Remdesivir in the treatment of COVID-19: An Inverse Probability of Treatment Weighting analysis

Tebe C[1], *Pallares N*[1], *Langohr K*[2], *Gomez Melis G*[2], *Videla S*[3], *Carratala J*[3]

[1] ctebe@idibell.cat,npallares@idibell.cat , IDIBELL, Barcelona, Catalonia, Spain
[2] lupe.gomez@upc.edu, klaus.langohr@upc.edu, UPC/BarcelonaTech, Barcelona, Spain
[3]svidela@bellvitgehospital.cat, jcarratala@bellvitgehospital.cat, Bellvitge Universitary Hospital, Barcelona, Spain

Introduction: Remdesivir is an antiviral drug approved for the treatment of severe COVID-19. In clinical trials, people who received remdesivir recovered faster than those who received placebo (median 10 vs 15 days), and mortality rates were also improved in those who received supplemental oxygen (4 % vs 13% on day 29 of treatment). There is still debate about the benefits of remdesivir from clinical trials. We used the multicentre DIVINE cohort to assess the effectiveness of remdesivir in COVID-19 hospitalised subjects in three different epidemic waves.

Methods: An inverse probability of treatment weighting (IPTW) propensity score analysis was performed to account for confounding by indication due to the lack of randomisation in treatment assignment in our cohort. Propensity scores were estimated using a logistic regression model stratified by wave. In both cohorts (unweighted and weighted), the incidence of mortality, ICU admission, nephrotoxicity and hepatotoxicity were compared between study groups. A Cox regression model was used to compare the risk of death and a log-binomial model for the other outcomes, resulting in hazard ratio (HR) and relative risk (RR) with a 95% confidence interval. A planned subgroup analysis was performed on identified clinically relevant groups. Analyses were performed using R software (survival, jskm, survey, and lme4).

Results: Among 5813 subjects from the DIVINE cohort, 477 remdesivir users and 1122 non-users were selected. Median age was 64 and 40% were women. During hospitalisation, 36 (7.6%) users and 118 (10.5%) non-users died. After adjustment for IPTW, remdesivir use was not associated with a lower risk of death (HR 0.73 95% CI 0.47 to 1.12), ICU admission (RR 0.84 95% CI 0.58 to 1.22), or nephrotoxicity and/or hepatotoxicity (RR 1.06 95% CI 0.75 to 1.50). Subgroup analysis suggested a potential pretective effect in subjects with early administration of remdesivir. Further research is needed to confirm these findings.

Conclusion: Our preliminary results using real-world data show a crude protective effect of remdesivir on in-hospital mortality, but the effect is minimised after adjustment for key confounders. No safety concerns with regards to renal and liver outcomes were raised in subjects with COVID-19 treated with remdesivir in our cohort. Further methodological approaches are planned to confirm these results.

Keywords: real world data, propensity score, inverse probability weighting, cox regression, log-binomial.