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Case Reports and Series

Use of remdesivir for COVID-19 pneumonia in patients with advanced kidney disease: A retrospective multicenter study

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A B S T R A C T

Background and objectives: Remdesivir, an antiviral drug routinely used in the treatment of COVID-19 has not yet received FDA approval for use in patients with advanced kidney disease defined as GFR < 30 mL/min/1.73 m². There is concern that an excipient in Veklury (Gilead’s proprietary name for remdesivir) called sulfobutylether-beta-cyclodextrin (SBECID), which is renally cleared, may accumulate and reach toxic levels in patients with advanced kidney disease. The aim of this study was to summarize characteristics and incidence of adverse events of chronic kidney disease (CKD) patients who received remdesivir during hospitalization. Design, setting, participants, and measurements. We retrospectively studied patients admitted to one of several hospitals of the Mayo Clinic Foundation with the diagnosis of COVID-19 pneumonia and CKD. Laboratory values were also measured when remdesivir was first administered and stopped. All analyses were performed in the overall patient group and three separate subgroups of patients with a GFR ≥ 15, a GFR < 15 and dialysis, and a GFR < 15 and no dialysis. Results: A total of 444 CKD patients who were admitted to the hospital with COVID-19 pneumonia between May 2020 and September 2021 were included. Information was collected on patient characteristics, hospitalization, and adverse events. In the overall cohort, median age was 72 years (Range: 21-100 years), 55.2 % of patients were male, and most (86.5 %) were Caucasian. CKD stage was 3 for 114 patients (25.7 %), 4 for 229 patients (51.6 %), and 5 for 101 patients (22.7 %). A total of 146 patients (32.9 %) were admitted to the ICU, 103 (23.2 %) died in the hospital, and 120 (27.0 %) were on dialysis. The proportion of patients with an adverse event did not differ dramatically between the GFR ≥ 15 (20.9 %), GFR < 15 and dialysis (30.2 %), and GFR < 15 and no dialysis (32.3 %) groups (P = 0.12). Conclusion: Our results suggest that the use of remdesivir in patients with very severe CKD is safe, even in those who are not on renal replacement therapy.

Introduction

Remdesivir, a viral RNA-dependent RNA-polymerase inhibitor, was developed by Gilead Science in collaboration with the Centers for Disease Control and Prevention (CDC) and the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) searching for treatments for respiratory syncytial virus and hepatitis C. Although found ineffective in treating Ebola virus disease (Yan and Muller, 2021), activity against numerous other viruses, including SARS-CoV-1 and MERS-CoV, was later documented (Mechinemi et al., 2021). In October of 2020, remdesivir became the first medication to receive FDA approval for the treatment of COVID-19 (Rubin et al., 2020). The results of several trials (Beigel et al., 2020; Goldman et al., 2020) support its use in hospitalized patients with COVID-19, and recent data indicate that treatment of outpatients with high risk for disease progression is highly beneficial. Despite its documented safety, concerns remain about the toxicity of remdesivir, particularly in patients with reduced kidney function. An excipient in Veklury (Gilead’s proprietary name for remdesivir) called sulfobutylether-beta-cyclodextrin (SBECID), is renally cleared and may accumulate and reach toxic levels in patients with advanced kidney disease. Therefore, remdesivir is not recommended for patients with a glomerular filtration rate (GFR) lower than 30 mL/min/1.73 m². However, there is clinical evidence that remdesivir is dialyzable and may be safe in patients with kidney disease (Pettit et al., 2020). REDPINE, a large ongoing randomized clinical trial, is likely to add evidence in that regard (https://clinicaltrials.gov/ct2/show/NCT04745351).

We performed a retrospective analysis of 444 hospitalized patients with advanced kidney disease who received remdesivir for the treatment...
of COVID-19 at several Mayo Clinic hospitals. We aimed to study the incidence and type of adverse effects experienced by patients with a GFR < 30 mL/min/1.73 m², who received remdesivir on a compassionate basis and define their clinical characteristics and incidence of adverse events.

