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 74-year-old man presented to the hospital for the third time in three weeks with recurrent fever, muscle aches, and vomiting. In the prior two hospitalizations, symptoms had self-resolved and broad work-up was unremarkable. He had traveled to Yosemite National Park one week prior to symptom onset. Physical examination was notable for rigors and diaphoresis. What is the most likely diagnosis? You are offered a Wright-stained peripheral blood smear that shows the organisms. The choices are: Babesiosis, Leptospirosis, Rocky Mountain spotted fever, Secondary syphilis, and Soft tick relapsing fever. The nonsteroidal mineralocorticoid receptor antagonist finerenone has been reported to improve kidney and cardiovascular outcomes in persons with type 2 diabetes and chronic kidney disease (CKD). The efficacy and safety of finerenone in persons with type 1 diabetes and CKD are unknown. Investigators conducted a phase 3 trial involving adults who had type 1 diabetes, CKD (estimated glomerular filtration rate [eGFR], 25 to <90 ml per minute), and albuminuria (urinary albumin-to-creatinine ratio >200) and were receiving an angiotensin-converting–enzyme (ACE) inhibitor or an angiotensin-receptor blocker. The primary outcome was the relative change in the urinary albumin-to-creatinine ratio over a period of 6 months. Finerenone beat placebo but would it have beaten spironolactone? The preferred timing of treatment of nonculprit lesions in patients with ST-segment elevation myocardial infarction (STEMI) remains uncertain. A comparison of immediate percutaneous coronary intervention (PCI) guided by instantaneous wave-free ratio (iFR) and deferred PCI guided by cardiac stress magnetic resonance imaging (MRI) in patients with STEMI and multivessel disease is warranted. Cardiologists randomized patients with STEMI and at least one nonculprit lesion who had undergone successful primary PCI to immediate iFR-guided PCI (in lesions with >50% stenosis and an iFR of ≤0.89 [normal value, >0.89]) or deferred cardiac stress MRI–guided PCI within 6 weeks after randomization. The primary end point was a composite of death from any cause, recurrent myocardial infarction, or hospitalization for heart failure at 3-year follow-up. Immediate PCI of nonculprit lesions could not beat

delayed PCI of nonculprit lesions. Dravet syndrome is a severe developmental and epileptic encephalopathy caused primarily by *SCN1A* haploinsufficiency. The autosomal-dominant condition involves a “poison” exon that leads to a splicing error. Risks of sudden unexpected death in epilepsy and cognitive deficits are higher among patients with this syndrome than in the general population with epilepsy. Is it possible to eliminate the mRNA of the poison exon to help patients with Dravet’s syndrome? The effects of zorevunersen, an antisense oligonucleotide designed to up-regulate NaV1.1 sodium channels, in patients with Dravet syndrome are not known. Investigators enrolled patients 2 to 18 years of age with Dravet syndrome who were receiving standard antiseizure medications in two phase 1–2a, open-label, multicenter studies. Patients were included in first a single-ascending-dose cohort and then a multidose regimen, in which zorevunersen was given intrathecally into the central nervous system. The safety and pharmacokinetics of zorevunersen were assessed; clinical effects were also evaluated. Zorevunersen seemed safe and might work. We learn something about poison exons. No neoadjuvant treatment has been considered to be standard therapy for patients with resectable intrahepatic cholangiocarcinoma with high-risk factors for recurrence. The GOLP regimen (gemcitabine–oxaliplatin, lenvatinib, and an anti–programmed death 1 antibody) has shown promising efficacy with a manageable safety profile in advanced intrahepatic cholangiocarcinoma and biliary tract cancer. In a phase 2–3 trial, Investigators randomly assigned patients with resectable high-risk intrahepatic cholangiocarcinoma to the neoadjuvant GOLP group, followed by curative resection) or a control group (curative resection and no neoadjuvant treatment). All patients received adjuvant capecitabine for eight cycles after surgery. The primary end point was event-free survival. The GOLP regimen increased event-free survival and was relatively tolerable. The N Engl J Med review is on the effects of radiation therapy on normal tissue; some progress here. The mystery case is a patient with puzzling cranial nerve palsies and progressive descending muscular weakness. In the Lancet, Finnish investigators studied the effects of obesity on infectious-disease risks. They confirmed their obesity-increases infectious-disease risk findings with the UK Biobank. What can we do for patients with marginal-zone B-cell lymphomas? Other than standard care, CAR T-cell therapy against CD19 is a reasonable strategy. Women with various breast cancers can benefit from radiation

therapy. We next learn that modern strategies could be employed to reduce the radiation dose without losing efficacy. Baxdrostat inhibits CYP11B2 and reduces aldosterone synthesis. Baxdrostat could reduce blood pressure in persons with poorly controlled hypertension. The Lancet presents a convincing randomized trial but alas, there was no spironolactone comparator. The Lancet review is on atrial fibrillation. There is good advice given here. The Lancet discusses “new treatments” for hard-to-control” hypertension. They were not-so-new. In Science Magazine, we confront a 36-item approach to climate change. Good ideas, but the USA administration denies that climate change exists and accepts not even a single approach. In Washington Post, we celebrate the oldest horse in the world. She is close to 37 years. The presentation is in English at 16:00, German at 17:00, and will take place will on Wednesday March 11, 2026.

Sincerely, Fred Luft

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