

Supplementary Table 1. Distribution of current illnesses in patients included in the studies

Illness	RA study (n = 738)*	LN study (n = 307)	MG study (n = 104)
Immune system disorders	6 (0.8) [6]	11 (3.6) [11]	2 (1.9) [2]
Lupus erythematosus syndrome	4 (0.5) [4]	–	NR
Rheumatoid arthritis	–	6 (2.0) [6]	NR
Auto-antibody response	NR	4 (1.3) [4]	NR
Multiple myositis	2 (0.3) [2]	1 (0.3) [1]	NR
Systemic lupus erythematosus (IT)	NR	NR	2 (1.9) [2]
General cardiovascular disorders	147 (19.9) [148]	106 (34.5) [109]	20 (19.2) [20]
Hypertension	145 (19.6) [145]	103 (33.6) [103]	20 (19.2) [20]
Heart failure	2 (0.3) [2]	3 (1.0) [3]	NR
Left heart failure	1 (0.1) [1]	NR	NR
Pulmonary hypertension	NR	3 (1.0) [3]	NR
Metabolism and nutrition disorders	82 (11.1) [86]	81 (26.4) [93]	33 (31.7) [44]
Hyperlipidemia	28 (3.8) [28]	45 (14.7) [45]	11 (10.6) [11]
Diabetes mellitus	44 (6.0) [44]	12 (3.9) [12]	11 (10.6) [11]
Lipid metabolism disorder NOS	7 (0.9) [7]	11 (3.6) [11]	NR
Hypocalcemia	NR	11 (3.6) [11]	NR
Hypercholesterolemia	3 (0.4) [3]	5 (1.6) [5]	6 (5.8) [6]
Vitamin D deficiency	NR	5 (1.6) [5]	NR
Gout	2 (0.3) [2]	2 (0.7) [2]	NR
Hyperuricemia	NR	1 (0.3) [1]	NR
Osteomalacia	NR	1 (0.3) [1]	NR
Dyslipidemia (IT)	NR	NR	8 (7.7) [8]
Xerophthalmia (IT)	1 (0.1) [1]	NR	4 (3.9) [4]
Non-insulin dependent diabetes mellitus (IT)	NR	NR	3 (2.9) [3]
Hyperglycemia	1 (0.1) [1]	NR	1 (1.0) [1]
Musculoskeletal and connective tissue disorders	145 (19.6) [156]	54 (17.6) [56]	28 (27.0) [32]
Osteoporosis	124 (16.8) [125]	24 (7.8) [24]	17 (16.4) [17]
Arthritis	4 (0.5) [4]	14 (4.6) [14]	4 (3.9) [4]
Bone avascular necrosis	1 (0.1) [1]	7 (2.3) [7]	1 (1.0) [1]
Myalgia	3 (0.4) [3]	3 (1.0) [3]	1 (1.0) [1]
Fibromyalgia	14 (1.9) [14]	3 (1.0) [3]	NR
Joint pain	NR	2 (0.7) [2]	NR
Arthrosis	2 (0.3) [2]	1 (0.3) [1]	NR
Myopathy	NR	1 (0.3) [1]	NR
Neuralgia	NR	1 (0.3) [1]	NR
Decreased bone mass	NR	NR	6 (5.8) [6]
Cramps (IT)	NR	NR	1 (1.0) [1]
Osteoarthritis localized (IT)	NR	NR	1 (1.0) [1]
Muscle cramp (IT)	NR	NR	1 (1.0) [1]
Tendonitis	1 (0.1) [1]	NR	NR
Tenosynovitis	1 (0.1) [1]	NR	NR
Osteomyelitis	1 (0.1) [1]	NR	NR
Fracture	1 (0.1) [1]	NR	NR
Bone disease	1 (0.1) [1]	NR	NR
Deformity	1 (0.1) [1]	NR	NR
Plantar fasciitis	1 (0.1) [1]	NR	NR

Supplementary Table 1. Continued 1

Illness	RA study (n = 738)*	LN study (n = 307)	MG study (n = 104)
Gastrointestinal disorders	55 (7.5) [62]	46 (15.0) [47]	26 (25.0) [29]
Gastritis	15 (2.0) [15]	33 (10.8) [33]	13 (12.5) [13]
Gastroesophageal reflux	13 (1.8) [13]	7 (2.3) [7]	6 (5.8) [6]
Constipation	3 (0.4) [3]	2 (0.7) [2]	1 (1.0) [1]
Esophagitis	2 (0.3) [2]	1 (0.3) [1]	1 (1.0) [1]
Gastric ulcer	14 (1.9) [14]	1 (0.3) [1]	NR
Gingivitis	NR	1 (0.3) [1]	NR
Tooth disorder	NR	1 (0.3) [1]	NR
Hemorrhoids	1 (0.1) [1]	1 (0.3) [1]	NR
Reflux esophagitis (IT)	NR	NR	3 (2.9) [3]
Gastroenteritis	NR	NR	3 (2.9) [3]
Erosive gastritis (IT)	NR	NR	1 (1.0) [1]
Diarrhea	NR	NR	1 (1.0) [1]
Gastrointestinal disorder NOS	5 (0.7) [5]	NR	NR
Xerostomia	2 (0.3) [2]	NR	NR
Peptic ulcer	2 (0.3) [2]	NR	NR
Pancreatitis	2 (0.3) [2]	NR	NR
Ulcerative colitis	1 (0.1) [1]	NR	NR
Duodenitis	1 (0.1) [1]	NR	NR
Gastrointestinal hemorrhage	1 (0.1) [1]	NR	NR
Blood and lymphatic system disorders	24 (3.3) [24]	28 (9.1) [29]	4 (3.9) [4]
Anemia	19 (2.6) [19]	19 (6.2) [19]	3 (2.0) [3]
Hypochromic anemia	4 (0.5) [4]	6 (2.0) [6]	NR
Folic acid deficiency anemia	NR	3 (1.0) [3]	NR
Hemolytic anemia	NR	1 (0.3) [1]	NR
Iron deficiency anemia (IT)	NR	NR	1 (1.0) [1]
Pancytopenia	1 (0.1) [1]	NR	NR
Psychiatric disorders	13 (1.8) [13]	27 (8.8) [30]	12 (11.5) [16]
Insomnia	6 (0.8) [6]	10 (3.3) [10]	5 (4.8) [5]
Depression	5 (0.7) [5]	10 (3.3) [11]	4 (3.9) [4]
Sleep disorders	NR	8 (2.6) [8]	NR
Delirium	NR	1 (0.3) [1]	NR
Agitation	1 (0.1) [1]	NR	6 (5.8) [6]
Panic reaction (IT)	NR	NR	1 (1.0) [1]
Agitation	1 (0.1) [1]	NR	NR
Endocrine disorders	17 (2.3) [18]	22 (7.2) [22]	13 (12.5) [14]
Hypothyroidism	8 (1.1) [8]	17 (5.5) [17]	4 (3.9) [4]
Goiter	NR	2 (0.7) [2]	NR
Increased glucocorticoids	NR	2 (0.7) [2]	NR
Thyroid disorder	NR	1 (0.3) [1]	2 (2.0) [2]
Hyperthyroidism	5 (0.7) [5]	NR	2 (2.0) [2]
Thyroid nodular (IT)	NR	NR	2 (2.0) [2]
Thymus hypertrophy	NR	NR	1 (1.0) [1]
Thyroiditis	3 (0.4) [3]	NR	1 (1.0) [1]
Thyrotoxicosis (IT)	NR	NR	1 (1.0) [1]
Graves' disease (IT)	NR	NR	1 (1.0) [1]
Adrenal insufficiency	2 (0.3) [2]	NR	NR

