

Table S1. Diagnostic guidelines for HLH as proposed by the Histiocyte Society (HLH-2004, adapted from Henter *et al.*¹⁾)

<p>The diagnosis of HLH can be established if one of either 1 or 2 below is fulfilled:</p> <p>1) A molecular diagnosis consistent with HLH</p> <p>2) Diagnostic criteria for HLH fulfilled (five out of the eight criteria below)</p>
Fever
Splenomegaly
<p>Cytopenias (affecting ≥ 2 of 3 lineages in the peripheral blood):</p> <p>Hemoglobin < 90 g/L (in infants < 4 weeks: hemoglobin < 100 g/L)</p> <p>Platelets $< 100 \times 10^9/L$</p> <p>Neutrophils $< 1.0 \times 10^9/L$</p>
<p>Hypertriglyceridemia and/or hypofibrinogenemia:</p> <p>Fasting triglycerides ≥ 3.0 mmol/L (<i>i.e.</i>, ≥ 265 mg/dl)</p> <p>Fibrinogen ≤ 1.5 g/L</p>
Hemophagocytosis in bone marrow or spleen or lymph nodes
Low or absent NK-cell activity
Ferritin ≥ 500 $\mu\text{g/L}$
Soluble CD25 (<i>i.e.</i> , soluble IL-2 receptor) $\geq 2,400$ U/mL

Table S2. Additional laboratory testing for lactate dehydrogenase and liver/biliary functional markers

Tested analyte (reference range)	Number of cases of total tested with elevated values (prevalence rate)	Median (interquartile range)
Lactate dehydrogenase (LDH) (115-221 U/L)	26 of 28 (93%)	514 U/L (311-916 U/L)
Aspartate transferase (AST) (12-38 U/L)	20 of 30 (67%)	109 U/L (31-292 U/L)
Alanine aminotransferase (ALT) (7-41 U/L)	16 of 30 (53%)	45 U/L (25-94 U/L)
Gamma-glutamyl transferase (GGT) (9-58 U/L)	13 of 16 (81)	199 U/L (73-721 U/L)
Total bilirubin (0.2-1.3 mg/dL)	15 of 29 (52%)	1.6 mg/dL (0.4-3.9 mg/dL)

Table S3. Detailed list of all immunosuppressive agents provided to patients in the setting of HLH

Immunosuppressive agent	Number of patients receiving (prevalence rate amongst all patients)
Corticosteroid*	22 (73%)
Methylprednisolone	14 (47%)
Prednisone	8 (27%)
Hydrocortisone	8 (27%)
Dexamethasone	2 (7%)
Mycophenolate mofetil	7 (23%)
Intravenous immune globulin	6 (20%)
Calcineurin inhibitor	5 (17%)
Cyclosporine	3 (10%)
Tacrolimus	2 (7%)
Hydroxychloroquine	4 (13%)
Anakinra	3 (10%)
Cyclophosphamide	2 (7%)
Etoposide	2 (7%)
Rituximab	2 (7%)
Daclizumab	1 (3%)
Antithymocyte globulin	1 (3%)
Alemtuzumab	1 (3%)
Infliximab	1 (3%)
Methotrexate	1 (3%)

*Nine patients received more than one corticosteroid for the management of HLH.