

Table S1. Items of diagnostic guidelines or classification criteria present in the patients with sec-HLH or MAS in sJIA included in the study, recruited in Rome (sec-HLH=11, sJIA with or without MAS=22), Genoa (sJIA with or without MAS=10) and Cincinnati (sJIA with or without MAS=22). The Table shows also the presence of each individual criterion at time of sampling in patients divided according to those who did not yet receive any treatment (Off therapy) and those who had already received one treatment for MAS/HLH including glucocorticoid pulses, cyclosporine-A, anakinra or cyclophosphamide (On therapy).

SEC-HLH	ALL PATIENTS	ACTIVE DISEASE (N=11)	
		Off therapy	On therapy
†Diagnostic guidelines for HLH-2004 [19]	N (%)	N (%)	N (%)
Fever	9/11 (81.8)	5/5 (100)	4/6 (66.7)
Splenomegaly	4/11 (36.4)	2/5 (40)	2/6 (33.3)
Cytopenias (affecting ≥ 2 of 3 lineages)	6/11 (54.5)	1/5 (20)	5/6 (83.3)
Hypertriglyceridemia (≥ 265 mg/dl)	7/11 (63.6)	4/5 (80)	3/6 (50)
Hypofibrinogenemia (≤ 1.5 g/l)	4/11 (36.4)	1/5 (20)	3/6 (50)
Hemophagocytosis	9/11 (81.8)	4/5 (80)	5/6 (83.3)
Ferritin (≥ 500 mcg/L)	10/11 (90.9)	5/5 (100)	5/6 (83.3)
Low or absent NK-cell activity*	2/3 (66.7)	NA	2/3 (66.7)
Met criteria	11/11 (100)		
MAS	ALL PATIENTS	ACTIVE DISEASE (N=20)	
Classification criteria for MAS complicating sJIA[17]	N (%)	Off therapy	On therapy
	N (%)	N (%)	N (%)
Fever	19/20 (95)	7/7 (100)	12/13 (92.3)
Increased ferritin (≥ 684 ng/mL)	19/20 (95)	6/6 (100)	13/13 (100)
Decreased platelet count ($\leq 181 \times 10^9/L$)	10/20 (50)	1/7 (14.3)	8/13 (61.5)
Increased aspartate aminotransferase (>48 U/L)	17/20 (85)	3/6 (50)	11/13 (84.6)
Decreased fibrinogen (≤ 360 mg/dl)	14/20 (70)	1/6 (16.7)	9/12 (75)
Increased triglycerides (>156 mg/dl)	12/19 (63.2)	3/5 (60)	6/11 (54.5)
Met criteria	17/20 (85)		

NA: Not Available

†sCD25 was not performed in the institution where these patients were recruited.

* In all patients, this was transient and normalized following resolution of the episode.