Supplementary Table 1. Continued 2

Illness	RA study (n = 738)*	LN study (n = 307)	MG study (n = 104)
Renal and urinary disorders	18 (2.4) [18]	18 (5.9) [19]	3 (2.9) [4]
Chronic renal failure	1 (0.1) [1]	4 (1.3) [4]	NR
Albuminuria	2 (0.3) [2]	3 (1.0) [3]	NR
Abnormal renal function	5 (0.7) [5]	2 (0.7) [2]	NR
Toxic nephropathy	NR	1 (0.3) [1]	NR
Cystitis	3 (0.4) [3]	1 (0.3) [1]	NR
Glomerulonephritis	NR	1 (0.3) [1]	NR
Renal calculus	NR	1 (0.3) [1]	NR
Renal infarction	NR	1 (0.3) [1]	NR
Nephritis	NR	1 (0.3) [1]	NR
Nephrosclerosis	NR	1 (0.3) [1]	NR
Urinary tract infection	NR	1 (0.3) [1]	NR
Urinary retention	NR	1 (0.3) [1]	NR
Decreased creatinine clearance	NR	1 (0.3) [1]	NR
Urinary incontinence	2 (0.3) [2]	NR	2 (1.9) [2]
Bladder irritability (IT)	NR	NR	1 (1.0) [1]
Neurogenic bladder (IT)	NR	NR	1 (1.0) [1]
Hematuria	2 (0.3) [2]	NR	NR
Pyelonephritis	1 (0.1) [1]	NR	NR
Nephrosis	1 (0.1) [1]	NR	NR
Urinary stasis	1 (0.1) [1]	NR	NR
Vascular disorders	9 (1.2) [9]	18 (5.9) [18]	6 (5.8) [6]
Peripheral vascular ischemia	3 (0.4) [3]	8 (2.6) [8]	NR
Deep thrombophlebitis	2 (0.3) [2]	4 (1.3) [4]	NR
Cerebral infarction	3 (0.4) [3]	2 (0.7) [2]	2 (1.9) [2]
Vasculitis	NR	2 (0.7) [2]	NR
Arteriosclerosis	1 (0.1) [1]	1 (0.3) [1]	NR
Atherosclerosis	NR	1 (0.3) [1]	NR
Cerebral arteriosclerosis (IT)	NR	NR	3 (2.9) [3]
Cerebral vascular lesion (IT)	NR	NR	1 (1.0) [1]
Nervous system disorders	16 (2.2) [18]	14 (4.6) [15]	11 (10.6) [16]
Headache	4 (0.5) [4]	3 (1.0) [3]	NR
Seizures	NR	3 (1.0) [3]	NR
Neuralgia	1 (0.1) [1]	3 (1.0) [3]	NR
Spinal stenosis	4 (0.5) [4]	2 (0.7) [2]	1 (1.0) [1]
Encephalopathy	NR	1 (0.3) [1]	NR
Neuritis	NR	1 (0.3) [1]	NR
Myelitis	NR	1 (0.3) [1]	1 (1.0) [1]
Dementia	2 (0.3) [2]	1 (0.3) [1]	2 (1.9) [2]
Dizziness	2 (0.3) [2]	NR	3 (2.9) [3]
Migraine	NR	NR	2 (1.9) [2]
Epilepsy (IT)	NR	NR	1 (1.0) [1]
MS-like syndrome	NR	NR	1 (1.0) [1]
Neurologic disorder NOS	NR	NR	1 (1.0) [1]
Gait disturbance (IT)	NR	NR	1 (1.0) [1]
Ptosis	NR	NR	1 (1.0) [1]
Parkinsonism (IT)	NR	NR	1 (1.0) [1]
Convulsions	2 (0.3) [2]	NR	NR
Myasthenia gravis-like syndrome	1 (0.1) [1]	NR	NR
Extrapyramidal disorder	1 (0.1) [1]	NR	NR
Complex regional pain syndrome	1 (0.1) [1]	NR	NR

