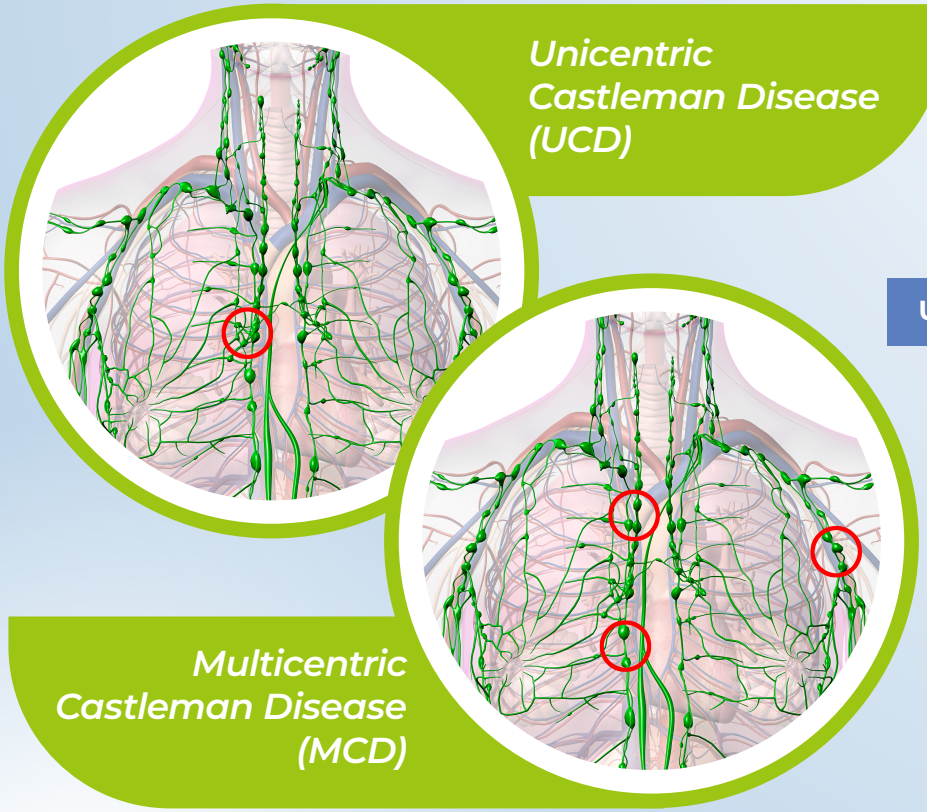
PATIENT JOURNEY: DIAGNOSIS AND MANAGEMENT PATHWAY

What Is Castleman Disease?

Castleman disease describes a group of distinct, nonmalignant lymphoproliferative disorders with a shared histology[1, 2]

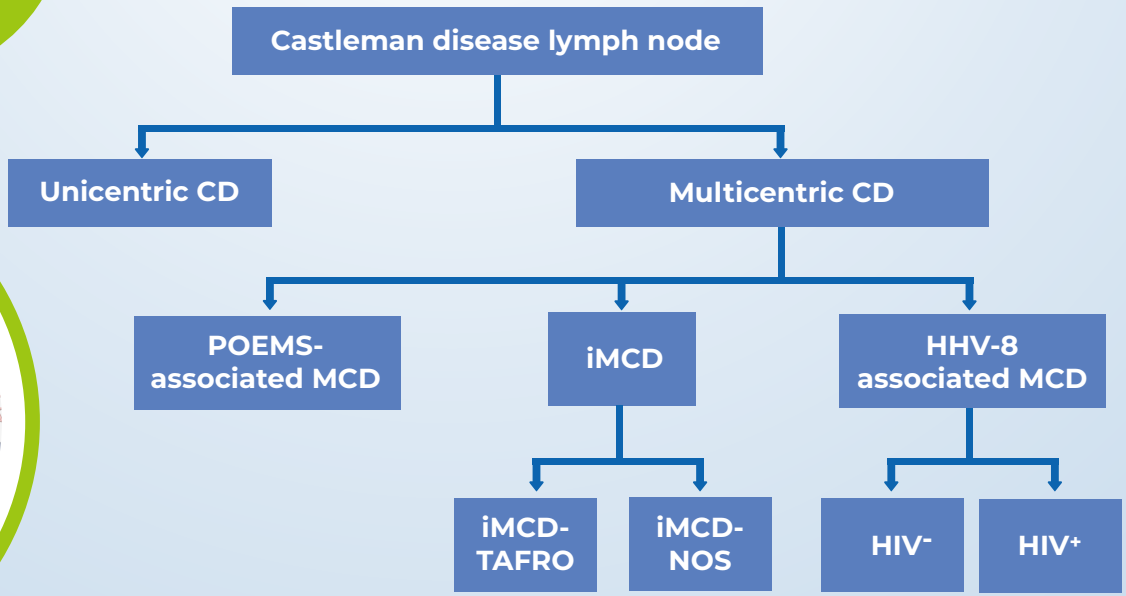
Classified into 2 Main Groups[1]



