

New drugs

Molnupiravir for Covid-19

Viral RNA polymerase inhibitor, given orally twice daily

Ongoing phase 3 trial in outpatients with mild-moderate Covid (n=775):

7.3% of patients in treatment group hospitalized/died vs. 14.1% in placebo group [NNT 15]

No deaths in treatment group as of [10/1 press release](#) (vs. 8 in placebo group)

Fewer adverse events in treatment group

FDA EUA application pending

Also being studied for post-exposure prophylaxis

Monoclonal Antibody Prophylaxis for Covid-19

Casirivimab/indevimab (Regeneron)

RCT of 1505 seronegative patients given 1.2 g SC or placebo within 96 hr of household contact testing positive for Covid-19 [\[34347950\]](#)

Risk of any infection decreased from 14.2% to 4.8% [NNT 10]

Risk of symptomatic infection decreased from 7.8% to 1.5% [NNT 15]

Average duration of symptoms decreased from 3.2 to 1.2 weeks

4% injection site reactions

Bamlanivimab/etesevimab (Lilly) also has EUA for this but uses IV formulation

Cabotegravir/rilpivarinine for HIV

Combination of INSTI/NNRTI for treatment of HIV; new IM formulation can be dosed once a month

Two trials [\[32130806\]](#), [\[32130809\]](#) showed comparable outcomes compared with standard oral therapy at 48 weeks of follow-up

28-day oral lead-in is needed before starting therapy to confirm tolerability

Injection site reactions should be expected (>80%)

Cabotegravir alone for HIV PrEP

3-year trial of cabotegravir alone every 8 weeks vs TDF-FTC (*Truvada*) in 4566 at-risk HIV-negative patients [\[34379922\]](#)

13 new HIV infections in cabotegravir group vs 39 in TDF-FTC group; hazard ratio 0.34 [95% CI 0.18-0.62]

Incident HIV infections were rare but INSTI resistance was common when this happened

May be a good option for patients who have trouble taking daily PrEP but neither licensed nor ready for prime time

Tirzepatide for T2DM

Novel agent that stimulates a second incretin pathway (GIP) along with GLP-1

RCT (n=1879) compared different doses of weekly SC tirzepatide to 1 mg SC semaglutide [\[34170647\]](#)

All doses had greater impact on A1C and weight, with dose response (especially for weight)

GI adverse effects were common but similar in all groups

Semaglutide dose was subtherapeutic for weight loss

Bempedoic acid for hyperlipidemia

Oral adenosine triphosphate-citrate lyase (ACL) inhibitor

Reduces LDL by 15-20% in addition to other agents (statins, ezetimibe)

Inhibits urate transport in the kidney: rate of gout was 1.5% vs 0.4% in placebo

Weak signal of increased risk for tendon rupture

Published trials are small (max 2200 patients) and lack hard endpoints

Cefiderocol for resistant gram-negatives

Cephalosporin that binds iron and uses bacterial iron transport system to penetrate cell membrane

Active against ESBL and carbapenemase producing gram-negatives including *Pseudomonas*, *Acinetobacter*, *Stenotrophomonas*

Non-inferior to cabapenems for complicated UTI, nosocomial pneumonia

May not be as effective as colistin when used as salvage therapy

\$1100/day

Aducanumab for Alzheimer's disease

Monoclonal antibody targeting aggregated β -amyloid in the brain [\[34320284\]](#)

Significant reduction in amyloid burden on PET imaging

Clinical trials enrolled 3285 patients with MCI or mild AD with positive PET

Trials were stopped early when they seemed unlikely to meet prespecified end points

Post-hoc analysis of one study showed small benefits in a few ADLs

Increased risk of cortical microhemorrhage in treatment group

Caplacizumab for iTTP

Immune-mediated TTP is caused by autoantibody to ADAMTS13

Standard treatment is plasma exchange + steroids/rituxumab

Caplacizumab binds vWF, preventing platelet adhesion

Placebo controlled RCT [\[30625070\]](#) found absolute reduction of 37% (NNT 3) in death, recurrent TTP in treatment group

Increased rate of "serious" bleeding including epistaxis, gingival bleeding, and UGIB

Once-weekly basal insulin for Type 2 DM

Insulin icodex has multiple AA substitutions and a fatty acid moiety to allow for binding to albumin; peaks at 16 hr, $t_{1/2} > 7$ days

RCT: of once weekly icodex vs once daily glargine in patients < 75 y/o with T2DM and A1C from 7.0-9.5%: [\[32960514\]](#)

Similar reductions in A1C (1.3 vs 1.2%)

No difference in hypoglycemia or injection-related adverse events

Drug updates

SGLT-2 inhibitors: an edge over GLP-1 agonists?