Supplementary Table 1. Continued 3

Illness	RA study (n = 738)*	LN study (n = 307)	MG study (n = 104)
Skin and subcutaneous tissue disorders	10 (1.4) [10]	12 (3.9) [12]	1 (1.0) [1]
Hyperkeratosis	NR	2 (0.7) [2]	NR
Pruritus	NR	2 (0.7) [2]	NR
Dermatitis	1 (0.1) [1]	2 (0.7) [2]	NR
Urticaria	1 (0.1) [1]	1 (0.3) [1]	NR
Rash	NR	1 (0.3) [1]	NR
Verruca	NR	1 (0.3) [1]	NR
Papilloma	NR	1 (0.3) [1]	NR
Seborrhea	NR	1 (0.3) [1]	NR
Erythematous rash	NR	1 (0.3) [1]	NR
Alopecia	NR	NR	1 (1.0) [1]
Psoriasis	2 (0.3) [2]	NR	NR
Dermatitis fungal	2 (0.3) [2]	NR	NR
Pyoderma gangrenosum	1 (0.1) [1]	NR	NR
Onychomycosis	1 (0.1) [1]	NR	NR
Eczema	1 (0.1) [1]	NR	NR
Sclerema	1 (0.1) [1]	NR	NR
Respiratory, thoracic and mediastinal disorders	40 (5.4) [40]	11 (3.6) [11]	1 (1.0) [1]
Asthma	4 (0.5) [4]	3 (1.0) [3]	1 (1.0) [1]
Rhinitis	2 (0.3) [2]	2 (0.7) [2]	1 (1.0) [1]
Pulmonary infiltrates	2 (0.3) [2]	2 (0.7) [2]	NR
Bronchitis	1 (0.1) [1]	1 (0.3) [1]	1 (1.0) [1]
Paranasal sinusitis	1 (0.1) [1]	1 (0.3) [1]	1 (1.0) [1]
Upper respiratory tract infections	2 (0.3) [2]	1 (0.3) [1]	NR
Lung disease	10 (1.4) [10]	1 (0.3) [1]	1 (1.0) [1]
Dyspnea	NR	NR	1 (1.0) [1]
Pulmonary fibrosis	4 (0.5) [4]	NR	NR
Bronchiectasis	3 (0.4) [3]	NR	NR
Pulmonary emphysema	3 (0.4) [3]	NR	NR
Pneumonia	3 (0.4) [3]	NR	NR
Interstitial pneumonia	2 (0.3) [2]	NR	NR
Pneumothorax	1 (0.1) [1]	NR	NR
Epistaxis	1 (0.1) [1]	NR	NR
Laryngitis	1 (0.1) [1]	NR	NR
General disorders and administration site conditions	10 (1.4) [11]	9 (2.9) [10]	3 (2.9) [3]
Tuberculosis infection	6 (0.8) [6]	5 (1.6) [5]	NR
Leg pain	NR	1 (0.3) [1]	NR
Back pain	1 (0.1) [1]	1 (0.3) [1]	1 (1.0) [1]
Oedema	NR	1 (0.3) [1]	NR
Allergy	NR	1 (0.3) [1]	NR
Activated inflammatory pain	NR	1 (0.3) [1]	NR
Chest discomfort (IT)	NR	NR	1 (1.0) [1]
Hernia NOS	NR	NR	1 (1.0) [1]
Carpel tunnel syndrome	4 (0.5) [4]	NR	NR
Infections and infestations	16 (2.2) [16]	8 (2.6) [9]	1 (1.0) [1]
Sjögren's syndrome	10 (1.4) [10]	4 (1.3) [4]	NR
Herpes zoster	3 (0.4) [3]	2 (0.7) [2]	NR
Infection	NR	1 (0.3) [1]	NR
Mycotic infection	NR	1 (0.3) [1]	NR
Moniliasis	NR	1 (0.3) [1]	NR
Perianal abscess (IT)	NR	NR	1 (1.0) [1]
Syphilis	1 (0.1) [1]	NR	NR
Polio	1 (0.1) [1]	NR	NR
Tympanitis	1 (0.1) [1]	NR	NR

Supplementary Table 1. Continued 4

Illness	RA study (n = 738)*	LN study (n = 307)	MG study (n = 104)
Hepatobiliary disorders	32 (4.3) [34]	6 (2.0) [6]	2 (1.9) [2]
Increased SGPT	NR	1 (0.3) [1]	NR
Cirrhosis of the liver	2 (0.3) [2]	1 (0.3) [1]	NR
Cholelithiasis	1 (0.1) [1]	1 (0.3) [1]	NR
Viral hepatitis	13 (1.8) [14]	1 (0.3) [1]	NR
Fatty liver	3 (0.4) [3]	1 (0.3) [1]	NR
Chronic active hepatitis	NR	1 (0.3) [1]	NR
Hepatitis C (IT)	NR	NR	2 (1.9) [2]
Abnormal liver function	12 (1.6) [12]	NR	NR
Hepatitis	1 (0.1) [1]	NR	NR
Jaundice	1 (0.1) [1]	NR	NR
Reproductive system and breast disorders (female)	12 (1.6) [12]	6 (2.0) [6]	2 (1.9) [2]
Endometriosis	1 (0.1) [1]	2 (0.7) [2]	NR
Menorrhagia	NR	1 (0.3) [1]	NR
Cervical dysplasia	NR	1 (0.3) [1]	NR
Uterine hemorrhage	NR	1 (0.3) [1]	NR
Vaginitis	NR	1 (0.3) [1]	NR
Salpingitis	NR	NR	1 (1.0) [1]
Female infertility	NR	NR	1 (1.0) [1]
Uteritis	5 (0.7) [5]	NR	NR
Cervicitis	3 (0.4) [3]	NR	NR
Endometrial hypertrophy	1 (0.1) [1]	NR	NR
Vaginal bleeding	1 (0.1) [1]	NR	NR
Menopausal symptoms	1 (0.1) [1]	NR	NR
Eye disorders	15 (2.0) [16]	5 (1.6) [5]	9 (8.7) [17]
Retinal disorder	2 (0.3) [2]	2 (0.7) [2]	1 (1.0) [1]
Glaucoma	3 (0.4) [3]	1 (0.3) [1]	2 (1.9) [2]
Retinal detachment	1 (0.1) [1]	1 (0.3) [1]	NR
Cataract	4 (0.5) [4]	1 (0.3) [1]	1 (1.0) [1]
Eye abnormality	NR	NR	4 (3.9) [4]
Diplopia	NR	NR	3 (2.9) [3]
Keratitis	NR	NR	1 (1.0) [1]
Diabetic retinopathy (IT)	NR	NR	1 (1.0) [1]
Retinopathy (IT)	NR	NR	1 (1.0) [1]
Strabismus	NR	NR	1 (1.0) [1]
Uveitis	1 (0.1) [1]	NR	1 (1.0) [1]
Macula lutea degeneration	NR	NR	1 (1.0) [1]
Conjunctivitis	3 (0.4) [3]	NR	NR
Scleritis	1 (0.1) [1]	NR	NR
Blepharitis	1 (0.1) [1]	NR	NR
Cardiac disorders	5 (0.7) [5]	3 (1.0) [3]	1 (1.0) [1]
Angina pectoris	2 (0.3) [2]	3 (1.0) [3]	NR
Cardiomyopathy	NR	NR	1 (1.0) [1]
Coronary artery disease	1 (0.1) [1]	NR	NR
Mitral insufficiency	1 (0.1) [1]	NR	NR
Mitral valve stenosis	1 (0.1) [1]	NR	NR
Reproductive disorders (male)	5 (0.7) [5]	NR	2 (1.9) [2]
Inguinal hernia	NR	NR	1 (1.0) [1]
Prostatic hyperplasia	5 (0.7) [5]	NR	1 (1.0) [1]

