Treatment aims and considerations for managing HLH/MAS

Treatment aims for suspected MAS in Still's disease

- **Suppress hyperinflammation while diagnostic tests are ongoing[1–3]**
- **Identify and treat the underlying disease or trigger[1–3]**
- **Balance treatment toxicity and need to control inflammation[3]**
- **Early and aggressive intervention is recommended while diagnostic testing is ongoing[2,3]**

Initial treatment options for suspected MAS include:

- Supportive therapies[2,3]
- Broad-spectrum antibacterials/antivirals[2,3]
- Immunomodulatory drugs[2,3]
- Therapy targeting the potential underlying disease and/or trigger[2–4]

Timely investigation and identification of the etiology of MAS is critical so that appropriate therapy can be promptly initiated[2,3]

EULAR/ACR points to consider for diagnosing and treating HLH/MAS[3]

Diagnosis

- Following initial laboratory evaluations, assessment of specialized biomarkers of inflammation (e.g., sCD25, CD163, IL-18, CXCL9, neopterin, if available) may further aid in the diagnosis of HLH/MAS
- Many of the biomarkers useful for diagnosing HLH/MAS also have prognostic relevance

Treatment

- Consider initiating immunomodulatory treatment if there is persistent, severe, or worsening inflammation or organ dysfunction while diagnostic testing is ongoing
- Initial empiric immunomodulatory therapy could include:
  - Glucocorticoids
  - IL-1 inhibitor
  - IVIg
- Antimicrobial and antiviral therapies should be administered for any underlying infectious triggers or disorders

Monitoring

- Initial response to treatment should be monitored at least daily and markers of systemic inflammation, in particular ferritin, monitored at least twice weekly
- Worsening or lack of improvement in laboratory parameters may indicate disease progression in patients with suspected HLH/MAS

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ACR, American College of Rheumatology; CXCL9, chemokine C-X-C motif ligand 9; EULAR, European Alliance of Associations for Rheumatology; HLH, hemophagocytic lymphohistiocytosis; IL, interleukin; IVIg, intravenous immunoglobulin; MAS, macrophage activation syndrome; sCD25, soluble CD25 (also known as soluble interleukin receptor α [sIL-2Rα]).

1. Carter SJ, et al. *Rheumatology (Oxford)* 2019;58:5–17; 2. Hines MR, et al. *Crit Care Med* 2022;50:860–872; 3. Shakoory B, et al. *Arthritis Rheumatol* 2023;75:1714–1732; 4. Onel KB, et al. *Arthritis Rheumatol* 2022;74:553–569.

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EULAR/ACR algorithm for early or suspected HLH/MAS

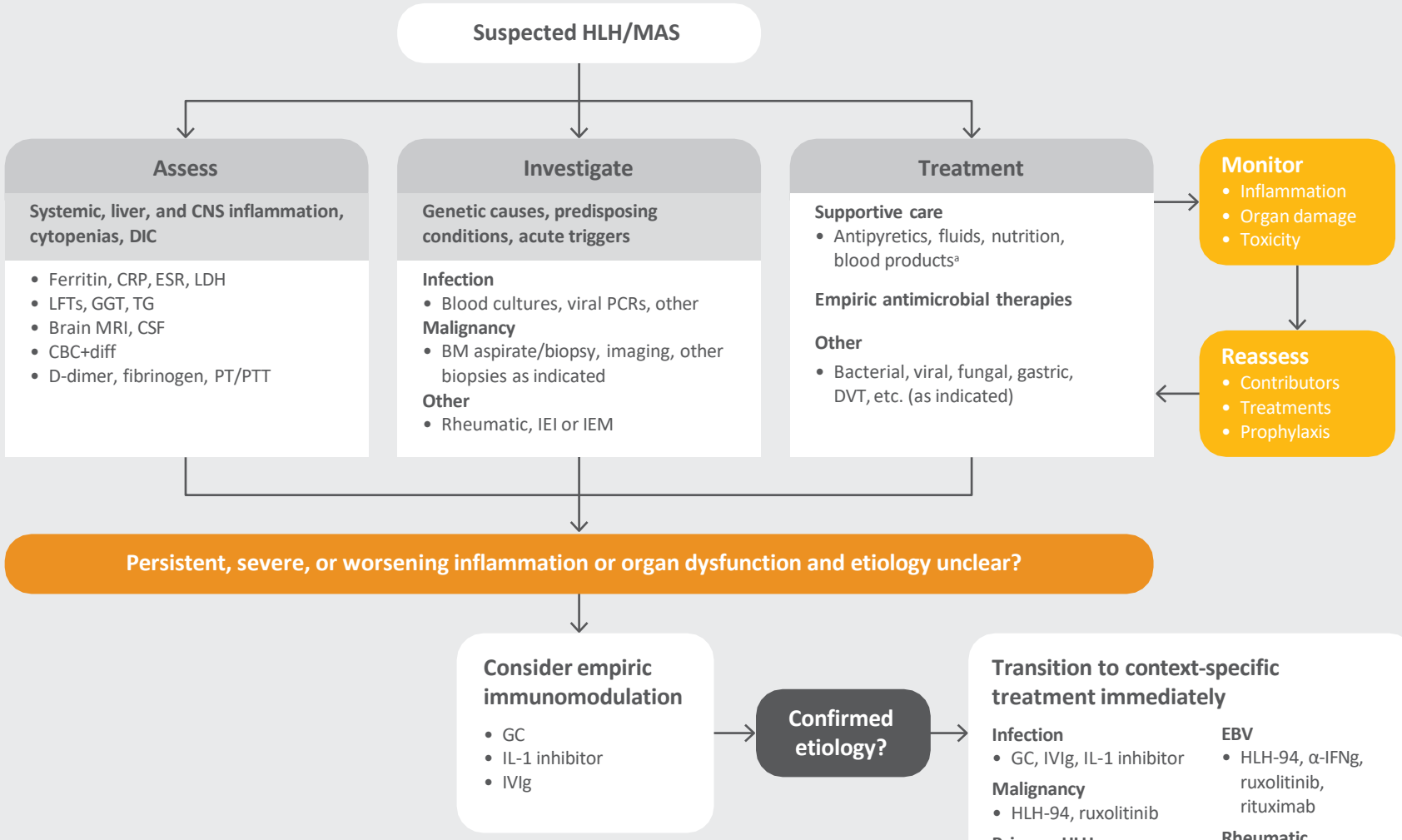

Figure adapted from Shakoory B, et al. *Arthritis Rheumatol* 2023;75:1714–1732.

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[a]Per local/national organ failure, DIC, shock guidelines.

ACR, American College of Rheumatology; BM, bone marrow; CBC+diff, complete blood cell count with leukocyte differential; CNS, central nervous system; CRP, C-reactive protein; CSF, cerebrospinal fluid; DIC, disseminated intravascular coagulopathy; DVT, deep vein thrombosis; EBV, Epstein-Barr virus; ESR, erythrocyte sedimentation rate; EULAR, European Alliance of Associations for Rheumatology; GC, glucocorticoid; GGT, γ-glutamyl transferase; HLH, hemophagocytic lymphohistiocytosis; IEI, inborn errors of immunity; IEM, inborn errors of metabolism; IL, interleukin; IVIg, intravenous immunoglobulin; LDH, lactate dehydrogenase; LFT, liver function test; MAS, macrophage activation syndrome; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; PT/PTT, prothrombin time/partial thromboplastin time; TG, triglycerides.

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