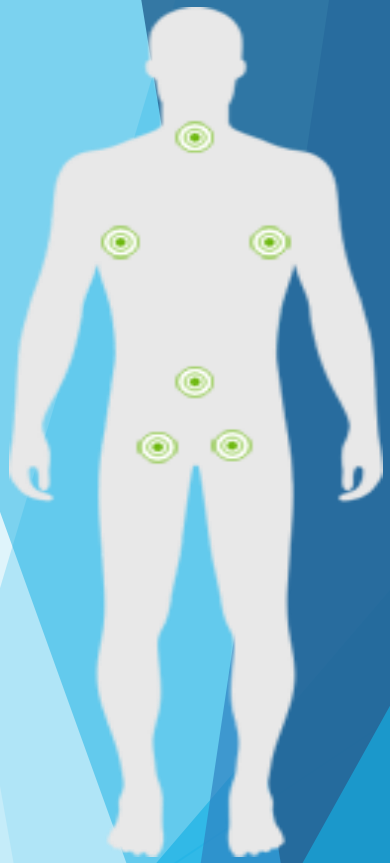
Suspect iMCD if the patient presents with a combination of common signs and symptoms shown in Figure [1].

Figure 1: Common signs and symptoms of iMCD (note, not all iMCD patients will present all of these symptoms)

Other symptoms and signs that are indicative of iMCD and can be helpful in leading towards a diagnosis include:[1]

- ❑ Elevated IL-6, sIL-2R, VEGF, IgA, IgE, lactate dehydrogenase and/or beta-2 microglobulin (B2M)
- ❑ Reticulin fibrosis of bone marrow
- ❑ Diagnosis of disorders that have been associated with iMCD: paraneoplastic pemphigus, bronchiolitis obliterans organising pneumonia, autoimmune cytopaenias, polyneuropathy (without diagnosis of POEMS-associated MCD), glomerular nephropathy, inflammatory myofibroblastic tumour

iMCD- Diagnostic criteria



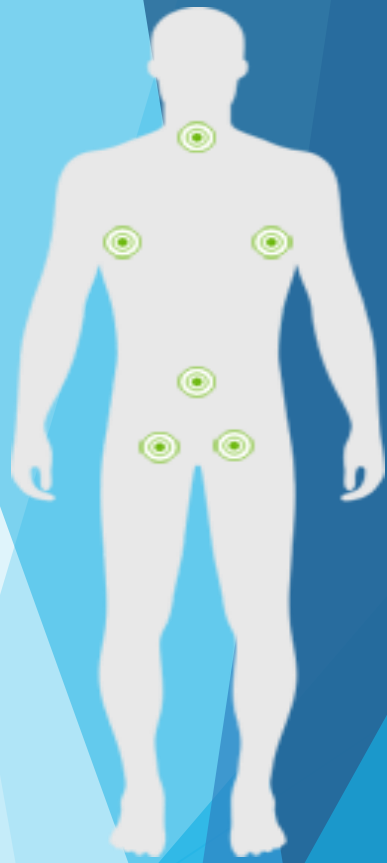
International guidelines have been published on the diagnosis of iMCD[1]

These guidelines recommend that patients with suspected iMCD should be examined for **major and minor diagnostic criteria** (covering lymph node pathology, clinical symptoms and laboratory abnormalities), as well as excluding conditions that mimic iMCD.[1]

References
1. Fajgenbaum DC, Uldrick TS, Bagg A, Frank D, Wu D, Srkalovic G, et al**. International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease. Blood. 2017**;129(12):1646-57

Diagnosing iMCD

- Three-part consensus diagnostic criteria have been proposed:
  - **Major criteria:** multicentric lymphadenopathy and characteristic lymph node histopathology
  - **Minor criteria:** ≥2 of 11 minor criteria, including ≥1 laboratory abnormality
  - **Exclusion criteria:** infectious, malignant and autoimmune diseases listed in the exclusion criteria must be ruled out



Diagnosing CD

Symptoms in CD often overlap with symptoms of many more common illnesses. This is why a Castleman disease diagnosis cannot be made with symptoms alone and requires further testing.

