Dear friends of clinical journal club - load the file down at https://www.mdc-berlin.de/cjc. This website also gives you access to my seminar on Wednesdays 16:00 English and 17:00 German. You need to click on *Besprechung beizutreten*. If it fails to work immediately, keep on clicking.

A 19-year-old man with a history of mild acne vulgaris presented with a 10-day history of rapidly worsening acne, along with fever, muscle aches, and knee pain. His temperature was 38.5°C. On physical examination, diffuse papulonodular and pustular lesions with areas of overlying crusting were noted across the forehead, nose, cheeks, and chin. There were similar lesions on the neck, shoulders, chest, back, and thighs. Laboratory studies were notable for neutrophilic leukocytosis and an elevated erythrocyte sedimentation rate and C-reactive protein level. A culture of a skin swab grew only *Cutibacterium* acnes. Histopathological examination of a skin-biopsy specimen taken from behind the left ear showed suppurative folliculitis with adjacent dermal edema. What is the most likely diagnosis? You are offered: Acne fulminans, Acute febrile neutrophilic dermatosis, Hidradenitis suppurativa, Pustular psoriasis, and Rosacea fulminans. Beta blockers decrease mortality after ST-segment elevation myocardial infarction. The appropriate duration of treatment with beta-blocker drugs after a myocardial infarction is unknown. Data are needed on the safety and efficacy of the interruption of long-term beta-blocker treatment to reduce side effects and improve quality of life in patients with a history of uncomplicated myocardial infarction. In a multicenter, open label, randomized, noninferiority trial conducted at 49 sites in France, investigators randomly assigned patients with a history of myocardial infarction, in a 1:1 ratio, to interruption or continuation of beta-blocker treatment. The primary end point was a composite of death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for cardiovascular reasons. Sad, but discontinuing beta blockers could not be shown to be “non-inferior” to consuming beta blockers. Cerebral adrenoleukodystrophy is a severe form of X-linked adrenoleukodystrophy, characterized by white-matter disease, loss of neurologic function, and early death. Elivaldogene autotemcel (eli-cel) gene therapy, which consists of autologous CD34+ cells transduced with Lenti-D lentiviral vector containing ABCD1 complementary DNA, is being tested in persons with cerebral adrenoleukodystrophy. In a phase 2–3 study, investigators evaluated the efficacy and safety of eli-cel therapy in boys with early-

stage cerebral adrenoleukodystrophy and evidence of active inflammation on magnetic resonance imaging (MRI). The primary efficacy end point was survival without any of six major functional disabilities at month 24. The secondary end points included overall survival at month 24 and the change from baseline to month 24 in the total neurologic function score. The eli-cel therapy met the therapeutic endpoint but there was concern about cancer in the recipients. The risk of oncogenesis with eli-cel is unclear. Other investigators performed integration-site analysis, genetic studies, flow cytometry, and morphologic studies in peripheral-blood and bone marrow samples from patients who received eli-cel therapy in two completed phase 2–3 studies. Hematologic cancer developed in a subgroup of patients who were treated with eli-cel; the cases are associated with clonal vector insertions within oncogenes and clonal evolution with acquisition of somatic genetic defects. Of 67 eli-cel treated patients, 6 developed myelodysplastic syndromes and 1 developed acute leukemia. PD-1 and PDL1 checkpoint inhibitors help for non-small-cell lung cancer, but how about small-cell lung cancer? Adjuvant therapy with durvalumab (PD-L1), with or without tremelimumab, may have efficacy in patients with limited-stage small-cell lung cancer who do not have disease progression after standard concurrent platinum-based chemoradiotherapy. In a phase 3, double-blind, randomized, placebo-controlled trial, investigators assigned patients to receive durvalumab at a dose of 1500 mg, durvalumab (1500 mg) plus tremelimumab at a dose of 75 mg (four doses only), or placebo every 4 weeks for up to 24 months. Checkpoint inhibition for small-cell lung cancer was also effective in prolonging progression-free survival. The N Engl J Med review is on “hairy-cell” leukemia. The N Engl J Med case is about a man who develops fever, jaundice, renal failure and diffuse pneumonia. He owned a dog and walked in the woods. In the Lancet, we encounter a massive analysis on breast cancer over the years. What we learn is that the prognosis improves, recurrence becomes less, and the reasons are related to earlier tumor diagnosis and somewhat to improved therapies. The Vi Tetatanus conjugate vaccine is not only directly against tetanus, but also against typhoid fever. A study in Bangladesh determines efficacy over time and determines that protection over 5 years decreases. But the issue is preventing typhoid fever, not tetanus. We then learn that cognitive behavior therapy may help British mothers of Asian background. The Lancet case concerns Olmesartan-induced

collagenous gastritis. A Lancet Commission deals with self-harm (suicides). In Science Magazine we learn that by eliminating certain epigenetic regulators, T-cell exhaustion (and failure to attack cancer cells) can be diminished. In the Washington Post, we learn about gluten intolerance in the US, although malabsorption and celiac disease have not increased. Widely available gluten-free foods seem of little help. The explanation for gastric discomfort in the US could be FODMAP foods, namely “food oligo-, di-, monosaccharides and polyols”. These products are not resorbed and converted into gas by bacteria in the colon.

No oral presentation this week. Join me on Wednesday, October 23 for another stunning clinical journal club, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

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