underway. The current study is a descriptive analysis of various therapeutic drugs in clinical trials against COVID-19 on the CURE ID platform.

Methods. Using clinicaltrials.gov we selected those trials addressing therapeutic strategies for COVID-19 and reviewed the drugs used, the current status of the trials, and the phases of development.

Results. As of May 2021, we identified 2,154 clinical trials and 933 drugs from clinicaltrials.gov that met the inclusion criteria. Hydrosorbocholine (n=251) was the most commonly investigated agent, followed by convalescent plasma (n=147), antihypoxmic (n=98), vremecin (n=68), mesenchymal stem cells (n=63), tocilizumab (n=58), desirnavir (n=41), and ibapenem (n=31). At the time of our analysis, the majority (45%) of the clinical trials were in the recruiting phase, 12% were in the active phase, and 13% of the studies were completed. The majority (31%) of trials were in phase two, followed by phase three (21%) and phase one (10%). The vast majority of the agents were repurposed (92%), while only 8% of the agents were new molecular entities. Remdesivir was the only drug approved for marketing for treatment of certain patients with COVID-19 at the time of our analysis.

Conclusion. Several repurposed and novel drugs are being investigated to treat COVID-19 in clinical trials. CURE ID provides a broad view of the various drugs being researched and serves to keep the scientific community informed. Such a platform may help prevent duplication of efforts and help the scientific community with more coordinated research efforts and larger platform trials that can robustly answer scientific questions during a pandemic.

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628. Pharmacokinetics, Safety and Tolerability of Co-administration of Nacubactam and β-lactams after Multiple Doses in Healthy Japanese Subjects

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Session: P-28. Clinical Trials

Background. Increase of carbapenem-resistant Enterobacteriaceae (CRE) is a serious problem in the clinical setting and drugs which can treat patients with CRE are still limited. Nacubactam (OP0959) is a novel dabcycloloctane-type β-lactamase inhibitor and being developed as a standalone drug to be co-administered with cefepime or aztreonam.

Methods. A randomized, double-blind multiple dose study of nacubactam in co-administration with cefepime (Cohort 1) or aztreonam (Cohort 2) in Japanese healthy subjects was performed to assess pharmacokinetics, safety, and tolerability of co-administrations of nacubactam and cefepime or aztreonam. In each cohort, 6 subjects received 3 mg/kg of nacubactam and 2 of co-concomitant drug (cefepime or aztreonam) and 2 subjects received placebo (saline) intravenously over 60 minutes, three times daily every 8 hours for 7 days. Plasma samples were collected and concentrations of each drug were analyzed by liquid chromatography-mass spectrometry (LC-MS/MS). Safety and tolerability assessments included treatment-emergent adverse events (TEAEs) and the evaluation of changes from baseline in safety laboratory test results, 12-lead electrocardiograms (ECGs), vital signs, and physical examinations.

Results. Profiles of Cmax, t1/2, AUC0-8, AUC0-∞, and t1/2 for nacubactam, cefepime and aztreonam are summarized in Table 1. Summary of Cmax for nacubactam, cefepime and aztreonam are summarized in Table 2. Plasma concentrations of nacubactam, cefepime and aztreonam reached the steady-state by Day 4, and the mean accumulation ratios of Cmax and AUC0-∞ on Day 7 to those of Day 1 were in the range of 0.91 to 1.10. As for the safety, no serious adverse event was observed in this study.

Conclusion. In conclusion, no remarkable change in pharmacokinetics was observed in each drug with multiple coadministration for 7 days and safety and tolerability of co-administrations of nacubactam and cefepime or aztreonam were confirmed. Based on these results, nacubactam is currently under further development.

Table 1. PK profiles of nacubactam and concomitant drugs on Day 1 and Day 7

Table 2. Summary of Ctrough of nacubactam and concomitant drugs

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629. High Efficacy of Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in African American Adults Including Those with Preexisting Resistance, Viral Blips, and Suboptimal Adherence

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Session: P-28. Clinical Trials

Background. BRAVE2020 demonstrated the efficacy of switching to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) among African American adults with suppressed HIV through Week (W) (48 Figure 1). We present resistance, viral blips, adherence, and virologic outcomes through W72.

