Changes in Pharmacodynamic Markers in Response to Emapalumab in Children and Adults with Macrophage Activation Syndrome in Still's Disease

Results from a Pooled Analysis of Two Prospective Trials

Sebastiaan J. Vastert,[1] Jordi Antón,[2] Pierre Quartier,[3] Bruno Fautrel,[4-6] Paul Brogan,[7,8] Ed Behrens,[9] Melissa Elder,[10] Francesca Minoia,[12] Pavla Dolezalova,[13] Robert Biesen,[14] Masaki Shimizu,[15] Uwe Ullmann,[16*] Adnan Mahmood,[17*] Andrew Danquah,[16] Elena Burillo,[16] Marco Petrimpol,[16] Steve Mallett,[17] Brian D. Jamieson,[18] Alexei A. Grom,[19] Fabrizio De Benedetti[20]

[1]Pediatric Rheumatology & Immunology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Utrecht, The Netherlands; [2]Hospital Sant Joan de Déu, Department of Pediatric Rheumatology, University of Barcelona, Barcelona, Spain; [3]Université Paris-Cité, IMAGINE Institute, RAISE reference centre, Pediatric Immuno-Hematology and Rheumatology Unit, Necker Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [4]Department of Rheumatology, Pitié-Salpêtriere Hospital, Assistance Publique-Hôpitaux de Paris, Sorbonne University, Paris, France; [5]CRI-IMIDIATE Clinical Research Network and ERN Rita, CEREMAIA Reference Center, Paris, France; [6]Pierre Louis Institute of Epidemiology and Public Health, INSERM UMR-S 1136, Paris, France; [7]Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK; [8]University College London Great Ormond Street Institute of Child Health, London, UK; [9]Division of Rheumatology, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; [10] College of Medicine, University of Florida, Gainesville, FL, USA; [12]Pediatric Immuno-Rheumatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [13]Paediatric Rheumatology and Autoinflammatory Diseases Unit, General University Hospital, Prague, Czechia; [14]Department of Rheumatology and Clinical Immunology, Charité Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität, Berlin, Germany; [15]Department of Pediatrics and Developmental Biology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan; [16]Sobi, Basel, Switzerland; [17]Sobi, Stockholm, Sweden; [18]Sobi, Inc., Morrisville, NC, USA; [19]Cincinnati Children's Hospital, Division of Rheumatology, Cincinnati, OH, USA; [20]Division of Rheumatology, Ospedale Pediatrico Bambino Gesù, IRCCS, Rome, Italy

*At time of study conduct

Disclosures for Sebastian J. Vastert

The speaker has the following financial relationships to disclose:

Shareholder	No relevant conflicts of interest to disclose
Grant/Research Support	Sobi
Consultant	Sobi, Novartis
Employee	No relevant conflicts of interest to disclose
Paid Instructor	No relevant conflicts of interest to disclose
Speaker Bureau	Sobi, Novartis
Other	No relevant conflicts of interest to disclose

Background

- MAS is a life-threatening complication of Still's disease, and is characterized by IFNγ-driven macrophage activation and systemic hyperinflammation[1–4]
- Emapalumab, an anti-IFNγ antibody, binds free and receptor-bound IFNγ, providing rapid and targeted neutralization of IFNγ[2]
- Emapalumab has demonstrated safety and efficacy in patients with MAS in two clinical trials (NCT03311854[5] and NCT05001737[6]).
- Emapalumab has been recently approved by FDA for adult and pediatric (newborn and older) patients with MAS in known or suspected Still's disease with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS[7].

