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

Methods. Using clinicaltrials.gov we selected those trials addressing therapeutics 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. Hydroxychloroquine (n=251) was the most commonly investigated agent, followed by convalescent plasma (n=147), azithromycin (n=98), ivermectin (n=68), mesenchymal Stem Cells (n=63), tocilizumab (n=58), remdesivir (n=53) and favipiravir (n=51). 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.

Disclosures. **All Authors**: No reported disclosures

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

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Session: P-28. Clinical Trials

Background. Increase of carbapenem-resistant Enterobacterales (CRE) is a serious problem in the clinical setting and drugs which can treat patients with CRE are still limited. Nacubactam (OP0595) is a novel diazabicyclooctane-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 2 g of nacubactam and 2 g of 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 C_{max}, t_{max}, AUC_{0-8}, $AUC_{0-\infty}$ and $t_{1/2}$ for nacubactam, cefepime and aztreonam are summarized in Table 1. Summary of C_{trough} 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 C_{max} and AUC_{0-8} 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. There was 1 TEAE (seborrhoeic dermatitis) leading to the discontinuation in 1 subject in nacubactam/cefepime group, but it was judged as "Not related to study drug".

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

Cohort	Drug	Measurement	Day	C_{max} (μg/mL)	t_{max} (hr)	AUC_{0-8} (μg·hr/mL)	$AUC_{0-\infty}$ (μg·hr/mL)	$t_{1/2}$ (hr)
1	Nacubactam : 2 g with Cefepime : 2 g	Nacubactam	1	107.0 ± 3.847	1.000 ± 0.000	253.9 ± 8.388	263.8 ± 10.70	1.669 ± 0.135
			7	115.4 ± 7.503	1.000 ± 0.000	255.0 ± 13.80	269.9 ± 15.69	2.788 ± 0.162
		Cefepime	1	116.5 ± 4.231	1.000 ± 0.000	291.4 ± 20.11	309.6 ± 24.97	1.941 ± 0.206
			7	126.4 ± 8.204	1.000 ± 0.000	296.2 ± 11.46	321.2 ± 14.12	2.859 ± 0.166
2	Nacubactam : 2 g with Aztreonam : 2 g	Nacubactam	1	118.4 ± 18.87	1.000 ± 0.000	263.4 ± 25.91	270.2 ± 26.84	1.459 ± 0.103
			7	121.0 ± 15.85	1.000 ± 0.000	263.2 ± 38.55	274.2 ± 40.97	2.819 ± 0.133
		Aztreonam	1	165.5 ± 23.75	1.000 ± 0.000	398.6 ± 36.41	421.4 ± 40.37	1.870 ± 0.226
			7	152.2 ± 14.12	1.000 ± 0.000	363.1 ± 36.97	385.8 ± 42.78	2.324 ± 0.099

Table 2. Summary of Ctrough of nacubactam and concomitant drugs

Cohort	Drug	Measurement	Descriptive Statistics	C_{trough} (μg/mL) Day 1 (8 hr)	Day 4 (Pre-dose)	Day 7 (Pre-dose)
1	Nacubactam : 2 g with Cefepime : 2 g	Nacubactam	Mean	4.083	7.568	7.054
			SD	0.945	1.311	1.450
		Cefepime	Mean	6.383	11.01	10.59
			SD	1.374	1.867	1.844
2	Nacubactam : 2 g with Aztreonam : 2 g	Nacubactam	Mean	3.173	6.808	4.520
			SD	0.812	1.825	1.158
		Aztreonam	Mean	8.257	13.92	8.685
			SD	1.953	3.330	2.539

SD : Standard Deviation

Conclusion. In conclusion, no remarkable change in pharmacokinetics was observed in each drug with multiple concomitant administration 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.