The assessment of adverse events in patients who receive SBECD drugs, particularly when administered in the setting of multiple comorbidities and/or acute critical illness, may be difficult. For instance, much of the clinical experience with an SBECD drug was collected from individuals who received intravenous voriconazole to treat systemic, life-threatening fungal infections including candidemia and invasive aspergillosis. Therefore, it may have been difficult to determine if an adverse event was caused by the index drug, the excipient or simply was a manifestation of the primary disease. There is also evidence indicating SBECD does not accumulate in renal epithelial cells or lead to worsening renal function (Lake et al., 2010; Oude Lashof et al., 2012).

Despite the limited clinical information on the actual risk associated with the use of SBECD drugs, clinicians continue to focus their attention on potential hepatic and renal toxicity, mainly based on the recommendations by European and U.S. regulatory agencies (Dearani et al., 2020; Aleem et al., 2021).

Aims

The aim of this study was to summarize clinical characteristics and incidence of adverse events of patients with advanced kidney disease who received remdesivir for the treatment of COVID-19 pneumonia.

Methods

Study subjects

A total of 444 CKD patients admitted to the Mayo Clinic hospitals between May 2020 and September 2021 were included in this retrospective study. Information was collected on patient characteristics, hospitalization, and adverse events by performing a retrospective review of electronic medical records. Laboratory values were also measured when remdesivir was first administered and stopped. As per institutional protocol, patients received a 5-day course of intravenous remdesivir consisting of a loading dose of 200 mg on day followed by 100 mg daily. All analyses were performed in the overall patient group and three separate subgroups of patients with a GFR ≥ 15, a GFR < 15 and dialysis, and a GFR < 15 and no dialysis. All patients had a history of chronic kidney disease in stages 3 to 5, and a GFR of <30 mL/kg/1.73 m² at the time of hospital admission. The Mayo Clinic COVID-19 Risk Score was used to predict severe disease (Nyman et al., 2022).

Statistical analysis

Continuous variables were summarized with the sample median and range. Categorical variables were summarized with number and percentage of patients. Comparisons of patient characteristics and adverse events of the GFR ≥ 15, GFR < 15 and dialysis, and GFR < 15 and no dialysis groups were made using a Kruskal-Wallis rank sum test (continuous and ordinal variables or Fisher’s exact test (categorical variables). Comparisons of laboratory values between when remdesivir was first administered and stopped were made using a paired Wilcoxon signed-rank test. P-values < 0.05 were considered as statistically significant. All statistical tests were two-sided. Statistical analyses were performed using R Statistical Software (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria).

Results

Of the 444 study patients, 350 (78.8 %) had a GFR ≥ 15, 63 (14.2 %) had a GFR < 15 and dialysis, and 31 (7.0 %) had a GFR < 15 and no dialysis. A summary of patient demographic and clinical characteristics and hospitalization information is displayed in Table 1 for the overall group and the three patient subgroups. In the overall cohort, median age was 72 years (Range: 21–100 years), 55.2 % of patients were male, and most (86.5 %) were Caucasian. Median BMI was 30.4 (Range: 2.9–79.9 %) and median Charlson comorbidity score was 7 (Range: 2–15). CKD stage was 3 for 114 patients (25.7 %), 4 for 229 patients (51.6 %), and 5 for 101 patients (22.7 %). A total of 146 patients (32.9 %) were admitted to the ICU, 103 (23.2 %) died in the hospital, and 120 (27.0 %) were on renal replacement therapy (RRT). The median length of remdesivir treatment was 5 days. When comparing characteristics of the three GFR subgroups, significant differences were noted for age (P < 0.001), race (P < 0.001), stage of CKD (P < 0.001), and RRT (P < 0.001). A total of 102 patients (23.0 %) experienced an adverse event, the most common of which were septic shock (11.5 %), nausea or vomiting (3.8 %), and pulmonary embolism (3.2 %) (Table 2). The proportion of patients with an adverse event did not differ dramatically when comparing the GFR ≥ 15 (20.9 %), GFR < 15 and RRT (30.2 %), and GFR < 15 and no RRT (32.3 %) groups (P = 0.12). Generalized seizure was more common for the GFR < 15 and RRT group (3.2 %) compared to the other two subgroups (both 0.0 %, P = 0.044). There were no other statistically significant differences in adverse events when comparing the three examined GFR/RRT subgroups (all P ≥ 0.13, Table 2). Comparisons of laboratory values between when remdesivir was first administered and when remdesivir was stopped are shown in Table 3. In the overall patient group, there were significant differences between these two time points regarding hemoglobin (P < 0.001), WBC (P < 0.001), platelets (P < 0.001), AST (P < 0.001), total bilirubin (P = 0.012), and GFR (P < 0.001).

