



# Back to the Future: Inflammation in CVD

A Conversation with  
Dr. Eileen O'Meara and  
Dr. Abhinav Sharma

# Accreditation

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada, and approved by the Canadian Cardiovascular Society. You may claim a maximum of 0.5 hour (credits are automatically calculated).

# Faculty

## Scientific Planning Committee:

- Shelley Zieroth (Chair), MD, FCCS, FHFSA (hon), FESC, FACC, FHFA, FRCPC
- Grace Chua, MD, FRCPC, FACC

## Presenters:

- Abhinav Sharma, MD, PhD
- Eileen O'Meara, MD, FRCPC, FCCS



# Disclosures

	Dr. Zieroth	Dr. Chua
Any direct financial payments including receipt of honoraria	No disclosures	Canadian Cardiovascular Society, Canadian Heart Failure Society, Canadian Society of Endocrinology and Metabolism, CPD Network, EOCI Pharmacomm, liV Medical Agency, Meducom Health Inc, Sei-Healthcare, University of Toronto Heart and Stroke Richard Lewar Center of Excellence, Canadian Medical and Surgical Knowledge Translation Research Group
Membership on advisory boards or speakers' bureaus	AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Cytokinetics, Eli Lilly, GSK, Janssen, Medtronic, Merck, Novartis, Novo-Nordisk, Otsuka, Pfizer, Roche, Salubrisbio, Servier and Vifor Pharma.	Amgen, Astra Zeneca, Bayer, Boehringer Ingelheim-Eli Lilly Alliance, Bristol Myers Squibb, GlaxoSmithKline, HLS Therapeutics, Novartis, Novo Nordisk, Pfizer, Servier, CPD Network, Canadian Collaborative Research Network, University of Toronto, CHEP +
Funded grants or clinical trials	AstraZeneca, Bayer, Boehringer Ingelheim, Merck, Novartis and Pfizer	Bayer, Novartis
All other investments or relationships that could be seen by a reasonable, well-informed participant as having the potential to influence the content of the educational activity	Canadian Medical and Surgical KT Group, CCS, CHFS, Charite, EOCI, Liv, Medscape, Ology, PACE-CME, Radcliffe, Reach MD, Translational Medicine Academy	No disclosures

This program has received an educational grant from Novo Nordisk Canada. This program was developed by the Canadian Heart Failure Society and was planned to achieve scientific integrity, objectivity and balance.

# Learning Objectives

1. Discuss the role of inflammation in driving ASCVD and HF pathophysiology
2. Review the historical and emerging evidence supporting the inflammation hypothesis
3. Appraise existing and future CVD therapies targeting inflammation

# Symposium Agenda

2 mins	Welcome and Introductions Dr. Shelley Zieroth
18 mins	Inflammation in CVD: Pathophysiology, Evidence, and Therapeutic Horizons Dr. Eileen O'Meara & Dr. Abhinav Sharma
8 mins	Q&A Period All panelists
2 mins	Conclusion Dr. Shelley Zieroth

# Housekeeping

- To collect your MOC Section 1 credits, please remember to complete both the session evaluation and the congress evaluation
- The evaluation QR code will be displayed on the screen after the presentation
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# Disclosures

	Dr. O'Meara	Dr. Sharma
Any direct financial payments including receipt of honoraria	Astra Zeneca, Boehringer Ingelheim, Bayer, HF Update, CCS	Boehringer Ingelheim, Novartis, Novo Nordisk, CHFS, HF Update, CCS
Membership on advisory boards or speakers' bureaus	Astra Zeneca, Boehringer Ingelheim, Bayer, Eli Lilly, Janssen	AstraZeneca, Boehringer Ingelheim, Eli-Lilly, Servier, Novo Nordisk, Abbott
Funded grants or clinical trials	CHFA – CIHR Team Grant (SC member) and SC member for DAPA-ACT (TIMI group and Astra Zeneca), NLI for DELIVER (AZ), SC member for HEART-FID (American Regent) and CARDINAL-HF (Cardurion)	AstraZeneca, Boehringer Ingelheim, Medtronic, Merck, Novartis, Novo Nordisk Takeda Development Center, Americas, Inc., Roche Diagnostics, Janssen
All other investments or relationships that could be seen by a reasonable, well-informed participant as having the potential to influence the content of the educational activity	No disclosures	Boehringer Ingelheim, Boston Scientific Corporation, Janssen

