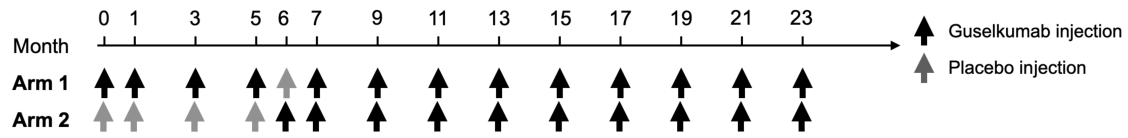


Supplement to
Efficacy of Guselkumab, a selective IL-23 inhibitor, in Preventing Arthritis in a Multi-center Psoriasis At-Risk cohort (PAMPA): protocol of a randomized, double-blind, placebo controlled multicenter trial

Rebecca H. Haberman, MD, MSCI¹⁺; Katrina A. MacFarlane, MSc¹⁺; Sydney Catron, BS¹⁺; Jonathan Samuels, MD¹; Rebecca B. Blank, MD, PhD¹; Michael Toprover, MD¹; Zakwan Uddin, BA¹; Jiyuan Hu, PhD²; Rochelle L. Castillo, MD, MSCI¹; Cinty Gong, PhD³; Kun Qian, MS²; Vincent Piguet, MD⁴, PhD; Francisco Tausk, MD⁵; Jensen Yeung, MD⁴; Andrea L. Neimann, MD⁶; Wayne P. Gulliver, MD⁷; Ralf G. Thiele, MD⁸; Joseph F. Merola, MD, MMSc⁹; Alexis Ogdie, MD, MSCE¹⁰; Proton Rahman, MD¹¹; Soumya D. Chakravarthy, MD, PhD^{3,12}; Lihi Eder, MD¹³; Christopher T. Ritchlin MD, MPH^{8*}; and Jose U. Scher, MD^{1*}



Supplementary Figure 1. Drug and placebo schedule. Black arrows indicate guselkumab injection, gray arrows indicate placebo injection.

Supplementary Methods

Participating Sites

New York University Langone Health and Langone Orthopedic Hospital (coordinating center)
University of Toronto and Women's College Hospital
University of Rochester Medical Center
Memorial University of Newfoundland
Brigham and Women's Hospital, Harvard Medical School
Perelman School of Medicine at the University of Pennsylvania (alternate site)

Ultrasound Protocol

All sites will be scanned longitudinally and any pathology detected in the longitudinal plane will be confirmed in the transverse plane. The following sites will be scanned bilaterally:

Enthesal sites:

1. Quadriceps insertion at the superior pole of patella
2. Patellar ligament origin at the distal pole of patella
3. Patellar ligament insertion at the tibial tuberosity
4. Achilles tendon insertion into the calcaneus
5. Plantar fascia insertion into the calcaneus
6. Common extensor tendon insertion into the lateral epicondyle

Joints:

1. Wrist (radio-carpal, mid-carpal)
2. Metacarpophalangeal, proximal interphalangeal, distal interphalangeal joints (digits 1-5)

Tendon sheaths and tendons:

1. In the dorsal wrist: Compartment 4 (extensor digitorum) and 6 (extensor carpi ulnaris)
2. In the dorsal hand: Extensor digitorum 1-5 at the level of the MCP joint
3. In the palmar hand: Flexor digitorum 1-5

Rochester-Modified PsASon Scoring System

The lowest RM-PsASon score a participant may have at baseline is 0. The highest RM-PsASon score a participant may have at baseline is 614.

- 1) **Synovitis and power Doppler signal/joint¹**: Graded from 0-3 as absent, mild, moderate or severe according to images of a reference atlas.
PD signal: 0=no PD-signal, 1=up to three single or two confluent signals, 2=less than half of the visible intracapsular area and 3=half or more of the visible intracapsular area covered by PD-signals.
- 2) **Bone erosions/joint²**: Score is based on maximal diameter of cortical break.
Grade 0: no erosion, grade 1: erosion of <2 mm, grade 2: erosion of >2 mm, grade 3: large destruction of the joint
- 3) **Osteophytes/joint²**: Score is based on maximal distance between the 'original' and new cortical lining (=maximal height)
Grade 0: no osteophyte, grade 1: osteophyte of <1 mm, grade 2: osteophyte of >1 mm, grade 3: large and diffuse osteophytes