Study limitations

The main limitation of this study is the retrospective design, which may have introduced biases into the data collection. Additionally, the sample sizes of several of the patient subgroups that were examined (particularly the two GFR < 15 subgroups) were relatively small, and therefore, the possibility of a type II error (i.e., a false-negative finding) is important to consider. We cannot conclude that no true difference exists simply due to the occurrence of a non-significant p-value in this study.

Discussion

Our study showed that hospitalized COVID-19 patients with advanced kidney disease defined as a GFR < 30 mL/1.73 m² had an incidence of adverse events of 23 % (102/444). Of those, the most common were septic shock (11.5 %), nausea or vomiting (3.8 %), and pulmonary embolism (3.2 %), with similar proportions in patients with a GFR of greater or <15 mL/1.73 m², with or without RRT. The diagnosis of septic shock was made in accordance with the 2021 Surviving Sepsis Campaign guidelines (Evans et al., 2021). Four major studies were conducted to assess the efficacy of remdesivir, but comparing their results has been difficult due to differences in design, length of treatment, dosing schedule, and endpoints (Beigel et al., 2020; Beigel, 2021; Wang et al., 2020; Spinner et al., 2020; Consortium WHO ST et al., 2021). In the NIH-sponsored Adaptive COVID-19 Treatment Trial (ACTT-1), the overall incidence of adverse events was 24.62 % for remdesivir compared to 31.59 % in those who received placebo.

A placebo-controlled study conducted in China in the early stages of the pandemic, yielded a very high withdrawal rate after 66 % of remdesivir patients experienced adverse events. Moreover, 18 % of the serious adverse events ultimately contributed to the discontinuation of that trial (Wang et al., 2020). Our lower adverse event rate may have been the result of a shorter treatment course of 5 days compared to 10 days in ACTT-1, and also the evolution of COVID-directed therapy. Our patients were treated with therapeutics that were not utilized in the
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early stages of the pandemic and a high percentage of them received dexamethasone (Tomasini et al., 2020). Not surprisingly, seizures were more common in our subgroup of patients with the poorest kidney function who required RRT. Approximately 10 % of patients with kidney failure and one-third of those with uremic encephalopathy develop seizures (Sazgar, 2021). Although their incidence is unknown, seizures have been occasionally reported as the presenting symptom of COVID-19 infection (Anand et al., 2020). In the ACTT-1, the incidence of seizures was lower in the placebo group (0.19 %, 1/516) compared to the remdesivir group (0.38 %, 2/532) but without statistical significance due to the low number of events (https://clinicaltrials.gov/ct2/show/results/NCT04280705). Additionally, a review of the World Health Organization global database revealed that remdesivir was not statistically associated with neurologic or psychiatric adverse events (Lee et al., 2021).

Remdesivir is not recommended for use in patients with a GFR < 30 mL/1.73 m (Mechineni et al., 2021) due to lack of sufficient safety data and concerns about toxicity, mainly due to accumulation of the renally excreted excipient sulfobutylether-beta-cyclodextrin (SBECD) (https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf). However, some of those concerns appear unjustified. Although most clinical studies on remdesivir have excluded patients with advanced renal disease, there is no clear evidence that the drug-excipient complex is nephrotoxic at usual dosing.