Massive meta-analysis [764 trials, 421,346 patients] of SGLT-2/GLP-1 vs multiple comparators: [\[33197395\]](#)

Odds ratio for all-cause mortality 0.88 with SGLT-2 vs GLP-1

Slightly greater weight loss with SGLT-2 (?!?)

No difference in CV mortality, ESRD

Significant increase in genital infections

SGLT-2 also shown to be beneficial for HFrEF [\[31535829\]](#), [\[32865377\]](#) & CKD [\[32970396\]](#).

Iron for HFrEF

AFFIRM-AHF: RCT of 1100 pts hospitalized with LVEF $< 50\%$ and ferritin < 100 (or < 300 with transferrin sat $< 20\%$) randomized to IV iron infusion vs placebo

Reduced rehospitalization for HF at 1 year (NNT 8) [\[33197395\]](#)

Improved HF-related QoL at 4 & 24 weeks (but not 1 year) [\[34080008\]](#)

3 additional trials ongoing but seems like a reasonable, safe intervention while they are pending

4 month therapy for active TB

Current standards for active TB treatment call for 4 drugs (RIPE) for eight weeks and then two drugs (RIF/INH) for 18 weeks for total of six months of directly observed therapy

Open label trial randomizing 2516 patients to standard treatment vs 4 months of new regimen consisting of four drugs (rifampin/isoniazid/moxifloxacin/pyrazinamide) for 8 weeks then 3 drugs (drop PZA) for 9 more weeks (total 4 months). [\[33951360\]](#)

Primary endpoint was disease-free survival at 12 months: 88% in intervention group vs 90% in control group, met threshold for non-inferiority

Could significantly shorten treatment for those with TB infection

Atrial fibrillation update

EAST-AFNET4: 2789 patients with new dx of AF (< 1 yr, median 36d) randomized to rhythm control vs rate control. At 5 yrs: 5.5% reduction in composite of CV death, stroke, hospitalization with CHF/ACS in rhythm control arm; 3.5% increase in serious adverse events related to treatment (mostly drug toxicity with a few ablation complications). [\[32865375\]](#)

Median age 70, 46% female

55% of patients in sinus rhythm at baseline; increased to 82% in rhythm control group and 60% in usual care group

90% of patients were anticoagulated with DOAC or VKA, continued through study end

AFIRE: 2236 pts with AF & stable CAD randomized to rivaroxaban 15 mg/d w/wo antiplatelet agent (70% aspirin). At 24 mos: 3.0% reduction in all-cause mortality in rivaroxaban monotherapy group (NNT 33). 2.2% reduction in major bleeding, 0.8% reduction in hemorrhagic stroke. No increase in revascularization, MI, embolic events. [[31475793](#)]

AVERROES subgroup analysis: in patients over 75, apixaban was more effective than aspirin alone at preventing stroke/embolism AND equally safe for major bleeding outcomes. [[26590293](#)]

Colchicine in CAD

COLCOT: 4745 patients (mean age 61, 81% male) with MI in last 30 days randomized to colchicine 0.5 mg/d vs placebo. At 23 mos: 1.6% reduction in composite of CV death, cardiac arrest, stroke, MI, urgent revascularization (NNT 63), driven largely by stroke and revascularization. Adverse effects included pneumonia (ARI 0.5%, NNH 200), nausea, flatulence. [[31733140](#)]

LoDoCo2: 5522 patients (mean age 66, 85% male) with stable CAD (84% had prior ACS/revascularization) randomized to colchicine 0.5 mg/d vs placebo. At 29 mos: 2.8% reduction in composite of CV death, MI, stroke, revascularization (NNT 35), driven by MI, revascularization. Reduced incidence of gout in treatment group, no increase in hospitalization for pneumonia. Nonsignificant increase in non-CV death in the colchicine group (0.6%). [[32865380](#)]

Hypertension update

With intensive therapy:

No increase in orthostatic hypotension [[31983312](#), [32909814](#)]

No increase in fear of falling [[31778222](#)]

No increase in actual falls [[33568342](#)]

RCT: 19168 patients (mean age 61, 56% male) randomized to take once-daily antihypertensives at bedtime or in the morning [[31641769](#)]