Supplementary Table 1. Continued 5

Illness	RA study (n = 738)*	LN study (n = 307)	MG study (n = 104)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	27 (3.7) [27]	2 (0.7) [2]	10 (9.6) [12]
Multiple myeloma	NR	1 (0.3) [1]	NR
Malignant neoplasm of female breast	1 (0.1) [1]	1 (0.3) [1]	1 (1.0) [1]
Malignant thymoma	NR	NR	5 (4.8) [5]
Thymoma (IT)	NR	NR	3 (2.9) [3]
Ovarian cyst	1 (0.1) [1]	NR	1 (1.0) [1]
Female breast neoplasm	NR	NR	1 (1.0) [1]
Uterine fibroid	4 (0.5) [4]	NR	1 (1.0) [1]
Ovarian carcinoma	4 (0.5) [4]	NR	NR
Gastric carcinoma	3 (0.4) [3]	NR	NR
Lung carcinoma	3 (0.4) [3]	NR	NR
Goiter	2 (0.3) [2]	NR	NR
Malignant neoplasm of goiter	2 (0.3) [2]	NR	NR
Teratoma	1 (0.1) [1]	NR	NR
Adrenal adenoma	1 (0.1) [1]	NR	NR
Malignant neoplasm of endometrium	1 (0.1) [1]	NR	NR
Breast fibroadenosis	1 (0.1) [1]	NR	NR
Squamous cell carcinoma	1 (0.1) [1]	NR	NR
Thrombocytosis	1 (0.1) [1]	NR	NR
Hemangioma acquired	1 (0.1) [1]	NR	NR
Platelet, bleeding & clotting disorders	2 (0.3) [2]	2 (0.7) [2]	NR
Thrombocytopenia	1 (0.1) [1]	1 (0.3) [1]	NR
Thrombosis	NR	1 (0.3) [1]	NR
Thromboembolism	1 (0.1) [1]	NR	NR
Heart rate and rhythm disorders	2 (0.3) [2]	NR	1 (1.0) [1]
Atrial fibrillation	NR	NR	1 (1.0) [1]
Arrhythmia	2 (0.3) [2]	NR	NR
Application site disorders	NR	NR	1 (1.0) [1]
Neovascularization	NR	NR	1 (1.0) [1]
Secondary terms	11 (1.5) [12]	1 (0.3) [1]	1 (1.0) [1]
Molluscum contagiosum	NR	1 (0.3) [1]	NR
Protrusion of intervertebral disc (IT)	NR	NR	1 (1.0) [1]
Intervertebral disc disorder	4 (0.5) [5]	NR	NR
Surgical intervention	4 (0.5) [4]	NR	NR
Arthroplasty	1 (0.1) [1]	NR	NR
Scoliosis	1 (0.1) [1]	NR	NR
Pemphigus	1 (0.1) [1]	NR	NR
White cell and RES disorders	1 (0.1) [1]	1 (0.3) [1]	NR
Lymphoedema	NR	1 (0.3) [1]	NR
Lymphadenopathy	1 (0.1) [1]	NR	NR
Ear and labyrinth disorders	1 (0.1) [1]	NR	NR
Tinnitus	1 (0.1) [1]	NR	NR

Data expressed as number of patients, number (%) [number of cases]. IT: included term, LN: lupus nephritis, MG: myasthenia gravis, NOS: nitrous oxide, NR: not reported, RA: rheumatoid arthritis, SGPT: serum glutamic pyruvic transaminase. *Current illness was unknown for two patients.

Supplementary Table 2. Types of concomitant medications received by patients included in the RA study

Medication	RA study (n = 740)
Central nervous system	610 (82.4)
Nonsteroidal anti-inflammatory agents	573 (77.4)
Non-narcotic analgesics and antifebriles	117 (15.8)
Antidepressants	29 (3.9)
Antianxiety agents	17 (2.3)
Therapeutic agents for neuropathic pain	14 (1.9)
Hypnotics, sedatives	6 (0.8)
Improvement agent for brain function	1 (0.1)
Narcotic analgesics	1 (0.1)
Antiepileptic agents	1 (0.1)
Antiparkinsonians	1 (0.1)
Hormones	559 (75.5)
Corticosteroid hormones	556 (75.1)
Estrogens/progesterones/relevant agents	4 (0.5)
Antineoplastics	548 (74.1)
Cytotoxic anticancer agents	548 (74.1)
Vitamins and minerals	
Vitamin agents for anemia/pregnant women	395 (53.4)
Calcium agent containing vitamins	142 (19.2)
Vitamins A, D, E	11 (1.5)
Mineral agents with or without vitamins	3 (0.4)
Vitamin C	2 (0.3)
Gastrointestinal and liver and biliary system	447 (60.4)
Antacid/antireflux/antiulcer agents	434 (58.6)
Gastrointestinal modifiers/antiflatulents/anti-inflammatory agents	68 (9.2)
Choleretics/gallstone dissolvents/liver protective agents	8 (1.1)
Digestive agents	6 (0.8)
Antispasmodics	5 (0.7)
Cathartics/drastic cathartics	4 (0.5)
Antidiarrhea agents	2 (0.3)
Musculoskeletal system	265 (35.8)
Antirheumatics	239 (32.3)
Muscle relaxants	24 (3.2)
Hyperuricemia/gout medicines	5 (0.7)
Other medicines for musculoskeletal system	3 (0.4)
Cardiovascular system and hematopoietic	163 (22.0)
Calcium antagonists	78 (10.5)
Other antihypertensive agents	39 (5.3)
Angiotensin II antagonists	35 (4.7)
Beta blockers	26 (3.5)
Anticoagulant/antiplatelet/fibrinolytic agents (thrombolytic agents)	21 (2.8)
Antihyperlipidemic agents	19 (2.6)
Diuretics	11 (1.5)
Peripheral vasodilators/brain function improving agents	10 (1.4)
Medicines for phlebitis and varix	4 (0.5)
ACE inhibitors	3 (0.4)
Cardiac drugs	2 (0.3)
Medicines for angina pectoris	1 (0.1)