- 4) **Peritendinitis/fingers**³: The presence of peritendinitis is assessed at dorsal scans of MCP 2-5 and is characterized by hypoechoic swelling of the soft tissue surrounding the extensor digitorum tendon, with or without peri-tendinous PD-signals. B-mode (B-perisyn) as well as PD-findings in perisynovial tissue (PD-perisyn) and is graded with 0=absent or 1=present.
- 5) **Enthesitis**⁴: Enthesitis is graded according to Madrid Sonographic Enthesis Index (MASEI): Structure is considered pathological (score=1) if there is a loss of fibrillar pattern, hypoechoic aspect, or fusiform thickening of the entheses. Erosions are defined as a cortical breakage with a step-down contour defect at the attachment of entheses at bone and graded with 0=absent or 3=present. Fascia and tendon thickness are measured at the point of maximal thickness on the bony insertion and graded with 0=normal or 1=thickened according to the reference values of the MASEI index. Enthesophytes are defined as calcifications at the entheses insertions into bone and graded with 0=absent, 1=small calcification, 2=clear presence of enthesophyte/calcification, 3= large calcifications or ossifications. PD-signals within entheses are scored with 0=absent or 3=present. Bursitis is investigated at the level of distal patellar tendon (infrapatellar bursitis) and the level of Achilles tendon insertion (retrocalcaneal bursitis) and graded with 0=absent and 1=present.

IDEOM MSK Questionnaire (IDEOM MSK-Q)

The IDEOM MSK-Q was developed by the International Dermatology Outcomes Measures (IDEOM). The IDEOM MSK-Q is patient-reported outcome measure (PROM) to identify musculoskeletal (MSK) symptoms and measure their intensity and impact on health-related quality of life in patients with psoriatic disease. It was developed to be used in research and clinical practice settings.

- The IDEOM MSK-Q consists of 9 questions evaluating 3 constructs
 - Musculoskeletal symptoms: pain, joint swelling, joint stiffness
 - Impact of musculoskeletal symptoms: work and/or school activities; family, social and/or leisure activities; physical activity, sleep, emotional state)
 - Fatigue.
- The content validity (i.e., relevance, comprehensiveness, and comprehensibility) of the tool was assessed in a multi-phase pilot testing study. This pilot testing study included: (1) an online survey with trained patient-research partners (PRPs) with psoriatic disease, in-person discussions, (2) voting including PRPs, clinicians, researchers, and other relevant stakeholders, and (3) semi-structured interviews with patients with psoriatic disease from a tertiary center using the Three-step test interview technique. Data was analyzed using NVivo Software. During the pilot testing, the instrument was modified, refined, and re-tested until the content validity of the instrument was deemed sufficient and no more changes were suggested by patients.

References

1. Hammer HB, Bolton-King P, Bakkeheim V, et al. Examination of intra and interrater reliability with a new ultrasonographic reference atlas for scoring of synovitis in patients with rheumatoid arthritis. *Ann Rheum Dis* 2011;70(11):1995-8. doi: 10.1136/ard.2011.152926 [published Online First: 2011/07/26]
2. Finzel S, Ohrndorf S, Englbrecht M, et al. A detailed comparative study of high-resolution ultrasound and micro-computed tomography for detection of arthritic bone erosions. *Arthritis Rheum* 2011;63(5):1231-6. doi: 10.1002/art.30285 [published Online First: 2011/05/04]

3. Gutierrez M, Filippucci E, De Angelis R, et al. Subclinical enthesal involvement in patients with psoriasis: an ultrasound study. *Semin Arthritis Rheum* 2011;40(5):407-12. doi: 10.1016/j.semarthrit.2010.05.009 [published Online First: 2010/08/07]
4. de Miguel E, Cobo T, Munoz-Fernandez S, et al. Validity of entheses ultrasound assessment in spondyloarthritis. *Ann Rheum Dis* 2009;68(2):169-74. doi: 10.1136/ard.2007.084251 [published Online First: 2008/04/09]