Figure 1. BRAVE2020 study design (phase 3, randomized, open-label, multicenter USA), active-controlled study) and virologic suppression at weeks 24 and 48

*Allowed 3rd agents: any FDA-approved protease inhibitor, nonnucleoside reverse transcriptase inhibitor (except etravirine), integrase strand transfer inhibitor (except bictegravir), or maraviroc.

Methods. Enrollment criteria permitted NNRTI resistance (–R), PI-R, and certain NRTI-R (M184V/I allowed; K65R/E/N, and T69N insertions excluded) and excluded known primary INSTI-R. Preexisting drug resistance was assessed with historical genotypes and retrospective baseline proviral DNA genotyping. Adherence was calculated by pill count. Viral blips (transient HIV-1 RNA ≥50 copies/mL) and outcomes based on last available on-treatment HIV-1 RNA were assessed.

Results. 489 participants received B/F/TAF and had ≥1 post-switch HIV-1 RNA measurement. Baseline genotypic data from cumulative historical and/or proviral genotypes were available for 96% (468/489) in protease/reverse transcriptase and 93% (453/489) in integrase. Preexisting NNRTI-R, M184V/I, ≥1 TAMs, NNRTI-R, and PI-R were observed in 15% (68/468), 11% (50/468), 8% (36/468), 22% (101/468), and 13% (61/468), respectively. Primary INSTI-R was detected post-randomization in 2% (11/453); all remained in the study and were included in efficacy analyses. Through W72, 99% (486/489) of participants had HIV-1 RNA < 50 copies/mL at their last visit study, including with all baseline NNRTI-R or INSTI-R (Figure 2). Mean frequency of viral blips was 1% per timepoint, and blips were not associated with virologic failure.

In conclusion, no remarkable change in pharmacokinetics was measured. B/F/TAF treatment, including those with preexisting resistance, viral blips, and suboptimal adherence. Continued HIV suppression and absence of treatment-emergent resistance demonstrate the efficacy of B/F/TAF in African Americans regardless of adherence or preexisting resistance to NNRTIs, PIs, or non-tenofovir NRTIs.

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630. Emergence of Colistin Resistance in the OVERCOME Trial: Impact of Combination Therapy with Meropenem

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Hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP) is associated with high rates of morbidity and mortality; this is often worse among patients who experience a delay in receiving appropriate therapy. Initial treatment choice and early adjustment occurs prior to pathogen susceptibility results and may be based on suspicion of a resistant infection and/or clinical deterioration. This study assesses the cost-effectiveness of Imipenem/cilastatin/relebactam (IMI/REL) in an early adjustment prescribing scenario compared to PIP/TAZ for patients with high risk of resistant infection from a US perspective.

Methods. Although early adjustment data was not directly available, pathogen susceptibility data derived from 2017-19 Study for Monitoring Antimicrobial Resistance Trends (SMART) surveillance program was applied to estimate patients who may have clinical worsening, likely due to a resistant infection. The efficacy and safety data for IMI/REL and PIP/TAZ were informed by the modified intent-to-treat population of a phase III trial (RESTORE-IMI 2). Our analysis comprised a decision tree (reflecting hospitalization period) followed by a yearly Markov model (capturing lifetime impact). The decision tree captured short-term outcomes (clinical cure, all-cause mortality, and hospital resource use). The Markov model translated short-term outcomes into quality-adjusted life years (QALYs). Results were expressed as an incremental cost-effectiveness ratio (ICER). Sensitivity analyses were conducted to test the robustness of model results.

Results. Compared with PIP/TAZ, IMI/REL in the early adjustment setting was associated with increased costs ($10,087 per patient) but a higher cure (+7%) and lower mortality (-3%) rate. The resulting ICER ($12,173/QALY) falls well below typical US willingness to pay thresholds. Model drivers were the SMART-based susceptibility profile, the RESTORE-IMI 2 mortality, and IMI/REL safety profile.

Conclusion. Our results suggest that IMI/REL used as an early adjustment option, could be considered cost effective for patients with worsening HABP/VABP in a US setting, when compared against PIP/TAZ.