totally asymptomatic for all their life. In most of the few true patients, no genetic abnormalities are found; in others, such as the family of Patient 4, the disorder is also consistent with Lenegre disease and arrhythmogenic cardiomyopathy.

In 1988 Andrea Nava,[2] demonstrated that a depolarization abnormality was the underlying cause of the ST-segment elevation. This theory has been heavily fought for two decades, during which everybody agreed that the syndrome was simply a functional repolarization disorder, simply erasing all the published data on structural abnormalities and depolarization disorders underlying the syndrome.[6,7]

Nowadays, the depolarization organic theory has been re-evaluated by all scientists and an ECG cure by means of epicardial ablation of the right ventricular outflow tract is becoming popular. The main problem is that nobody has sufficient criteria to correctly stratify the subjects with the discussed ECG, so there is a serious risk of unjustified overtreatment.

In my personal opinion, we are still far from a correct scientific approach to the true syndrome, and ignorance does not justify submitting healthy young people with a strange ECG to invasive investigations and treatments, only because of a Brugadophobia, not based on scientific data but only on Google and Blog references.

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References

References are available as supplementary material at *European Heart Journal* online.

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Weekly Journal Scan

Conflicting results on the efficacy of remdesivir in hospitalized Covid-19 patients: *comment on the Adaptive Covid-19 Treatment Trial*

The results of the Adaptive Covid-19 Treatment Trial (ACTT-1) Trial have been published in *the New England Journal of Medicine.* https://doi:10.1056/NEJMoa2007764.

Key Points

- In the double-blind, randomized, multinational ACTT-1 trial,[1] the antiviral drug remdesivir was administered intravenously at the loading dose of 200 mg on Day 1, followed by 100 mg for up to 9 additional days, and compared with placebo in 1062 hospitalized adults with laboratory-confirmed coronavirus disease 2019 (Covid-19) who had evidence of lower respiratory tract infection. Of these, 159 (15%) were categorized as having mild-to-moderate disease and 903 (85%) were considered to have severe disease.

- The primary outcome was the time to recovery defined as the first day, during the 28 days after enrolment, on which a patient met the criteria for the less severe categories of clinical status on the eight-category ordinal scale.

- Patients who received remdesivir had a shorter time to recovery [10 days; 95% confidence interval (CI), 9–11], as compared with those who received placebo [15 days; 95% CI, 13–18; rate ratio (RR) for recovery, 1.29; 95% CI, 1.12–1.49; $P < 0.001$]. In the severe disease stratum, the median time to recovery was 11 days, as compared with 18 days (RR for recovery, 1.31; 95% CI, 1.12–1.52). The benefit of remdesivir was larger when given earlier in the disease course. Moreover, the benefit in recovery persisted when adjustment was made for glucocorticoid use, which suggests that the benefit of remdesivir may be additive to that of dexamethasone.

- Kaplan–Meier estimates of mortality (one of many secondary outcomes) by Day 15 were 6.7% in the remdesivir group and 11.9% in the placebo group [hazard ratio (HR), 0.55; 95% CI, 0.36–0.83]; K–M estimates by Day 29 were 11.4% and 15.2% in the two groups, respectively (HR, 0.73; 95% CI, 0.52–1.03).

- Serious adverse events, including serious respiratory failure, occurred less frequently in the remdesivir group (24.6%) than in the placebo group (31.6%).

Comment

Remdesivir, an inhibitor of the viral RNA-dependent RNA polymerase, was identified early as a promising candidate for Covid-19 treatment because of its ability to inhibit severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at relatively low concentrations *in vitro*. Early on, there were a series of studies testing the potential clinical efficacy of remdesivir in Covid-19 patients with conflicting results, at least in part, reflecting the small sample size and/or uncontrolled nature of the studies.

Strengths of the ACTT-1 trial are represented by its double-blind, placebo-controlled design, a potentially valuable primary endpoint in terms of resource utilization, and adequate statistical power to test a moderate treatment effect.[1] Weaknesses are related to the numerous challenges encountered by participating centres during the Covid-19 pandemic, resulting in less-than-optimal staff training, available resources, and study monitoring. Moreover, although randomization was stratified by disease severity at enrolment, 54 of the patients who were in the mild-to-moderate stratum at randomization were subsequently found to meet the criteria for severe disease, resulting in 105 patients in the mild-to-moderate disease stratum and 957 in the severe stratum, thereby precluding the assessment of remdesivir efficacy in patients with less severe disease.[1] As emphasized by the US National Institutes of Health Expert Panel,[2] because viral replication may be particularly active early in the course of Covid-19, antiviral therapy may have the greatest impact before the illness progresses into the later stages of disease. For this reason, it would be desirable to understand the dynamics of SARS-CoV-2 infection and the role of antiviral drugs in treating mild, moderate, severe, and critical disease, to optimize the treatment for people with Covid-19.[2]

In March 2020, the World Health Organization (WHO) began a large, simple, multi-country, open-label randomized (SOLIDARITY) trial among hospitalized Covid-19 patients of the effects of four re-purposed antiviral drugs that were expected to have at least a moderate effect on mortality: remdesivir, hydroxychloroquine, lopinavir, and interferon-β1a.[3] The WHO SOLIDARITY trial consortium has just reported interim mortality results for these drugs.[3] With 604 deaths in ~5400 randomized to the same remdesivir regimen used in the ACTT-1 trial (136 deaths in ~1000), the in-hospital death RR was 0.95 (95% CI, 0.81–1.11, $P = 0.50$).[3] Moreover, in the SOLIDARITY trial, there were no material effects on ventilation initiation or time to discharge (secondary endpoints).[3]

While waiting for the final results of the WHO SOLIDARITY trial to be published in a peer-reviewed journal, the overall negative findings of the largest, independent study of existing antiviral strategies suggest the opportunity of rethinking current treatment guidelines for Covid-19 and redefine the size of the unmet therapeutic need in this setting.

Supplementary material

supplementary material is available at *European Heart Journal* online.

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