- **Lymph node biopsy:** Diagnosis of CD requires an excisional lymph node biopsy that shows features of Castleman disease.
  - "Excisional" means that the lymph node must be surgically removed entirely so that it can be specially prepared and evaluated by a pathologist.
- **Imaging:** shows how many lymph nodes are affected and can help to distinguish between UCD and MCD.
  - CT scan: can detect enlarged lymph nodes
  - PET-CT scan: uses a radiotracer to detect enlarged lymph nodes and the activity of those lymph nodes
- **Laboratory tests:**
  - Complete blood count: hemoglobin, white blood cells, platelets
  - Inflammation markers: CRP/ESR
  - Markers of organ function: liver function tests, albumin, creatinine (tests kidney function), HIV/HHV8 testing (used to test for HHV8-positive MCD).

Treating iMCD

SYLVANT® (siltuximab) is the first and only FDA/EMA approved therapy for Multicentric Castleman Disease (MCD)* and is recommended as a preferred first line therapy by clinical guidelines.[1]

- *Adult iMCD patients who are HHV-8 and HIV negative.[1]

Reference
1. van Rhee F, Voohees P, Dispenzieri A, et al. International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease. Blood. 2018; 132 (20): 2115-2125.

Treating iMCD

- Siltuximab is recommended as front-line therapy for patients with non-severe iMCD, due to the good quality data on safety and efficacy[1]
- Severely ill patients should be treated with siltuximab and high-dose steroids as a first-line therapy due to the high quality and volume of efficacy and safety data[1]
- Severe disease must be closely monitored, as life-threatening events may occur in this population[1]