Unicentric Castleman Disease (UCD)

Multicentric Castleman Disease (MCD)

MCD is classified based on its etiology[3]



CD = Castleman disease; HHV-8 = human herpesvirus 8; HIV = human immunodeficiency virus; iMCD = idiopathic multicentric Castleman disease; MCD = multicentric Castleman disease; NOS = not otherwise specified; POEMS = polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin abnormalities; TAFRO = thrombocytopenia, ascites, reticulin fibrosis, renal dysfunction, organomegaly

iMCD is not associated with HHV-8, HIV, or POEMS and has no identifiable cause[4]

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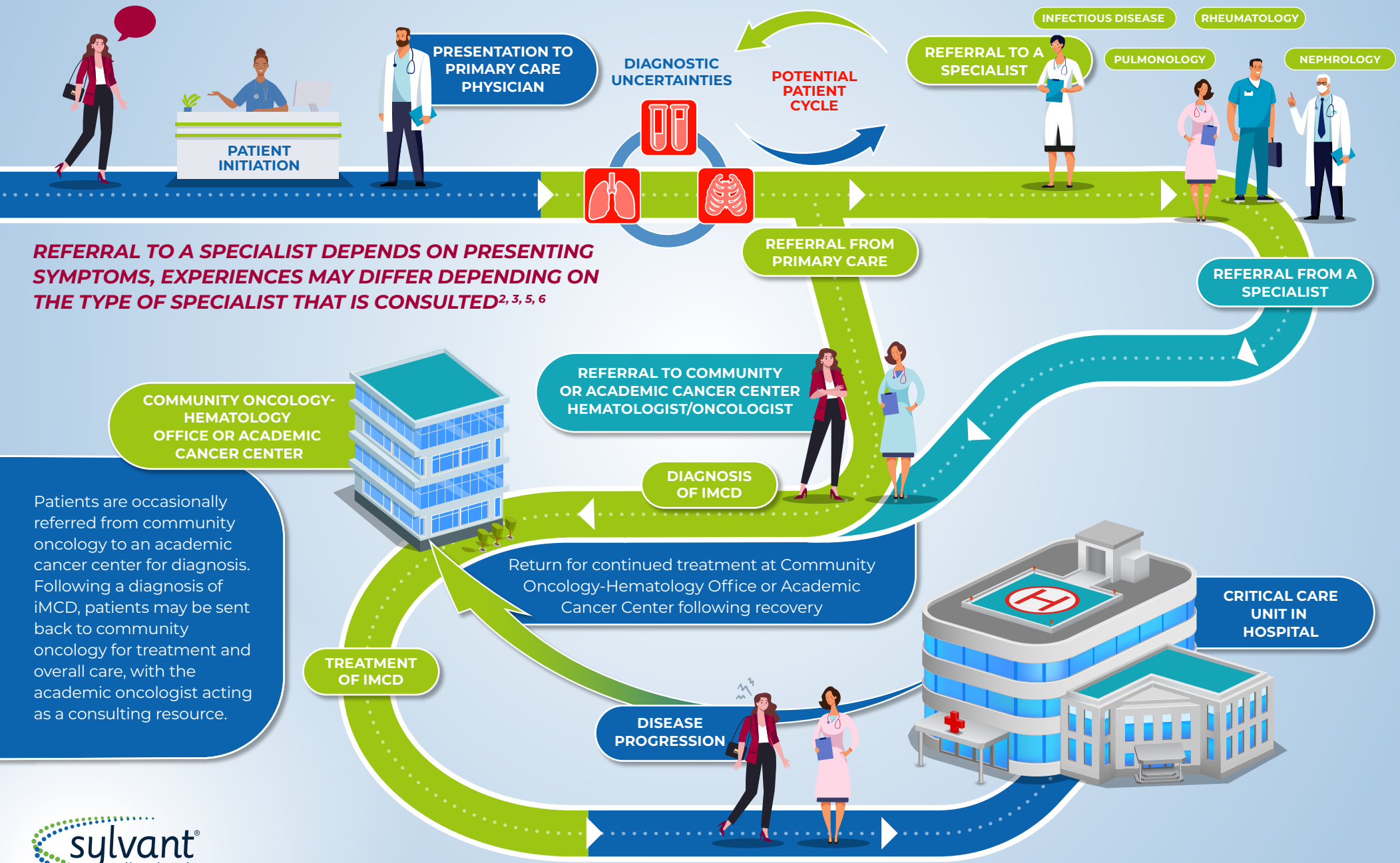
PATIENT JOURNEY is VARIABLE due to DIVERSITY of DISEASE MANIFESTATIONS



