

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.

39-year-old woman with obesity presented to an ophthalmology clinic with a 6-week history of a foreign-body sensation and tearing in both eyes. Symptoms were worse upon awakening. She also reported daytime fatigue, snoring, and difficulty sleeping at night. Ophthalmologic examination and findings with attempted closure of both eyes are shown. What is the most appropriate next step? You are offered a list of what to do: Blepharoplasty, Computed tomography of the chest to look for a superior sulcus tumor, Ice pack test, Referral for a sleep study, and Topical antimicrobials. Which test is the most reasonable and would do the least harm?

Patients with severe hypertriglyceridemia have an increased risk of acute pancreatitis. Apolipoprotein C-III negatively regulates lipoprotein lipase. The efficacy and safety of olezarsen, an antisense oligonucleotide targeting apolipoprotein C-III messenger RNA, have not been established in this population. Investigators conducted two double-blind, randomized, placebo-controlled trials (CORE-TIMI 72a and CORE2-TIMI 72b). Patients with severe hypertriglyceridemia were assigned in a 1:1:1 ratio to receive olezarsen at a dose of 50 mg, olezarsen at a dose of 80 mg, or placebo monthly for 12 months. The primary outcome was the percent change in the triglyceride level at 6 months, reported as the difference between each olezarsen dose group and the placebo group (placebo-adjusted change). Secondary lipid outcomes included the percent change in the triglyceride level at 12 months and in apolipoprotein C-III, remnant cholesterol, and non-high-density lipoprotein (non-HDL) cholesterol at 6 months and 12 months. Acute pancreatitis events were assessed across both trials. The antisense strategy lowered triglycerides substantially and markedly reduced episodes of acute pancreatitis.

Central retinal artery occlusion can result in permanent vision loss. Effective treatment is lacking. There is no treatment. Investigators conducted a phase 3, double-blind, double-dummy, randomized, controlled trial involving adults with acute, nonarteritic central retinal artery occlusion who had symptom onset within 4.5 hours before treatment. Patients were assigned, in a 1:1 ratio, to receive intravenous tenecteplase (at a dose of 0.25 mg per kilogram of body

weight) and oral placebo or intravenous placebo and oral aspirin (at a dose of 300 mg). The primary end point was vision recovery, defined as a best corrected visual acuity (BCVA) in the affected eye at 30 days of up to 0.7 logMAR. Tenecteplase did not improve vision and one person in the tenecteplase group died of hemorrhage. Dual anti-human epidermal growth factor receptor 2 (HER2) therapy plus chemotherapy followed by maintenance treatment with HER2-targeted and endocrine therapies is standard first-line treatment for hormone-receptor-positive, HER2-positive metastatic breast cancer. On the basis of preclinical and clinical data, the addition of palbociclib (a selective inhibitor of cyclin-dependent kinases 4 and 6) may overcome resistance to both endocrine and HER2-directed therapies. Investigators enrolled patients with hormone-receptor-positive, HER2-positive metastatic breast cancer who did not have disease progression after four to eight cycles of chemotherapy plus HER2-targeted therapy. Patients were randomly assigned in a 1:1 ratio to receive maintenance HER2-targeted and endocrine therapies with or without palbociclib. The primary end point was investigator-assessed progression-free survival. Progression-free survival was improved with palbociclib.

Queen Victoria (1819–1901) was a carrier of Hemophilia B (factor IX deficiency), likely due to a spontaneous mutation, introducing it into European royalty. She passed the gene to three of her nine children—Leopold, Alice, and Beatrice—leading to its spread through the German, Russian, and Spanish royal houses. Prophylactic treatment for hemophilia B necessitates lifelong, regular intravenous factor IX infusions. Gene therapy offers the possibility of a single-dose treatment that produces durable endogenous factor IX expression and disease control. Etranacogene dezaparvovec comprises an adeno-associated virus serotype 5 (AAV5) vector and a codon-optimized cDNA of the highly active Padua factor IX variant. We now review 5 years of this gene therapy for hemophilia B. Annualized bleeding rates remained low, and a marked decrease in exogenous factor IX consumption was observed. Furthermore, most gene therapy-related adverse events occurred in the first 6 months after the infusion, and no AAV-related oncogenicity had been reported at 5 years after infusion. Peripheral artery disease affects approximately 236 million persons worldwide and is diagnosed with an ankle-brachial index of less than 0.90. *N Engl J Med* reviews the topic. The weekly mystery patient is an 80-year-old woman with cough. She has a ground-glass pneumonia on chest roentgenogram and recently

developed Herpes Zoster. Her pO₂ is 48 mm Hg. The CD4 cell count was reduced. Yellow fever was in scourge in the 19th century and is still a lethal disease. In the Lancet, a randomized trial of vaccine efficacy in children showed that reducing the dose of vaccine material from 13000 IU to 500 IU is not wise; noninferiority criteria were not met. Next, the Lancet presents a trial showing that artificial intelligence improves the interpretation of mammography. Patients with cancer enjoy much longer survival than earlier. However, now more-and-more cancer patients are showing up with acute coronary syndromes. How should these cancer patients be managed for their coronary disease? ONCO-ACS is a computerized program to generate a score indicating increased risk of hemorrhage or other adverse events in cancer patients with coronary syndromes. A prospective study showed that ONCO-ASC is a reliable practical tool. The Lancet review is about heart failure with reduced ejection fraction. The Lancet policy paper holds powerful corporations accountable for their health impacts. Is longevity heritable? The estimates vary from 6 – 30%. In Science Magazine we review a study of DZ and MZ twins from Scandinavia. This study raises the heritability index for longevity to about 50%. In the Washington Post, we discuss whether-or-not dogs should be outfitted with coats and sweaters in winter. The next oral presentation English at 16:00, German at 17:00 will be on Wednesday February 4, 2026.

Sincerely, Fred Luft

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