**Dr. O'Meara,**

# **What is inflammation exactly?**

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**Which biomarker best measures inflammation in CVD?**

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**Dr. Sharma,**

**How is inflammation  
diagnosed?**

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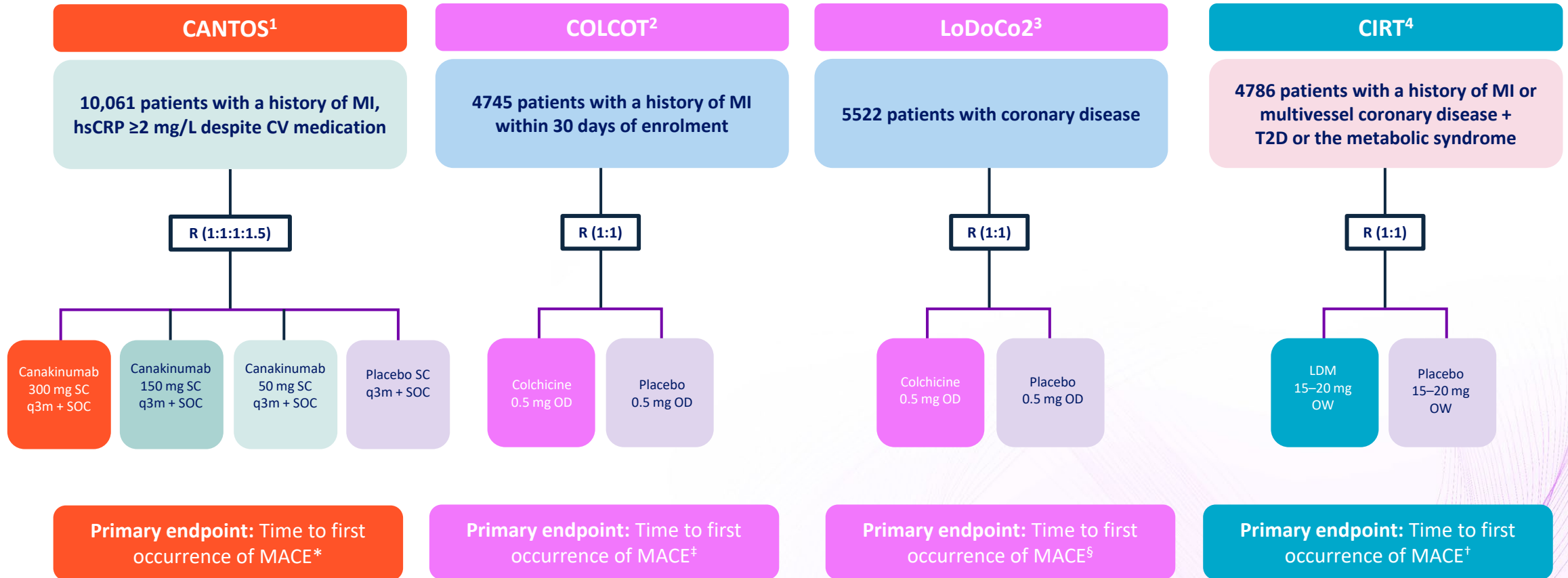
**Dr. Sharma,**

**About agents tested in  
ASCVD...**

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# Inflammation and CVOTs: Trial designs



\*Including non-fatal MI, non-fatal stroke and CV death; †Including CV death, non-fatal MI, non-fatal stroke or hospitalisation for unstable angina that led to urgent coronary revascularisation; ‡Including resuscitated CV death, cardiac arrest, MI, stroke or urgent hospitalisation for angina leading to coronary revascularisation; §CV death, spontaneous MI, ischaemic stroke or ischaemia-driven coronary revascularisation.

