Effects of riociguat in treatment-naïve vs pretreated patients with pulmonary arterial hypertension (PAH): 2-year efficacy results from the PATENT-2 study

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Introduction

Riociguat showed sustained efficacy in patients with PAH in the PATENT-2 study. We compared treatment-naïve and pretreated patients from the final datacut of PATENT-2.

Methods

Patients with PAH who were treatment-naïve or pretreated with ERAs or prostanoids entered PATENT-2 after completing PATENT-1 without ongoing riociguat-related SAEs. All patients received riociguat individually adjusted up to a maximum of 2.5 mg tid. Primary endpoints were safety and tolerability; secondary endpoints included 6MWD, WHO FC, survival, and clinical worsening-free survival.

Results

In total, 396 patients entered PATENT-2; 197 (50%) were treatment-naïve and 199 (50%) were pretreated. Median treatment duration was >2 years (139 weeks). Of the treatment-naïve patients who reached 2 years (n=141), 24 (17%) had initiated concomitant therapy with ERAs and/or prostanoids. Improvements in 6MWD, NT-proBNP, Borg dyspnea score, and EQ-5D were more pronounced in the treatment-naïve subgroup compared with the pretreated subgroup (Table 1). The most frequent AEs in the treatment-naïve and pretreated subgroups were nasopharyngitis (27% vs 33%), dizziness (25% vs 26%), and peripheral edema (21% vs 28%). Fewer patients in the treatment-naïve subgroup compared with the pretreated subgroup experienced SAEs (52% vs 68%), drug-related SAEs (7% vs 13%), clinical worsening (25% vs 29%), and death (11% vs 14%).

Conclusions

Riociguat provided long-term clinical benefit in treatment-naïve and pretreated patients with PAH. No new safety signals identified, but more SAEs were observed in the pretreated subgroup. The improvements in 6MWD and WHO FC observed with riociguat treatment in PATENT-1 were sustained at 2 years in PATENT-2 in both subgroups.

Table 1. Secondary efficacy endpoints in PATENT-2

Endpoint	Treatment-naïve subgroup					Pretreated subgroup				
	Baseline	Change from baseline at timepoint, months				Baseline	Change from baseline at timepoint, months			
		6	12	18	24		6	12	18	24
6MWD, m	369±68 (n=197)	+59±60 (n=189)	+54±71 (n=179)	+58±74 (n=169)	+53±84 (n=154)	365±66 (n=199)	+46±67 (n=177)	+46±74 (n=172)	+42±82 (n=160)	+40±86 (n=142)
WHO FC, %										
I/II/III/IV	5/51/44/1 (n=197)	–	–	–	–	2/34/64/1 (n=198)	–	–	–	–
Improved/stabilized/ worsened	–	28/69/4 (n=192)	29/65/7 (n=184)	30/63/7 (n=176)	28/63/9 (n=158)	–	37/58/5 (n=185)	36/59/6 (n=179)	34/56/10 (n=167)	37/54/9 (n=148)
NT-proBNP, pg/mL	1209±1891 (n=181)	–482±1688 (n=174)	–386±2097 (n=166)	–510±1934 (n=138)	–291±1626 (n=104)	912±1152 (n=173)	–159±911 (n=160)	–210±879 (n=155)	–70±984 (n=122)	+19±1553 (n=92)
Borg dyspnea score	3.2±2.0 (n=197)	–0.6±1.7 (n=188)	–0.5±1.8 (n=177)	–0.3±1.8 (n=150)	–0.2±1.8 (n=115)	4.3±2.2 (n=199)	–0.5±1.8 (n=177)	–0.4±2.0 (n=169)	–0.4±2.3 (n=132)	–0.6±1.9 (n=98)
EQ-5D	0.69±0.24 (n=195)	+0.08±0.22 (n=187)	+0.06±0.26 (n=176)	+0.06±0.24 (n=152)	+0.48±0.26 (n=115)	0.68±.0.23 (n=197)	+0.08±0.21 (n=181)	+0.09±0.19 (n=171)	+0.06±.0.22 (n=131)	+0.08±0.24 (n=102)

Data are mean±SD unless otherwise stated.
6MWD, 6-minute walking distance; EQ-5D, EuroQol 5-Dimensions questionnaire; NT-proBNP, *N*-terminal prohormone of brain natriuretic peptide; WHO FC, World Health Organization functional class.