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 46-year-old man with cirrhosis presented to the emergency department with a 1-week history of left flank pain. He reported no recent trauma, medical procedures, or use of anticoagulant or antiplatelet medications. His heart rate was 128 beats per minute, and his blood pressure was 64/37 mm Hg. Laboratory studies were notable for anemia, severe thrombocytopenia, and findings consistent with advanced liver disease. Physical examination and contrast-enhanced computed tomography of the abdomen are shown. What is the most likely diagnosis? You are offered: Acute hemorrhagic pancreatitis, Splenic rupture, Spontaneous retroperitoneal hemorrhage, Rectus sheath hematoma, and Ruptured abdominal aortic aneurysm. Observe the presence of Grey-Turner's sign, but it is not pancreatitis. For patients who are ineligible (too old or too sick) for induction chemotherapy (cytarabine and anthracyclines), hypomethylating therapy plus venetoclax is the standard treatment owing to its efficacy and side-effect profile. In a multicenter, phase 2 trial, investigators randomly assigned previously untreated adults with AML who were eligible for induction chemotherapy to receive either azacitidine plus venetoclax or induction chemotherapy. Venetoclax and azacitidine therapy was at least as good and was less toxic. This combination should probably replace standard induction therapy for AML. Achondroplasia is a genetic skeletal condition caused by FGFR3 pathogenic variants that are inherited as autosomal-dominant, gain-of-function mutations. Infigratinib, an oral FGFR1–3 tyrosine kinase inhibitor, down-regulates key pathways in the pathogenesis of achondroplasia. In a phase 3, multicenter, double-blind, placebo-controlled trial, investigators randomly assigned children with achondroplasia (3 to 17 years of age) to receive infigratinib (at a dose of 0.25 mg per kilogram of body weight) or placebo once daily for 52 weeks. The primary end point was the change from baseline in the annualized height velocity. The infigratinib group grew a bit but had no side effects of note. Whether treatment with balanced crystalloid fluid leads to better outcomes than 0.9% saline in children treated for septic shock is debated. In a pragmatic clinical trial conducted at 47 emergency departments in five countries, patients (2 months to <18

years of age) with suspected septic shock and abnormal perfusion were randomly assigned to receive fluid resuscitation with either balanced fluid or 0.9% saline for up to 48 hours. The primary outcome was a major adverse kidney event. Similar to results in septic adults, there was no difference in saline versus balanced electrolyte solutions in these critically ill young patients. Daraxonrasib has shown efficacy in patients with pancreas cancer harboring RAS mutations. RAS mutations, as a group, are the most common oncogenic drivers of non–small-cell lung cancer (NSCLC), and they occur in approximately 30% of patients. Whether daraxonrasib (RMC-6236) — an oral RAS(ON) multiselective, tri-complex inhibitor of guanosine triphosphate–bound mutant and wild-type RAS protein isoforms — is safe and effective in patients with RAS-mutant NSCLC is unknown. In a phase 1–2, multicenter, dose-escalation and dose-expansion study of daraxonrasib, investigators enrolled patients with previously treated advanced RAS-mutant NSCLC and administered daraxonrasib in doses of 10 to 400 mg orally once daily in 21-day cycles. The primary end point was safety. Secondary end points included investigator-assessed objective response (complete or partial response). Safety was acceptable and daraxonrasib showed efficacy on NSCLC patients harboring RAS mutations. The N Engl J Med review is on the management of isolated pulmonary nodules (“coin lesions”). The mystery patient of the week is a 46-year-old woman, who develops spontaneous fractures over a period of years and since calcium, phosphorus, PTH, and vitamin D are normal the fractures are ascribed to osteoporosis. Turns out she is 20 cm shorter than her sister and her alkaline phosphatase levels are low. In the Lancet, we are confronted with Lp(a), a lipoprotein of ill repute that is largely inherited. Lp(a) sits on LDL molecules so lowering LDL is the current treatment. Lancet presents an siRNA strategy to knock down Lp(a). Kylo-11 has been engineered to have an extremely long half-life. Kylo-11 lowered Lp(a) for a year after only a single dose! Lipoedema is a genetic condition of extremity obesity occurring only in women. Diet, exercise, and weight loss are all not helpful treatments. In a randomized trial, liposuction in lipoedema patients decreased pain and increased quality of life. Robotic joint replacement is replacing traditional surgery in total knee-replacement patients. But do robotic arms improve outcomes? A randomized trial in Lancet suggests that robotic arms to not improve outcomes. Lancet next presents two reviews on cardiovascular disease and pregnancy. In Science

Magazine, we inspect how Protostomia and Deuterostomia develop their hearts. We learn that animal hearts share more than 60% of gene modules and a conserved cellular foundation. Notably, certain atrial and ventricular characteristics were inherited by both protostomes and deuterostomes, pointing to an ancient origin possibly traceable to the last common bilaterian ancestor. Washington Post reports on Adrian, a man who actually exists without owning a smart phone. Load down the file and join me again on September 9, 16:00 English and 17:00 German.

Sincerely, Fred Luft

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