Disclosures. **All Authors**: No reported disclosures

629. High Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in African American Adults with HIV Including Those with Preexisting Resistance, Viral Blips, and Suboptimal Adherence

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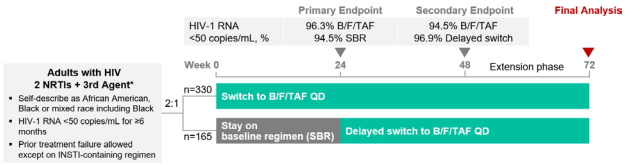
Session: P-28. Clinical Trials

Background. BRAAVE 2020 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. BRAAVE 2020 study design (phase 3, randomized, open-label, multicenter [USA], active-controlled study) and virologic suppression at weeks 24 and 48

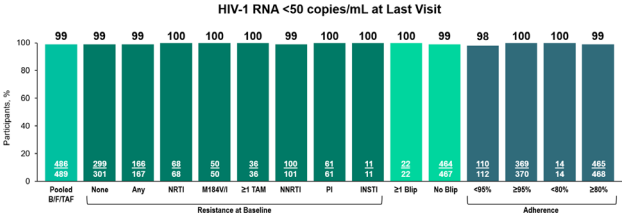


*Allowed 3rd agents: any FDA-approved protease inhibitor, nonnucleoside reverse transcriptase inhibitor (except etravirine), integrase strand transfer inhibitor (except bictegravir), or maraviroc.

Methods. Enrollment criteria permitted NNRTI resistance (-R), PI-R, and certain NRTI-R (M184V/I allowed; K65R/E/N, ≥3 thymidine analog mutations [TAMs], or T69-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 NRTI-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 study visit, including all with baseline NRTI-R or INSTI-R (Figure 2). Mean frequency of viral blips was 1% per timepoint, and blips were not associated with virologic failure. 112 participants (23%) had < 95% adherence by pill count, 98% (110/112) of whom had HIV-1 RNA < 50 copies/mL at last visit, including 14 of 14 (100%) with < 80% adherence. No participant discontinued due to lack of efficacy or had treatment emergent resistance to study drugs.

Figure 2. Virologic suppression by preexisting resistance, viral blips, and adherence



Conclusion. Virologic suppression was maintained through W72 of 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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Session: P-28. Clinical Trials

Background. Colistin (COL) remains an important therapeutic option for carbapenem-resistant (CR) Gram-negative bacilli (GNB). COL is often utilized in combination with meropenem (MEM), in part due to concerns regarding the development of COL resistance with monotherapy. We recently completed a randomized controlled trial comparing outcomes in patients receiving COL + placebo to those receiving COL + MEM; herein we present data on the emergence of COL resistance in this trial.

Methods. OVERCOME was an international, multicenter, randomized, double-blind, placebo-controlled study comparing COL and COL + MEM for the treatment of bloodstream infection and/or pneumonia due to CR GNB. Subjects were included in the modified intent to treat population (mITT) if their enrollment pathogen had a COL MIC ≤2 mg/L, as determined by broth microdilution (BMD). Daily blood and/or respiratory samples were obtained in patients per protocol until two consecutive negatives were obtained or the end of study treatment. All subsequent isolates were evaluated for COL resistance via BMD, defined as MIC ≥ 4 mg/L.

Results. Of the 425 patients in the mITT population, 380 (191 COL; 189 COL + MEM) were evaluable for the endpoint of COL resistance development. The median age of the cohort was 70, 38% were female, 47% were white, and 45% were Asian. 70% had an index infection of pneumonia, 68% were in the intensive care unit at the onset of their infection, and *A. baumannii* was the most common pathogen (78% of patients). Baseline characteristics, infection type, severity of illness, and index pathogen were similar amongst treatment arms. No significant difference in resistance development was seen between the COL and COL + MEM groups overall (12% vs. 8%; p = 0.31), or in any subgroup (Table). In patients with *A. baumannii*, there was a trend towards decreased resistance development with COL + MEM (13.3% vs 7.5%; p = 0.13).

Conclusion. We were unable to identify a significant difference in resistance emergence between treatment arms, but given the low incidence of this outcome, were underpowered to do so. The impact of COL + MEM on preventing emergence of COL resistance in *A. baumannii* warrants further clinical study.