In our study, there was no significant decline in GFR after 5 days of remdesivir administration in any of the subgroups; on the contrary, the GFR improves in those with a baseline above 15 mL/1.73 m (Mechineni et al., 2021). Biancalana et al. reported that renal function improved after the administration of remdesivir in patients with COVID-19 pneumonia and CKD III. A higher GFR had prognostic value in their univariate analysis (Biancalana et al., 2021). The renal function of our patients, which was much poorer than Biancalana’s cohort at study entry, may have improved due to organ recovery induced by COVID-19 directed therapy, or simply as the result of fluid administration in patients who were febrile and hypovolemic at the time of hospital admission (Biancalana et al., 2021). The renal function of our patients, which was much poorer than Biancalana’s cohort at study entry, may have improved due to organ recovery induced by COVID-19 directed therapy, or simply as the result of fluid administration in patients who were febrile and hypovolemic at the time of hospital admission (Biancalana et al., 2021).

Table 1

| Variable                   | Median (minimum, maximum) or No. (%) of patients | P-value |
|----------------------------|--------------------------------------------------|---------|
| Patient characteristics    |                                                 |         |
| Age (years)                | 72 (21, 100)                                     | <0.001  |
| Sex (male)                 | 245 (55.2 %)                                     | 0.81    |
| Race                       | 443                                              |         |
| Caucasian                  | 383 (86.5 %)                                     | 0.001   |
| African American           | 36 (8.1 %)                                       |         |
| Asian                      | 5 (1.1 %)                                        |         |
| Other                      | 19 (4.3 %)                                       |         |
| Ethnicity (not Hispanic or Latino) | 442 (95.7 %)                              | 0.82    |
| BMI                        | 30.4 (2.9, 79.9)                                 | 0.22    |
| Charlson comorbidity score | 7 (2, 15)                                        | 0.96    |
| Mayo Clinic site           | 444                                              | 0.95    |
| Florida                    | 113 (25.5 %)                                     |         |
| Arizona                    | 0 (0.0 %)                                        |         |
| Rochester                  | 82 (18.5 %)                                      |         |
| Health system              | 249 (56.1 %)                                     |         |
| Vaccinated                 | 147 (30.9 %)                                     | 1.00    |
| Mayo Clinic COVID-19 Risk Score | 6 (0, 11)                              | 0.096   |
| Stage of chronic kidney disease | 444                                             | <0.001  |
| 3                          | 114 (25.7 %)                                     | 9.15    |
| 4                          | 229 (51.6 %)                                     | 8.25    |
| 5                          | 101 (22.7 %)                                     | 18.51   |
| Hospitalization information|                                                 |         |
| ICU during hospitalization | 444 (32.9 %)                                     | 0.95    |
| Mechanical ventilation     | 444 (19.1 %)                                     | 0.35    |
| Died in the ICU            | 444 (18.0 %)                                     | 0.90    |
| Etofose                    | 444 (7.6 %)                                      | 1.00    |
| Died in the hospital outside of the ICU | 364 (63.3 %)                        | 0.72    |
| Died in the hospital (ICU or non-ICU) | 444 (23.2 %)                               | 1.00    |
| RRT                        | 444 (27.0 %)                                     | <0.001  |
| Other COVID-19 treatments  |                                                 |         |
| Tocilizumab                | 444 (5.6 %)                                      | 0.40    |
| Monoclonal antibodies      | 444 (6.4 %)                                      | 0.74    |
| Desmamethone               | 444 (70.5 %)                                     | 0.42    |
| Codex                      | 444 (7.6 %)                                      | 0.76    |
| CP                         | 444 (16.4 %)                                     | 0.97    |
| Tofacitinib                | 444 (0.0 %)                                      | 1.00    |
| Baricitinib                | 444 (12.5 %)                                     | 0.49    |
| Ravilumab                  | 444 (0.7 %)                                      | 1.00    |
| Lenzilumab                 | 444 (0.5 %)                                      | 1.00    |
| MMF                        | 444 (0.0 %)                                      | 1.00    |
| Camostat                   | 444 (0.0 %)                                      | 1.00    |
| Length of remdesivir treatment (days) | 444 (5, 135)                          | 0.25    |

P-values result from a Kruskal-Wallis rank sum test (continuous and ordinal variables) or Fisher’s exact test (categorical variables).
lymphocytopenia, and anemia, as well as elevation of liver enzymes have been described in patients with COVID-19 (Mao et al., 2021; Neofytos et al., 2020). Treatment route nor the baseline renal function were predictors of worsening renal function. The serum concentration of voriconazole; however, the serum concentration of SBECID, its solubilizing agent, was 50–100 times higher than the ones reached during a standard remdesivir infusion course of 5 to 10 days (Luke et al., 2010; Sorgel et al., 2021). SBECID is also easily removed by continuous replacement therapy and RRT (Luke et al., 2012). In a study of 166 patients with reduced renal dysfunction who received voriconazole, Neofytos et al. found that neither the administration route nor the baseline renal function were predictors of worsening kidney disease (Neofytos et al., 2012).

