Inherit trial: discussion

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Background

• Current therapies for HCM are palliative for symptoms only
• No randomized controlled trials
• Medical
  – Beta blockers
  – Non-dihydropyridine CCBs: verapamil, diltiazem
  – Disopyramide
• Septal reduction
  – Myectomy
  – Alcohol ablation
• Sudden death
  – Exercise limitation
  – ICD
INHERIT trial

• In 58 obstructive and non-obstructive adult HCM patients (52yrs+/- 12), when compared to 66 patients who received placebo, losartan 100mg daily did not alter the change in LV mass, or any secondary endpoint, after 372 days of therapy.
• No significant change in symptoms or resting LVOT gradient
• 92/137 screen failures were already on ACEi/ARB
Inherit trial – major learning points

- Studies in rare disease are hard to do
- Randomized, double blind, placebo controlled study
- No safety issues identified in giving “vasodilator”
- No dramatic change in LV mass or secondary endpoints
- Smaller but important effects not yet ruled out
What is the right endpoint?

Regression of Hypertensive Left Ventricular Hypertrophy by Losartan Compared With Atenolol
The Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Trial

Richard B. Devereux, MD; Björn Dahlöf, MD, PhD; Eva Gerdts, MD, PhD; Kurt Boman, MD; Markku S. Nieminen, MD; Vasilios Papademetriou, MD; Jens Rokkedal, MD; Katherine E. Harris, DrPH; Jonathan M. Edelman, MD; Kristian Wachtell, MD, PhD

960 patients total
What’s coming next?

• VANISH
  – Valsartan, younger patients, composite endpoint

• Liberty-HCM
  – Late sodium channel inhibitor

- 8-30 years
- Must have sarcomere variant
- 7 component composite outcome
- G+/P- group