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 47-year-old woman presented to the dermatology clinic with a 1-year history of a crawling sensation on her chin that caused her to scratch the area. The right corneal reflex was decreased, and pinprick and temperature sensation around the mouth, lip, and chin on the right side was reduced. With occlusive dressings, the ulcer healed, but it later recurred after being left uncovered. What is the diagnosis? You are offered: Cutaneous lupus erythematosus; Cutaneous malignancy; Herpes simplex virus infection; Sarcoidosis; and Trigeminal trophic syndrome. All hints point to a 5th nerve lesion. Patients with human epidermal growth factor receptor 2 (HER2)–positive early breast cancer and residual disease after neoadjuvant therapy are at high risk for recurrence. In a phase 3, open-label, international, randomized trial, investigators studied post-neoadjuvant trastuzumab (topoisomerase I inhibitor) deruxtecan (T-DXd; 5.4 mg per kilogram of body weight) as compared with trastuzumab (microtubular blocker) emtansine (T-DM1; 3.6 mg per kilogram), the current standard treatment, in patients with HER2-positive breast cancer with residual invasive disease and node-positive disease at surgery or inoperable disease at diagnosis. The primary end point was invasive disease–free survival, and the key secondary end point was disease-free survival (including survival free from noninvasive breast cancers and second primary nonbreast cancers). Other end points included overall survival, distant recurrence–free interval, brain metastasis–free interval, and safety. T-Dx beat T-DM1. Randomized trials of long-acting injectable antiretroviral therapy (ART) in persons with human immunodeficiency virus (HIV) who face challenges with adherence to oral medication are lacking. Investigators conducted an open-label, randomized trial involving persons with HIV who had inadequate adherence to ART (a persistent HIV-1 RNA level of >200 copies per milliliter or loss to follow-up). Participants who had an HIV-1 RNA level of 200 copies per milliliter or lower in step 1 were randomly assigned in a 1:1 ratio to either continue standard care or switch to monthly injections of long-acting cabotegravir plus rilpivirine with or without oral lead-in therapy. The primary outcome was regimen failure, defined as confirmed virologic failure (two consecutive HIV-1 RNA

measurements of >200 copies per milliliter) or treatment discontinuation during step 2. New regimen beats old. The transcription factor protein, P53, encoded by the gene *TP53* is a tumor suppressor commonly mutated and defective in cancer patients. The Y220C somatic missense mutation is a “hotspot” mutation causing cancer. Rezatapopt is an investigational, first-in-class, oral, selective p53 reactivator that specifically binds to Y220C-mutated p53, which stabilizes p53 in its wild-type conformation and restores its functionality. In a phase 1, single-group, dose-escalation and dose-optimization study, investigators assigned heavily pretreated patients with locally advanced or metastatic solid tumors harboring a TP53 Y220C mutation to receive rezatapopt during continuous 21-day treatment cycles. The primary objectives were to determine the maximum tolerated dose and recommended phase 2 dose. Primary end points included dose-limiting toxic effects and adverse events. Secondary end points included preliminary efficacy and pharmacokinetic features. These was some nausea and vomiting but rezetapopt seems to work. This study ushers in a new era of P53-directed cancer treatments. Tecovirimat is approved for smallpox treatment under the Food and Drug Administration Animal Rule on the basis of efficacy in nonhuman primate models of mpox (previously known as monkeypox). However, the clinical efficacy of tecovirimat against human clade II mpox is unclear. In a phase 3, international, double-blind, randomized, placebo-controlled trial, we evaluated the efficacy of oral tecovirimat in adults with laboratory-confirmed clade II mpox. Participants were randomly assigned in a 2:1 ratio to receive tecovirimat or placebo for 14 days. The primary outcome was clinical resolution. Tecovirimat was useless in all respects so better stick with the vaccine. The N Engl J Med review is on Group B streptococcal disease. We pay homage to Rebecca Lancefield. The N Engl J Med mystery patient is a 91-year-old with pain in his knee prosthesis. In the Lancet, we review in a meta-analysis, 30 years of hip replacement; the news is good. Treating myelomeningocele operatively, in utero, with placentally-derived stem cells seems far-fetched. A Lancet paper provides good safety and promising clinical results. Next, the Lancet reviews efficacy and tolerability of antidopaminergic and muscarinic antipsychotic drugs for schizophrenia. My personal and only experience is with haloperidol. This old workhorse actually comes off pretty well! The Lancet review is on GLP-1 agonists. Much of (about half) healthcare advice on “Tic-Toc” is largely BS.

Lancet next comes to grips with social-media-directed health-care advice. In Science Magazine we are introduced to “our dad” the Neanderthal man. In Washington Post we learn about how Lindsay Vonn’s leg was saved and who saved it! The presentation is in English at 16:00, German at 17:00, and will take place will on Wednesday March 4, 2026.

Sincerely, Fred Luft

Friedrich.luft@charite.de
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