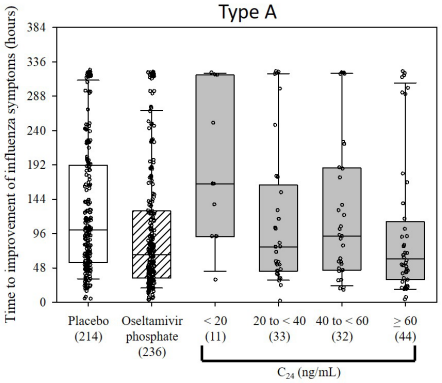
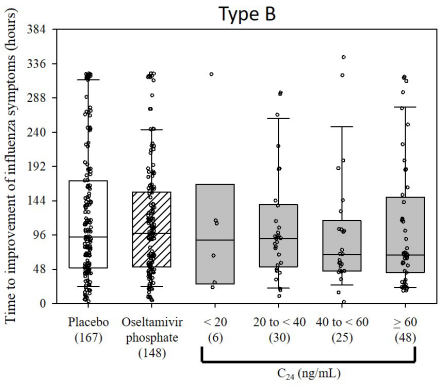
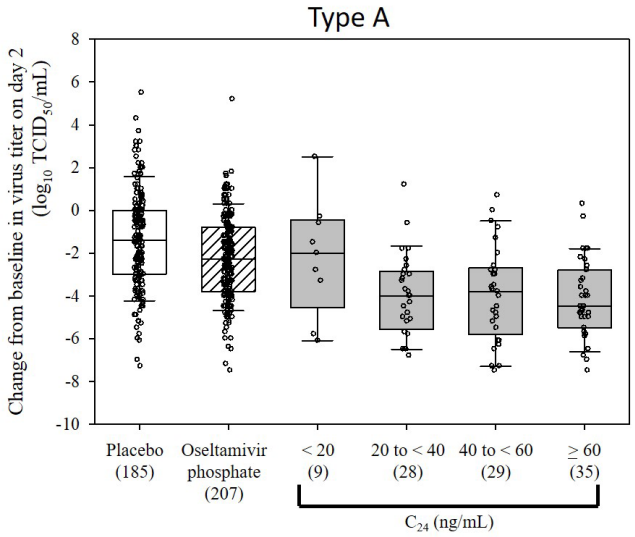
was assessed on the PK of baloxavir acid. The individual C_{max} and AUC were estimated with an empirical Bayesian approach. Exposure-response analysis was conducted for TTIIS and virus titer in the high-risk patients.

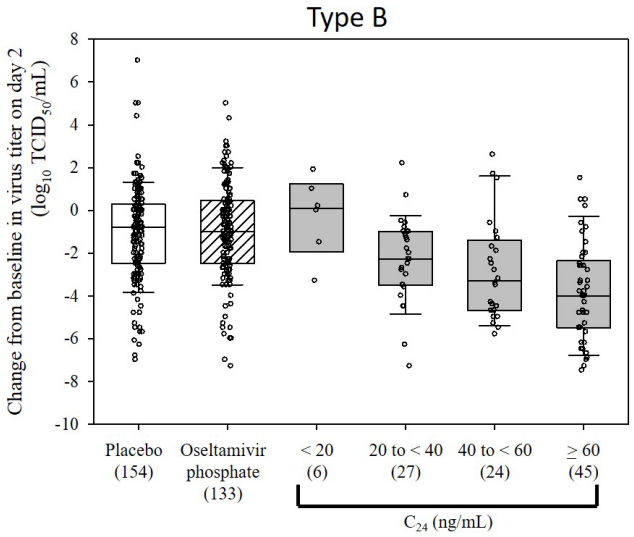
Results. A 3-compartment model with first-order absorption and lag time was selected as a structural PK model, and well described the plasma concentrations. The population PK analysis suggested that (1) AUC in non-Asians was 30.7% lower than that in Asians, (2) body weight significantly affected the exposures to baloxavir acid, (3) the exposures in high-risk patients were similar to those in otherwise healthy patients, and (4) no PK differences were identified regarding the risk factors for influenza complications. The exposure-response analyses showed that the body weight-based dose regimen (40 mg for the patients weighing <80 kg and 80 mg for the patients weighing ≥80 kg) shortened TTIIS and reduced virus titer for both type A and B influenza, across the entire range of baloxavir acid exposures observed in CAPSTONE-2 although subject number in the lowest exposure group was limited and it was difficult to discuss the magnitude of the responses accurately.

