SUPPLEMENTAL ONLINE TEXT

Opportunistic infection. In the golimumab 100mg group, one patient had histoplasmosis and another had pulmonary tuberculosis. Histoplasmosis was reported 6 days following the prior administration of study agent (day 560) in a 67-year-old man from Illinois who previously smoked cigarettes and was receiving background methotrexate (7.5mg/wk). He presented with fever, sweats and a 30-pound weight loss. A chest radiograph revealed bilateral ground-glass opacities, and bronchoscopic lung biopsy demonstrated non-necrotizing granulomatous inflammation and organism consistent with *Histoplasma capsulatum*. He discontinued golimumab and was treated with itraconazole. The sole case of tuberculosis occurred in a 76-year-old woman from Germany with no known risk factors for tuberculosis. She presented with recurrent hemoptysis and cavitary lesions in both upper lung lobes after the week-100 visit. A bronchoscopically-obtained specimen culture confirmed the presence of *Mycobacterium tuberculosis*. At baseline, purified protein derivative skin testing and interferon-gamma release assay for tuberculosis both yielded negative results and chest radiographs were interpreted as normal. She was discharged from the hospital having initiated anti-tuberculosis therapy with rifampin, isoniazid, pyrazinamide and ethambutol.

Deaths. The death due to an aggressive lymphoma occurred in a 61-year-old woman with a history of colon cancer (in remission >5 years), coronary artery disease, gastroesophageal reflux disease (GERD), hypertension, depression, peripheral neuropathy and hyperlipidemia. She presented with acute onset of throat infection and left earache followed by the appearance of significant bilateral cervical and supraclavicular lymphadenopathy, thromobocytopenia (platelet count=30,000/mm^3), markedly elevated serum lactate dehydrogenase (16,000 IU/L), and hepatomegaly. Three weeks after her initial presentation the patient was found to be hypotensive,

lost consciousness, and then died. An autopsy confirmed the cause of death as aggressive lymphoma (diffuse large B-cell lymphoma, CD20+, cyclin D1+, BCL2-, CD23+ and 5+); Epstein-Barr virus (EBV) testing was negative.

The three other deaths were attributed to cardiopulmonary causes. A 72–year-old woman, with atypical chest pain, anemia, anxiety/depression, hypothyroidism and GERD, was presumed to have died from a cardiovascular event (no autopsy was performed). A 52-year-old morbidly obese (169 kg) woman who had insulin-dependent diabetes mellitus, hypertension, sleep apnea, chronic venous stasis, recurrent edema, gastroparesis, and hypothyroidism, died with congestive heart failure. She presented with anasarca and weight gain due to cardiomyopathy with right-sided heart failure and hypoventilation syndrome. Results of rectal biopsy showed no evidence of amyloidosis; no autopsy was performed. A 79-year-old woman died of pneumonia. She had a history of cigarette smoking, asthma, chronic obstructive pulmonary disease, coronary artery disease, cerebrovascular disease, chronic renal insufficiency, hypertension, hyperlipidemia, paroxysmal atrial fibrillation and chronic dyspnea while receiving methotrexate. She experienced a 36-pound weight loss over 6 months and was hospitalized with sudden-onset altered mentation, anemia and possible pneumonia. Bilateral bronchopneumonia and pleural effusions were documented via chest radiograph and computed tomography scanning. However, results of broncoscopy with culture, performed 6 weeks earlier, were unremarkable and negative. She developed respiratory distress and hypotension and was found to have a myocardial infarction (non-ST elevation) and right common femoral vein thrombosis. Blood cultures yielded no growth. She died of pneumonia and resulting respiratory failure; no autopsy was performed.

Malignancies. In addition to the placebo-treated patient with pancreatic cancer described above and the patients with squamous cell skin carcinoma (50mg) and lymphoma (100mg) reported through wk24 of GO-AFTER,[1] 13 other patients have been reported to have developed malignancies through wk160. These include three patients with B-cell lymphomas who were receiving golimumab 100mg (yielding four patients with lymphoma on golimumab 100mg; see Supplementary Table 1); breast cancer in two patients (both 100mg); non-melanoma skin cancer in five patients (four basal cell carcinomas, one squamous cell carcinoma) who received 100mg; and one patient each with cervical cancer (50mg), pancreatic cancer (50mg), rectal cancer (100mg) and a papillary urothelial neoplasm of low malignant potential according to World Health Organization criteria (100mg) that was classified as a malignancy for analytical purposes. Since the wk160 database lock, no additional reports of lymphoma have been received; however, there has been one report of T-cell leukemia (prolymphocytic leukemia) in a 71-year-old man who had received leflunomide, methotrexate and etanercept before study enrollment. He was randomized to golimumab 50mg and had his dose escalated to 100mg after wk100. More than 20 months later, leukocytosis was noted on routine laboratory monitoring; T-cell prolymphocytic leukemia was diagnosed by peripheral blood flow cytometry.

With regard to the four GO-AFTER patients diagnosed with lymphoma, only one of four patients achieved an ACR50 response prior to lymphoma diagnosis and two patients did not achieve an ACR20 response, together indicating persistent disease activity. Two of four patients with lymphoma died, one prior to and the other following the wk160 database lock. Among the three patients with EBV testing performed by *in situ* hybridization, only the patient with the shortest disease duration had positive findings. This patient had RA of 4.7-year's duration with secondary Sjogren's syndrome and was diagnosed with reversible methotrexate-associated

lymphoproliferative disease 1 year before diffuse large B-cell lymphoma diagnosis (Supplementary Table 1). These findings are of interest because lymphoma related to immunosuppressive therapy, as that seen in transplant patients, tends to have a higher rate of EBV positivity.[25] Despite this context, the risk of malignancy, particularly lymphoma, with anti-TNF therapy requires close monitoring. The increased lymphoma occurrence in this study is an important observation; however, the relative contributions of longstanding severe disease and golimumab therapy cannot be discerned with these few cases.