UNDERSTANDING THE IMPACT OF PLACEBO ON PATIENT-REPORTED HEALTH STATUS: AN ANALYSIS FROM SEQUOIA-HCM

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BACKGROUND

- As clinical trials increasingly use patient-reported outcomes (eg, the Kansas City Cardiomyopathy Questionnaire [KCCQ]) in obstructive hypertrophic cardiomyopathy (oHCM), there is growing interest in understanding placebo effects on these outcomes.
- While improvements in placebo-treated patients are often ascribed to a placebo effect, other important benefits from trial participation can improve participants' health status, including treatment at expert centers and changes in patient behavior. Regression to the mean may also play a role.
- In SEQUOIA-HCM (NCT05186818), we evaluated the differences in KCCQ Overall Summary Scores (OSS) following blinded treatment withdrawal to estimate the magnitude of the placebo effect on KCCQ scores.

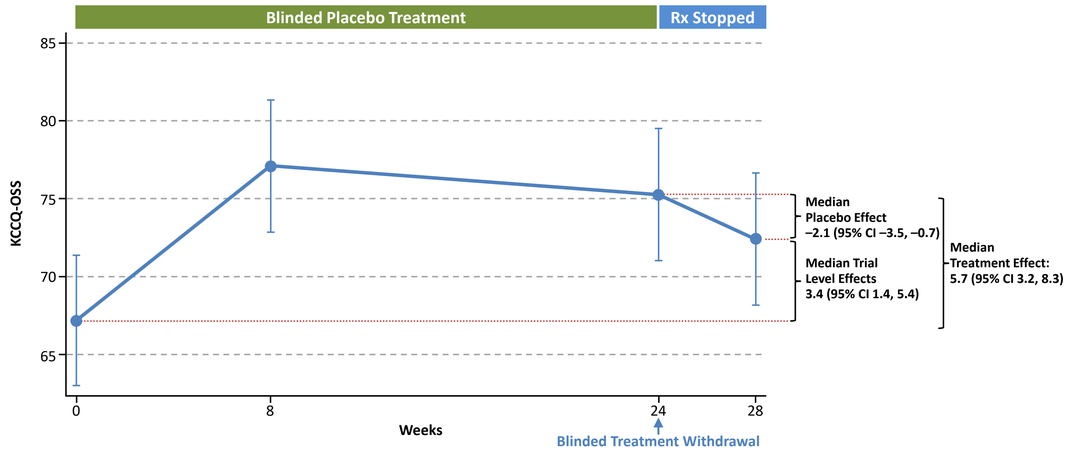
OBJECTIVE

- To separate placebo effects from other trial-related benefits on the KCCQ-OSS.

METHODS

- SEQUOIA-HCM was a phase 3 double-blind placebo-controlled trial that randomized participants 1:1 to aficamten or placebo for 24 weeks of treatment followed by known treatment withdrawal while participants remained blinded to treatment assignment.
- The KCCQ is a valid measure of patients' health status in oHCM, and score ranges from 0–100 with higher scores representing better health status. The KCCQ was collected throughout the study.
- Median changes in KCCQ-OSS after treatment withdrawal were compared using quantile regression, adjusted for baseline score, in those receiving placebo treatment.
  - Combined placebo and trial effects = the change from baseline to Week 24.
  - Placebo effects = the change from Weeks 24 to 28, after blinded treatment withdrawal.
  - Other clinical trial effects = the change from baseline to Week 28 minus the placebo effect.

Figure: KCCQ-OSS Over Time In Placebo-treated Patients



KCCQ-OSS, Kansas City Cardiomyopathy Questionnaire Overall Summary Score, Rx, assigned treatment.

RESULTS

- Among 140 (49%) patients who were assigned to placebo, 59 (42%) were women, mean age was 59 ± 13, 115 (82%) were White, and 45 (32%) were North American.
- Background medications: 62% beta-blockers, 26% calcium channel-blockers, 14% disopyramide.
- Median baseline KCCQ-OSS was 67.2 (95% CI: 62.9, 71.5) and the median improvement was 5.7 (95% CI: 3.2, 8.3; *P*<0.01) at Week 24 (**Figure**).
- After withdrawal of study treatment, the median score decrement (placebo effect) was –2.1 (95% CI: – 3.5, – 0.7; *P*<0.01) from Weeks 24 to 28.

LIMITATIONS

- Inclusion and exclusion criteria may limit the generalizability of these results.
- Although most changes by 28 weeks in the placebo group were not attributed to placebo effects, the categories of other trial effects (eg, adherence, regression to mean) could not be separated.

CONCLUSIONS

- Placebo effects represented a minority of the observed improvement in KCCQ scores in placebo-treated patients, with the remainder attributed to other trial effects.
- Better quantifying the magnitude of placebo effects can increase confidence in patient-reported outcomes.

DISCLOSURES

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