Supplementary Information (Web Only Files)
Behrens et al., Anti-GM-CSF in RA

Study drug manufacturer and administration

The MOR103 drug substance was manufactured by DSM Biologics Company BV (Groningen, The Netherlands) and the drug product (sterile liquid formulation in glass vials) was manufactured by Rentschler Biotechnologie GmbH (Laupheim, Germany). MOR103 or placebo was administered by intravenous infusion at a fixed rate (500 mL over 1 hour) under medical supervision.

Effect of MOR103 on lung function

An evaluation of subjects with a ≥20% decrease in DLCO was performed. Between 1 and 5 subjects in each treatment group showed a ≥20% decrease in DLCO from screening at the time points evaluated (weeks 2, 4, 10, and 16). There was no trend toward an increased incidence of reduced DLCO over time, and there were no differences between placebo and active treatment groups in the proportion of patients with decreased DLCO. One subject in the MOR103 0.3 mg/kg group experienced a decrease in FEV1 that was considered related to treatment, and 1 subject in the MOR103 1.0 mg/kg group had abnormal spirometry results (not related to treatment). Other PFTs showed minimal changes during the course of the trial and no differences were noted between placebo and active treatment groups.

Anti-MOR103 antibodies

Serum samples were tested for anti-MOR103 IgG and IgM antibodies. One sample collected at week 10 from a subject treated with MOR103 1.0 mg/kg was confirmed positive for anti-MOR103 IgG antibodies. Because all later samples of the same subject tested negative, the immune response was recorded as a transient positive.

As there was no appropriate positive control available for the detection of anti-MOR103 IgM antibodies, study samples were only screened for potential positive samples. Results from pre-dose (screening visit) values and placebo-treated patients were compared to results in MOR103-treated patients. At the screening visit, ELISA results for anti-MOR103 IgM antibodies were positive in 4 placebo subjects and 0, 3, and 4 subjects in the MOR103 0.3, 1.0, and 1.5 mg/kg groups, respectively. Post-treatment positive samples were found to be in the same range; 0 to 4 subjects were positive for potential anti-MOR103 IgM antibodies in each treatment group at weeks 10, 13, and 16. Based on these results it was concluded that there were no obvious differences in the numbers of positive ELISA samples between placebo and MOR103 groups. Overall, there was no evidence that anti-MOR103 antibodies affected MOR103 serum concentrations or clinical outcomes.

Table S1. Treatment distribution by country

Country	Pooled placebo N = 27	MOR103 0.3 mg/kg N = 24	MOR103 1.0 mg/kg N = 22	MOR103 1.5 mg/kg N = 23	Total patients N = 96
Bulgaria	6	12	7	4	29
Germany	4	4	7	2	17
The Netherlands	2	0	0	1	3
Poland	8	8	4	3	23
Ukraine	7	0	4	13	24

Table S2. Treatment-emergent AEs occurring in any MOR103 subject by system organ class and preferred term. Patients may have experienced more than one AE.

Adverse event	Placebo N = 27	MOR103 0.3 mg/kg N = 24	MOR103 1.0 mg/kg N = 22	MOR103 1.5 mg/kg N = 23	MOR103 Pooled active N = 69
Infections and infestations	8 (29.6)	3 (12.5)	10 (43.5)	5 (25.7)	18 (26.1)
Nasopharyngitis	3 (11.1)	1 (4.2)	7 (31.8)	1 (4.3)	9 (13.0)
Viral respiratory tract infection	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.7)	2 (2.9)

Adverse event	Placebo N = 27	MOR103 0.3 mg/kg N = 24	MOR103 1.0 mg/kg N = 22	MOR103 1.5 mg/kg N = 23	MOR103 Pooled active N = 69
Rhinitis	0 (0.0)	0 (0.0)	2 (9.1)	0 (0.0)	2 (2.9)
Bronchitis	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Influenza	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Oral herpes	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4
Otitis media	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Tonsillitis	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Viral infection	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Musculoskeletal and connective tissue disorders	1 (3.7)	6 (25.0)	4 (18.2)	3 (13.0)	13 (18.8)
Rheumatoid arthritis*	0 (0.0)	3 (12.5)	4 (18.2)	2 (8.7)	9 (13.0)
Back pain	0 (0.0)	1 (4.2)	1 (4.5)	0 (0.0)	2 (2.9)
Arthralgia	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Muscle spasms	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Myalgia	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Neck pain	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Pain in extremity	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)