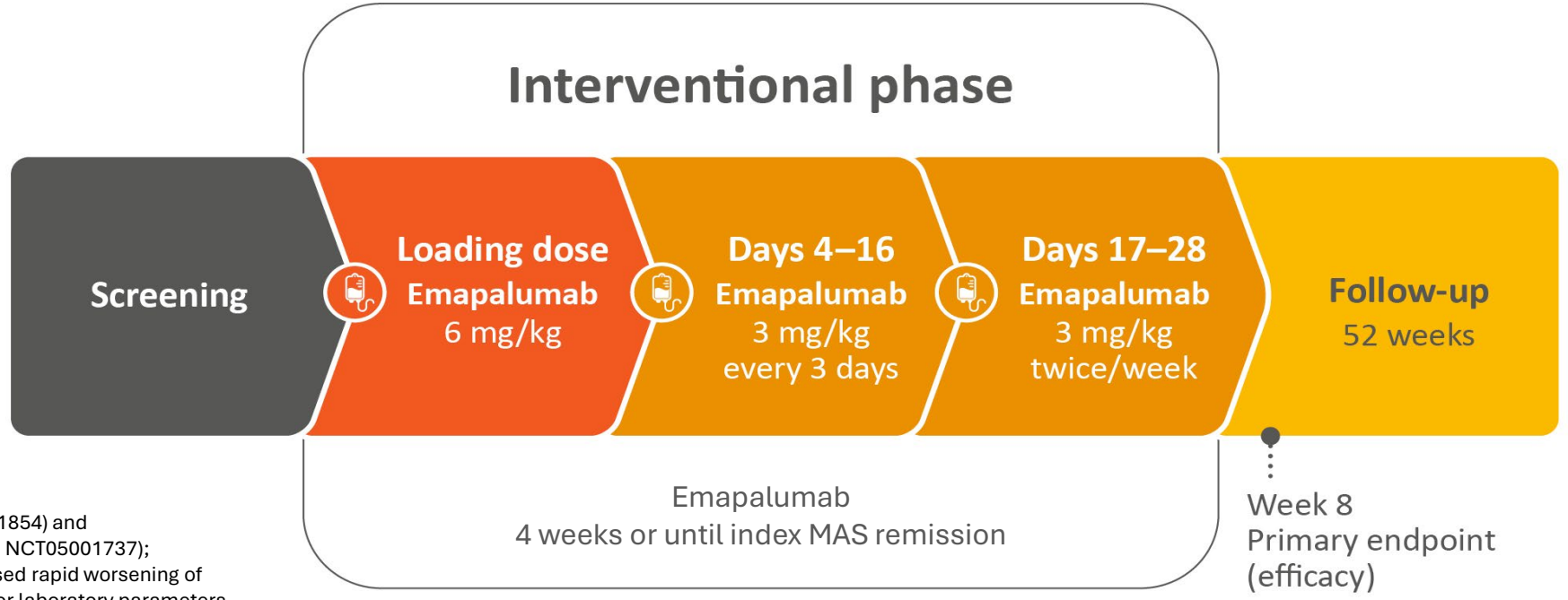
IFNγ, interferon gamma; MAS, macrophage activation syndrome.

1. Fautrel B, et al. *Ann Rheum Dis* 2024;83:1614–1627; 2. Jacqmin P, et al. *Br J Clin Pharmacol* 2022;88:2128–2139; 3. Fajgenbaum DC, June CH. *N Engl J Med* 2020;383:2255–2273;
4. De Benedetti F, et al. *Nat Rev Rheumatol* 2021;17:678–691; 5. De Benedetti F, et al. *Ann Rheum Dis* 2023;82:857–865; 6. Study Details | NCT05001737 | Evaluate Efficacy, Safety and Tolerability, PK and PD of Emapalumab in Children and Adults With MAS in Still's or SLE | ClinicalTrials.gov; 7. FDA PI last accessed on September 2nd 2025

Study design

Data were pooled from two prospective, open-label, single-arm interventional studies[a] in patients with MAS in Still's disease who had an inadequate response to high-dose glucocorticoids[b]

- Enrollment in EMERALD was extended to patients with adult-onset Still's disease after encouraging preliminary results in the NI-0501-06 study[1]



[a]NI-0501-06 (NCT03311854) and NI-0501-14 (EMERALD; NCT05001737);
[b]Or investigator-assessed rapid worsening of clinical condition and/or laboratory parameters.
MAS, macrophage activation syndrome.

