Measurement of remdesivir and its metabolite in plasma for COVID-19 research

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Introduction: Remdesivir is a therapy with the potential to be used to treat COVID-19 and is approved for use in relevant patients in Australia and globally. In order to understand optimal dosing in patients with COVID-19 we have developed an assay that can measure therapeutic concentrations of remdesivir and its active metabolite GS-441524 in plasma.

Method: Instrument: Shimadzu Nexera-8050 UHPLC-MS/MS.

Chromatography: The stationary phase was a Kinetex C8, 100 x 2.1 mm, 1.7 μm analytical column and the mobile phase was a gradient of 0.02% formic acid and acetonitrile (v/v). Detection: Remdesivir and GS-441524 were monitored using positive mode electrospray (ESI+) with selective reaction monitoring (SRM) of 603.20→229.05 and 291.95→163.15, respectively. The stable isotope labelled internal standards (IS) [13C6]-remdesivir and [13C5]-GS-441524 were monitored using ESI+ with SRM of 609.00→206.00 and 297.15→148.10.

Sample Preparation: A 100 μL plasma sample was mixed with isopropyl alcohol and acetonitrile (containing the IS) to precipitate the plasma proteins.

Results: The assay has been validated to the industry standard (FDA 2018 guidelines). The calibration line was linear for remdesivir from 5 to 5000 ng/mL with acceptable precision and accuracy (within 9.1%). The calibration line for GS-441524 was linear from 5 to 500 ng/mL with acceptable precision and accuracy (within 9.3%). The assay also meets the criteria for matrix effects (within 10.6%) and stability testing.

Application: This assay will be used in an ex vivo study investigating the impact of extracorporeal membrane oxygenation (ECMO) on the dosing of remdesivir (funded by RBWH Foundation), as well as for a dosing study of remdesivir in COVID-19 patients hospitalized in Spain (funded by CRE REDUCE).

Conclusion: High quality bioanalytical capabilities available at UQCCR, based on the RBWH campus, are being directed to inform clinicians on optimal dosing for potential COVID-19 treatments.

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