REFERRAL TO A SPECIALIST DEPENDS ON PRESENTING SYMPTOMS, EXPERIENCES MAY DIFFER DEPENDING ON THE TYPE OF SPECIALIST THAT IS CONSULTED[2, 3, 5, 6]

Patients are occasionally referred from community oncology to an academic cancer center for diagnosis. Following a diagnosis of iMCD, patients may be sent back to community oncology for treatment and overall care, with the academic oncologist acting as a consulting resource.

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Initial Presentation of iMCD

Patients with iMCD may experience a wide spectrum of clinical and laboratory abnormalities that come and go[3]

PCPs may perform medical histories, physical examinations, bloodwork, and medical tests[8, 9]

PRIMARY CARE PHYSICIANS (PCPS)

PRESENTING SYMPTOMS

Patients may present with enlarged lymph nodes, fever, weight loss, fatigue, autoimmune or respiratory symptoms, arthritis, or kidney disease.[3, 4]

DELAY OF DIAGNOSIS

Symptoms of iMCD overlap other malignant, autoimmune, and infectious disorders that need to be ruled out[2]

Secondary Management

Dependent on presentation of symptoms, treatment may include multiple specialists

HEMATOLOGIST/ONCOLOGIST

- Specializes in the treatment of blood disorders, including blood cancers and cancer of the blood-forming tissues[9]
- May perform tests to rule out malignant disorders, such as lymphoma or multiple myeloma[2]
- May see patients who present with enlarged lymph nodes, abnormal blood work, weight loss, or fatigue[3, 9, 10]

INFECTIOUS DISEASE SPECIALIST

- Specializes in the diagnosis and treatment of conditions caused by microbial agents[11]
- May see patients who present with persistent fever or enlarged lymph nodes, liver, or spleen[10,11]
- May perform virus serology to rule out infections, such as human herpesvirus-8, Epstein-Barr virus, or cytomegalovirus, that can drive Castleman disease symptoms[2, 3, 10]

PULMONOLOGIST

- Specializes in the diagnosis and treatment of lung conditions and diseases[9]
- May see patients who present with cough or pleural effusion[9, 10]
- May perform tests to provide information about ventilation, airflow, lung volume and capacity, and the diffusion of gas if a patient is experiencing pulmonary symptoms[2, 11]

RHEUMATOLOGIST

- Specializes in the diagnosis and treatment of conditions of the musculoskeletal system[11]
- May see patients who present with decreased performance status or signs of muscle or joint damage[10, 11]
- May perform tests to identify any autoimmune or inflammatory diseases, such as systemic lupus erythematosus or rheumatoid arthritis[2]

NEPHROLOGIST

- Specializes in the diagnosis and treatment of kidney diseases[9]
- May see patients who present with high levels of protein in the urine or blood[3, 9]
- May perform tests to identify causes of high amounts of protein in the urine[3, 10, 12]

