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 5-week-old boy was brought in for evaluation of a painful lump on his scalp that had been present since birth. The otherwise healthy baby had been born at term. Ultrasonography of the lesion showed a subcutaneous structure of mixed echogenicity. Physical examination and magnetic resonance imaging of the head is shown. What is the most likely etiology of the lump? You are offered. Atretic cephalocele, Cephalohematoma, Dermoid cyst, Lipoma, and Meningocele. Quickly rule out 4 and you are left with the correct answer. Asian patients with nonsmall-cell lung cancer (NSCLC) commonly have mutated epidermal growth factor receptor (EGFR) drivers. Sacituzumab tirumotecan (sac-TMT) is an antibody–drug conjugate targeting trophoblast cell-surface antigen 2 (anti-TROP2 antibody carrying a tropoisomerase inhibitor payload) that has shown significant survival benefits in patients with EGFR-mutated non–small-cell lung cancer (NSCLC) that has progressed after EGFR tyrosine-kinase inhibitor (TKI) therapy and platinum-based chemotherapy. In a phase 3 trial, investigators enrolled patients with EGFR-mutated locally advanced or metastatic nonsquamous NSCLC that had progressed after EGFR-TKI therapy. The patients were randomly assigned, in a 1:1 ratio, to receive sac-TMT monotherapy or pemetrexed plus platinum-based chemotherapy. The primary end point was progression-free survival as assessed by blinded independent review. Overall survival was a hierarchically tested key secondary end point. Sac-TMT met both primary and secondary endpoints. The initial therapy of NSCLC and EGFR-mutations is osimertinib, an inhibitor of the mutated EGFR driver. Results from the planned final analysis of overall survival are needed. In a phase 3, international, open-label trial, invesitgators randomly assigned in a 1:1 ratio patients with EGFR-mutated (exon 19 deletion or L858R mutation) advanced NSCLC who had not previously received treatment for advanced disease to receive either osimertinib (80 mg once daily) plus chemotherapy with pemetrexed and a platinum-based agent or osimertinib monotherapy (80 mg once daily). The key secondary end point was overall survival. Now, we learn about the resulting follow-up study. Osimertinib plus chemotherapy

improved survival compared to osimertinib alone. Earlier, we learned that the blood-brain-barrier can be overcome by fusion proteins that bind to the brain's transferrin-receptor (TFR) binding Fc domain. Tividenofusp-alfa, comprising iduronate-2-sulfatase fused to an engineered transferrin receptor–binding Fc domain, has been developed to treat neurologic and peripheral manifestations of mucopolysaccharidosis type II (MPS II or Hunter's syndrome), a rare lysosomal disorder causing progressive multisystem and neurologic decline. In a phase-1 study, tividenofusp-alfa showed reasonable safety with relatively promising results, suggesting that this fusion-protein TFR Fc-domain binding strategy may work. Multiple myeloma is a lethal disease, but salvage strategies continue to be developed. Patients with plasmacytomas that are noncontiguous with bone marrow (true extramedullary myeloma) are at high risk for disease progression or relapse. Phase 1 of the RedirecTT-1 study showed promising efficacy with dual-antigen targeting of myeloma with talquetamab (anti–G protein–coupled receptor family C group 5 member D) plus teclistamab (anti–B-cell maturation antigen) in patients with triple-class–exposed relapsed or refractory multiple myeloma, including those with true extramedullary myeloma. Most patients with drug-resistant, true extramedullary myeloma had a response with talquetamab plus teclistamab. The N Engl J Med review is on cardiogenic shock. Refer these patients to a center equipped to deal with this problem. The mystery patient this week has combined immunodeficiency syndrome. In the Lancet, the Global Burden of Disease project deals with intimate partner violence against female partners and children. The ROCKET-IGNITE studies were directed at atopic dermatitis. Rocatinimab is an antibody directed against the OX-40 receptor, belonging to the TNF-protein family. Rocatinimab beat placebo. Preeclampsia risk can be assessed with the 11.-13 SSW risk-assessment tool. This computerized tool was centrally used to establish a preeclampsia probability > 1-in-50 in pregnant patients. Such patients were then randomized to scheduled birth compared to usual care. The outcome was birth with pre-eclampsia. Pre-eclampsia was significantly reduced. The first Lancet review is on hyperemesis gravidarum. The differential diagnosis of the condition has increased but treatment is largely unchanged. The second Lancet review is on chronic kidney disease. SGLT-2 inhibitors should routinely be given; GLP-1 agonists might help obese CKD patients with type-2 diabetes. Aptamers are short synthetic nucleic acids

that form complex three-dimensional structures, enabling them to bind to cell-surface target molecules. Investigators in Science Magazine now describe single-cell perturbation-driven aptamer recognition and kinetics sequencing (SPARK-seq), a method that combines the binding properties and sequencing capabilities of aptamers with gene inactivation studies. This approach enables the simultaneous mapping of thousands of aptamer-target interactions and the identification of aptamers that bind to low-abundance targets. Washington Post gives advice on 5 little daily habits that increase health. The next oral presentation will be on January 7, 2026.

Sincerely, Fred Luft

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