CV, cardiovascular; CVOT, cardiovascular outcomes trial; hsCRP, high-sensitivity C-reactive protein; LDM, low-dose methotrexate; MACE, major adverse cardiovascular events; MI, myocardial infarction; OD, once daily; OW, once weekly; q3m, every 3 months; R, randomisation; SC, subcutaneous; SOC, standard of care; T2D, type 2 diabetes

1. Ridker PM et al. *N Engl J Med* 2017;377:1119–1131; 2. Tardif JC et al. *N Engl J Med* 2019;381:2497–2505; 3. Nidorf SM et al. *N Engl J Med* 2020;383:1838–1847; 4. Ridker PM et al. *N Engl J Med* 2019;380:752–762



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**Which agent has not been or is not being tested to reduce inflammation in HF?**

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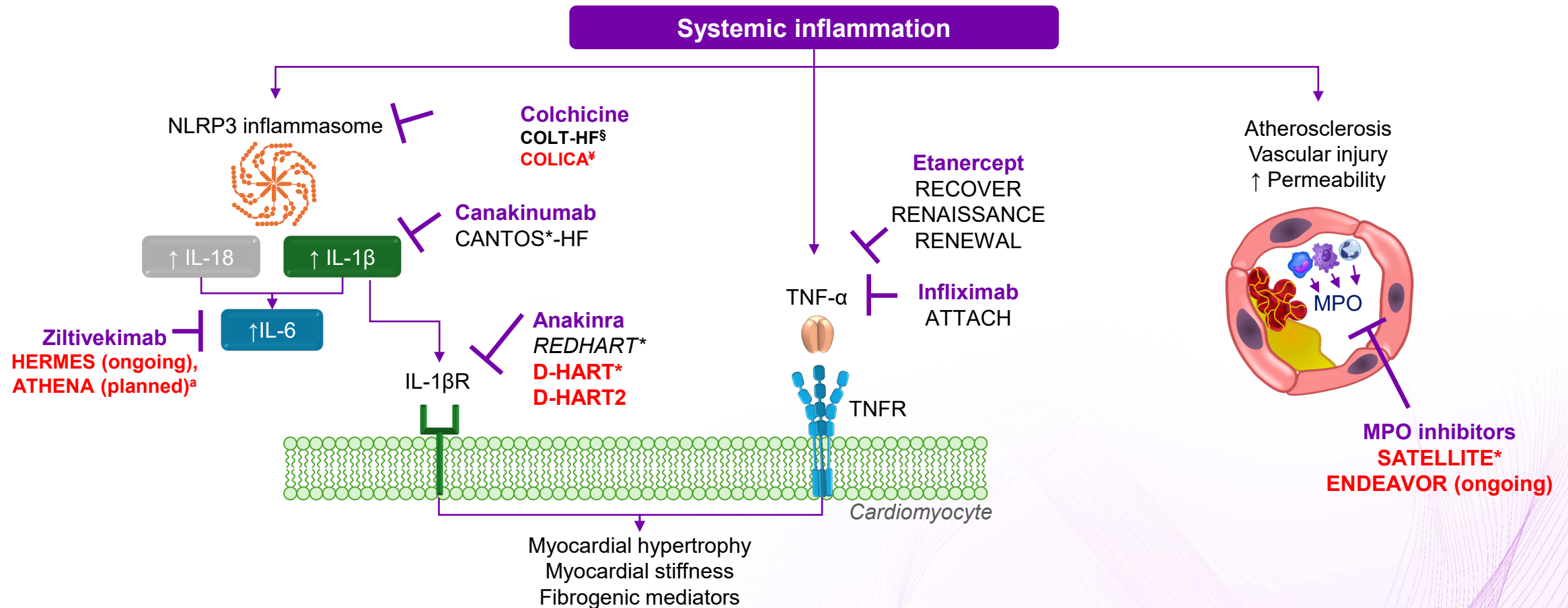
**Dr. O'Meara,**

**About agents tested in HF...**

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# Clinical trials of anti-inflammatory therapies for HF



**Trials that included patients with HFpEF are highlighted in red**

\*Trial met its primary endpoint; §LVEF ≤ 45% within 1 year prior to enrollment; ¥Across LVEF; aConfidential