Table: Incidence of resistance development per treatment arm

	Colistin*	Colistin + Meropenem*	P value
Overall	23/191 (12)	16/189 (8)	0.31
XDR-AB	20/150 (13)	11/146 (8)	0.13
XDR-PA	2/20 (10)	4/19 (21)	0.40
CRE	1/29 (3)	4/32 (13)	0.36
Pneumonia	21/137 (15)	15/128 (12)	0.47
BSI	2/54 (4)	1/61 (2)	0.60

* Data are listed as number where resistance developed/number of patients evaluated; XDR = extensively drug resistant; AB = *A. baumannii*; PA = *P. aeruginosa*; CRE = carbapenem-resistant enterobacteriaceae; BSI = bloodstream infection

Disclosures. **Jason M Pogue, PharmD, BCPS, BCIDP**, **Merck** (Consultant)**QPex** (Consultant)**Shionogi** (Consultant)**Utility Therapeutics** (Consultant)**VenatoRX** (Consultant) **Michael J. Rybak, PharmD, MPH, PhD**, **Paratek Pharmaceuticals** (Research Grant or Support) **Emmanuel Roilides, MD, PhD, FIDSA, FAAM, FESCMID**, **Merck Sharp & Dohme Corp.** (Consultant, Grant/Research Support) **Matthew Sims, MD, PhD**, **Astra Zeneca** (Independent Contractor)**Diasorin Molecular** (Independent Contractor)**Epigenomics Inc** (Independent Contractor)**Finch** (Independent Contractor)**Genentech** (Independent Contractor)**Janssen Pharmaceuticals NV** (Independent Contractor)**Kinevant Sciences gmBH** (Independent Contractor)**Leonard-Meron Biosciences** (Independent Contractor)**Merck and Co** (Independent Contractor)**OpGen** (Independent Contractor)**Prenosis** (Independent Contractor)**Regeneron Pharmaceuticals Inc** (Independent Contractor)**Seres Therapeutics Inc** (Independent Contractor)**Shire** (Independent Contractor)**Summit Therapeutics** (Independent Contractor)

631. Economic Analysis of Imipenem/Cilastatin/Relebactam Compared to Piperacillin/Tazobactam for Treating Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia

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Session: P-28. Clinical Trials

Background. 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 profiles and RESTORE-IMI 2 response and mortality rates.

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.

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632. Clinical Experience with a New Fully Liquid Presentation of the MenACWY-CRM Vaccine. Results from Two Multicenter, Randomized, Controlled, Observer-Blind, Phase 2b Studies

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Session: P-28. Clinical Trials

Background. Currently, licensed MenACWY-CRM conjugate vaccine presentation (Lyo/Liq) consists of two vials (lyophilized MenA, liquid MenCWY) to be reconstituted before injection. A new, fully liquid, single vial formulation has been developed and evaluated in two clinical studies in adolescents and adults aimed at demonstrating immunological non-inferiority of the liquid presentation for MenA.

Methods. Overall, 1337 subjects, 10 to 40 years of age (y), were exposed to a single 0.5 mL intramuscular dose of MenACWY Liquid and 1332 to MenACWY-CRM(Lyo/Liq). MenACWY-CRM Liquid was aged before administration, to test the vaccine immunogenicity at the end of the intended shelf-life and establish release and end of shelf life specifications. MenACWY-CRM(Lyo/Liq) was used as comparator and was not aged. In study 1 (NCT03652610), the Liquid vaccine underwent an ageing process under controlled conditions to reach ~30% MenA free saccharide (FS). In study 2 (NCT03433482), the Liquid vaccine was naturally aged at 2–8°C for approximately 24 and 30 months. Primary immunogenicity objective in both studies was non-inferiority of MenACWY-CRM liquid to licensed vaccine, as measured by human serum bactericidal assay (hSBA) geometric mean titers (GMTs) against MenA, 1-month post-vaccination.

Results. In both studies, for each between-group ratio of MenA hSBA GMTs, lower limits of the 95% confidence intervals (CIs) were greater than the prespecified non-inferiority margin (0.5), thus meeting the non-inferiority immunogenicity objective. Irrespectively of the vaccine presentation tested, over 82% of participants achieved MenA hSBA titers ≥ 8 in study 1 and at least 92% in study 2. The immunogenicity of MenACWY-CRM Liquid was similar to that of MenACWY-CRM(Lyo/Liq) when analyzed by serogroup, overall. No related serious adverse events were reported for both presentations.

Conclusion. After ageing, the new MenACWY-CRM Liquid demonstrated the ability to elicit non-inferior bactericidal responses against MenA compared to licensed formulation. The new full-liquid presentation is expected to increase the user-friendliness of the vaccine as well as to reduce reconstitution errors in the future, with a similar safety profile to that of the licensed vaccine presentation.

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