

ONLINE SUPPLEMENTARY INFORMATION

TABLE S1 Rates of adverse events per 100 patient-years in CHEST-1 and CHEST-2

AE, n (rate per 100 patient-years) [#]	CHEST-1		CHEST-2
	Riociguat (n=173)	Placebo (n=88)	Total (n=237)
Any AE	889 (1732.5)	405 (1525.0)	2081 (550.9)
Five most frequent AEs in CHEST-2			
Nasopharyngitis	29 (56.5)	10 (37.7)	86 (22.8)
Dizziness	57 (111.1)	13 (49.0)	61 (16.2)
Peripheral oedema	30 (58.5)	20 (75.3)	61 (16.2)
Upper respiratory tract infection	11 (21.4)	4 (15.1)	40 (10.6)
Diarrhoea	27 (52.6)	4 (15.1)	39 (10.3)
Dyspnoea	9 (17.5)	14 (52.7)	39 (10.3)
AEs of special interest			
Syncope	4 (7.8)	4 (15.1)	22 (5.8)
Hypotension	16 (31.2)	3 (11.3)	17 (4.5)
Other AEs of interest			
Haemoptysis/pulmonary haemorrhage	4 (7.8)	0	11 (2.9)

[#]: total number of events are shown; a patient may have more than one event.
AE: adverse event.

TABLE S2 Missing data sensitivity analyses for 6MWD and WHO FC at week 12 and 1 year of CHEST-2

	Change from baseline in 6MWD, mean±SD (m)			WHO FC improved/ stabilised/worsened (%) [#]	
	CHEST-2 Week 12	CHEST-2 1 year		CHEST-2 Week 12	CHEST-2 1 year
	LOCF ^{***}	LOCF [¶]	Mixed-model for repeated measures ⁺	LOCF ^{***}	LOCF [§]
Former riociguat group (n=155)	+57±69 m	+51±67 m	+54±6 m	41/55/4%	45/48/7%
Former placebo group (n=82)	+43±72 m	+36±71 m	+38±8 m	40/57/4% ^f	40/57/4% ^f
Overall population (n=237)	+52±70 m	+46±69 m	+48±5 m	40/56/4% ^{##}	43/51/6% ^{##}

[#]: data do not always add up to 100% due to rounding.

^{***}: with worst value imputation.

[¶]: without worst value imputation.

⁺: data are LS mean±SEM.

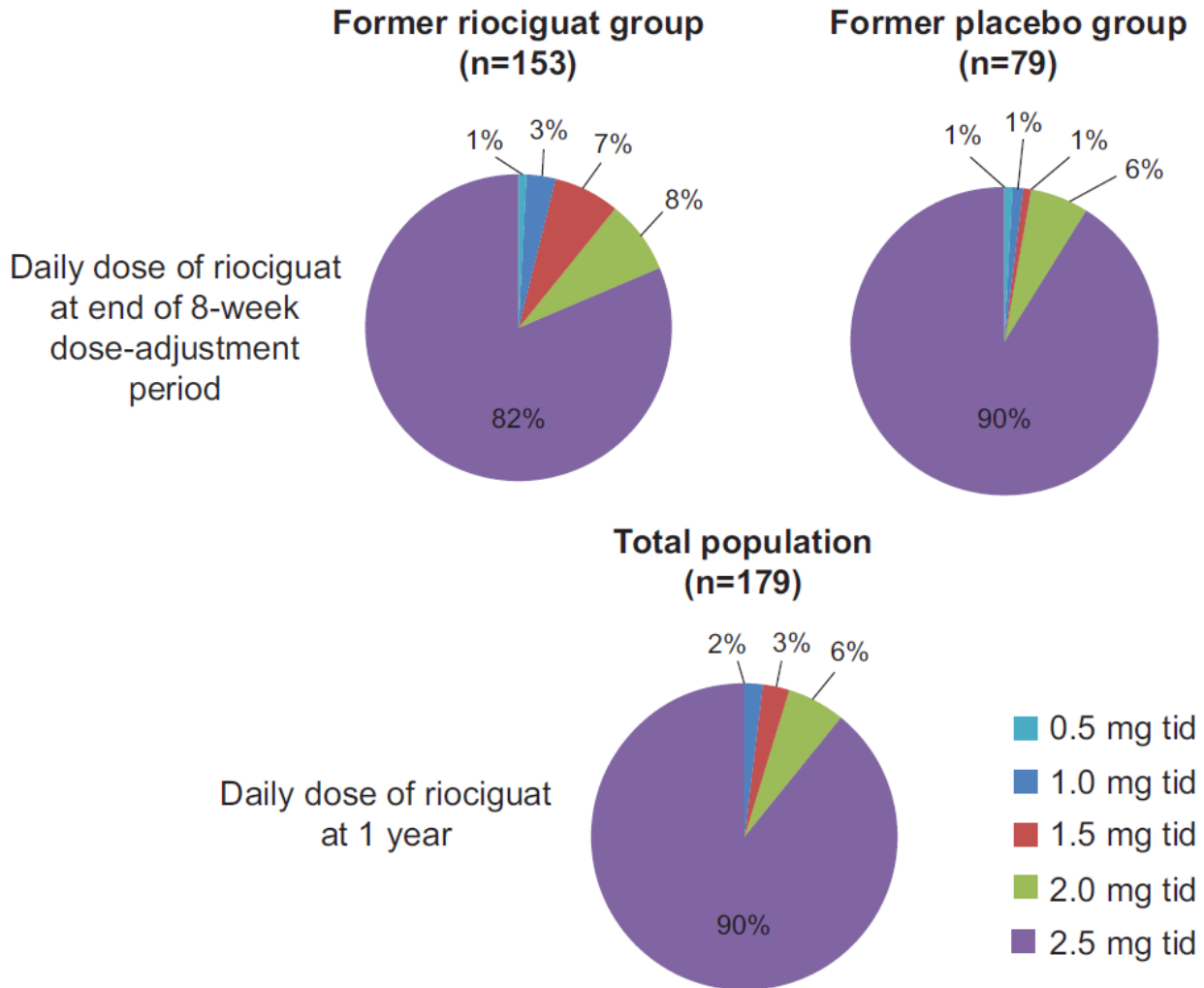
[§]: with worst value plus 1 (V) in cases of death.

^f: n=81.

^{##}: n=236.

6MWD: 6-minute walking distance; FC: functional class; LOCF: last observation carried forward; LS: least-squares; SD: standard deviation; SEM: standard error of the mean.

FIGURE S1 Daily dose of riociguat received during CHEST-2



tid: three times daily.

Percentages may not add up to 100% due to rounding.