

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 6-month-old baby boy was referred to a pediatric neurology clinic in Brazil for evaluation of developmental delay. At the beginning of the second trimester, the baby's mother had had a rash. At birth, the baby had microcephaly. He subsequently developed severe developmental delay and epilepsy. Prenatal ultrasonography at 12 weeks' gestation and at 29 weeks' gestation are shown. What is the underlying etiology? You are offered: Congenital cytomegalovirus, Congenital toxoplasmosis, Congenital Zika syndrome, Inborn error of metabolism, and In-utero toxin exposure. Think Brazil, rash, and microcephaly.

ctDNA-guided treatment means using circulating tumor DNA (ctDNA) from a blood test (liquid biopsy) to personalize and manage cancer therapy. Patients with muscle-invasive bladder cancer have varied outcomes after cystectomy. ctDNA)-based detection of molecular residual disease may identify patients at high risk for recurrence after cystectomy who can benefit from adjuvant immunotherapy, thus sparing patients at lower risk from unnecessary treatment burden. In a phase 3, double-blind, randomized trial, investigators used serial ctDNA testing to monitor (for up to 1 year) patients with muscle-invasive bladder cancer and no radiographic evidence of disease after surgery. Eligible patients who tested ctDNA-positive during surveillance were randomly assigned in a 2:1 ratio to receive intravenous atezolizumab or placebo every 4 weeks for up to 1 year. The primary end point was investigator-assessed disease-free survival. ctDNA proved highly predictive of outcomes and atezolizumab beat (placebo) usual care.

Tirzepatide, a dual incretin agonist of the glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide receptors, has favorable effects on glycemic control and body weight. The effects on cardiovascular outcomes are uncertain. Investigators conducted an active-comparator-controlled, double-blind, noninferiority trial in which patients with type 2 diabetes and atherosclerotic cardiovascular disease were randomly assigned in a 1:1 ratio to receive a weekly subcutaneous injection of tirzepatide (up to 15 mg) or dulaglutide (1.5 mg), an agent that has been shown to reduce the incidence of cardiovascular events (both drugs are Eli Lilly products). The primary end point was a

composite of death from cardiovascular causes, myocardial infarction, or stroke and was tested for noninferiority of tirzepatide to dulaglutide with a margin of 1.05 for the upper limit of the 95.3% confidence interval for the hazard ratio. An upper limit of less than 1.00 was considered to indicate superiority of tirzepatide to dulaglutide. Tirzepatide induced greater weight loss and was, “no-worse but no-better than” dulaglutide. Multidose human papillomavirus (HPV) vaccination is efficacious, yet the vaccine has been underused globally. Human papilloma virus (HPV) can cause cervical cancer, but we have an HPV vaccine to avoid this cancer. Emerging data suggest that a single dose may provide protection. Whether a single dose of HPV vaccine would provide similar protection to two doses is uncertain. In this trial, investigators assessed whether one dose of an HPV vaccine was noninferior to two doses. Girls 12 to 16 years of age were randomly assigned, in a 1:1:1:1 ratio, to receive one or two doses of a bivalent HPV vaccine or one or two doses of a nonavalent HPV vaccine. The primary end point was new HPV type 16 or 18 infection occurring from month 12 to month 60 and persisting for at least 6 months. One shot HPV vaccine was as good as two shots! Tuberculous meningitis is often lethal (about 50%), and many survivors have disabilities despite antimicrobial treatment and adjunctive glucocorticoid therapy. Standard-dose rifampin has limited central nervous system penetration. Whether high-dose rifampin could improve survival outcomes is unknown. Investigators performed a double-blind, randomized, placebo-controlled clinical trial involving adults with tuberculous meningitis in Indonesia, South Africa, and Uganda. We assigned persons with and those without human immunodeficiency virus (HIV) coinfection to receive standard daily isoniazid, rifampin (at a dose of 10 mg per kilogram of body weight), ethambutol, and pyrazinamide plus either additional rifampin (for a cumulative dose of 35 mg per kilogram; high-dose group) or matched placebo (standard-dose group) for 8 weeks; participants in both groups received standard therapy for the remainder of the 9-to-12-month treatment course. The primary outcome was 6-month mortality. Unfortunately, high-dose rifampin was not better than low-dose, when given in addition to the standard anti-TB regimen. The N Engl J Med review is on measles. Do not forget about vitamin A and pneumococcal vaccine. The mystery patient has mysterious gastrointestinal blood loss. In the Lancet, investigators tested the oral GLT-agonist, orforglipron (Eli Lilly), against placebo in obese patients with

type-2 diabetes. Weight reduction with the highest dose approached that of parenteral GLP-1 agonists and disease parameters were substantially improved. Side effects were gastro-intestinal in nature. Ductal pancreatic cancer chemotherapy is not satisfactory. The PAXG combination was slightly better than the usual FOLFIRINOX regimen. The half-time event-free survival was increased by about six months. Acute-pain management after trauma in the ambulance or helicopter is not clear. Successful iv placement is not reliable and is also not easy. Inhalational methoxyflurane, intranasal fentanyl, and iv morphine were compared. Inhalational methoxyflurane proved to be perhaps the best acute-pain approach. CAR-T cell management has arrived in patients with aggressive systemic lupus erythematosus. Chinese investigators performed an allogenic (off the shelf) CAR-T cell approach and documented efficacy. Amylin agonists cause weight loss, improve diabetic control and lower blood pressure. However, amylin induces renin release. A Lancet review suggests that since these patients receive ACE inhibitors and ARBs, the blood pressure-lowering effect could be related to Ang 1-7 and MAS receptor signaling. In Science Magazine, we learn that photovoltaics received recognition as technology “breakthrough” of-the-year, since photovoltaics have earned a first-place in production of “green” electricity. Most of these products come from China. In the Washington Post, we learn that the Trump-appointed regulatory board of the Kennedy Center in Washington, DC has renamed the entire Center as the “Donald J. Trump and John F. Kennedy Center”. Trump is also the self-appointed board chairman. Who came up with this idea? I wish you all happy holidays. The next oral presentation will be on January 7, 2026.

Sincerely, Fred Luft

Friedrich.luft@charite.de

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