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 60-year-old man presented with a 1-month history of postprandial epigastric pain. The physical examination was normal, with no jaundice or abdominal tenderness observed. Laboratory testing showed mild elevations in levels of alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase. CT of the abdomen with contrast showed a diffusely enlarged pancreas with a capsule-like rim of low attenuation. The serum IgG4 level was elevated. Endoscopic retrograde cholangiopancreatography identified an intrapancreatic distal bile-duct stricture. Histopathological analysis of a fine-needle aspiration biopsy specimen from the pancreas was limited by crush artifact but showed lymphoplasmacytic infiltration, fibrosis, chronic inflammation, and no cancer. Which of the following is the most appropriate next step in management? You are offered: Begin glucocorticoid therapy with a gradual taper, Initiate pancreatic enzyme replacement therapy, Observe with repeat imaging in 6 months, Schedule pancreaticoduodenectomy, and Treat with intravenous immunoglobulin. We learn about IgG4-related syndromes. A previous trial involving patients with metastatic prostate cancer that was resistant to androgen pathway modulation (formerly referred to as castration-resistant) showed that adding talazoparib to enzalutamide significantly improved imaging-based progression-free survival and overall survival, with the greatest benefit observed in the cohort with alterations in homologous recombination repair genes. In an ongoing, phase 3, double-blind trial assessing talazoparib in patients with metastatic androgen pathway modulation–sensitive [APMS] prostate cancer harboring alterations in homologous recombination repair genes, investigators randomly assigned patients to receive talazoparib at a dose of 0.5 mg plus enzalutamide at a dose of 160 mg once daily (talazoparib group) or placebo plus enzalutamide at a dose of 160 mg once daily (control group). In these APMS patients with repair-gene mutations, the poly-ADP-ribose polymerase (PARP) inhibitor plus enzalutamide strategy beat placebo, also in terms of overall survival. The efficacy of teclistamab, a bispecific antibody targeting B-cell maturation antigen and CD3, as early-line monotherapy in relapsed or refractory

multiple myeloma is unclear. Investigators randomly assigned patients with relapsed or refractory multiple myeloma who had previously received one, two, or three lines of therapy, including an anti-CD38 monoclonal antibody and lenalidomide, to receive teclistamab or the investigator's choice of pomalidomide, bortezomib, and dexamethasone (PVd) or carfilzomib and dexamethasone (Kd). Teclistamab beat both PVd and Kd. Furthermore, overall survival was improved. Nav1.8, a voltage-gated sodium channel expressed in the peripheral nervous system, has a critical role in pain signaling. Previous trials of NaV1.8 inhibitors have shown effectiveness in reducing postoperative pain. Investigators conducted a phase 2b, double-blind, randomized, placebo-controlled trial to evaluate LTG-001, a selective Nav1.8 inhibitor, in patients with moderate-to-severe pain after abdominoplasty. Patients were randomly assigned to receive a 300-mg loading dose of LTG-001, followed by 150 mg every 12 hours (low-dose group); a 450-mg loading dose of LTG-001, followed by 300 mg every 12 hours (high-dose group); hydrocodone bitartrate–acetaminophen (5 mg of hydrocodone bitartrate and 325 mg of acetaminophen) every 6 hours; or placebo every 6 hours. All doses were administered orally over a 48-hour period. The primary end point was the time-weighted sum of the pain-intensity difference (SPID) over the 48-hour treatment period (SPID48). Inhibiting Nav1.8 should be competitive over current "pain"-treatment strategies. Overactivation of the alternative complement pathway contributes to IgA nephropathy and glomerular inflammation. In the 9-month interim analysis of this phase 3 trial, iptacopan, a complement factor B inhibitor, led to a significant reduction of 38.3% in the 24-hour urinary protein-to-creatinine ratio as compared with placebo and had an acceptable safety profile. In a phase-3 trial, investigators enrolled adults who had IgA nephropathy, an estimated glomerular filtration rate (eGFR) of at least 30 ml per minute per 1.73 m2 of body-surface area, and a 24-hour urinary protein-to-creatinine ratio of 1 or higher despite supportive care. Patients were randomly assigned, to receive oral iptacopan (200 mg) or placebo twice daily. The primary end point for the final analysis was the annualized total eGFR slope as estimated over a 24-month period. Iptacopan met the primary endpoint. Side effect profile was not a problem. Platelet-activating antibodies against platelet factor 4 (PF4) cause highly prothrombotic disorders with reduced platelet counts. Vaccine-induced immune thrombocytopenia and thrombosis (VITT) antibodies directly target PF4. N

Engl J Med reviews the topic. The N Engl J Med mystery patient is a 37-year-old woman from Honduras with an intra-nasal ulcer that has persisted for years. The Lancet reports the death of Eugene Braunwald, an iconic cardiologist, who died at age 96 years. Numerous South American countries collaborated on the Lat-Am-Fingers study. This randomized trial investigated life-style interventions in terms of improving outcomes in the elderly. The investigators claim acceptance of the intervention and improvements in mental abilities in the more-intensive intervention. Carbapenems are a mainstay of treatment in severe gram-negative infections. A randomized trial reveals that a new beta-lactam antibiotic, temocillin, is noninferior to carbapenems. Side effects were not different. The OPTIMA-AF trial tested dual platelet inhibition after percutaneous interventions in patients with atrial fibrillation. One month was “no worse than” 12 months in terms of MACE and caused less bleeding. Does adding a Bruton tyrosine kinase inhibitor to venetoclax plus rituximab lead to better outcomes in treating chronic lymphocytic leukemia? Pirtobrutinib administration proved that it does. Lancet next reviews light-chain caused amyloidosis and thyretin-induced amyloidosis. Treatments and outcomes for both have improved. In Science Magazine, we learn about ancient DNA research regarding small-pox spread from Europe to the Americas. In Washington Post, we confront a man with the auto-brewery syndrome. Load down the file and join me again on August 6, 16:00 English and 17:00 German.

Sincerely, Fred Luft

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