Hematologic abnormalities that include eosinopenia, monocytosis, lymphocytopenia, and anemia, as well as elevation of liver enzymes levels have been described in patients with COVID-19 (Mao et al., 2021; Hasel et al., 2022). As shown in Table 3, our patients experienced a significant improvement in hemoglobin, white cell count, platelet count, and AST levels during the course of the remdesivir infusion. These favorable changes do not necessarily relate to the administration of remdesivir but instead, to an overall improvement of hemodynamic conditions and reduced inflammatory burden.

### Conclusions

To our knowledge, this is the most extensive retrospective study of patients with a GFR < 30 mL/1.73 m² who received remdesivir for the treatment of COVID-19 pneumonia. Our results suggest that the use of remdesivir in patients with very severe CKD is safe, even in those who continued on next page
are not on renal replacement therapy. An ongoing placebo-controlled trial in which remdesivir is given to COVID-19 patients with GFR < 30 (REDPINE) is expected to complete enrollment and yield additional information on the safety of this antiviral agent later this year.

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None.

**Institutional approval**

Approved by Mayo Clinic Institutional Review Board.

**Disclosures**

FS, PK, and CRL are investigators for the Study to Evaluate the Efficacy and Safety of Remdesivir in Participants With Severely Reduced Kidney Function Who Are Hospitalized for Coronavirus Disease 2019 (COVID-19) (REDPINE), sponsored by Gilead.

**Ethical approval statement**

Our study, “Use of Remdesivir for COVID-19 Pneumonia in Patients with Advanced Kidney Disease: A Retrospective Multicenter Study,” was approved by the Mayo Clinic Institutional Review Board (IRB), and the Mayo Clinic COVID-19 Task Force. Our work, which was deemed to be a “Minimal Risk Study” by IRB, is original and has not been published elsewhere. Given the nature of the study (chart review), including its retrospective design, a patient consent waiver was granted to the investigators.

All authors actively participated in the study and none received monetary compensation.

**CRediT authorship contribution statement**

F. Stancampiano: Conceptualization, Writing – original draft, Writing – review & editing. N. Jhawar: W. Alsafi: J. Valery: D.M. Harris: P. Kempaiah: S. Shah: M.G. Heckman: H. Siddiqui: C.R. Libertin: Supervision, Conceptualization.

**Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

**References**

Ackley, T.W., McManus, D., Topal, J.E., Cicali, B., Shah, S., 2021. A Valid Warning or Clinical Lore: an Evaluation of Safety Outcomes of Remdesivir in Patients with Impaired Renal Function from a Multicenter Matched Cohort. Antimicrob. Agents Chemother. 65 (2).

Akleem, A., Mahadeviah, G., Sharriff, N., Kothadia, J.P., 2021. Hepatic manifestations of COVID-19 and effect of remdesivir on liver function in patients with COVID-19 illness. Proc. (Baylor. Univ. Med. Cent.) 34 (4), 473–477.

Anand, P., Al-Faraj, A., Sader, E., et al., 2020. Seizure as the presenting symptom of COVID-19: A retrospective case series. Epilepsy Behav. 112, 107355.

Beigel, J.H., 2021. What is the role of remdesivir in patients with COVID-19? Curr. Opin. Crit. Care 27 (5), 487–492.

Beigel, J.H., Tomashek, K.M., Dodd, L.E., et al., 2020. Remdesivir for the Treatment of COVID-19: Final Report. N. Engl. J. Med. 383 (19), 1813–1826.

Biancalana, E., Chiriaco, M., Sciaronne, P., et al., 2021. Remdesivir, Renal Function and Short-Term Clinical Outcomes in Elderly COVID-19 Pneumonia Patients: A Single-Centre Study. Clin. Infect. Dis. Aging 16, 1037–1046.

