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 42-year-old man on prolonged immunosuppressive therapy for chronic graft-versus-host disease after stem-cell transplantation for acute lymphoblastic leukemia presented to clinic with a 2-week history of urinary frequency and weak stream. Physical examination was notable for several small papules on the penile shaft. Urinalysis showed 9 white cells per high-power field, and a urine culture was negative. Testing for human immunodeficiency virus was also negative. Resected urethral tissue showed papillomatous squamous proliferation with koilocytic atypia. Which of the following causes this condition? You are offered: Herpes simplex virus, Human papillomavirus, Poxvirus, Treponema pallidum, and Ureaplasma urealyticum. The tissue fronds give the diagnosis away. Assessing intermediate coronary lesions with an intracoronary pressure wire improves clinical outcomes in patients undergoing cardiac catheterization and percutaneous coronary intervention (PCI). However, clinical use of pressure-wire–based physiological assessment remains low. Measurement of fractional flow reserve (FFR) computer-derived from coronary angiographic images alone correlates well with pressure-wire–based FFR measurements and may simplify procedures, but its effect on clinical outcomes is unknown. Investigators randomly assigned patients undergoing coronary angiography who were found to have at least one intermediate coronary stenosis to physiological assessment with measurements computer-derived from angiographic images (FFRangio) or with pressure-wire–based measurements. The primary end point was a composite of death, myocardial infarction, or unplanned, clinically indicated coronary revascularization at 1 year. The noninferiority margin was 3.5 percentage points. Computer-derived was just as good as pressure-wire FFR. Thereupon follows a second paper on the same issue with the same results. Thus, FFRangio is “no worse than” FFRpressure-wire. Renal-cell cancer commonly involves mutations in oxygen-sensing genes such as the von-Hippel-Lindau (vHL) gene. Adjuvant pembrolizumab improves disease-free and overall survival among patients with resected clear-cell renal-cell carcinoma. The hypoxia-inducible factor 2α inhibitor, belzutifan, has activity

in advanced disease. Adjuvant pembrolizumab with belzutifan may further improve outcomes in patients with clear-cell renal-cell carcinoma at increased risk for recurrence. In a phase 3, double-blind trial, investigators randomly assigned participants to receive intravenous pembrolizumab at a dose of 400 mg every 6 weeks (≤9 doses) and either daily oral belzutifan at a dose of 120 mg (pembrolizumab–belzutifan) or placebo (pembrolizumab–placebo) for up to 1 year. The primary end point was disease-free survival as assessed by the investigator; secondary end points included overall survival and safety. The HIF 2α inhibitor, belzutifan, helped a bit. Anti-CD20 monoclonal antibodies are effective for relapsing multiple sclerosis. However, data from head-to-head trials are lacking. In a phase 3, multicenter, double-blind, noninferiority investigators, investigators randomly assigned adults with newly diagnosed relapsing multiple sclerosis and recent disease activity in a 3:2 ratio to receive rituximab or ocrelizumab every 6 months for 24 months. The primary end point was the absence of new or enlarging lesions on T2-weighted magnetic resonance imaging (MRI) from month 6 to month 24. Ocrelizumab was “as good as” rituximab. The N Engl J Med review is on advances in multiple sclerosis; incremental progress is being made here. The weekly mystery patient is a 54-year-old woman, who underwent a hip replacement years ago, and now develops peripheral neuropathy, ataxia, and memory impairment. In the Lancet, we encounter first a transplant involving both kidney and bladder. The bladder function is the marker of success. Amylin is an incretin with receptors in many tissues. Cargrilintide is an amylin agonist. The combination of cargrilintide+semaglutide could be a super combination to treat type-2 diabetes. Lancet reports that the combination performed well with type-2 diabetes patients. Patellar resurfacing is routine with knee replacement surgery, but is it really all that helpful and necessary? Lancet publishes a randomized trial, and we learn that endpoint was not met with patellar resurfacing. But the “quality of life” was better with patellar resurfacing. That finding alone would be something. Next, Lancet publishes three seminars on post-partum hemorrhage, epidemiology, prevention, and treatment. Discovery of the gene “wingless” in fruit files and the integrator gene (Int) in mice with breast cancer led to the discovery of the *Wnt* signaling pathway. Wnt signaling is pivotal to embryologic development, cancer, and much more. In Science Magazine we learn how Wnt signaling is used to elucidate renal development and can be applied to

kidney organoids, which hopefully will make them more like organs. In Washington Post, we observe that Americans are discovering the bidet. An article informs us on the comforts of this European invention. July 8, Wednesday is the next oral presentation in English at 16:00 and German at 17:00.

Sincerely, Fred Luft

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