Adverse event	Placebo N = 27	MOR103 0.3 mg/kg N = 24	MOR103 1.0 mg/kg N = 22	MOR103 1.5 mg/kg N = 23	MOR103 Pooled active N = 69
Respiratory, thoracic and mediastinal disorders	3 (11.1)	2 (8.3)	3 (13.6)	4 (17.4)	9 (13.0)
Cough	0 (0.0)	1 (4.2)	0 (0.0)	2 (9.7)	3 (4.3)
Oropharyngeal pain	1 (3.7)	0 (0.0)	2 (9.1)	0 (0.0)	2 (2.9)
Rhinorrhea	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.7)	2 (2.9)
Dyspnoea	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Dyspnoea exertional	1 (3.7)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Pleurisy	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Rales	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Gastrointestinal disorders	2 (7.4)	3 (12.5)	4 (18.2)	1 (4.3)	8 (11.6)
Diarrhoea	1 (3.7)	1 (4.2)	0 (0.0)	1 (4.3)	2 (2.9)
Nausea	0 (0.0)	1 (4.2)	1 (4.5)	0 (0.0)	2 (2.9)
Abdominal pain	1 (3.7)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Dry mouth	1 (3.7)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Flatulence	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Gingivitis	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Toothache	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)

Adverse event	Placebo N = 27	MOR103 0.3 mg/kg N = 24	MOR103 1.0 mg/kg N = 22	MOR103 1.5 mg/kg N = 23	MOR103 Pooled active N = 69
General disorders and administration site conditions	3 (11.1)	1 (4.2)	6 (27.3)	1 (4.3)	8 (11.6)
Fatigue	1 (3.7)	1 (4.2)	4 (18.2)	1 (4.3)	6 (8.7)
Impaired healing	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Influenza-like illness	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Oedema	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Oedema peripheral	2 (7.4)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Investigations	5 (18.5)	4 (16.7)	3 (13.6)	1 (4.3)	8 (11.6)
Decreased DLCO	2 (7.4)	2 (8.3)	0 (0.0)	0 (0.0)	2 (2.9)
Alanine aminotransferase increased	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Anti-glutamic acid decarboxylase antibody positive	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Blood creatinine increased	1 (3.7)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)

Adverse event	Placebo N = 27	MOR103 0.3 mg/kg N = 24	MOR103 1.0 mg/kg N = 22	MOR103 1.5 mg/kg N = 23	MOR103 Pooled active N = 69
Body temperature increased	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
C-reactive protein increased	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Forced expiratory volume decreased	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Spirometry abnormal	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Vascular disorders	2 (7.4)	1 (4.2)	2 (9.1)	3 (13.0)	6 (8.7)
Hypertension	1 (3.7)	1 (4.2)	2 (9.1)	2 (8.7)	5 (7.2)
Hypotension	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Nervous system disorders	1 (3.7)	1 (4.2)	1 (4.5)	3 (13.0)	5 (7.2)
Headache	1 (3.7)	1 (4.2)	0 (0.0)	2 (8.7)	3 (4.3)
Dizziness	1 (3.7)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Presyncope	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Cardiac disorders	0 (0.0)	1 (4.2)	0 (0.0)	2 (8.7)	3 (4.3)
Sinus tachycardia	0 (0.0)	1 (4.2)	0 (0.0)	1 (4.3)	2 (2.9)
Arrhythmia	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)

Adverse event	Placebo N = 27	MOR103 0.3 mg/kg N = 24	MOR103 1.0 mg/kg N = 22	MOR103 1.5 mg/kg N = 23	MOR103 Pooled active N = 69
Injury, poisoning and procedural complications	0 (0.0)	1 (4.2)	1 (4.5)	1 (4.3)	3 (4.3)
Burns first degree	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Fall	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Foot fracture	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Skin and subcutaneous tissue disorders	3 (11.1)	1 (4.2)	2 (9.1)	0 (0.0)	3 (4.3)
Alopecia	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Dermatitis allergic	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)
Rash	2 (7.4)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Blood and lymphatic system disorders	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.7)	2 (2.9)
Anaemia	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.7)	2 (2.9)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	0 (0.0)	0 (0.0)	1 (4.5)	1 (4.3)	2 (2.9)
Basal cell carcinoma	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	1 (1.4)

Adverse event	Placebo N = 27	MOR103 0.3 mg/kg N = 24	MOR103 1.0 mg/kg N = 22	MOR103 1.5 mg/kg N = 23	MOR103 Pooled active N = 69
Skin cancer	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Renal and urinary disorders	0 (0.0)	2 (8.3)	0 (0.0)	0 (0.0)	2 (2.9)
Leukocyturia	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Renal colic	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.4)
Metabolism and nutrition disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)
Hyperkalaemia	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (1.4)

*Worsening or exacerbation of existing RA (flares). Except for one patient in the MOR103 0.3 mg/kg group (date of flare not reported), all events occurred from 10 days to > 12 weeks following the last dose of active treatment

Figure S1. Mean DAS28 scores from baseline through week 16. Error bars indicate standard deviation for each data point. Statistical significance was not evaluated prior to the week 4 visit as specified in the study protocol. DAS28, Disease Activity Score-28 joints.