1. De Benedetti F, et al. *Ann Rheum Dis* 2023;82:857–865.

Objective: To evaluate **changes in key PD markers** by response status at week 8 after treatment initiation and time to response

Methods:

Data were pooled from two prospective, open-label, single-arm interventional studies[a] in patients with MAS in Still's disease who had an inadequate response to high-dose glucocorticoids[b]

8-component composite endpoint

Complete response:

- Absence of MAS clinical signs and symptoms (VAS ≤1 cm)
- Normalization of 7 lab parameters

+

Measurement and analysis of key PD biomarkers

- Ferritin
- CXCL9
- sCD25

[a]NI-0501-06 (NCT03311854) and NI-0501-14 (EMERALD; NCT05001737); [b]Or investigator-assessed rapid worsening of clinical condition and/or laboratory parameters.

CXCL9, chemokine C-X-C motif ligand 9; MAS, macrophage activation syndrome; PD, pharmacodynamic; sCD25, soluble CD25; VAS, visual analog scale.

Cohort Demographics, Heterogeneous Population

Baseline characteristics	N=39
Age, years, median (range)[1]	12 (9 months–64 years)
Age <17 years, n (%)[2]	30 (76.9)
Age ≥17 years, n (%)[2]	9 (23.1)
Age at diagnosis, years, median (range)[1]	9 (9 months–64 years)[a]
Sex, female, n (%)[1]	31 (79.5)
Underlying disease, n (%)[2]	
sJIA	**35 (89.7)**
AOSD	4 (10.3)
Geographic region, n (%)[1]	
North America	6 (15.4)
Europe/UK	**30 (76.9)**
Japan	2 (5.1)
China	1 (2.6)
Weight, kg, median (range)[1]	45.0 (9.5–80.0)
Previous MAS episode, n (%)[2]	**14 (35.9)**
Herpes zoster virus prophylaxis, n (%)	32 (82.1)

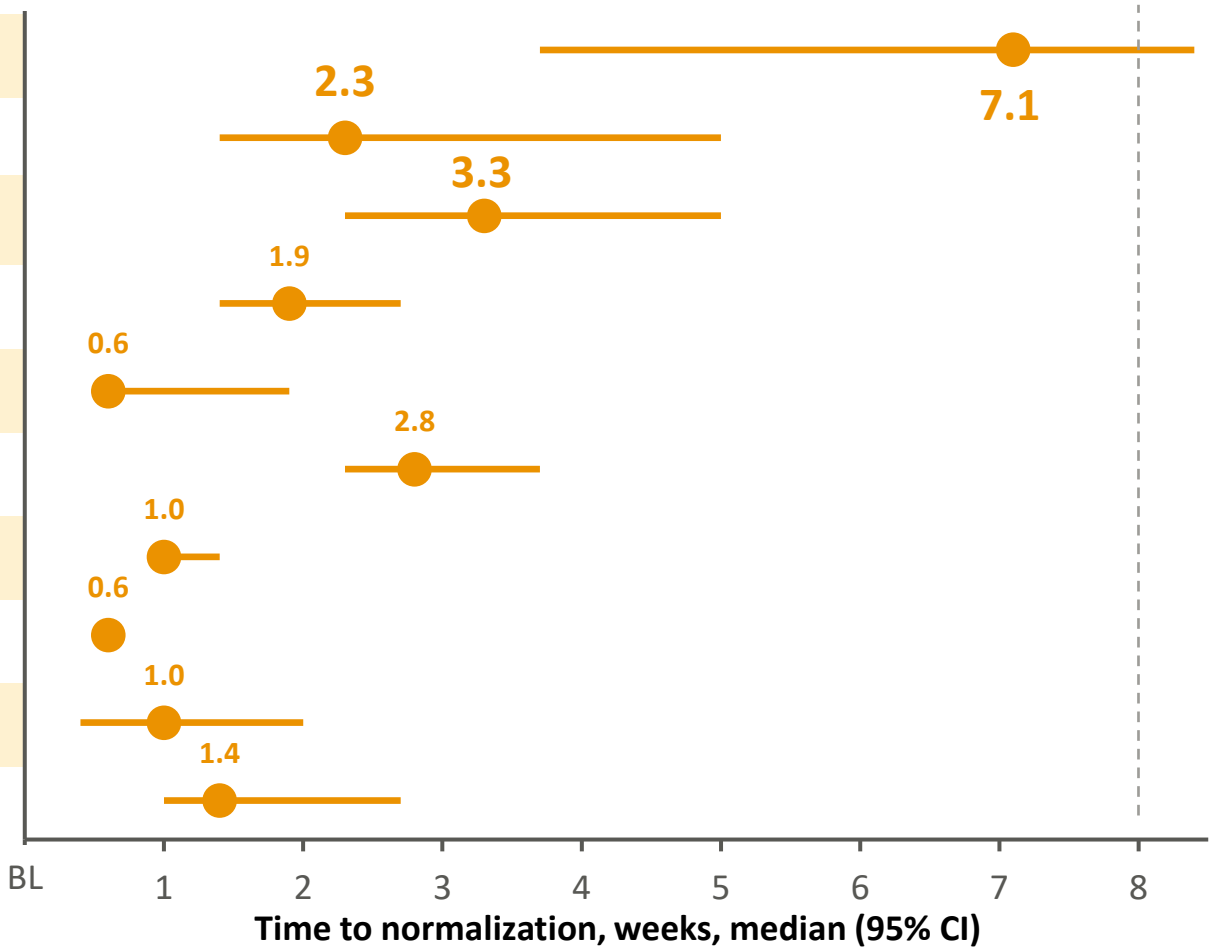
A majority of patients received concomitant anakinra for Still's disease