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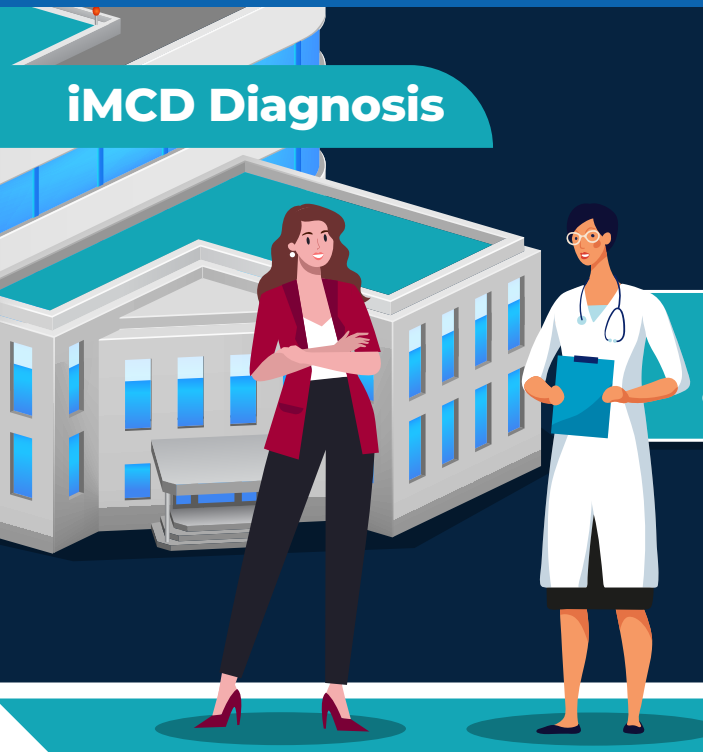
iMCD Diagnosis



Diagnostic criteria for iMCD includes major criteria, minor criteria, and exclusion criteria[3]

Diagnostic criteria for iMCD[3]

MAJOR CRITERIA: Patient must meet both major criteria for diagnosis[2]

MINOR CRITERIA: Patient must have 2 of 11 criteria, including at least 1 laboratory abnormality[2]

EXCLUSION CRITERIA: Must rule out autoimmune, malignant, and infectious diseases[2]

2 TYPES OF iMCD[3]

iMCD TAFRO

T HROMBOCYTOPENIA

A NASARCA

F EVERS

R ENAL FAILURE

O RGANOMEGALY

Homogeneous constellation of abnormal laboratory tests and clinical features

iMCD NOS

N OT

O THERWISE

S PECIFIED

No known cause and no characteristics of TAFRO

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iMCD Management

The Castleman Disease Collaborative Network and National Comprehensive Cancer Network both recommend anti-IL-6 therapy as preferred treatment for iMCD[5,10]

CDCN CASTLEMAN DISEASE COLLABORATIVE NETWORK

NCCN National Comprehensive Cancer Network®

Nonsevere disease[5]
- Typically diagnosed in outpatient setting
- Varied symptoms
- May affect ability to function or require hospitalization but typically not intensive care

Severe disease[5]
- Marked organ dysfunction
- Poor performance status
- Requires critical care

Patients with severe iMCD often present with **iMCD-TAFRO**[5]

10%–20% of patients with iMCD have severe disease[5]

Siltuximab is the only U.S. Food and Drug Administration (FDA)-approved drug specifically for the treatment of iMCD[3]

Siltuximab is a monoclonal antibody that binds directly to human IL-6 and prevents the binding of IL-6 to its soluble and membrane-bound receptors[13]

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iMCD Physician Views and Pain Points

OPPORTUNITIES TO EDUCATE[3,14]

- Perception that disease is benign and does not have an aggressive clinical course
- No defined threshold at which to initiate treatment
- Misconception that anti-IL-6 therapy is only for highly symptomatic patients