van Rhee *et al*. *Blood* 2018; 132(20): 2115–24

International Prognostic Index

valuable tool for iMCD prognostic prediction and treatment decision making

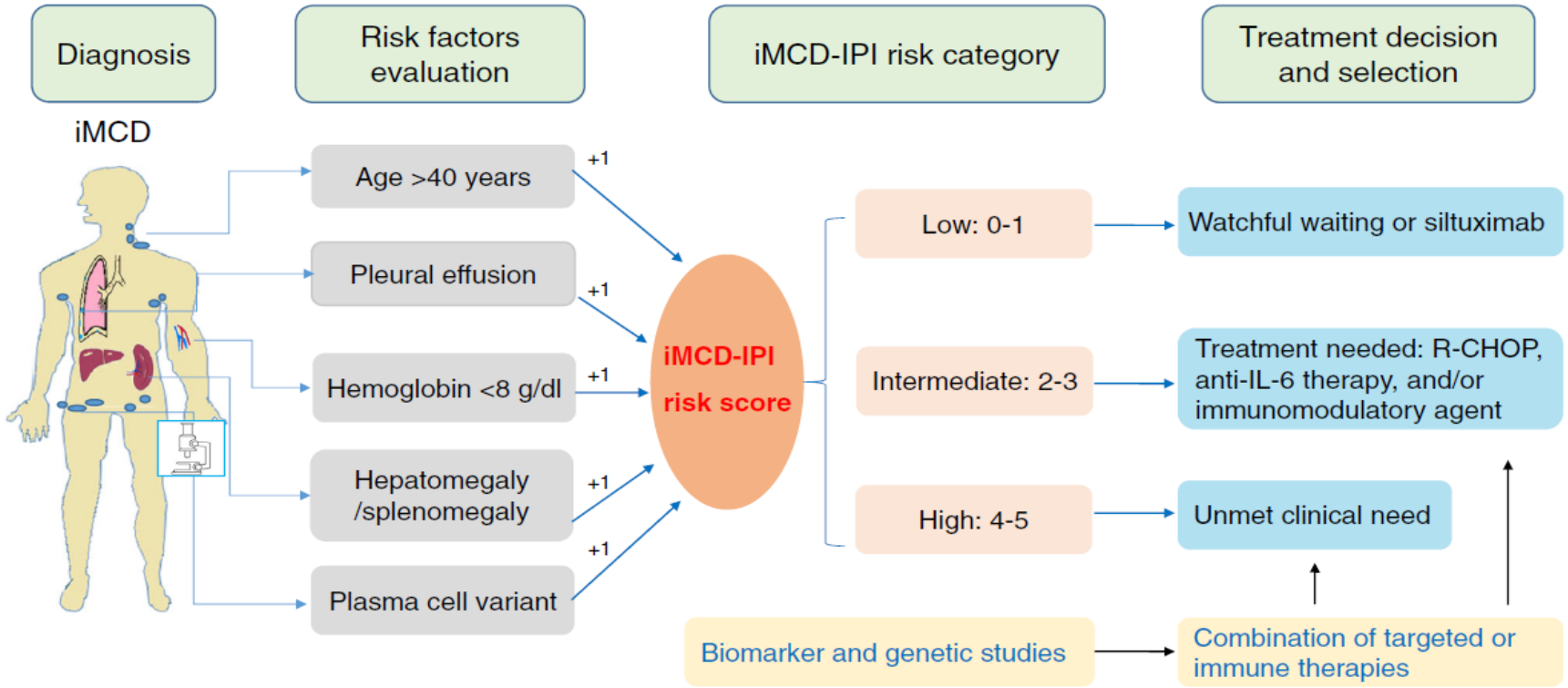


Figure 1. Schematic illustration of risk stratification of iMCD (idiopathic multicentric Castleman disease, HIV/HHV-8-negative) and proposed optimal treatment

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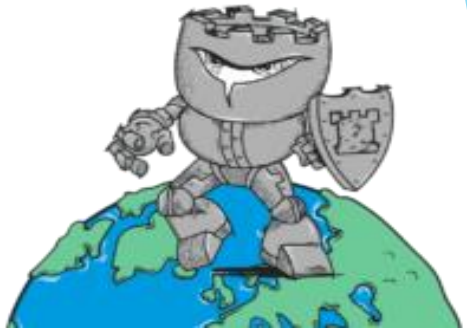
NETWORKING & COLLABORATION CDCN; CSTL



The Castleman Disease Collaborative Network (CDCN) is dedicated to accelerating research and treatment for Castleman disease, a disease at the intersection of cancer and autoimmunity, and revolutionizing biomedical research to cure many more diseases.

CDCN story began when third-year medical student David Fajgenbaum was struck and almost killed by Castleman disease.
After several relapses and recoveries, plus a completed medical degree, the Castleman Disease Collaborative Network (CDCN) was co-founded in 2012 by Dr. David Fajgenbaum and Dr. Frits van Rhee (of the University of Arkansas for Medical Sciences).

•**The Center for Study & Treatment of Castleman & Inflammatory Lymphadenopathies (CSTL)** was started by CDCN Co-Founder Dr. Fagjenbaum at the Perelman School of Medicine at the University of Pennsylvania

