The Adaptive COVID-19 Trial (ACTT) is a double blinded placebo controlled RCT of up to 1063 patients (400 recovery needed for primary outcome) in **hospitalised patients who had advanced COVID-19 with lung involvement** has shown (**interim results)** that Remdesivir 200mg IV on day one and then 100mg daily for up to 10 days (IV)vs placebo:

1. recovered faster -time to recovery (ie, being well enough for hospital discharge or to return to normal activity level) was 31% faster for patients who received remdesivir vs placebo ($P <$ .001). Median time to recovery was 11 days (remdesivir) vs 15 days (placebo); the primary outcome time to recovery by day 29.
    - Day of recovery is defined as the first day on which the subject satisfies one of the following three categories from the ordinal scale: 1) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 2) Not hospitalized, limitation on activities and/or requiring home oxygen; 3) Not hospitalized, no limitations on activities.

2. Secondary outcome mortality showed a non-significant statistical survival benefit: mortality rate of 8.0% vs 11.6%; ($P = 0.059$).

In contrast the Wuhan study, the first randomised placebo-controlled clinical trial of remdesivir among hospitalized patients with severe COVID-19 and with laboratory-confirmed SARS-CoV-2 infection within 12 days of symptom onset, having oxygen saturation of 94% or less on room air, and having radiologically confirmed pneumonia in China was inconclusive (Lancet). Drug dosing was similar - 200 mg on day 1 followed by 100 mg on days 2–10 in single daily infusions) or placebo infusions for 10 days It showed nonsignificant trends toward benefit but the study was stopped early after 237 [remdesivir = 158 and placebo = 79).of the intended 453 patients were enrolled, owing to a lack of additional patients who met the eligibility criteria. The trial was underpowered. The primary endpoint was time to clinical improvement to day 28, defined as the time (in days) from randomization to the point of a decline of two levels on a six-point ordinal scale of clinical status (on that scale, 1 indicated that the patient was discharged, and 6 indicated death) or to the patient's being discharged alive from hospital, whichever came first.

- Remdesivir did not significantly speed recovery: Average time to clinical improvement 21 days for remdesivir group vs 23 days placebo group.
    - Hazard ratio [HR], 1.23; 95% confidence interval [CI], 0.87 – 1.75).
2. Remdesivir did not or reduce deaths from COVID-19 within 28 days of randomisation: (14% (22/158) remdesivir died vs 13% (10/78) placebo).
3. There was no signal that viral load decreased differentially over time between the two groups.
4. Prespecified secondary outcomes, time to clinical improvement and duration of invasive mechanical ventilation were shorter among a subgroup of patients who began undergoing treatment with remdesivir within 10 days of showing symptoms, in comparison with patients who received standard care. (median, 18 days vs 23 days; HR, 1.52; 95% CI, 0.95 – 2.43). However there was no statistically significant, difference in mortality, with 11% (8/71) patients dying compared with 15% (7/47) receiving placebo.

5. Adverse events in 65% of remdesivir recipients, vs 64% of those who received placebo.

6. Overall proportion of serious adverse events: remdesivir vs placebo (18%; 28/155 vs 26%; 20/78).

7. Remdesivir group discontinued treatment because of adverse events including gastrointestinal symptoms (eg, nausea, vomiting) and cardiopulmonary failure (18 remdesivir group; 12% vs 4 placebo; 5%).

**Synopsis**

Therefore the Chinese study has not shown that remdesivir treatment meets least clinically important difference but it has not ruled such a benefit out. The sub group analysis suggested possible benefit for those treated within 10 days but this is hypothesis generating and mere speculation. It was safe and reasonably tolerated.

The new study is better powered with a similar design so should confirm if this trend was statistically true in reducing duration of illness. To me once the new study is released as they are similar in design pooling the data may be the ideal way to get a definitive answer. More importantly the secondary analysis which I concede is speculation for both may show a mortality benefit but I have not done a power calculation to estimate the size of s study that would be needed with a hard outcome of death. I would be several thousand depending on the effect size desired.

In addition we need to remember that Remdesivir could be part of the armoury with other meds to block other pathways or viral enzymes. The Chinese study did allow patients to have concomitant use of lopinavir-ritonavir, interferons, and corticosteroids, which may be a confounder.

Finally should one consider giving the drug even earlier in the disease but economically may not be viable?