Changes in high-sensitivity cardiac troponin I and associated cardiovascular risk

Analyses From The FOURIER Trial In Patients With Stable ASCVD

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BACKGROUND

- Circulating **high-sensitivity cardiac troponin I** (hs-cTnI) **is associated with the risk of future cardiovascular (CV) events** in stable patients with atherosclerotic CV disease (ASCVD).
- **Data are scarce** regarding changes of hs-cTnI in this setting and **if changes are associated with subsequent risk** of major cardiovascular events.

AIM: To **study changes of hs-cTnI** in stable patients with ASCVD and **the association with risk of future major CV events.**

METHODS

- The **FOURIER** trial tested the PCSK9i evolocumab vs. placebo in **patients with ASCVD receiving statin** therapy with LDL-C ≥70 or non-HDL-C ≥100 mg/dL.
- **In 20,718 patients, hs-cTnI** (Abbott ARCHITECT) was measured at **baseline** (BL) **and after 24 weeks** as part of a nested biomarker study. The lower limit of quantification (LLOQ) = 3.6ng/L.
- The **primary endpoint** was an **adjudicated composite of CV death, MI, stroke, hosp. for unstable angina, or coronary revascularization**.
- The **3-year risk** of a future event, **landmarked from 24 weeks**, was assessed across change in hs-cTnI from baseline to 24 weeks.
- Restricted-cubic splines and Cox-PH models were adjusted for sex, age, LDL-C, prior MI, treatment group, eGFR, DM, HTN, prior HF, and BMI.
- A Generalized Additive Model was used to predict event rates as a function of hs-cTn$_{BL}$ & absolute hs-cTn change, including a non-linear interaction.

RESULTS

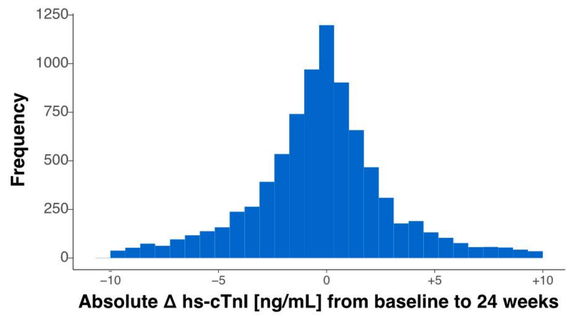
- Of **20,718 pts**, **11,021 (53.2%) had quantifiable hs-cTnI at baseline and 24 weeks (Table 1)**

Table 1: Baseline characteristics

	Baseline hs-cTnI				
	<LLOQ N=8852	**Q1 N=2,967**	**Q2 N=2,967**	**Q3 N=2,966**	**Q4 N=2,966**
Age	61 (54 - 67)	64 (57 - 69)	65 (58 - 70)	65 (59 - 71)	65 (58 - 71)
Male (%)	69	78	80	83	81
Diabetes	30	34	34	38	42
CAD	82	87	89	90	91
PAD	13	13	13	14	17
Cerebrovasc. Disease	25	23	22	23	23
Heart failure	19	22	24	31	38
Kidney disease	12	19	21	26	29
Hs-cTnI$_{BL}$	-	4.1 (3.8, 4.5)	5.7 (5.2, 6.3)	8.8 (7.7, 10.3)	22.6 (16.0, 41.7)
Hs-cTnI$_{24wks}$	-	4.80 (4.1, 5.9)	5.60 (4.6, 7.2)	8.00 (6.1, 10.8)	18.1 (11.6, 35.0)

Data in median (25th, 75th percentile) or %. LLOQ – lower limit of quantification

Fig 1: Absolute hs-cTnI Δ from baseline to 24 weeks.



