

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 44-year-old man presented with a 4-day history of an itchy rash and a 2-day history of fever and malaise. The rash had first appeared on the scalp and then spread across the body within 24 hours. What is the most likely diagnosis? You are offered: Cutaneous T-cell lymphoma, Dengue fever, Disseminated gonococcal infection, Primary varicella infection, and Smallpox. Hint: the lesions vary in age, and they are prominent centrally instead of peripherally or general.

Aficamten reduces myocardial contractility (inotropy) by directly binding to cardiac myosin, which stabilizes the myosin pre-power stroke state and reduces the number of excessive myosin-actin cross-bridges, thus decreasing force generation in hypertrophic cardiomyopathy (HCM). This mechanism directly addresses the hypercontractility that causes left ventricular outflow tract (LVOT) obstruction in HCM. Beta-blockers have been the initial treatment for symptomatic obstructive hypertrophic cardiomyopathy (HCM) despite limited evidence of their efficacy. Whether aficamten as monotherapy provides greater clinical benefit than beta-blockers as monotherapy remains unknown. Investigators conducted an international, double-blind, double-dummy trial in which adults with symptomatic obstructive HCM were randomly assigned. The primary end point was the change in peak oxygen uptake at week 24; secondary end points were improvement at week 24 in New York Heart Association (NYHA) functional class and changes at week 24. Aficamten beat beta-blockers in obstructive HCM. Mavacamten (similar to aficamten) is approved to treat adults with symptomatic obstructive hypertrophic cardiomyopathy (HCM). However, its effects in nonobstructive HCM remain uncertain. Investigators conducted a phase 3, international, double-blind, placebo-controlled, clinical trial to determine whether mavacamten improves functional capacity and patient-reported health status among adults with symptomatic nonobstructive HCM. Mavacamten did not work in patients with non-obstructive HCM. The benefit of rehabilitation interventions in patients who are 65 years of age or older with myocardial infarction and impaired physical performance remains unclear. In a multicenter, randomized trial conducted in Italy, investigators assigned older patients

with impaired physical performance 1 month after myocardial infarction in a 2:1 ratio to receive either an intervention consisting of control of cardiovascular risk factors, dietary counseling, and exercise training (intervention group) or usual care (control group – general advice). The primary outcome was a composite of cardiovascular death or unplanned hospitalization for cardiovascular causes within 1 year. The intervention met the primary endpoint. On September 27, 2024, Rwanda reported an outbreak of Marburg virus disease (MVD), after a cluster of cases of viral hemorrhagic fever was detected at two urban hospitals. Investigators report key aspects of the epidemiology, clinical manifestations, and treatment of MVD during this outbreak, as well as the overall response to the outbreak. They performed a retrospective epidemiologic and clinical analysis of data compiled across all pillars of the outbreak response and a case-series analysis to characterize clinical features, disease progression, and outcomes among patients who received supportive care and investigational therapeutic agents. Aggressive measures were helpful against Marburg virus in this epidemic. The N Engl J Med review is on HCM. The weekly patient is a 93-year-old woman with aortic stenosis. She decides to eschew TAVR and elects to join the hospice group. The Lancet presents another systematic analysis of long-term clopidogrel versus aspirin for secondary prevention after myocardial infarction. Clopidogrel may be a bit better; however, the clinical relevance was not clear to me. The SWEDEPAD studies compared paclitaxel-coated versus control stents for peripheral vascular occlusive disease. In both these studies, the control stents actually looked a bit better than the paclitaxel stents. Next, we inspect a randomized controlled trial of beta-blocker against placebo in post-myocardial infarction patients with EF between 40 and 50 percent. Beta-blockers improved the prognosis in these patients. There are three reviews in Lancet this week. The first is on heart failure prevention, the second on heart failure prevention after myocardial infarction, and the third on heart failure in the face of renal and metabolic disease. I was aware of circular RNA but had not heard about circular DNA. This extrachromosomal DNA (ecDNA) is common in tumors. We learn from Science Magazine that unusually large swaths of unpacked ecDNA explain regions where the genome seemed to be bent and rewired to drive massive bursts of oncogene expression in malignant tumors. In the Washington Post, we learn that processed foods are bad for us and that five types of chemical additives

are responsible for the deleterious effects. Join me on Wednesday, September 17 for the above and more in another stunning, orally presented, clinical journal club, 16:00 in English and 17:00 in German.

Sincerely, Fred Luft

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