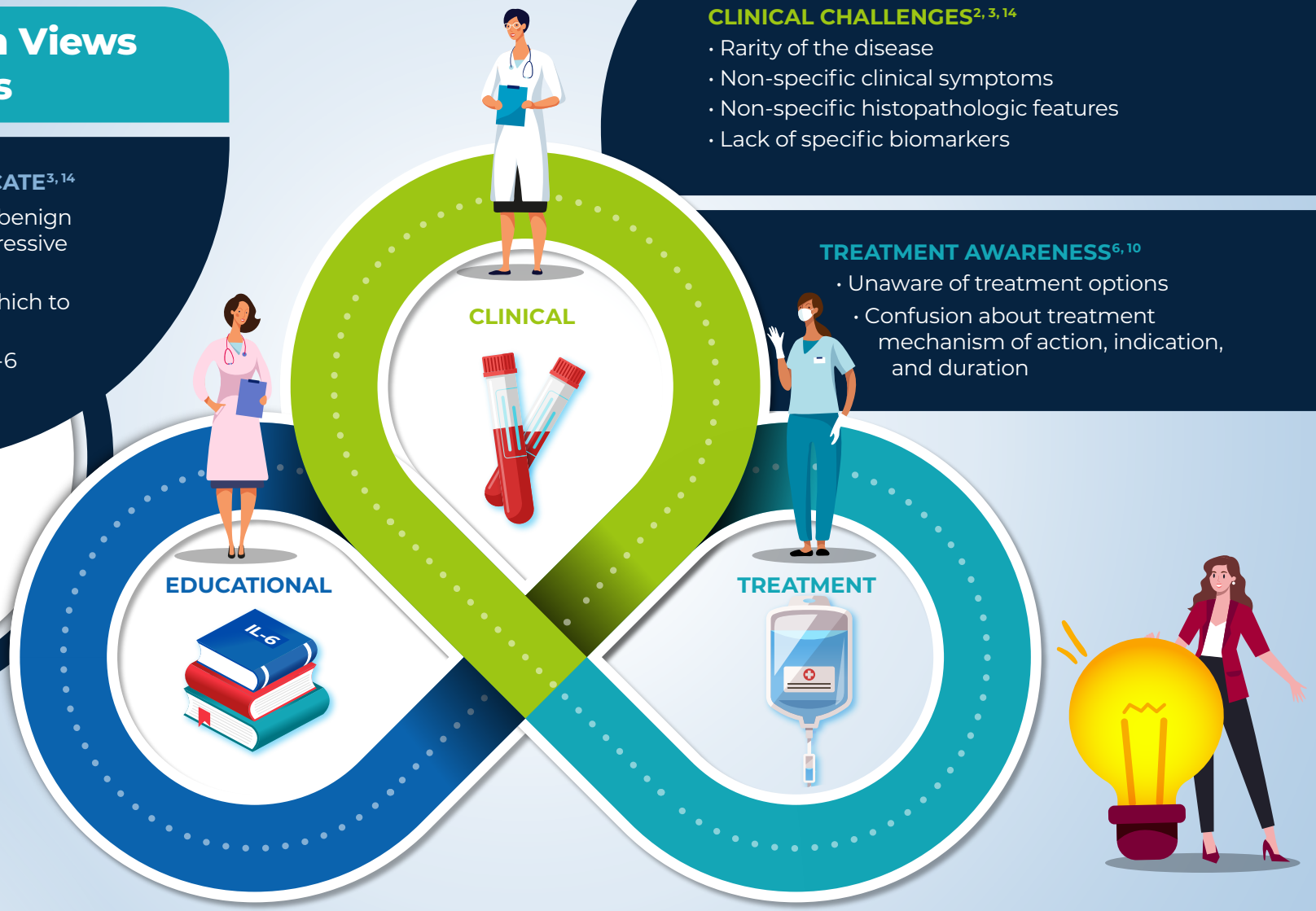
Despite recommendations from the CDCN and NCCN, only ~10% of patients with iMCD receive anti-IL-6 treatment[14]

CLINICAL CHALLENGES[2,3,14]

- Rarity of the disease
- Non-specific clinical symptoms
- Non-specific histopathologic features
- Lack of specific biomarkers

TREATMENT AWARENESS[6,10]

- Unaware of treatment options
- Confusion about treatment mechanism of action, indication, and duration



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