- Median hs-cTnI change was -0.2 ng/L (25th, 75th percentile: -1.6, 1.0), distribution shown in **Fig. 1.**
- There was no interaction of hs-cTnI with evolocumab regarding the primary CV endpoint.
- The median absolute change of hs-cTnI from baseline to 24 weeks across baseline values is depicted in **Fig. 2**.
- **Absolute decreases and increases of hs-cTnI from baseline to 24 weeks were associated with a gradient of risk for future events**, across hs-cTnI$_{BL}$ (**Fig 3**).
- **Relative decreases and increases** of hs-cTnI were associated with **lower and higher relative risk, respectively** (**Fig. 4**).

Fig. 2. Median Δ in hs-cTnI from baseline to 24 weeks across baseline hs-cTnI deciles.

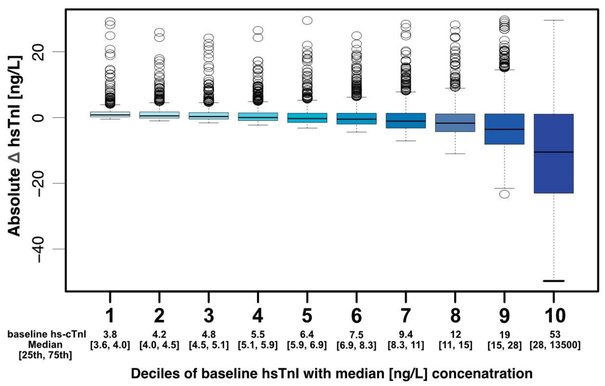


Fig. 3: Categories of absolute risk through 3 years for absolute change of hs-cTnI across starting baseline concentrations

(CV death, MI, stroke, hosp. for unstable angina, or coronary revascularization)

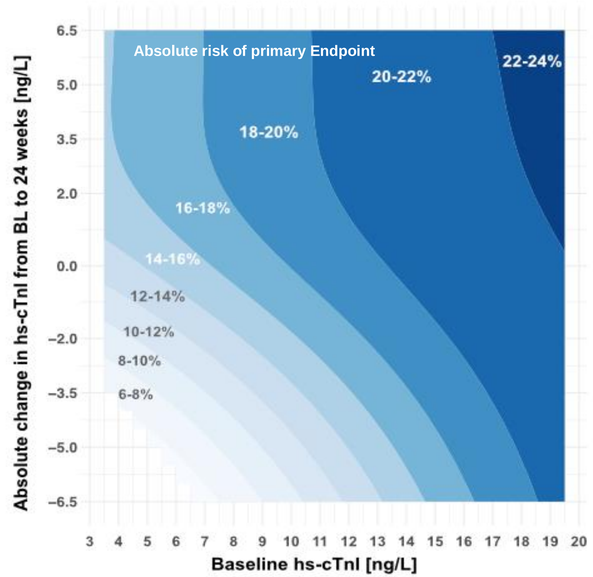
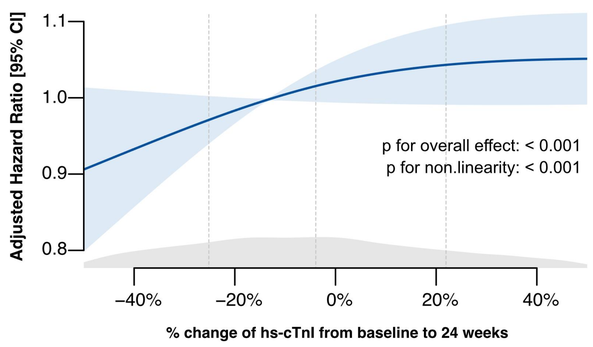


Fig. 4: Adjusted HR for primary endpoint by % Δ in hs-cTnI from baseline to 24 wks.



CONCLUSION

- In stable patients with established ASCVD, small **changes in hs-cTnI over 6 months are associated with the changes in the risk of future major CV events**.
- **Serial measurements of hs-cTnI** over time **may be useful for risk assessment** in secondary prevention, identifying patients whose CV risk changes with time.

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