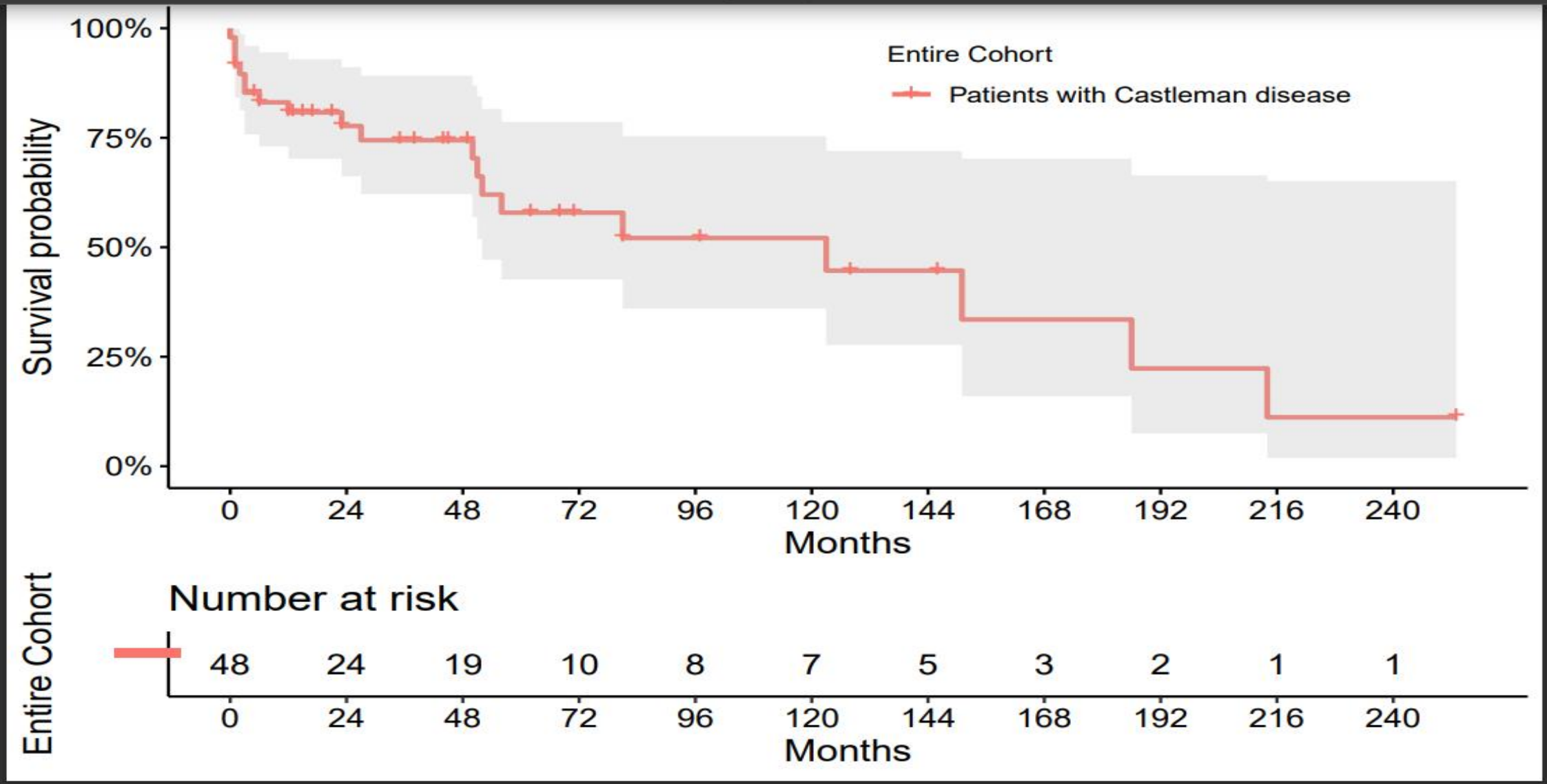
Reference: https://cdcn.org/

CDCN Connect: Physicians & Researchers

Table 1. Patient Characteristics

Variable	N	Overall, N = 48[1]	Cohort	
			G, N = 28[1]	R, N = 20[1]
Sex	48			
Female		15 / 48 (31%)	6 / 28 (21%)	9 / 20 (45%)
Male		33 / 48 (69%)	22 / 28 (79%)	11 / 20 (55%)
Age	48	65 (19)	74 (18)	54 (14)
Primary cause of death	19			
Death from AE		3 / 19 (16%)	3 / 16 (19%)	0 / 3 (0%)
Death from malignant disease under study		6 / 19 (32%)	5 / 16 (31%)	1 / 3 (33%)
Death other		10 / 19 (53%)	8 / 16 (50%)	2 / 3 (67%)
Disease status at last known follow-up	48			
Disease progression		19 / 48 (40%)	14 / 28 (50%)	5 / 20 (25%)
Progression free		23 / 48 (48%)	9 / 28 (32%)	14 / 20 (70%)

Response	48				0.44
Complete response		21 / 48 (44%)	10 / 28 (36%)	11 / 20 (55%)	
No response or stable disease		3 / 48 (6.2%)	2 / 28 (7.1%)	1 / 20 (5.0%)	
Other		2 / 48 (4.2%)	2 / 28 (7.1%)	0 / 20 (0%)	
Partial response		7 / 48 (15%)	3 / 28 (11%)	4 / 20 (20%)	
Progressive		8 / 48 (17%)	5 / 28 (18%)	3 / 20 (15%)	
Unknown		7 / 48 (15%)	6 / 28 (21%)	1 / 20 (5.0%)	
Best Response	48				0.17
Complete response		21 / 48 (44%)	10 / 28 (36%)	11 / 20 (55%)	
No response or stable disease		6 / 48 (12%)	4 / 28 (14%)	2 / 20 (10%)	



THANK YOU!

Cooperation strategy for knowledge transfer, internationalization and curricula innovation in the field of research education at the 3rd level of study - AURORA

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