At 6.3 yr: 5.5% reduction in composite of stroke, CHD, CHF (NNT 19) with significant decreases in all three subgroups

C/w previous small trial, another big trial expected to report soon

DOACs for VTE in Cancer

Two meta-analyses of DOAC vs LMWH for treatment of cancer associated VTE. [[32548553](#), [32788122](#)] For 6 mo f/u:

VTE recurrence down from 8.2→5.2% (NNT 33)

Major bleeding up from 3.3→4.3% (p=NS)

- Risk of major bleeding significantly increased with GI malignancy: 4.0→9.3% (NNH 19)

Clinically relevant non-major bleeding up from 6.4→10.4% (NNH 25)

Addiction Medicine update

RCT: 96 patients with AUD, h/o withdrawal, consumption of ≥ 5 drinks per day, and ≥ 3 days of abstinence were randomized to gabapentin (300-300-600 mg) vs placebo for 16 weeks: [[32150232](#)]

In patients with high baseline withdrawal severity, abstinence increased from 4→41% (NNT 3)

No effect in patients with low withdrawal severity

Cochrane review of e-cigarettes for smoking cessation: more effective than other NRT (NNT 25), non-nicotine pharmacotherapy (NNT 25), and behavioral support alone (NNT 17). Evidence was moderate certainty for pharmacotherapy and very low certainty for behavioral support. [[33052602](#)]

Atypical femur fractures with bisphosphonates

Retrospective cohort study using Kaiser Permanente data: 196,129 million women over 50 who had used bisphosphonates from 2007-2017 [[32813950](#)]

Risk of atypical femur fracture was overall very low, but increased dramatically with duration of bisphosphonate use: those using for 5-8 years had double the risk of those using for 3-5 years, and those using for over 8 years had 5x increase in risk

Risk of AFF also varied by race: Asian >> White/Hispanic >> Black; no variation by age

Many more hip fractures prevented than AFFs but yield highest in older patients at highest risk of hip fracture

Validates current guidelines recommending “holiday” after 3-5 years of bisphosphonate therapy. [[30907953](#)]

Ca/Vit D for recurrent BPPV

RCT: 1050 patients with typical BPPV randomized to test-and-treat strategy with calcium/vit D vs. usual care after canalith repositioning maneuvers. [[32759193](#)]

70% of intervention group had vitamin D level < 20 ng/mL; they were treated with CaCO₃ 500 mg/ vit D 400 IU twice daily. At 1 yr f/u:
Recurrence rate reduced from 46.7→37.8% in the intervention group (NNT 11); subgroups suggested effect more pronounced in older, overweight patients
Study conducted in South Korea, where prevalence of Vitamin D deficiency is 70% [\[29952942\]](#)

Those aren't drugs!

PT vs steroids for knee OA

RCT: 156 patients in US military health system (mean age 56, 52% male) with clinical and radiographic osteoarthritis of the knee randomized to PT (8 sessions over 4-6 weeks + up to 3 sessions at 4 & 9 month visits) vs steroid injections (40 mg triamcinolone, up to three over 12 months). [\[32268027\]](#) At 1 year:

Pts in PT arm had lower WOMAC scores than glucocorticoid (37 vs 56)

Pts in PT arm were more likely to have meaningful reduction in WOMAC score (90% vs 74%, NNT 7)

Self-monitored Home BP

RCT of web-based home BP monitoring intervention in 612 treated pts with baseline BP > 140/90 [\[33468518\]](#)

Pts in intervention arm were asked to record BP on web portal 7 days per month and given online feedback

If BP above target for two consecutive months, clinician got email recommending medication adjustment

SBP reduction 9.8 points in usual care group, 13.2 points in intervention group

Larger effect in pts < 67 y/o

Adding Psychotherapy for Depression

Meta-analysis of 17 randomized trials of psychotherapy after early pharmacotherapy for major depressive disorder [\[33237285\]](#)

RR for relapse 0.84 when psychotherapy was added after three months of medications

Worth an extra nudge to try to get patients treated with drugs alone to engage with psychotherapy

Pharmanure

The 2021 Pharmanure List

Zerivate eyedrops: Prescription-only cetirizine for \$230/bottle

Brexafemme (Ibexafungerp) for vaginal candidiasis: \$475

Orphenagesic forte: Orphenadrine (remember *Norgesic*?) + ASA + caffeine for \$1590 per 60 tablets

Consensi: amlodipine/celecoxib fixed dose combination for \$1287/month

Palforzia: peanut allergen powder for \$890/month