

Another week, another top 5! The team faced well over 2,000 papers this week, along with a couple of big-hitters which sneaked themselves in. We've all noticed a jump in quality and so whittling down to just five hasn't been easy. Luckily, if you have the head space for ten more which couldn't quite fit the page, check out the Director's Cut. If an interactive live journal club captures your interest then tune in to the webinar Tuesdays at 11:00, click here to register.



The following papers have been split into 3 categories that will allow you to focus on those that are most vital to your practice.

- Worth a peek: interesting, but not yet ready for prime time
- Head Turner: new concepts
- Game Changer: this paper should change practice

Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study by Docherty et al ¹

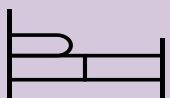
Topic: Observational

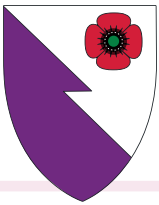
Rating: Head turner

Scout: Dr Anisa Jafar

The benefit of being several months into the pandemic is of course potential for big data. Over 20,000 hospitalised UK patients with COVID-19. The headlines remind us of the independent risk factors for in-hospital mortality, which are increasing age, being male, and having chronic co-morbidities i.e. cardiovascular disease, liver disease, chronic kidney disease, chronic respiratory disease and dementia. One thing the authors are keen to highlight is that

obesity was noted to be an independent risk factor. Interestingly diabetes didn't quite reach significance as an independent predictor of in-hospital mortality. So what else? Median of 4 days symptomatic pre-admission; median age of admission 73; 41% discharged alive (26% died, the rest still remain in hospital). If ventilated, 17% discharged alive (37% died, the rest remain in hospital). Too much to summarise here, definitely worth spending your next coffee break getting into the detail.





Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial by Wang et al ²

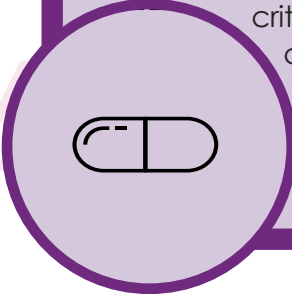
Topic: Treatment

Rating: Head turner

Scout: Dr Daniel Darbyshire



This is a well-designed and clearly reported negative trial of an antiviral therapy for patients with COVID-19 admitted to hospital in Wuhan. 237 patients split 2:1 remdesivir vs placebo, enrolled if 12-days or less since symptoms started (so, again lots of 'late' administration of the therapy). Underpowered overall however interim analysis at this number of patients was accounted for. The study used a 6-point severity scale: death=6; extracorporeal membrane oxygenation or mechanical ventilation=5; noninvasive ventilation or high-flow oxygen therapy=4; oxygen therapy (NOT high-flow/non-invasive ventilation)=3; hospital admission but not requiring oxygen therapy=2; discharged/reached discharge criteria=1. This is both objective and likely to be important to patients - a good candidate for something for all studies to report so we have a hope of any meaningful meta-analyses. The study found a numerically median reduction in time to improvement between the remdesivir and placebo group which was not statistically significant. Not sure this outcome means we should be writing remdesivir off just yet: watching closely.



Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial by Zhu et al ³

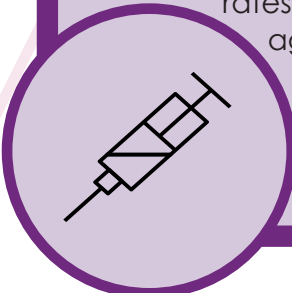
Topic: Vaccine

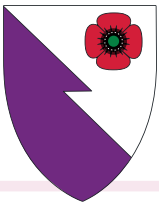
Rating: Worth a peek

Scout: Dr Anisa Jafar



We are going to see more and more of these studies as the months go on. Here we have a recombinant adenovirus expressing the infamous spike glycoprotein being used as a COVID-19 vaccine. 3 groups of healthy adults (36 in each) received different doses and immune response was measured. Mild to moderate side effects were experienced, none serious (but increasing severity with increased dose) and peak antibodies were seen at 28 days, specific T-cell response peaked at 14 days. A number of issues relating to pre-existing antibodies to the adenovirus itself and lower seroconversion rates in older adults were noted. The team admit it is a small group, with no-one aged over 60 and with no control group, furthermore as it is first-in-human it does not measure efficacy. Importantly the study was not powered for safety outcomes. Bear in mind that antibody response was only measured at the latest at 28-days, so let's keep our eyes on the upcoming later measurements. Very much a work in progress.





Game changer summary

Mehra et al signal trouble for HCQ, thank goodness no-one stockpiled...⁴



Summary of the rest

ISARIC give us the headlines on 20,000 hospitalised UK patients with COVID-19¹
Wang et al leave us hanging with a non-significant result using remdesivir²
Zhu et al have us brushing up on our vaccine science with a recombinant adenovirus offering³
Holmes et al throw us a curveball in the quest to understand where all the regular pathology went⁵



References

- 1) Docherty AB, Harrison EM, Green CA. Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;369:m1985 <http://dx.doi.org/10.1136/bmj.m1985>
- 2) Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet*. 2020;395(10236):1569-1578. doi:10.1016/S0140-6736(20)31022-9
- 3) Zhu FC, Li YH, Guan XH, et al. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. *Lancet*. 2020. doi:10.1016/S0140-6736(20)31208-3
- 4) Mehra MR, Desai SS, Ruschitzka F, et al. Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. [published online ahead of print, 2020 May 22]. *Lancet*. 2020 doi: 10.1016/S0140-6736(20)31180-6
- 5) Holmes JL, Brake S, Docherty M, Lilford R, Watson S. Emergency ambulance services for heart attack and stroke during UK's COVID-19 lockdown [published online ahead of print, 2020 May 14]. *Lancet*. 2020;S0140-6736(20)31031-X. doi:10.1016/S0140-6736(20)31031-X

