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Title: Riociguat for the treatment of pulmonary arterial hypertension (PAH): A responder analysis from the phase III PATENT-1 study

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Body: Background In PATENT-1, riociguat significantly improved 6-min walking distance (6MWD) and a range of secondary endpoints, including hemodynamics, NT-proBNP, and WHO functional class (FC), in patients (pts) with PAH. For several of these endpoints, threshold criteria have been defined that correlate with favorable clinical outcome. Aims To investigate the proportion of pts who fulfilled these criteria in PATENT-1. Methods PATENT-1 was a double-blind randomized trial in which pts with PAH received 12 wks' oral treatment with placebo, an individual titration of riociguat (up to 2.5 mg tid), or a capped titration of riociguat (up to 1.5 mg tid). Increase in 6MWD ≥40 m, 6MWD ≥380 m, cardiac index (CI) ≥2.5 L/min/m^2, PVR <500 dyn·s·cm^{-5}, mixed venous oxygen saturation (SvO_2) ≥65%, FC I/II, and NT-proBNP <1800 pg/mL were chosen as criteria of a positive response based on studies showing their prognostic relevance at baseline (BL) and after targeted therapy. Results Similar proportions of pts met the selected criteria in the riociguat and placebo groups at baseline. The proportion of pts who met these criteria at Wk 12 was increased in the riociguat group, while it remained unchanged or decreased in the placebo group.

Criteria, %	Riociguat individual titration	Placebo

	N	BL	Wk 12	N	BL	Wk 12
6MWD increase ≥40 m	254	n/a	43	126	n/a	23
6MWD ≥380 m	254	45	63	126	58	55
CI ≥2.5 L/min/m^2	233	45	76	108	48	44
PVR <500 dyn•s•cm^{-5}	232	30	49	107	27	30
SvO_2 ≥65%	210	56	73	100	61	47
FC I/II	254	44	60	125	51	54
NT-proBNP <1800 pg/mL	228	82	89	106	79	73

Conclusions Riociguat increased the proportion of pts who fulfilled criteria defining a positive response to therapy.