Supplementary Table 2. Continued

Medication	RA study (n = 740)
Endocrine system and metabolic system	122 (16.5)
Bone metabolism agents	98 (13.2)
Oral antidiabetics	16 (2.2)
Agents for hyperthyroidism	12 (1.6)
Other metabolism agents	1 (0.1)
Anti-obesity agents	1 (0.1)
Allergies and immune system	21 (2.8)
Immunosuppressants	13 (1.8)
Antihistaminic/antiallergic agents	8 (1.1)
Respiratory system	19 (2.6)
Cough and cold medicines	13 (1.8)
Medicines for asthma and COPD	7 (0.9)
Nasal decongestants/other nasal agents	1 (0.1)
Treatments for systemic infection	14 (1.9)
Antiviral agents	4 (0.5)
Antituberculous agent	3 (0.4)
Cephalosporins	3 (0.4)
Penicillins	3 (0.4)
Complex antimicrobial agents	2 (0.3)
Quinolones	1 (0.1)
Antifungals	1 (0.1)
Medicines for ear, mouth and throat	7 (0.9)
Medicines for mouth and throat	7 (0.9)
Urogenital system	6 (0.8)
Therapeutic agents for bladder and prostatic diseases	5 (0.7)
Vaginopathy medicines	1 (0.1)
Local and general anesthetics	2 (0.3)
Local and general anesthetics	2 (0.3)
Nutritional supplements	2 (0.3)
Appetite stimulant	2 (0.3)
Intravenous and other sterilants	1 (0.1)
Intravenous and other sterilants	1 (0.1)
Dermatologic agents	1 (0.1)
Topical antiphlogistics	1 (0.1)
Other dermatologic agents	1 (0.1)

Values are presented as number (%). ACE: angiotensin converting enzyme, COPD: chronic obstructive pulmonary disease, RA: rheumatoid arthritis.

Supplementary Table 3. Adverse events and adverse drug reactions reported in patients ≥ 65 years of age in the RA study

Event	No. patients (%)	
	AEs	ADRs
Blood and lymphatic system disorders		
Anemia	1 (0.63)	1 (0.63)
Panhematopenia	1 (0.63)	1 (0.63)
Cardiac disorders		
Hypertension	2 (1.25)	2 (1.25)
Eye disorders		
Dysopia	1 (0.63)	0
Gastrointestinal disorders		
Abdominal pain	2 (1.25)	2 (1.25)
Hiccups	1 (0.63)	1 (0.63)
Nausea	2 (1.25)	2 (1.25)
Constipation	1 (0.63)	1 (0.63)
Unspecified GI disorder	1 (0.63)	1 (0.63)
Indigestion	1 (0.63)	1 (0.63)
Gastritis	1 (0.63)	0
General disorders and administration site conditions		
ESR increased	2 (1.25)	1 (0.63)
Asthenia	1 (0.63)	1 (0.63)
Edema	1 (0.63)	1 (0.63)
Hepatobiliary disorders		
SGPT increased	1 (0.63)	1 (0.63)
SGOT increased	1 (0.63)	1 (0.63)
Investigations		
Urine creatinine increased	1 (0.63)	0
CRP increased	1 (0.63)	1 (0.63)
Metabolism and nutrition disorders		
Loss of appetite	1 (0.63)	0
Musculoskeletal and connective tissue disorders		
Worsening RA	1 (0.63)	1 (0.63)
Infectious arthritis	1 (0.63)	1 (0.63)
Osteoporosis	1 (0.63)	1 (0.63)
Nervous system disorders		
Headache	1 (0.63)	0
Dizziness	1 (0.63)	0
Respiratory, thoracic and mediastinal disorders		
Cough	1 (0.63)	1 (0.63)
Pharyngitis	1 (0.63)	0
Pneumonia	1 (0.63)	0

ADR: adverse drug reaction, AE: adverse event, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, NR: not reported, RA: rheumatoid arthritis, SGOT: serum glutamic-oxaloacetic transaminase, SGPT: serum glutamic-pyruvic transaminase.

Supplementary Table 4. Univariable analysis of the association of patients' demographic and medical characteristics with the incidence of AEs (RA study)

