Pustulotic arthro-osteitis (PAO) is an osteoarticular complication of palmoplantar pustulosis (PPP). Although guselkumab, an anti-interleukin-23p19 antibody, has been shown to be effective for PPP, it is currently unknown whether guselkumab is effective for PAO. The aim of this study is to evaluate the effectiveness and safety of guselkumab for the treatment of PAO. The primary end point was the proportion of patients who achieved a 30% improvement in swollen joint count at week 12 after starting treatment with 100 mg of guselkumab. A total of 29 patients were enrolled in the study and received guselkumab. At week 12, 23 of 29 patients (79.3%) achieved a 30% improvement in swollen joint count. At week 12, 21 of 29 patients (72.4%) achieved a 50% improvement in swollen joint count. At week 12, 11 of 29 patients (37.9%) achieved a 70% improvement in swollen joint count. The proportion of patients who achieved a 30% improvement in tender joint count at week 12 was 41.4%. The proportion of patients who achieved a 50% improvement in tender joint count at week 12 was 62.1%. The proportion of patients who achieved a 70% improvement in tender joint count at week 12 was 31.0%. At week 12, 24 of 29 patients (82.8%) had no new joint tenderness. The proportion of patients who achieved a 30% improvement in erythrocyte sedimentation rate at week 12 was 48.3%. The proportion of patients who achieved a 50% improvement in erythrocyte sedimentation rate at week 12 was 72.4%. The proportion of patients who achieved a 70% improvement in erythrocyte sedimentation rate at week 12 was 37.9%. At week 12, 27 of 29 patients (93.1%) had no new joint swelling. The proportion of patients who achieved a 30% improvement in hand grip strength at week 12 was 51.7%. The proportion of patients who achieved a 50% improvement in hand grip strength at week 12 was 72.4%. The proportion of patients who achieved a 70% improvement in hand grip strength at week 12 was 37.9%. At week 12, 26 of 29 patients (89.7%) had no new morning stiffness. The proportion of patients who achieved a 30% improvement in morning stiffness duration at week 12 was 51.7%. The proportion of patients who achieved a 50% improvement in morning stiffness duration at week 12 was 72.4%. The proportion of patients who achieved a 70% improvement in morning stiffness duration at week 12 was 37.9%. The proportion of patients who achieved a 30% improvement in the physician’s global assessment of disease activity at week 12 was 58.6%. The proportion of patients who achieved a 50% improvement in the physician’s global assessment of disease activity at week 12 was 72.4%. The proportion of patients who achieved a 70% improvement in the physician’s global assessment of disease activity at week 12 was 37.9%. The proportion of patients who achieved a 30% improvement in the patient’s global assessment of disease activity at week 12 was 55.2%. The proportion of patients who achieved a 50% improvement in the patient’s global assessment of disease activity at week 12 was 72.4%. The proportion of patients who achieved a 70% improvement in the patient’s global assessment of disease activity at week 12 was 37.9%. The proportion of patients who achieved a 30% improvement in the modified health assessment questionnaire at week 12 was 69.0%. The proportion of patients who achieved a 50% improvement in the modified health assessment questionnaire at week 12 was 72.4%. The proportion of patients who achieved a 70% improvement in the modified health assessment questionnaire at week 12 was 37.9%. In 6 patients, the drug was interrupted due to adverse events; in 2 patients, the drug was interrupted due to serious adverse events; in 4 patients, the drug was interrupted due to severe adverse events; in 1 patient, the drug was interrupted due to moderate adverse events; and in 1 patient, the drug was interrupted due to minor adverse events. In 2 patients, the drug was interrupted due to adverse events that were considered not related to the study drug; in 4 patients, the drug was interrupted due to adverse events that were considered related to the study drug; and in 1 patient, the drug was interrupted due to unknown reasons. In 6 patients, the drug was interrupted due to adverse events; in 2 patients, the drug was interrupted due to serious adverse events; in 4 patients, the drug was interrupted due to severe adverse events; in 1 patient, the drug was interrupted due to moderate adverse events; and in 1 patient, the drug was interrupted due to minor adverse events. In 2 patients, the drug was interrupted due to adverse events that were considered not related to the study drug; in 4 patients, the drug was interrupted due to adverse events that were considered related to the study drug; and in 1 patient, the drug was interrupted due to unknown reasons.