Concomitant medications to control Still's disease n (%)	N=39
Any	32 (82.1)
Anakinra (≤ 4mg/kg/day)	22 (56.4)
Calcineurin inhibitors	18 (46.2)

[a]n=33.[2]
AOSD, adult-onset Still's disease; MAS, macrophage activation syndrome; sJIA, systemic juvenile idiopathic arthritis.
1. Grom A, et al. *Ann Rheum Dis* 2025;84(suppl 1):172–173; 2. Sobi. Data on file.

Laboratory parameters normalised quickly in the majority of patients

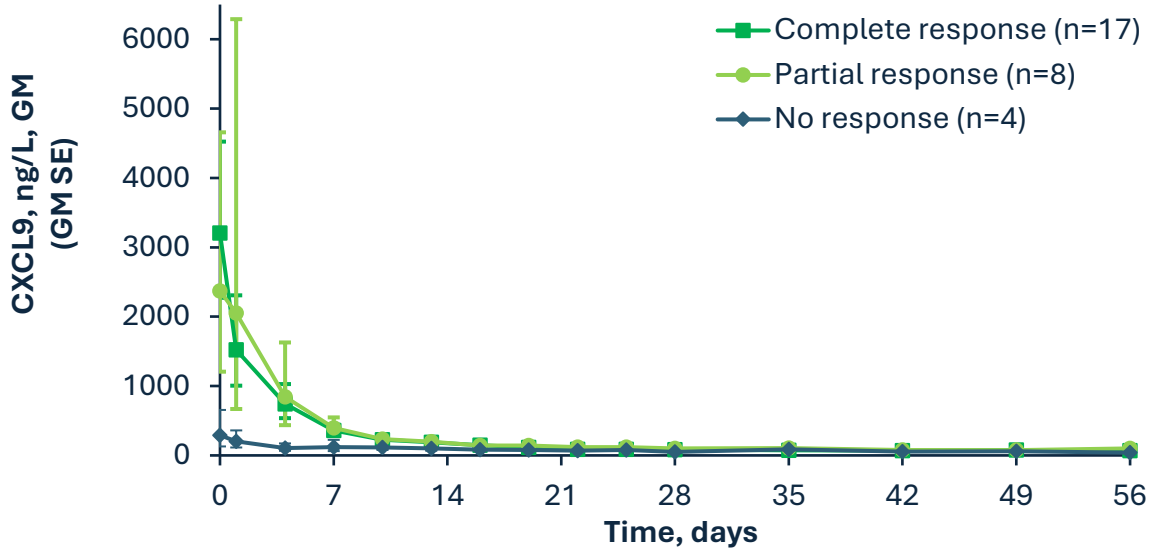
	Abnormal at baseline, n	Normalized at Week 8, n (%)
Complete response (CR)	39	21 (53.8)
Overall response (CR or PR)	38	29 (76.3)
MAS clinical activity score VAS ≤1/10 cm	39	32 (82.1)
Ferritin	39	33 (84.6)
Platelet count	20	17 (85.0)
ALT	32	28 (87.5)
AST	26	24 (92.3)
Fibrinogen	7	6 (85.7)
WBC	10	9 (90.0)
LDH	37	24 (64.9)

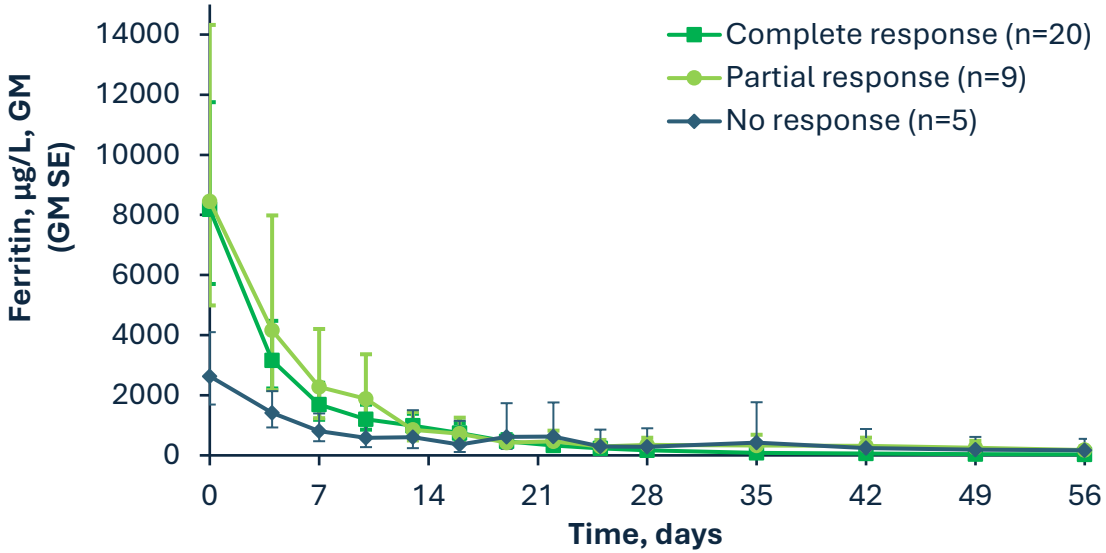


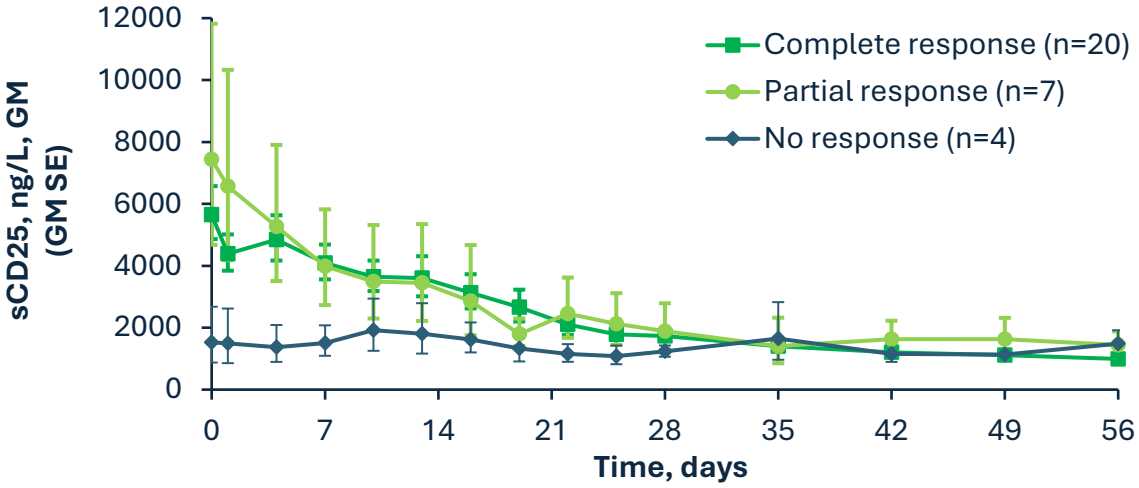
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BL, baseline; CI, confidence interval; LDH, lactate dehydrogenate; PR, (VAS <4 cm and normalisation of at least 3 abnormal baseline laboratory parameters included in the composite primary endpoint) ; MAS, macrophage activation syndrome; VAS, visual analog scale; WBC, white blood cell.

Grom A, et al. *Ann Rheum Dis* 2025;84(suppl 1):172–173.

CXCL9, ferritin and sCD25 improved within the 1st week of treatment in patients achieving a defined response at Week 8







Week 8 median percentage reduction from baseline

	CXCL9	Ferritin	sCD25
CR/PR	-98%	-99%	-80%
NR	-86%	-89%	+21%

[a]Evaluable Set -Patients with response status of "NO CR/NOT APPLICABLE PR", "NOT EVALUABLE" or missing status are excluded from the analysis
CXCL9, chemokine C-X-C motif ligand 9; GM, geometric mean; sCD25, soluble CD25; SE, standard error. Sobi. Data on file.

Summary

The pooled analysis from two prospective studies in patients with MAS in Still's disease with an inadequate response to high-dose glucocorticoid treatment demonstrated:

- Emapalumab treatment rapidly controlled signs and symptoms of MAS in 82.1% of patients[a]
- Emapalumab enabled reduction of key inflammatory PD markers by IFNγ inhibition in patients with MAS in Still's disease
- Predefined complete and partial responses at Week 8 were associated with higher levels of inflammatory biomarkers of MAS at baseline, although all improved after emapalumab treatment initiation

[a]MAS clinical activity score VAS ≤1/10 cm
CXCL9, chemokine C-X-C motif ligand 9; IFNγ, interferon gamma; LDH, lactate dehydrogenase; MAS, macrophage activation syndrome; VAS, visual analog scale.

Thank you to the NI-0501-06 and EMERALD investigators

The authors also wish to acknowledge the participants and their families for their contribution of the study

Studies NI-0501-06 (NCT03311854) and NI-0501-14 (EMERALD; NCT05001737) were funded by Sobi.

Additional author disclosures: **J. Antón:** Grant / Research Support with: Sobi, Speaker Bureau with: Sobi; **P. Quartier**: None Declared; **B. Fautrel:** Grant / Research Support with: AbbVie, Eli Lilly & Co, MSD, Pfizer, Consultant with: AbbVie, Alternative, Biogen, BMS, Celgene, Celltrion, Chugai, Eli Lilly & Co, Fresenius Kabi, Galapagos, Janssen, Medac, MSD, Nordic Pharma, Novartis, Pfizer, Roche, Room, Sandoz, Sanogi-Genzyme, UCB; **P. Brogan:** Speaker Bureau with: Sobi; **E. Behrens:** Grant / Research Support with: Sobi, Consultant with: Sobi, Ab2Bio; **M. Elder:** None Declared; **F. Minoia:** Consultant with: Sobi, Novartis, Speaker Bureau with: Sobi, Novartis; **P. Dolezalova:** Speaker Bureau with: Sobi, Novartis, Pfizer, Medac, **R. Biesen:** None Declared; **M. Shimizu:** Grant / Research Support with: Medical and Biological Laboratories Co., Ltd; **U. Ullmann:** Consultant with: Sobi; **A. Mahmood:** Consultant with: Sobi; **A. Danquah:** Employee with: Sobi; **E. Burillo:** Employee with: Sobi; **M. Petrimpol:** Employee with: Sobi; **S. Mallett:** Consultant with: Sobi; **B. Jamieson:** Employee with: Sobi, Inc.; **A. Grom:** Grant / Research Support with: National Institutes of Health, Novartis, SJIA Foundation, Sobi, Consultant with: Kiniksa, Novartis, Sobi; **F. De Benedetti:** Grant / Research Support with: Abbvie, Apollo, Elixiron, Kiniska, Novartis, Sanofi, Sobi, Consultant with: Abbvie, Apollo, Elixiron, Kiniska, Novartis, Sanofi, Sobi