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# Long-term sotatercept in pulmonary arterial hypertension (PAH): an update from all completed studies and follow-up in SOTERIA

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Background: The first-in-class activin-signalling inhibitor, sotatercept, has demonstrated broad clinical benefit and manageable safety in PAH across multiple placebo-controlled studies and in previously reported data from an open-label, long-term follow-up (f/u) study (SOTERIA, NCT04796337).

Aims: Assess outcomes associated with long-term sotatercept, capturing the longest exposure duration to date from all completed parent studies and f/u in SOTERIA.

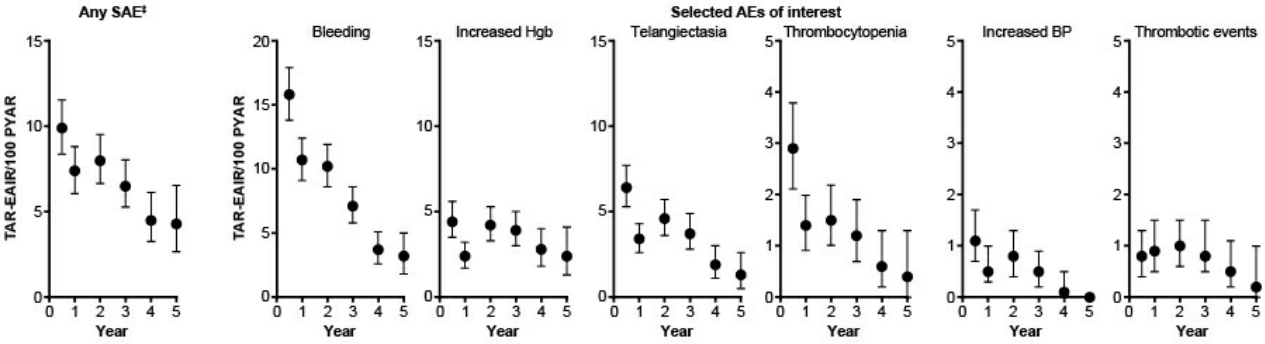
Methods: This post-hoc analysis pooled participant (pt)-level data from SPECTRA (NCT03738150), PULSAR (NCT03496207), STELLAR (NCT04576988), ZENITH (NCT04896008), HYPERION (NCT04811092) and SOTERIA, reported from sotatercept treatment (tx) initiation to discontinuation or data cutoff.

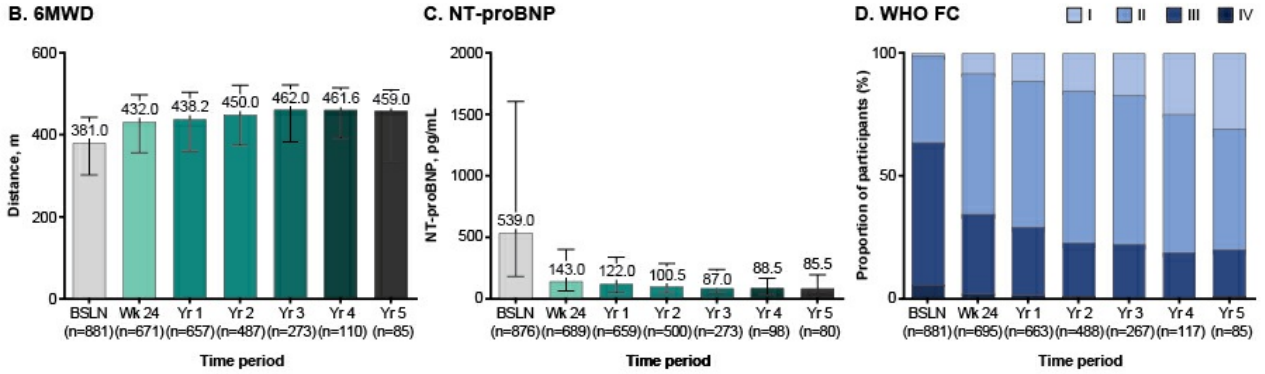
Results: By 14 April 2025, 881 pts had received sotatercept in the above trials; baseline mean (SD) age was 52 (15.6) yrs, time since diagnosis was 5.9 (6.1) yrs, WHO functional class distribution: I=1%, II=34%, III=59%, IV=6% with 47% receiving double and 50% triple background tx. After median (range) 2.1 (0.1–6.8) yrs and 1894 total person-yrs of exposure, 92% had ≥1 adverse event (AE); 44% had a serious AE. AEs led to dose delays, tx discontinuation, and death in 36%, 6%, and 6% respectively. Figure shows exposure-adjusted AE incidence rates (EAIR) and efficacy measures. Over time, efficacy was sustained and incidence of AEs did not increase.

Conclusion: Pooled data from six clinical trials and up to 5 yrs f/u support sustained, favourable benefit–risk for sotatercept in PAH.

**Figure.** Safety and efficacy of sotatercept up to Year 5 of treatment

**A. Exposure-adjusted incidence rates† (6 months to 5 years of treatment)**




Data cutoff: April 14, 2025, indexed to the start of sotatercept treatment. The following number of participants contributed to EAIR analyses at 6 months and years 1-5, respectively: 881, 705, 617, 454, 243, and 100.
†Each pt was counted once based on the earliest reported selected AE; for any SAE, each pt is counted once based on the earliest reported SAE. PYAR for each participant and each type of event is defined as the time between the sotatercept start date and the earlier of: first event date, death date, last dose date + 56 days, or the data cutoff date, plus 1 day. Incidence rate per 100 person-years at risk = number of pts with events * 100 / person-years at risk. Between-group 95% CI is computed using the Miettinen and Nurminen method.
‡Includes all reported serious events.
Bar graphs for 6MWD and NT-proBNP show the median and IQR for each timepoint.
6MWD, 6-minute walk distance; BSLN, baseline; BP, blood pressure; CI, confidence interval; EAIR, exposure-adjusted incidence rate; Hgb, haemoglobin; IQR, interquartile range; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PYAR, person-years at risk; Pt, participant; SAE, serious adverse event; TAR-EAIR, time-at-risk exposure-adjusted incidence rate; WHO FC, World Health Organization functional class; Wk, week; Yr, year.