Conclusion. The results of the population PK analysis and exposure-response analyses provide useful information for understanding the pharmacokinetic and pharmacodynamic characteristics of baloxavir marboxil.









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

1537. Multicenter Study with Therapeutic Drug Monitoring (TDM) of Voriconazole (VRCZ) in Japanese Patients

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Background. TDM of VRCZ might be useful, especially in Asian people because of CYP2C19 genetic polymorphisms. However, limited data are available because of the small sample size.

Methods. Patients who received VRCZ and had TDM were reviewed retrospectively at five institutions. Adequate VRCZ dosage was defined as a loading dose of 5–6 ± 0.5 mg/kg twice daily followed by a maintenance dose of 3–4 ± 0.5 mg/kg twice daily. For prophylaxis, the loading dose was left to the physician's discretion. Optimal timing of TDM was defined as 4–7 days after starting therapy. Patients with adequate dosing and optimal timing of TDM were evaluated for analysis of trough levels (Cmin). Target Cmin was set at 1–5 μg/mL.

Results. The study included 584 patients (treatment: 402; prophylaxis: 182). TDM was conducted on days 4–7 in 66.5% of patients (>7, 30.2%). A low adequate dosage (44.5%) was observed for treatment mainly because of a low performance of the loading dose (46.8%). Achievement of target Cmin was obtained in 62.7% (>5 μg/mL, 32.2%) in the treatment group and in 67.6% (11.0%) in the prophylaxis group. Seventy-one of 81 (81.7%) patients who required a dose reduction reached target Cmin by the second TDM. In 38 patients whose dose was not altered at oral switching, Cmin was significantly reduced from 2.5 ± 1.6 to 1.2 ± 1.3 μg/mL ($P = 0.002$), which indicated the necessity of TDM after oral switching. Hepatotoxicity occurred in 4.6% and visual symptoms in 7.9% of patients. Visual symptoms resolved without discontinuation of VRCZ in 73.9% of patients. Because of dosage adjustment based on TDM, high Cmin did not cause hepatotoxicity. However, the incidence of visual symptoms was significantly higher in patients with a high Cmin (12.7% vs. 5.4%, $P = 0.002$).

Conclusion. One-third of Japanese patients who underwent VRCZ treatment with a loading dose showed high Cmin. Occurrence of hepatotoxicity was prevented with alteration of dosage in these patients (AMED, JP18fk0108045).

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

1538. Who Will Benefit From Therapeutic Drug Monitoring of Ganciclovir?

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Background. Oral valganciclovir and intravenous ganciclovir are used for prophylaxis, treatment, and pre-emptive treatment of cytomegalovirus and human herpesvirus 6. It is important to estimate the exposure to these antivirals, as deviating levels can cause adverse events or induce acquired drug resistance, which can both lead to treatment failure. Therapeutic drug monitoring (TDM) is a good tool to estimate drug exposure in these patients. With this observational study we aimed to evaluate which patients would benefit most from TDM.

Methods. An observational study was performed in adult solid-organ and stem cell transplant recipients on routine (val)ganciclovir (dosed according to renal function, weight and indication). As valganciclovir is a prodrug of ganciclovir, only the latter was measured. Ganciclovir trough (C_{trough}) and peak (C_{peak}) concentrations were measured with a validated LC-MS/MS assay. The target concentrations defined for the study were 1–2 mg/L and 2–4 mg/L for prophylaxis and treatment, respectively, and over 5 mg/L toxic.

Results. From June 2018 to April 2019, 66 patients were included. Within this timeframe, 236 C_{trough} and 52 C_{peak} were measured with median of 4 samples per patient. The median C_{trough} was 1.1 mg/L and 2.3 mg/L for prophylaxis and treatment, respectively. Over 50% of the concentrations were out of the therapeutic window. The median creatinine for all measurements was 100 µmol/L. Observational analysis showed patients with kidney failure and on continuous renal replacement therapy (CVVH) had more concentrations measured out of the predefined range (Figures 1 and 2). For one individual with augmented renal clearance we observed significantly lower concentrations during routine dosing. 6 toxic concentrations were measured (5 subjects); creatinine concentrations ranged 71–527 µmol/L in these individuals. A preliminary linear-mixed model analysis did not show drug formulation, age or gender as a significant predictor for ganciclovir concentrations.

