emapalumab intravenously for 4 weeks (6mg/kg on Day 1; 3mg/kg every 3 days from Days 4–16, then 3mg/kg twice weekly from Days 17–28) until protocol-defined complete response (CR). Patients will be followed up for 1 year after study completion.

Key inclusion criteria
- Run-in phase
- Informed consent
- Male and female patients aged 6 months to 80 years at diagnosis of MAS
- Patients with a diagnosis of MAS having shown an inadequate response to high dose GCs as per local standard clinical practice

MAS diagnostic criteria
- Febrile patient presenting with NHL, CRP >4 mg/mL
- And any two of:
  - Platelet count ≤180 x10^9/L
  - Aspartate aminotransferase levels >48 U/L
  - Triglycerides >156 mg/dL
  - Fibrinogen levels ≤360 mg/dL

Results: Protocol-defined CR at Week 8 after first emapalumab administration is the primary endpoint of the EMERALD study. Secondary efficacy endpoints include GC tapering, survival, time to first CR, overall response (CR and partial response), time to first overall response, MAS recurrence, pharmacokinetic/pharmacodynamic profile of emapalumab, and patient-reported outcomes. Adverse events, abnormal laboratory parameters, and anti-drug antibodies will be monitored as safety endpoints.

Conclusion: The ongoing EMERALD study is designed to address the unmet need for efficacious and safe therapies for the treatment of MAS, particularly for patients who are refractory to high-dose GCs.

Acknowledgements: Medical writing assistance was provided by Blair Hesp PhD. Support and lung transplantation in severe anti-melanoma differentiation-associated gene 5 (MDA5)-rapidly progressive interstitial lung disease: a systematic review

Keywords: Systematic review, Rare/orphan diseases, Lungs

Background: Anti-melanoma differentiation-associated gene 5 antibody (MDA5) associated dermatomyositis is associated with rapidly progressive interstitial lung disease (RP-ILD), high mortality, and progression despite aggressive immunosuppression. Extra corporeal membrane oxygenation (ECMO), as bridge to recovery or lung transplantation, is potentially life-saving therapy for MDAS RP-ILD but their roles are unclear, and its use in practice is often debated.

Methods: We systematically reviewed the clinical outcomes of patients with MDA5 RP-ILD receiving ECMO and/or lung transplantation.

Results: The sixteen identified manuscripts reported outcomes for 33 patients with serological evidence of MDA5 (14 case reports, 2 case series). Most presented with respiratory symptoms, classic dermatomyositis cutaneous features, were amyopathic and had pulmonary radiological ground glass opacifications. Time to clinical diagnosis was usually less than 3 months from symptom onset. Treatment with emapalumab, and patient-reported outcomes. Adverse events, abnormal laboratory parameters, and antidrug antibodies will be monitored as safety endpoints.

Conclusion: The ongoing EMERALD study is designed to address the unmet need for efficacious and safe therapies for the treatment of MAS, particularly for patients who are refractory to high-dose GCs.

Acknowledgements: Medical writing assistance was provided by Blair Hesp PhD.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.3216

AB1482 SPECIFIC BLOOD MONOCYTE DISTRIBUTION IN HISTIOCYTOSES CORRELATES WITH VASCULAR INVOLVEMENT AND DISEASE ACTIVITY

Keywords: Innate immunity

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Background: Histiocytoses are rare clonal disorders characterized by the proliferation and accumulation of CD68+ histiocytes in tissues[1]. During histiocytosis, circulating monocytes arising from bone marrow progenitors carry most MAP-kinase gene mutations, but only “classical” monocytes can differentiate into tissue histiocytes[2]. However, little is known about the circulating monocyte subset distribution in histiocytoses[3] and their differences from other myeloid/lymphoid disorders.

Objectives: We aimed to evaluate the circulating monocyte subset distribution in patients with histiocytoses compared to patients with myeloproliferative disorders (Chronic myelomonocytic leukemia (CMMIL) and essential thrombocythemia (ET)) and healthy donors (HD).

Methods: Peripheral blood cells were obtained from patients diagnosed in Dijon University hospital between 2020 and 2021, with histiocytoses (n=17), CMMIL (n=7), ET (n=7), and from 21 HD at steady state. Monocytes were separated on a CD14/CD16 scattergram into CD14+CD16- (classical), CD14+CD16+ (intermediate), and CD14+CD16+ (non-classical) subsets after stained cell separation.

Results: During histiocytoses, an increase in “classical” monocytes was observed, compared to ET (p=0.01) while “intermediate” (vs. ET, p=0.02) and “non-classical” monocytes (vs. HD; p=0.04) were decreased. The distribution of monocyte subsets in histiocytoses was close to that in CMMIL and homogeneous among the different types of histiocytoses. Compared to CMMIL patients, clonal hematopoiesis in patients with histiocytoses was associated with a decrease in “classical” monocytes (67.50% vs. 97%; p=0.002), with an increase in intermediate and “non-classical” monocytes: 5% vs. 2.5% (p=0.03) and 4% vs. 0.5% (p=0.01), excepted when MAP-kinase mutation was considered, as monocyte distribution was similar. Patients with vascular involvement (ET included 5 RDD and 1 ID) had an increase in classical monocytes (96.00% [92.0-96.0] vs. 86.00% [82.5%-92.0%; p=0.008) and a decrease in “non-classical” monocytes (1.00% [1.0-2.0] vs. 5.00% [3.50-9.50]; p=0.007). The correlation between “non-classical” monocytes and vascular involvement was confirmed by Pearson model (0.648; [0.25-0.86]; p=0.005). Histiocytoses patients achieving a metabolic response had a lower percentage of “intermediate” monocytes (3.5% [2.00-5.00] vs. 7.0% [4.00-13.00]; p= 0.04) and lower CRP levels (3.0 [1.1-8.75] vs. 33.65 [5.5-39.5]; mg/L; p=0.04). The only factor influencing the monocytes subset repartition (“classical” monocytes) was the presence of clonal hematopoiesis (95% CI: [16.83 to 4.737]; p<0.002) in patients with histiocytoses.

Conclusion: The monocyte subset distribution is singular in histiocytoses compared to other myeloproliferative neoplasms and is influenced by clonal hematopoiesis. The decrease in the “non-classical” subset could represent a surrogate marker of vascular involvement, while the decrease of the intermediate fraction is associated with a metabolized response.

REFERENCES: