Long-term Safety and Effectiveness of Canakinumab in Patients with MKD/HIDS: Interim Analysis of the RELIANCE Registry

Prasad T. Oommen[1], Tilmann Kallinich[2–4], Juergen Rech[5–7], Norbert Blank[8], Julia Weber-Arden[9], Jasmin B. Kuemmerle-Deschner[10]

[1]Department of Paediatric Oncology, Haematology and Clinical Immunology, Division of Paediatric Rheumatology, Medical Faculty, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany;

[2]Department of Paediatric Respiratory Medicine, Immunology and Critical Care Medicine, Charité Universitätsmedizin, Berlin, Germany;

[3]Deutsches Rheuma-Forschungszentrum (DRFZ), an Institute of the Leibniz Association, Berlin, Germany;

[4]German Center for Child and Adolescent Health (DZKJ), partner site Berlin, Berlin, Germany;

[5]Department of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany;
[6]DZI (Deutsches Zentrum für Immuntherapie), Erlangen, Germany;

[7]Centre for Rare Diseases Erlangen (ZSEER), Erlangen, Germany;

[8]Division of Rheumatology, Department of Internal Medicine, Heidelberg University Hospital, Heidelberg, Germany;

[9]Novartis Pharma GmbH, Nuernberg, Germany;

[10]Division of Paediatric Rheumatology and autoinflammation reference centre Tübingen, Department of Paediatrics, University Hospital Tübingen, Tübingen, Germany; member of ERN-RITA.

Correspondence to:

Prasad T. Oommen,

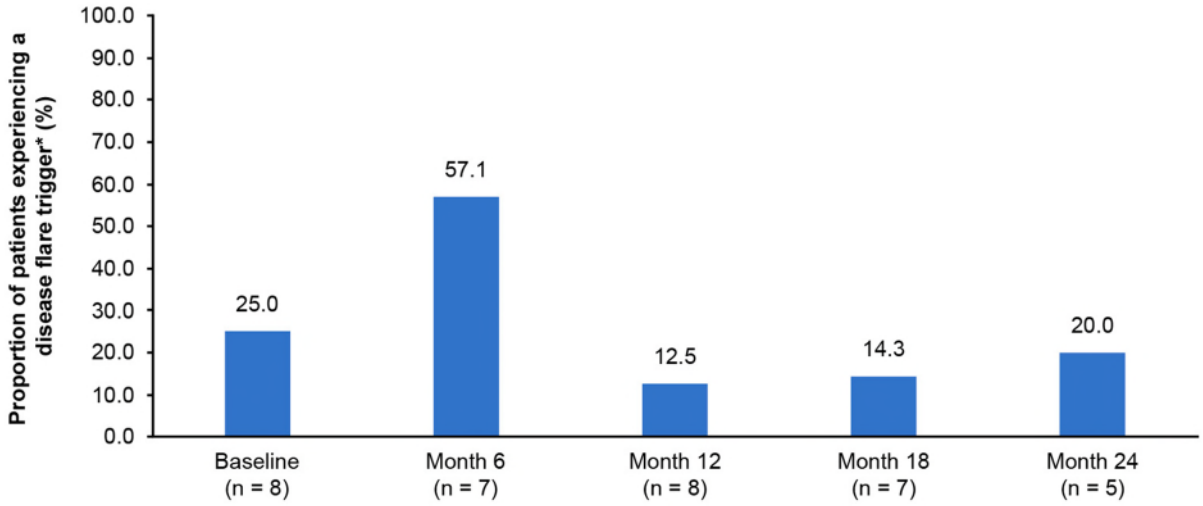
Department of Paediatric Oncology, Haematology and Clinical Immunology, Division of Paediatric Rheumatology, Medical Faculty, Heinrich-Heine-University Duesseldorf, Duesseldorf,

