

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 35-year-old woman presented with a 20-day history of a painless nipple ulcer without other associated symptoms or skin findings. Histopathologic analysis of a nipple-biopsy specimen showed epidermal necrosis with inflammatory exudate, dermal capillary proliferation, and dense perivascular lymphoplasmacytic infiltrates. Physical examination and immunohistochemical analysis of the biopsy are shown. What is the most likely diagnosis? You are offered Eczema, Erosive adenomatosis, Idiopathic granulomatous mastitis, Mammary Paget disease, and Syphilitic chancre. The photomicrograph shows linear structures about 6-15 μ in length; enough said. The effectiveness and safety of statins for the primary prevention of cardiovascular events and the extension of disability-free survival among older adults remain uncertain. Investigators conducted a double-blind, randomized, placebo-controlled trial at general medical practices across Australia. Community-dwelling adults at least 70 years of age with no history of cardiovascular disease, diabetes, or dementia were randomly assigned to receive atorvastatin at a dose of 40 mg once daily or identical placebo. The two primary end points were a composite of death from cardiovascular causes, nonfatal myocardial infarction or stroke, or coronary revascularization and a composite of death from any cause, dementia, or persistent physical disability. There was a modest effect on the cardiovascular outcome, none on dementia or survival. IgG4-related disease is a chronic fibroinflammatory condition that can affect virtually any organ system. Glucocorticoid agents are a cornerstone of therapy but are limited by toxic effects, and relapse is common after discontinuation. Obexelimab is a bifunctional monoclonal antibody that inhibits B-cell activity through coengagement of CD19 and Fc γ RIIb without inducing B-cell depletion. In a phase 3, double-blind, randomized, placebo-controlled trial, patients with active IgG4-related disease received subcutaneous obexelimab at a dose of 250 mg or placebo once weekly for 52 weeks. For patients in both groups, glucocorticoids were tapered in a standardized schedule over 8. The primary end point was the time to the first flare of IgG4-related disease. Obexelimab led to a better result. Giredestrant and everolimus target the

estrogen receptor (ER) pathway and the phosphatidylinositol 3-kinase (PI3K)–protein kinase B (AKT)–mammalian target of rapamycin (mTOR) pathway, respectively, which are implicated in endocrine-therapy resistance. Investigators enrolled patients with ER-positive, human epidermal growth factor receptor 2 (HER2)–negative locally advanced or metastatic breast cancer who had disease progression or recurrence after receipt of a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor plus endocrine therapy. Patients receive giredestrant plus everolimus (each given orally) or standard endocrine therapy (i.e., exemestane, fulvestrant, or tamoxifen) plus everolimus. The primary end point was investigator-assessed progression-free survival. Giredestrant led to a better progression-free survival. Once-daily, single-tablet regimens have transformed care for persons living with human immunodeficiency virus type 1 (HIV-1); however, challenges to adherence continue to limit effective treatment. Long-acting oral-drug combinations could offer new options with less frequent dose administration. Investigators conducted a noninferiority trial to evaluate the efficacy and safety of a switch to once-weekly oral islatravir–lenacapavir (ISL/LEN) from once-daily oral bictegravir–emtricitabine–tenofovir alafenamide (B/F/TAF) in adults in whom HIV-1 had been virologically suppressed for at least 6 months while they were receiving B/F/TAF. Participants were assigned to receive once-weekly ISL/LEN (2 mg/300 mg) or to continue once-daily B/F/TAF for 96 weeks; all received matched placebo for the alternative regimen. The primary end point was the percentage of participants with an HIV-1 RNA level of 50 copies per milliliter or higher at week 48. The once-per-week regimen was non-inferior. Remember the cruise ship where tourists came down with Hanta virus infection? Turns out it was Andes virus (ANDV). ANDV is the sole orthohantavirus with documented human-to-human transmission. N Engl J Med reviews the subject. The N Engl J Med mystery patient of the week is a 58-year-old woman who rituximab and develops rapid bilateral hearing loss. In the Lancet, investigators randomized patients with inoperable non-small-cell lung cancer (NSCLC) to receive stereotactic irradiation alone or stereotactic irradiation plus a checkpoint inhibitor. Outcomes were not improved by checkpoint inhibition in these patients. Persons with acute aches-and-pains commonly present in emergency departments (ED). In the UK, such departments were randomized to having a physiotherapist in the ED or not, to see these patients. Time in ED and patient satisfaction were greatly

improved by the presence of a physiotherapist. “Most-favored-nation” strategy has been introduced in the USA to reduce drug prices. A cohort study indicates that this strategy is likely to fail. Lancet next examines wealth redistribution policies (soak the rich) as a strategy to mitigate the impact of development assistance defunding. Basically, this strategy involves taking from the rich to help the poor. Presumably, the rich will resist. Lancet presents a three-part review on peripheral artery disease. In Science Magazine we review an astounding study linking arterial hypertension to osteoarthritis. The link involves arginine vasopressin the V1 receptor which is expressed in cartilage. In the Washington Post, Donald Trump announces plans to send \$90 payments to all seniors. The direct purpose of this bribe is unclear. But I can hardly wait to get mine. Load down the file and join me again on October 7, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

Friedrich.luft@charite.de

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