

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 45-year-old man presented with a 2-month history of worsening pain and swelling in his right shoulder. He worked in construction and had chronic intermittent pain in the joint. An MRI showed destructive arthropathy of the glenohumeral joint associated with a large effusion, free-floating calcific fragments, and full-thickness tears of the rotator cuff tendons. Analysis of the synovial fluid revealed hemorrhagic, noninflammatory fluid with negative cultures and no visible crystals. What is the most likely diagnosis? You are offered: Avascular necrosis of the humeral head, Calcium pyrophosphate deposition disease, Joint sarcoma, Milwaukee shoulder syndrome, and Rotator cuff tear arthropathy. The roentgenogram shows a destructive arthropathy characterized by the deposition of hydroxyapatite crystals, humeral head destruction, and severe rotator-cuff damage. Current therapies offer limited benefit for patients with previously treated metastatic pancreatic ductal adenocarcinoma (mPDAC). Aberrant activation of the RAS pathway is the key driver of PDAC, with oncogenic RAS mutations present in more than 90% of cases. Daraxonrasib is an oral RAS(ON) multiselective, tri-complex inhibitor of the active guanosine triphosphate-bound state of mutant and wild-type RAS. In a phase 3, international, open-label, randomized trial, investigators randomly assigned patients with previously treated mPDAC to receive daraxonrasib or chemotherapy of the investigator's choice. The dual primary end points were overall survival and progression-free survival in the subpopulation of patients with RAS G12 mutations (the RAS G12 population). Key secondary end points included overall survival and progression-free survival. Daraxonrasib increased survival in these mPDAC patients that almost invariably had a RAS mutation. Neoadjuvant cisplatin-based chemotherapy is a standard therapy for muscle-invasive bladder cancer. The efficacy and safety of neoadjuvant and adjuvant (perioperative) enfortumab vedotin–pembrolizumab as compared with neoadjuvant cisplatin-based chemotherapy in persons with this cancer are unclear. Investigators conducted a phase 3, open-label, randomized trial involving adults with muscle-invasive bladder cancer eligible for cisplatin-based chemotherapy and radical cystectomy with pelvic lymph-node

dissection (cystectomy). Participants were assigned to receive neoadjuvant enfortumab vedotin–pembrolizumab every 3 weeks), cystectomy, and 5 cycles of enfortumab vedotin and 13 cycles of pembrolizumab as adjuvant therapy or to receive neoadjuvant cisplatin–gemcitabine and cystectomy. The primary end point was event-free survival; key secondary end points were overall survival and pathological complete response. Safety was also assessed. Enfortumab vedotin plus pembrolizumab beat cisplatin-gemcitabine. No vaccines are currently licensed for the prevention of *Neisseria gonorrhoeae* infection. Observational studies suggest that the four-component meningococcal serogroup B vaccine (4CMenB) may reduce the risk of gonorrhea. In a multicenter, double-blind, randomized, placebo-controlled trial, investigators assigned men who have sex with men (MSM) to receive two doses of 4CMenB or placebo. Unfortunately 4CMenB provided no protection against gonorrhea. Approved pharmacologic therapies for pediatric hypertrophic cardiomyopathy are lacking, and surgical intervention may be indicated in patients with left ventricular outflow tract obstruction. The efficacy and safety of mavacamten, a cardiac myosin inhibitor (reduces inotropy) that is available for adults, warrant evaluation in adolescents. Investigators conducted a phase 3, double-blind, randomized, placebo-controlled trial involving symptomatic adolescents (12 to <18 years of age) with New York Heart Association class II or III obstructive hypertrophic cardiomyopathy. The patients were randomly assigned to receive mavacamten or placebo. Mavacamten helped these patients. The N Engl J Med review is on antiretroviral therapy (50 years of successful progress). The mystery N Engl J Med patient is a 28-year-old man, who was admitted to a hospital for a headache and vision loss in the right eye. He owned cats and a dog. In the Lancet, a multi-country analysis of population-based studies shows that blood pressure and cholesterol have been similarly reduced in the general population and in obese persons. Thus, these groups seem to receive similar care. Dual mobility hip prostheses appear to be associated with fewer hip dislocations than conventional total hip replacements. Unfractionated heparin (UFH) has been available since the 1950's but may have an increased bleeding risk and could cause heparin-associated thrombocytopenia with thrombosis (HIT). Fractionated low-molecular-weight heparin (LMWH) might be better but costs more. The two were compared in the anticoagulation of extracorporeal membrane oxygenation (ECMO). ECMO

duration was about 7 days. LMWH was “no worse” and could be better. The Lancet review is on genetic causes of retinal degeneration (about 20 syndromes). To my knowledge, there are 5 types of chemical bonds (ionic, metallic, covalent, hydrogen and van der Waals). Drugs generally rely on the latter two bonds; however, covalent bonding could sometimes be better. In Science Magazine, we inspect a technique involving an underexplored warhead type with well-tempered reactivity. Bicyclobutane is a structure that exhibits spring-like behavior and results in a better covalent bond. You will recall that the USA recalled the hapless alcohol prohibition amendment years ago, but some counties in various USA states are recalcitrant and choose to remain “dry”. In one such county in Alaska, a bush pilot was discovered harboring a six pack of Budweiser beer in his plane. Now, the state of Alaska wants to confiscate his airplane, despite the fact that he already paid a \$1500 fine, 20 years ago. The US Supreme Court will now decide the matter says the Washington Post. Load down the file and join me again on July 29, 16:00 English 17:00 German.

Sincerely, Fred Luft

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