**Supplementary Material:**

**Listing of SAEs and AEs leading to discontinuation**

*SAEs by treatment arm and age group (from Table 2)*

**Placebo <50 years SAEs were** supraventricular tachycardia, bronchitis, gastroenteritis, urinary tract infection, wound infection staphylococcal, fall, patella fracture, back pain, depression, insomnia, suicidal ideation, nasal septum perforation, hysterectomy

**Bari 4 mg <50 years SAEs were** cholecystitis acute, bacterial infection, cellulitis, lower respiratory tract infection, sepsis, viral infection, animal bite, ankle fracture, muscular weakness, myalgia, myositis, metrorrhagia, thrombophlebitis

**Placebo 50 to <65 years SAEs were** myocardial infarction, pneumonia, gastroenteritis, muscle abscess, pyelonephritis, urinary tract infection, back pain, chondrocalcinosis pyrophosphate, intervertebral disc protrusion, rheumatoid arthritis, synovial cyst, ovarian cancer, subarachnoid haemorrhage, acute kidney injury, renal failure, subcutaneous emphysema

**Bari 4 mg 50 to <65 years SAEs were** anaemia, lymphocytosis, angina pectoris, sinus bradycardia, duodenal ulcer haemorrhage, dyspepsia, drug-induced liver injury, disseminated tuberculosis, pneumonia, femoral neck fracture, tibia fracture, ulna fracture, increased alanine and aspartate aminotransferase, lung squamous cell carcinoma stage III, interstitial lung disease (n=2), allergic bronchitis, pleural effusion, dermatitis allergic, circulatory collapse

**Placebo ≥65 years SAEs were** anaemia, cardiac failure, ventricular tachycardia, diverticulum intestinal, gastrointestinal haemorrhage (n=2), large intestine polyp, pancreatitis acute, bile duct stone (n=2), cholangitis sclerosing, cholelithiasis, bronchitis, kidney infection, fall, upper limb fracture, dehydration, diabetes mellitus, hypoproteinaemia, transient ischemic attack, nephrosclerosis, renal impairment

**Bari 4 mg ≥65 years SAEs were** anaemia, cardiac failure, myocardial infarction, gastric ulcer, herpes zoster (n=2), cellulitis, epiglottitis, pneumonia, humerus fracture, spinal pain, breast cancer, chronic obstructive pulmonary disease, pulmonary embolism, rash pruritic

*Serious infections*

**Placebo <50 years serious infections were** bronchitis, gastroenteritis, urinary tract infection, wound infection

**Bari 4 mg <50 years serious infections were** bacterial infection, cellulitis, lower respiratory tract infection, sepsis, viral infection

**Placebo 50 to <65 years serious infections were** pneumonia, gastroenteritis, muscle abscess, pyelonephritis, urinary tract infection

**Bari 4 mg 50 to <65 years serious infections were** disseminated tuberculosis, pneumonia

**Placebo ≥65 serious infections were** bronchitis, kidney infection

**Bari 4 mg ≥65 years serious infections were** herpes zoster (n=2), cellulitis, epiglottitis, pneumonia

*AEs leading to discontinuation by treatment arm and age group (from Table 2)*

**Placebo <50 years AEs were** pregnancy, myopathy, suicidal ideation, depression, decreased lymphocyte counts, upper respiratory tract infection

**Bari 4 mg <50 years AEs were** increased alanine aminotransferase, herpes zoster (n=2), urinary tract infection, cholecystitis acute, amenorrhoea

**Placebo 50 to <65 years AEs were** diarrhoea, dermatitis allergic, skin necrosis, rheumatoid arthritis aggravated (n=2), herpes zoster (n=2), cancer (breast, ovarian), abnormal liver function test, subarachnoid haemorrhage, myocardial infarction, lung cyst, renal failure

**Bari 4 mg 50 to <65 years AEs were** urinary tract infection, pneumonia, interstitial lung disease (n=2), disseminated tuberculosis, herpes zoster (n=4), increased blood triglycerides, drug-induced liver injury, circulatory collapse, alanine aminotransferase increased, hepatitis B DNA assay positive, lung squamous cell carcinoma stage III, lymphocytosis, drug intolerance, dermatitis allergic

**Placebo ≥65 years AEs were** gastrointestinal haemorrhage, mood altered, decreased glomerular filtration rate, acute pancreatitis, renal impairment, squamous cell carcinoma of skin, kidney infection

**Bari 4 mg ≥65 years AEs were** hypersensitivity, decreased lymphocyte count, pneumonia, breast cancer, cardiac failure, herpes zoster (n=3), asthenia, gastric ulcer, nasopharyngitis, thrombocytosis