Factor	Patients, n	Patients with AE, n (%)	95% CI	p-value	
Demographics					
Sex	Male	131	13 (9.9)	5.39 ~ 16.37	0.2924*
	Female	609	81 (13.3)	10.70 ~ 16.26	
	Total	740	94 (12.7)		
Age (yr)	<10	1	0	-	0.4820*
	10 to <20	0	0	-	
	20 to <30	30	3 (10.0)	2.11 ~ 26.53	
	30 to <40	87	7 (8.0)	3.30 ~ 15.88	
	40 to <50	155	21 (13.5)	8.59 ~ 19.96	
	50 to <60	195	21 (10.8)	6.79 ~ 15.99	
	60 to <70	178	24 (13.5)	8.83 ~ 19.39	
	70 to <80	85	16 (18.8)	11.16 ~ 28.76	
	≥80	9	2 (22.2)	2.81 ~ 60.01	
	Total	740	94 (12.7)		
Currently pregnant	Yes	0	0	-	-
	No	609	81 (13.3)	10.70 ~ 16.26	
	Total	609	81 (13.3)		
Patient status	Inpatient	5	1 (20.0)	0.51 ~ 71.64	0.5812 [†]
	Outpatient	697	88 (12.6)	10.25 ~ 15.32	
	Inpatient↔outpatient	38	5 (13.2)	4.41 ~ 28.09	
	Total	740	94 (12.7)		
Medical background					
Complication/comorbidity	Yes	409	66 (16.1)	12.71 ~ 20.07	0.0020 [†]
	No	329	28 (8.51)	5.73 ~ 12.07	
	Total	738	94 (12.7)		
Hepatic impairment	Yes	30	4 (13.3)	3.76 ~ 30.72	0.7848 [†]
	No	710	90 (12.7)	10.32 ~ 15.35	
	Total	740	94 (12.7)		
Renal impairment	Yes	10	5 (50.0)	18.71 ~ 81.29	0.0045 [†]
	No	730	89 (12.2)	9.91 ~ 14.79	
	Total	740	94 (12.7)		
Severity of RA	Mild	116	13 (11.2)	6.10 ~ 18.40	0.6864*
	Moderate	539	68 (12.6)	9.93 ~ 15.72	
	Severe	85	13 (15.3)	8.40 ~ 24.73	
	Total	740	94 (12.7)		
Any antirheumatic or biologic withdrawn before study drug administration (within 4 weeks)	Yes	327	37 (11.3)	8.09 ~ 15.26	0.3131*
	No	413	57 (13.8)	10.62 ~ 17.51	
	Total	740	94 (12.7)		
Concomitant medication	Yes	738	94 (12.7)	10.42 ~ 15.36	1.0000 [†]
	No	2	0	-	
	Total	740	94 (12.7)		
Duration of illness	<12 months	55	10 (18.2)	9.08 ~ 30.90	0.3302*
	12 to <60 months	289	31 (10.7)	7.41 ~ 14.88	
	60 to <120 months	121	19 (15.7)	9.73 ~ 23.43	
	≥120 months	140	18 (12.9)	7.80 ~ 19.56	
	Total	605	78 (12.9)		

AE: adverse event, CI: confidence interval, RA: rheumatoid arthritis. *Pearson's chi-squared test. [†]Fisher's exact test.

Supplementary Table 5. Types of concomitant medications received by patients included in the LN study

Medication	LN study (n = 307)
Hormones	296 (96.4)
Corticosteroid hormones	296 (96.4)
Androgens/relevant agents	4 (1.3)
Estrogens/progesterones/relevant agents	2 (0.7)
Cardiovascular system and hematopoietic	255 (83.1)
Angiotensin II antagonists	119 (38.8)
Antihyperlipidemic agents	93 (30.3)
Calcium antagonists	69 (22.5)
Anticoagulant/antiplatelet/fibrinolytic agents (thrombolytic agents)	55 (17.9)
ACE inhibitors	54 (17.6)
Diuretics	50 (16.3)
Other antihypertensive agents	28 (9.1)
Beta blockers	26 (8.5)
Peripheral vasodilators/brain function improving agents	14 (4.6)
Medicines for phlebitis and varix	9 (2.9)
Medicines for angina pectoris	3 (1.0)
Gastrointestinal & liver and biliary system	182 (59.3)
Antacid/antireflux/antiulcer agents	171 (55.7)
Gastrointestinal modifiers/antiflatulents/anti-inflammatory agents	23 (7.5)
Choleretics/gallstone dissolvents/liver protective agents	7 (2.3)
Antidiarrhea agents	7 (2.3)
Cathartics/drastic cathartics	7 (2.3)
Digestive agents	2 (0.7)
Antispasmodics	2 (0.7)
Antiemetic agents	1 (0.3)
Musculoskeletal system	181 (59.0)
Antirheumatics	174 (56.7)
Hyperuricemia/gout medicines	6 (2.0)
Other medicines for musculoskeletal system	6 (2.0)
Muscle relaxants	5 (1.6)
Vitamins and minerals	139 (45.3)
Calcium agent containing vitamins	99 (32.3)
Vitamin agents for anemia/pregnant women	38 (12.4)
Vitamins A, D, E	16 (5.2)
B-vitamin (containing vitamin C)	7 (2.3)
Mineral agents with or without vitamins	7 (2.3)
Vitamin C	1 (0.3)
Central nervous system	100 (32.6)
Non-narcotic analgesics and antifebriles	40 (13.0)
Nonsteroidal anti-inflammatory agents	35 (11.4)
Antianxiety agents	20 (6.5)
Antidepressants	17 (5.5)
Hypnotics, sedatives	14 (4.6)
Therapeutic agents for neuropathic pain	12 (3.9)
Antiepileptic agents	6 (2.0)
Narcotic analgesics	5 (1.6)
Antipsychotics	3 (1.0)
Antihemichranins	1 (0.3)
Antiparkinsonians	1 (0.3)
Allergies and immune system	76 (24.8)
Immunosuppressants	55 (17.9)
Antihistaminic/antiallergic agents	22 (7.2)
Vaccines/antiserum & immunizing agents	4 (1.3)

