

**Appendix from Frey et al., “Assessment of the effects of hepatic impairment and smoking on the pharmacokinetics of a single oral dose of the soluble guanylate cyclase stimulator riociguat (BAY 63-2521)”
(Pulm. Circ., vol. 6, no. S1, p. S5)**

Supplemental table

Table S1. Pharmacokinetic parameters for riociguat and metabolite M1 in nonsmoking healthy individuals (controls) and patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment, following a single oral dose of riociguat 1.0 mg

Parameter	Child-Pugh A (<i>n</i> = 13)	Child-Pugh B (<i>n</i> = 11)	Control A (<i>n</i> = 14)	Control B (<i>n</i> = 14)
Riociguat				
AUC, $\mu\text{g}\cdot\text{h}/\text{L}$	453 (60)	552 (56)	344 (70)	369 (64)
AUC _{norm} , $\text{kg}\cdot\text{h}/\text{L}$	38.1 (59)	44.2 (59)	28.1 (69)	29.3 (67)
C_{max} , $\mu\text{g}/\text{L}$	43.5 (36)	43.1 (44)	42.8 (24)	40.2 (30)
$C_{\text{max, norm}}$, kg/L	3.66 (36)	3.45 (29)	3.50 (19)	3.18 (22)
t_{max} , hours	1.00 (0.500–3.00)	1.50 (0.750–4.00)	0.750 (0.500–3.00)	1.50 (0.500–3.00)
$t_{1/2}$, hours	10.9 (36)	15.2 (47)	8.9 (63)	9.2 (58)
CL/F, L/h	2.21 (60)	1.81 (56)	2.90 (70)	2.71 (64)
f_{u} , %	3.34 (14)	4.28 (36)	3.35 (18)	3.43 (24)
AUC _{u, norm} , $\text{kg}\cdot\text{h}/\text{L}$	1.27 (53)	1.89 (75)	0.941 (69)	1.00 (69)
$C_{\text{max, u, norm}}$, kg/L	0.122 (33)	0.148 (26)	0.117 (24)	0.109 (25)
$A_{\text{E, ur}}$, %	10.7 \pm 4.48	14.0 \pm 9.51	11.0 \pm 5.29	10.7 \pm 4.15
CL _R , L/h	0.217 (60)	0.221 (110)	0.281 (32)	0.267 (44)
Metabolite M1				
AUC, $\mu\text{g}\cdot\text{h}/\text{L}$	267 (51)	226 (55)	219 (40)	221 (37)
AUC _{norm} , $\text{kg}\cdot\text{h}/\text{L}$	23.2 (46)	18.7 (62)	18.5 (37)	18.1 (33)
C_{max} , $\mu\text{g}/\text{L}$	6.83 (56)	4.98 (70)	7.06 (74)	6.98 (69)
$C_{\text{max, norm}}$, kg/L	0.594 (53)	0.412 (59)	0.597 (70)	0.572 (60)
t_{max} , hours	12.0 (2.00–48.0)	12.0 (4.00–48.0)	8.00 (2.00–24.0)	12.0 (4.00–24.0)
$t_{1/2}$, hours	20.0 (30)	23.0 (54)	15.2 (30)	16.5 (33)
CL/F, L/h	3.62 (51)	4.28 (55)	4.41 (41)	4.37 (37)
f_{u} , %	2.70 (14)	3.80 (37)	2.91 (17)	2.98 (20)
AUC _{u, norm} , $\text{kg}\cdot\text{h}/\text{L}$	0.627 (47)	0.715 (61)	0.541 (49)	0.541 (40)
$C_{\text{max, u, norm}}$, kg/L	0.0161 (51)	0.0157 (38)	0.0174 (76)	0.0171 (63)
$A_{\text{E, ur}}$, %	12.2 \pm 7.50	5.72 \pm 4.49 ^a	15.1 \pm 8.81	13.3 \pm 6.75
CL _R , L/h	0.391 (93)	0.209 (126) ^a	0.594 (48)	0.529 (61)

Note: Data are geometric means (percentage coefficient of variation) except for t_{max} , which is expressed as median (range), and $A_{\text{E, ur}}$, which is expressed as arithmetic mean \pm standard deviation. $A_{\text{E, ur}}$: amount excreted into urine from time 0 to infinity; AUC: area under the plasma concentration–time curve from time 0 to infinity; AUC_{norm}: AUC divided by dose of riociguat per kilogram of body weight for total (bound and unbound) riociguat/M1; AUC_{u, norm}: AUC divided by dose of riociguat per kilogram of body weight for unbound riociguat/M1; CL/F: apparent oral clearance for total riociguat/M1; CL_R: renal clearance of riociguat/M1; C_{max} : maximum concentration in plasma; $C_{\text{max, norm}}$: C_{max} divided by dose of riociguat per kilogram of body weight for total riociguat/M1; $C_{\text{max, u, norm}}$: C_{max} divided by dose of riociguat per kilogram of body weight for unbound riociguat/M1; f_{u} : fraction unbound; t_{max} : time to C_{max} of total riociguat/M1; $t_{1/2}$: terminal elimination half-life for total riociguat/M1.

^a Data were available from 10 patients.