Conclusion. We believe that patients with decreased renal function, on CVVH or showing changes in renal function might benefit from TDM to guide therapy. TDM of ganciclovir for patients without renal failure remains debatable. Further studies with specific patient groups are needed to confirm these results.

Table 1. Patient characteristics (n=66)

Characteristic	No. (%) of patients or median (IQR)
Gender	
Female	**25 (62%)**
Male	**41 (38%)**
Age (years)	**58 (48.5-64)**
BMI (kg/m²)	**23.5 (20.7-26.4)**
Weight	**71.1 (60.9-83.1)**
Height	**176 (169-182)**
Transplant type	
Stem cell transplant	**21 (31)**
Kidney	**9 (14)**
Lung	**13 (20)**
Liver	**9 (14)**
Heart	**8 (12)**
Other*	**6 (9)**
*Small intestine, liver/pancreas/small intestine, kidney/pancreas, lung/liver	
Ganciclovir treatment	
Therapeutic issue	
CMV prophylaxis	**37 (56)**
CMV treatment	**16 (24)**
HHV 6 treatment	**13 (20)**
Route of administration	

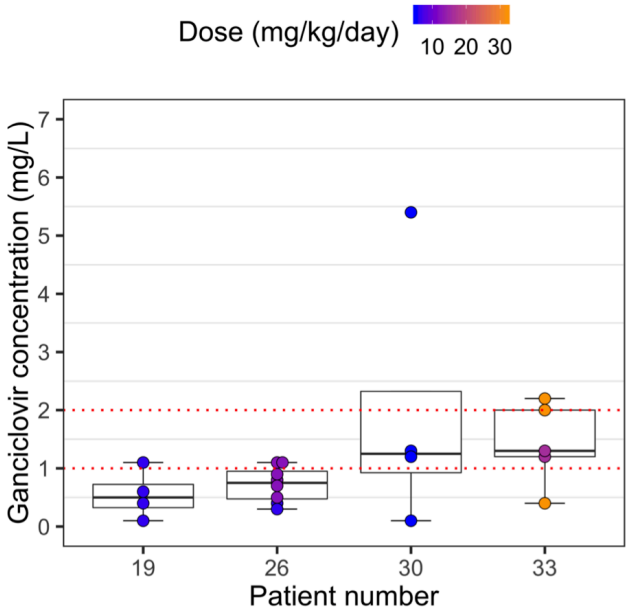

Figure 1. Variability of Ganciclovir concentrations during oral prophylaxis.

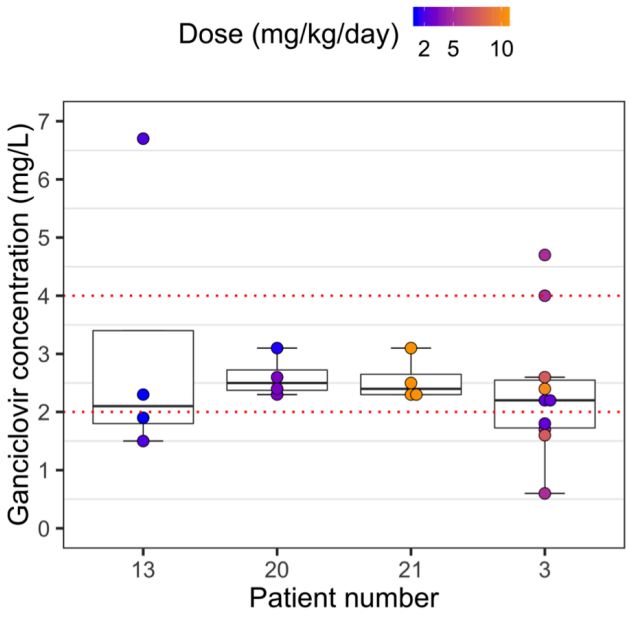

Figure 2. Variability of Ganciclovir concentrations during intravenous treatment.

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

1539. Dalbavancin, Vancomycin, and Daptomycin Alone and in Combination with Cefazolin Against Vancomycin Intermediate-Resistant (VISA) and Daptomycin Non-Susceptible (DNS) *Staphylococcus aureus*

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Background. Glycopeptides and lipopeptides, more specifically vancomycin (VAN) and daptomycin (DAP) have been principally utilized in treating MRSA infections. Due to continued use, MRSA strains have developed resistance to these antibiotics