SUPPLEMENTAL MATERIAL

MATERIALS AND METHODS

Renal impairment study design. Cohort assignments (eight subjects per group) included the control group (estimated glomerular filtration rate [eGFR] ≥80.0 ml/min/1.73 m^2) that was matched (by age, sex, and body mass index [BMI]) to severe renally impaired subjects (eGFR <30.0 ml/min/1.73 m^2) and to subjects with end-stage renal disease (ESRD) requiring hemodialysis (eGFR <15.0 ml/min/1.73 m^2).

Individuals in both the control group and the nondialyzed severe renal impairment group received a single 60-min infusion of 200-mg tedizolid phosphate. Those in the ESRD group received two separate 60-min infusions of 200-mg tedizolid phosphate in a nonrandomized crossover design, with half of all subjects first receiving an infusion starting 1 to 1.5 h before hemodialysis (using high-flux hemodialysis and non-reuse filters) and the other half initially receiving an infusion starting within 1 h of completing hemodialysis. All subjects subsequently underwent the reverse sequence to the one to which they were initially assigned, with a minimum 7-day washout period between infusions.

Hepatic impairment study design. Cohort assignments (eight subjects in each group) were as follows: moderate hepatic impairment (Child-Pugh classification B; score of 7–9); severe hepatic impairment (Child-Pugh classification C; score of 10–15); and 16 controls (eight subjects matched to the moderate hepatic control group, eight matched to the severe hepatic impairment control group) with normal hepatic function. Control subjects were matched for age, sex, and

BMI to each of the hepatic impairment groups. Group enrollment was sequential; the moderate hepatic impairment group was enrolled before the severe impairment group. Study drug was administered to subjects in a fasted (for at least 8 h) state.

Sample collection. Serial plasma samples were collected from predose through 72 h post dose for the renal study and predose through 96 h post dose for the hepatic study. Afferent and efferent plasma samples and dialysate samples (ESRD group only) were collected before hemodialysis and every 30 min during hemodialysis. Samples were extracted with acetonitrile and precipitated with hydrochloric acid, followed by low-speed [3,800 × *g*] centrifugation at room temperature for 5 min. Supernatants were evaporated to dryness and reconstituted in methanol/water (3:7, v/v). Tedizolid and tedizolid phosphate were separated by high-power liquid chromatography (1200 series; Agilent Technologies, Santa Clara, CA, USA) with a Hypersil GOLD aQ column (50 × 3 mm, 5-micron particle size; Thermo Fisher Scientific, Waltham, MA, USA). Samples were eluted using a gradient from 80% 20 mM ammonium phosphate (pH 9.0)/20% methanol to 80% methanol over 4.5 min at a flow rate of 0.5 ml/min. The column eluent was directed to an API 4000 triple quadrupole mass spectrometer (AB SCIEX, Framingham, MA, USA) for compound quantification. Data were processed using the Analyst 1.4.1 software package (AB SCIEX) and the Watson LIMS laboratory information management system (Thermo Fisher Scientific).

TABLE S1. Renal impairment study: baseline demographics[a-c]

Characteristic[b]	Controls (*n* = 8)	Nondialysis severe group (*n* = 8)	ESRD dialysis group (*n* = 8)
Age, yrs	57.8 (7.3)	61.0 (10.0)	50.4 (8.1)
Male sex	4 (50.0%)	4 (50.0%)	7 (87.5%)
Race			
White	7 (87.5%)	4 (50.0%)	0
Black/African American	1 (12.5%)	3 (37.5%)	8 (100.0%)
American Indian/Alaska Native	0	1 (12.5%)	0
eGFR (ml/min/1.73 m^2)	92.6 (9.1)	18.3 (6.5)	7.9 (2.2)[c]
BMI (kg/m^2)	28.7 (3.9)	29.4 (5.4)	27.5 (5.2)

[a] BMI, body mass index; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease.

[b] Demographic data are presented as the mean (SD) or as the number and percentage of the study population.

[c] The estimated calculation of the GFR using the four-variable Modification of Diet in Renal Disease calculation can overestimate GFR as a result of fluctuating plasma creatinine levels during and between dialysis sessions.

TABLE S2. Hepatic impairment study: baseline demographics[a,b]

Characteristic[b]	Moderate impairment (*n* =8)	Matched control (*n* = 8)	Severe impairment (*n* = 8)	Matched control (*n* = 8)
Age, yrs	53.8 (3.9)	55.3 (7.0)	55.8 (8.4)	53.0 (8.7)
Male sex	7 (87.5%)	7 (87.5%)	5 (62.5%)	5 (62.5%)
Race				
White	8 (100.0%)	5 (62.5%)	7 (87.5%)	6 (75.0%)
Black/African American	0	3 (37.5%)	0	2 (25.0%)
American Indian/Alaskan Native	0	0	1 (12.5%)	0
CLcr, ml/min	130.1 (30.1)	111.9 (23.9)	140.5 (39.1)	132.1 (31.1)
BMI, kg/m^2	29.8 (5.1)	27.3 (4.2)	34.0 (3.5)	32.9 (4.3)

[a] BMI, body mass index; CLcr, creatinine clearance calculated using the Cockcroft-Gault equation.

[b] Demographic data are presented as the mean (SD) or as the number and percentage of the study population.