Supplementary Table 5. Continued

Medication	LN study (n = 307)
Endocrine system and metabolic system	56 (18.2)
Bone metabolism agents	33 (10.8)
Agents for hyperthyroidism	17 (5.5)
Antidiabetics	8 (2.6)
Agents for hypothyroidism	1 (0.3)
Treatments for systemic infection	30 (9.8)
Complex antimicrobial agents	10 (3.3)
Quinolones	8 (2.6)
Tuberculostatics	8 (2.6)
Cephalosporins	6 (2.0)
Penicillins	5 (1.6)
Antifungals	4 (1.0)
Tetracyclines	3 (1.0)
Antiviral agents	3 (1.0)
Other antibiotics	1 (0.3)
Macrolides	1 (0.3)
Antiprotozoals	1 (0.3)
Respiratory system	24 (7.8)
Cough and cold medicines	18 (5.9)
Nasal decongestants/other nasal agents	7 (2.3)
Medicines for asthma and chronic obstructive pulmonary disease	5 (1.6)
Antineoplastics	12 (3.9)
Cytotoxic anticancer agents	12 (3.9)
Supportive therapies	2 (0.7)
Dermatologic agents	7 (2.3)
Topical corticosteroids	5 (1.6)
Topical antifungals and antiparasitics	2 (0.7)
Topical antiphlogistics	1 (0.3)
Medicines for mouth and throat	4 (1.3)
Eye	4 (1.3)
Glaucoma medicine	2 (0.7)
Ocular lubricants	2 (0.7)
Urogenital system	4 (1.3)
Therapeutic agents for bladder and prostatic diseases	3 (1.0)
Other medicines for urogenital system	1 (0.3)
Vaginopathy medicines	1 (0.3)
Nutritional supplements	4 (1.3)
Electrolyte agents	4 (1.3)
Parenteral nutritional supplements	1 (0.3)
Antidotes, therapeutic agents for substance dependence	3 (1.0)
Intravenous and other sterilants	2 (0.7)
Other agents	1 (0.3)

Values are presented as number (%). ACE: angiotensin-converting enzyme, LN: lupus nephritis.

Supplementary Table 6. Univariable analysis of the association of patients' demographic and medical characteristics with the incidence of AEs (LN study)

Factor		Patients, n	Patients with AE, n (%)	95% CI	p-value
Demographics					
Sex	Male	34	9 (26.5)	12.88 ~ 44.36	0.3920*
	Female	273	55 (20.1)	15.55 ~ 25.40	
	Total	307	64 (20.8)		
Age (yr)	< 20	15	4 (26.7)	7.79 ~ 55.10	0.8637 [†]
	20 to < 40	169	34 (20.1)	14.35 ~ 26.96	
	40 to < 60	110	24 (21.8)	14.51 ~ 30.70	
	≥ 60	13	2 (15.4)	1.92 ~ 45.45	
	Total	307	64 (20.8)		
Pediatric patient (< 19 yr)	Yes	10	4 (40.0)	12.16 ~ 73.76	0.2256 [†]
	No	297	60 (20.2)	15.78 ~ 25.22	
	Total	307	64 (20.8)		
Elderly patient (≥ 65 yr)	Yes	4	0	-	0.5835 [†]
	No	303	64 (21.1)	16.66 ~ 26.16	
	Total	307	64 (20.8)		
Patient status	Inpatient	5	0	-	0.3574 [†]
	Outpatient	262	53 (20.2)	15.54 ~ 25.61	
	Inpatient outpatient	40	11 (27.5)	14.60 ~ 43.89	
	Total	307	64 (20.8)		
Medical background					
Current illness	Yes	307	64 (20.8)	16.44 ~ 25.83	-
	No	0	0		
	Unknown	0	0		
	Total	307	64 (20.8)		
Previous illness	Yes	90	26 (28.9)	19.82 ~ 39.40	0.0800*
	No	202	35 (17.3)	12.38 ~ 23.26	
	Unknown	15	3 (20.0)	4.33 ~ 48.0	
	Total	307	64 (20.8)		
Hepatic impairment	Yes	11	5 (45.5)	16.75 ~ 76.62	0.0557 [†]
	No	296	59 (19.9)	15.53 ~ 24.94	
	Unknown	0	0		
	Total	307	64 (20.8)		
Renal impairment	Yes	108	30 (27.8)	19.59 ~ 37.22	0.0276*
	No	199	34 (17.1)	12.13 ~ 23.05	
	Unknown	0	0	-	
	Total	307	64 (20.8)		
Cardiac impairment	Yes	10	4 (40.0)	12.16 ~ 73.76	0.3874 [†]
	No	296	60 (20.3)	15.84 ~ 25.31	
	Unknown	1	0	-	
	Total	307	64 (20.8)		
Severity of LN	Mild	64	9 (14.1)	6.64 ~ 25.02	0.0624*
	Moderate	189	38 (20.1)	14.64 ~ 26.54	
	Severe	54	17 (31.5)	19.52 ~ 45.55	
	Total	307	64 (20.8)		

Supplementary Table 6. Continued

Factor		Patients, n	Patients with AE, n (%)	95% CI	p-value
History of treatment with immunosuppressants	Yes	198	38 (19.2)	13.95 ~ 25.38	0.4094 [†]
	No	106	26 (24.5)	16.69 ~ 33.84	
	Unknown	3	0		
	Total	307	64 (20.8)		
Concomitant medication	Yes	307	64 (20.8)	16.44 ~ 25.83	-
	No	0	0		
	Total	307	64 (20.8)		
Reason for additional prescription of the investigational product	Insufficient therapeutic effect of steroids	285	61 (21.4)	16.79 ~ 26.63	0.5859 [†]
	Side effect of steroids	22	3 (13.6)	2.91 ~ 34.91	
	Other	0	0	-	
	Total	307	64 (20.8)		

AE: adverse event, CI: confidence interval, LN: lupus nephritis. *Pearson's chi-squared test. [†]Fisher's exact test.

