

Dear friends of clinical journal club - load the latest 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 65-year-old woman with diabetes, hypertension, and dyslipidemia presented to the ophthalmology clinic with a 14-hour history of painless, progressively worsening, blurry vision in the right eye. Physical examination was notable for a visual acuity of 20/400 in the right eye, with the patient unable to see fingers in the peripheral visual fields. There was a relative afferent pupillary defect in the right eye. What is the primary cause of this condition? You are offered: Acute ischemia of the optic nerve head, Compression of a distal retinal vein by an overlying arteriole, Degeneration of photoreceptors and retinal pigment epithelium, Obstruction of venous outflow from a proximal retinal vein, and Occlusion of a central retinal artery from an embolism. Hint: the process took 14 hours, not minutes and not days.

Complex percutaneous coronary intervention (PCI) in patients with severely impaired left ventricular function carries a high risk of death and complications. Whether percutaneous left ventricular unloading improves outcomes remains unclear. Investigators randomly assigned 300 patients with severe left ventricular dysfunction and extensive coronary artery disease to a strategy of elective unloading with a microaxial flow pump or to standard care during planned complex PCI. The primary outcome was a hierarchical composite. However, the flow pump did not improve outcomes.

Current therapies for patients with pancreatic ductal adenocarcinoma (PDAC) provide modest benefit. Activating RAS mutations occur in more than 90% of PDAC tumors. Daraxonrasib (RMC-6236) is an oral RAS(ON) multiselective inhibitor that targets guanosine triphosphate-bound mutant and wild-type RAS. In a phase 1–2 study, investigators evaluated daraxonrasib in patients with advanced solid tumors with activating RAS mutations. Patients received 10 to 400 mg of daraxonrasib orally once daily. Daraxonrasib appears effective; however, a RAS mutation (G12D most common) seems to be required.

We are still allowed to be vaccinated against influenza virus. An investigational messenger RNA (mRNA)-based vaccine called mRNA-1010 encodes hemagglutinin glycoproteins from World Health Organization-recommended influenza strains. In a phase 3, double-blind, active-controlled trial, investigators randomly assigned adults 50 years

of age or older to receive trivalent mRNA-1010 (37.5 µg, which includes 12.5 µg of each strain) or a licensed standard-dose comparator. The primary efficacy end point was relative vaccine efficacy. The new mRNA flu vaccine was actually - better than the older vaccine. Generalized scabies (mites burrowing under your skin) can be a devastating skin disease. A combination of standard-dose oral ivermectin (blocks invertebrate chloride channels) and topical scabicides is recommended for treatment. However, data from randomized clinical trials are lacking, and the probability of cure is uncertain. Ivermectin at higher doses has been effective in the treatment of some parasitic diseases. Investigators conducted a blinded randomized trial involving adults with severe scabies in which the standard ivermectin dose was compared to double the standard dose. The old dose was enough and was effective. The HBG1 and HBG2 hemoglobin-chain promoters respond to BCL11A at birth to convert hemoglobin F (alpha and gamma chain) to hemoglobin A (alpha and beta chain) at birth. In sickle cell anemia, the beta chain is defective so that hemoglobin F would be better during adulthood. Ristocel is a gene editing treatment to reverse the effects of BCL11A. Investigators enrolled patients 12 to 35 years of age with sickle cell disease who had had at least four severe vaso-occlusive crises in the 2 years before enrollment. After myeloablative conditioning with pharmacokinetically guided administration of busulfan, patients received a single infusion of risto-cel (at a dose of $\geq 3.0 \times 10^6$ viable CD34+ cells per kilogram of body weight). The primary efficacy end point was freedom from severe vaso-occlusive crises for 12 consecutive months. Ristocel was effective in stopping severe vaso-occlusive crises. Beta amyloid is a peptide that plays a crucial role in normal brain function, including regulating synaptic plasticity, supporting neuron growth and repair, and defending against oxidative stress. While infamous for aggregating into plaques in Alzheimer's disease, in its soluble form, it serves as a normal metabolic product involved in protection against pathogens and maintaining the blood-brain barrier. The N Engl J Med review is on cerebral amyloid angiopathy. The N Engl J Med mystery patient has an immune reaction to an obscure atypical Mycobacterial infection and then develops antibodies against interferon gamma. In the Lancet we inspect a prospective trial of colonoscopy screening for colorectal cancer. Cancer-related deaths were (somewhat) lower, but overall survival was not reduced. RTS,S/AS01 (Mosquirix) is an approved antimalarial vaccine that is directed against

sporozoites. This vaccine was tested on mortality of children in various African countries with a randomized controlled cluster trial. The vaccine could avoid one in eight malaria-related deaths. Toll-like receptors play a role in systemic lupus erythematosus. Lancet reports a trial in such patients using enpatoran, a Toll-like 7/8 receptor inhibitor. The drug reduced the BICLA score, but the results were not bombastic. Safety was not an issue. A Lancet Commission reports (in about 50 pages) on the impact of liver disease. Actually, much can be done to ameliorate various causes, including the effects of alcohol. Enlicitide is a macro-cyclic peptide drug directed against PCSK9 and lowers cholesterol. The drug works (a ring-like peptide) as an oral formulation. In Science Magazine, we learn how pharmacologists did it. They reduced the synthesis steps from about 60 to a very few (three or so) steps to make enlicitide in kilogram quantities. In Washington Post, we learn that Bobby Kennedy Jr. contacted the editors of *Ann Intern Med* and tried to bully them into retracting a paper reporting that childhood vaccinations did not cause autism (a favorite delusion of his). The editors courageously refused to do so. There is no presentation this week. The next in English at 16:00, German at 17:00, and will take place will on Wednesday May 20, 2026.

Sincerely, Fred Luft

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