ClinicalInfection.pdf (c) 2021 CCR Rev. https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf.

Consortium WHOST, Pan, H., Peto, R., et al., 2021. Repurposed Antiviral Drugs for COVID-19 - Interim WHO Solidarity Trial Results. N. Engl. J. Med. 384 (6), 497–511.

Dearani, J.A., Stephens, E.H., Guleria, K.J., et al., 2020. COVID-19: FAQs-Congenital Heart Surgery Recovery and Defining a ‘New Normal’. World J. Pediatr. Congenit. Heart Surg. 11 (5), 548–556.

Evans, L., Rhodes, A., Alhazzani, W., et al., 2021. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. Crit. Care Med. 49 (11), e1063–e1143.

Goldman, J.D., Lye, D.C.B., Hui, D.S., et al., 2020. Remdesivir for 5 or 10 Days in Patients with Severe COVID-19. N. Engl. J. Med. 383 (19), 1827–1837.

Hasel, K., Salim, A., Verma, S., et al., 2022. Prevalence of Gastrointestinal Symptoms, Hepatic Dysfunction, and Outcomes in Hospitalized Patients with COVID-19 infection: An Early Experience. Cureus 14 (2), e22152.

Lee, S., Yang, J.W., Jung, S.Y., et al., 2021. Neuropsychological adverse drug reactions of Remdesivir: analysis using Vigibase, the WHO global database of individual case safety reports. Eur. Rev. Med. Pharmacol. Sci. 25 (23), 7390–7397.

Luke, D.R., Tomaszewski, K., Danile, B., Schlamm, H.T., 2011. Review of the basic and clinical pharmacology of sulfobutylether-beta-cyclodextrin (SBEDC). J. Pharm. Sci. 99 (8), 3291–3301.

Luke, D.R., Wood, N.D., Tomaszewski, K.E., Danile, B., 2012. Pharmacokinetics of sulfobutylether-beta-cyclodextrin (SBEDC) in subjects on hemodialysis. Nephrol. Dial.Transplant. 27 (3), 1207–1212.

Mao, J., Bai, S., Du, R.C., Zhu, Y., Shi, L.P., Zhu, X.H., 2021. Hemolymphatic changes when remdesivir was stopped.

Mochi, K., Yamazaki, S., Shigematsu, Y., et al., 2021. Role of vitamin D in the pathogenesis and treatment of COVID-19. J. Prim. Care Commun. Health 14, 21501319211069748.

Nyman, M.A., Jose, T., Croghan, I.T., et al., 2022. Utilization of an Electronic Health Record Integrated Risk Score to Predict Hospitalization Among COVID-19 Patients. N. Engl. J. Med. 383 (19), 1813–1821.

Oude Lashof, A.M., Sobel, J.D., Ruhnke, M., et al., 2012. Safety and tolerability of voriconazole in patients with baseline renal insufficiency and candidemia. Antimicrob. Agents Chemother. 56 (6), 3313–3317.

Pettit, N.N., Pisano, J., Nguyen, C.T., et al., 2020. Remdesivir Use in the Setting of Severe Renal Impairment: A Theoretical Concern or Real Risk? Clin. Infect. Dis. 70 (9), 1307–1316.

Rubin, D., Chan-Tack, K., Farley, J., Sherwat, A., 2020. FDA Approval of Remdesivir - A Step in the Right Direction. N. Engl. J. Med. 383 (27), 2598–2600.

Saggar, M., 2021. Kidney Disease and Epilepsy. J. Stroke Cerebrovasc. Dis. 30 (9), 105651.

Sedgel, F., Malin, J.J., Haggmann, H., et al., 2021. Pharmacokinetics of remdesivir in a COVID-19 patient with end-stage renal disease on intermittent haemodialysis. Nephrol. Dial. Transplant. 27 (3), 1207–1212.

Shi, L., Zhao, H., Zhang, H., et al., 2021. Remdesivir Alleviates Acute Kidney Injury by Improving Renal Function From a Multicenter Matched Cohort. Antimicrob. Agents Chemother. 65 (2)