Supplementary Table 7. Types of concomitant medications received by patients included in the MG study

Medication	MG study (n = 104)
Systemic hormonal preparations, excl. sex hormones and insulins	85 (81.7)
Corticosteroids for systemic use	84 (80.8)
Thyroid therapy	4 (3.9)
Pituitary and hypothalamic hormones and analogues	1 (1.0)
Nervous system	63 (60.6)
Other nervous system drugs	58 (55.8)
Psychoanaleptics	11 (10.6)
Psycholeptics	8 (7.7)
Analgesics	6 (5.8)
Antiepileptics	6 (5.8)
Anesthetics	2 (1.9)
Alimentary tract and metabolism	51 (49.0)
Drugs for acid related disorders	27 (26.0)
Mineral supplements	23 (22.1)
Vitamins	12 (11.5)
Drugs used in diabetes	10 (9.6)
Drugs for functional gastrointestinal disorders	5 (4.8)
Antidiarrheals, intestinal anti-inflammatory/anti-infective agents	3 (2.9)
Other alimentary tract and metabolism products	2 (1.9)
Antiemetics and antinauseants	1 (1.0)
Drugs for constipation	1 (1.0)
Cardiovascular system	30 (28.9)
Lipid modifying agents	20 (19.2)
Agents acting on the renin-angiotensin system	7 (6.7)
Calcium channel blockers	6 (5.8)
Cardiac therapy	4 (3.9)
Beta blocking agents	3 (2.9)
Vasoprotectives	3 (2.9)
Peripheral vasodilators	2 (1.9)
Diuretics	1 (1.0)
Antineoplastic and immunomodulating agents	15 (14.4)
Immunosuppressants	13 (12.5)
Endocrine therapy	1 (1.0)
Immunostimulants	1 (1.0)
Musculoskeletal system	15 (14.4)
Anti-inflammatory and antirheumatic products	7 (6.7)
Drugs for treatment of bone diseases	5 (4.8)
Muscle relaxants	4 (3.9)
Blood and blood forming organs	10 (9.6)
Antithrombotic agents	7 (6.7)
Antianemic preparations	3 (2.9)
Blood substitutes and perfusion solutions	1 (1.0)
Anti-infectives for systemic use	7 (6.7)
Antibacterials for systemic use	6 (5.8)
Antivirals for systemic use	2 (1.9)
Immune sera and immunoglobulins	1 (1.0)
Sensory organs	5 (4.8)
Ophthalmologicals	5 (4.8)
Dermatologicals	3 (2.9)
Antibiotics and chemotherapeutics for dermatological use	2 (1.9)
Other dermatological preparations	1 (1.0)

Supplementary Table 7. Continued

Medication	MG study (n = 104)
Genito urinary system and sex hormones	3 (2.9)
Urologicals	3 (2.9)
Respiratory system	1 (1.0)
Cough and cold preparations	1 (1.0)
Unknown	1 (1.0)
Unknown	1 (1.0)
Various	1 (1.0)
All other therapeutic products	1 (1.0)

Values are presented as number (%). MG: myasthenia gravis.

Supplementary Table 8. Univariable analysis of the association of patients' demographic and medical characteristics with the incidence of AEs (MG study)

Factor		Patients, n	Patients with AE, n (%)	95% CI	p-value
Demographics					
Sex	Male	44	8 (18.2)	8.19 ~ 32.71	0.0264*
	Female	60	23 (38.3)	26.07 ~ 51.79	
	Total	104	31 (29.8)		
Age (yr)	≥ 19 to < 30	3	0	0.00 ~ 70.76	0.1760 [†]
	≥ 30 to < 40	12	4 (33.3)	9.92 ~ 65.11	
	≥ 40 to < 50	26	10 (38.5)	20.23 ~ 59.43	
	≥ 50 to < 60	28	8 (28.6)	13.22 ~ 48.67	
	≥ 60 to < 70	23	3 (13.0)	2.78 ~ 33.59	
	≥ 70	12	6 (50.0)	21.09 ~ 78.91	
Elderly age (yr)	Total	104	31 (29.8)		0.4490*
	≥ 65	22	8 (36.4)	17.20 ~ 59.34	
	< 65	82	23 (28.0)	18.68 ~ 39.06	
Total	Total	104	31 (29.8)		
	Medical background				
	Duration of MG (yr)	< Median	63	18 (28.6)	17.89 ~ 41.35
≥ Median		41	13 (31.7)	18.08 ~ 48.09	
Total		104	31 (29.8)		
MGFA clinical classification	1	20	5 (25.0)	8.66 ~ 49.10	0.0291 [†]
	2a	31	10 (32.3)	16.68 ~ 51.37	
	2b	20	5 (25.0)	8.66 ~ 49.10	
	3a	11	4 (36.4)	10.93 ~ 69.21	
	3b	8	6 (75.0)	34.91 ~ 96.81	
	4a	0	0	-	
	4b	1	0	0.00 ~ 97.50	
	5	2	1 (50.0)	1.26 ~ 98.74	
	Unknown	11	0	0.00 ~ 28.49	
	Total	104	31 (29.8)		
Acetylcholine receptor antibody	Yes	82	26 (31.7)	21.87 ~ 42.92	0.8954 [†]
	No	20	5 (25.0)	8.66 ~ 49.10	
	Unknown	2	0	0.00 ~ 84.19	
Total	Total	104	31 (29.8)		
	Previous illness				
	Yes	28	14 (50.0)	30.65 ~ 69.35	0.0063*
No	76	17 (22.4)	13.60 ~ 33.38		
Total	104	31 (29.8)			
Current illness	Yes	82	29 (35.4)	25.12 ~ 46.70	0.0167*
	No	22	2 (9.1)	1.12 ~ 29.16	
	Total	104	31 (29.8)		
Hepatic impairment	Yes	2	0	0.00 ~ 84.19	1.0000 [†]
	No	102	31 (30.4)	21.67 ~ 40.29	
	Total	104	31 (29.8)		
Renal impairment	Yes	0	0	-	-
	No	104	31 (29.8)	21.23 ~ 39.57	
	Total	104	31 (29.8)		

Supplementary Table 8. Continued

	Factor	Patients, n	Patients with AE, n (%)	95% CI	p-value
Thymectomy	Yes (before administration of investigational product)	41	16 (39.0)	24.20 ~ 55.50	0.2233 [†]
	Yes (after administration of investigational product)	0	0	-	
	No	59	14 (23.7)	13.62 ~ 36.59	
	Unknown	4	1 (25.0)	0.63 ~ 80.59	
	Total	104	31 (29.8)		
Concomitant medication	Yes	101	31 (30.7)	21.90 ~ 40.66	0.5526 [†]
	No	3	0	0.00 ~ 70.76	
	Total	104	31 (29.8)		

AE: adverse event, CI: confidence interval, MG: myasthenia gravis, MGFA: Myasthenia Gravis Foundation of America. *Pearson’s chi-squared test. [†]Fisher’s exact test.