Germany,

Email: Prasad.Oommen@med.uni-duesseldorf.de

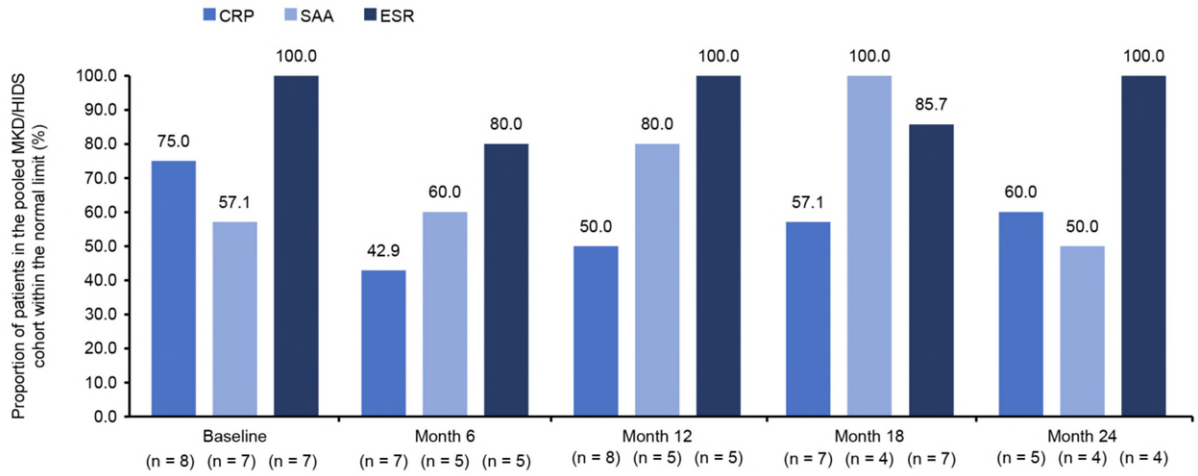
SUPPLEMENTARY FIGURES AND TABLES

Figure S1. Proportion of patients experiencing a disease flare trigger



*Cold, stress, infections, vaccinations and/or menstrual cycle hormones

Figure S2. Proportion of patients with CRP, SAA and ESR within normal limits in the pooled patient cohort. *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *MKD/HIDS* mevalonate kinase deficiency/hyperimmunoglobulin-D syndrome, *SAA* serum amyloid A



Normal limits of inflammatory markers: CRP (≤ 0.5 mg/dL), SAA (≤ 1.0 mg/dL), ESR (≤ 15.0–20.0 mm/h)

Table S1. Adverse events and adverse drug reactions

Preferred Term, n (%)	AE (*N* = 8)	ADR (*N* = 8)	SAE (*N* = 8)	SADR (*N* = 8)	Any (*N* = 8)	Incidence rate (IR/100PY)
Acrodermatitis	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Aphthous ulcer	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Concussion	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (12.5)	4.5
C-reactive protein increased	1 (12.5)	1 (12.5)	0 (0.0)	0 (0.0)	2 (25.0)	9.1
Cough	0 (0.0)	3 (37.5)	0 (0.0)	0 (0.0)	3 (37.5)	13.6
COVID-19	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Drug ineffective	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)	2 (25.0)	9.1
Epistaxis	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Fall	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	1 (12.5)	4.5
Gamma-glutamyl transferase increased	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Hand-foot-and-mouth disease	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Hyper IgD syndrome	2 (25.0)	1 (12.5)	0 (0.0)	0 (0.0)	3 (37.5)	13.6
Immunisation reaction	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (25.0)	9.1
Infection	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Intermenstrual bleeding	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Leukopenia	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)	2 (25.0)	9.1
Lymphadenopathy	3 (37.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (37.5)	13.6
Nasopharyngitis	2 (25.0)	2 (25.0)	0 (0.0)	0 (0.0)	4 (50.0)	18.2
Nausea	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Neutropenia	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)	2 (25.0)	9.1
Oropharyngeal pain	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Pyrexia	4 (50.0)	2 (25.0)	0 (0.0)	0 (0.0)	6 (75.0)	27.3
S100 protein increased	2 (25.0)	2 (25.0)	0 (0.0)	0 (0.0)	4 (50.0)	18.2
Transaminases increased	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Vaccination site lymphadenopathy	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5
Vomiting	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	4.5

A patient with multiple occurrences of an AE is counted only once in the corresponding AE category. IR/100PY = number of events multiplied by 36,525 / sum of observation days (= 8,039)

ADR adverse drug reaction, *AE* adverse event, *Ig* immunoglobulin, *IR* incidence rates, *PY* patient years, *SAR* serious ADR, *SAE* serious AE