HF, heart failure; HFpEF, heart failure with preserved ejection fraction; IL-18, interleukin-18; IL-1β, interleukin-1β; IL-1β-R, interleukin-1β receptor; IL-6, interleukin-6; MPO, myeloperoxidase; NLRP3, NOD [nucleotide oligomerization domain]-, LRR [leucine-rich repeat]- and PYD [pyrin domain]-containing protein 3; TNFR, tumour necrosis factor receptor; TNF-α, tumour necrosis factor-α

Figure adapted from Pugliese NR et al. Cardiovasc Res 2022;118:3536–3555; NCT05873881, <https://classic.clinicaltrials.gov/ct2/show/NCT05873881> accessed Dec 2023; NCT04705987

[https://clinicaltrials.gov/study/NCT04705987?term=Randomized%20Double-blind%20Trial%20to%20Study%20the%20Benefit%20of%20Colchicine%20in%20Patients%20With%20Acutely%20Decompensated%20Heart%20Failure%20\(COLICA\)&rank=1](https://clinicaltrials.gov/study/NCT04705987?term=Randomized%20Double-blind%20Trial%20to%20Study%20the%20Benefit%20of%20Colchicine%20in%20Patients%20With%20Acutely%20Decompensated%20Heart%20Failure%20(COLICA)&rank=1)

(Accessed Dec 2023)



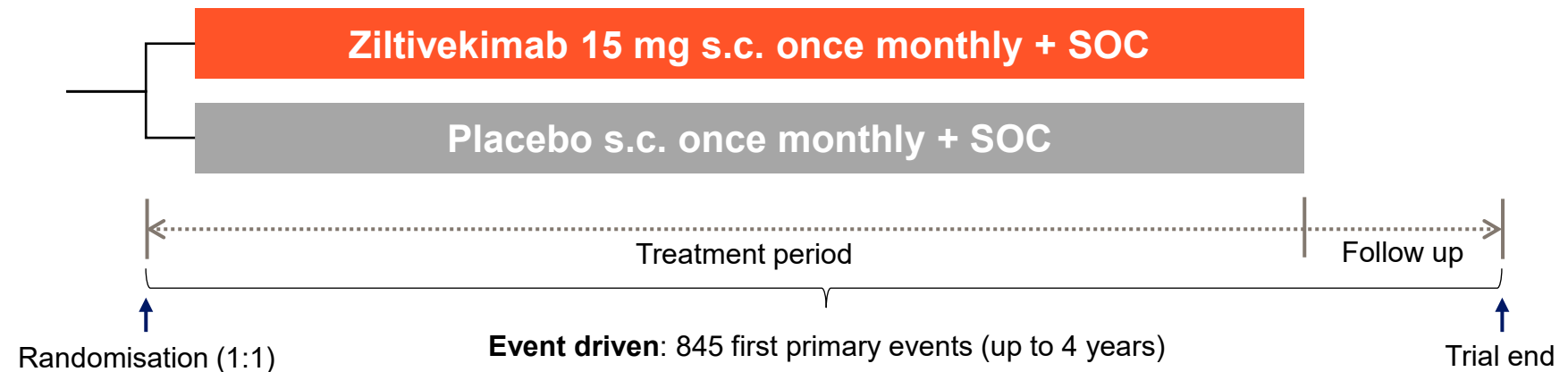
# HERMES<sup>1,2</sup>

## A Phase 3, randomised, double-blind, cardiovascular outcomes trial

Estimated completion date: July 2027

### 5,600 patients

- Elevated hsCRP  $\geq 2$  mg/L
- NYHA class II–IV
- LVEF  $>40\%$
- Elevated NT-proBNP levels
- Echocardiographic signs of HFmrEF or HFpEF



### Primary endpoint:

Time to the first occurrence of:

- CV death
- HHF
- Urgent HF visit

### Confirmatory secondary endpoints:

- Time to the first occurrence of cardiovascular death, HHF or urgent heart failure visit, non-fatal myocardial infarction or non-fatal stroke
- Number of CV death, HHF or urgent heart failure visits (first and recurrent)
- Time to occurrence of CV death
- Time to occurrence of all-cause death

\*NT-proBNP  $\geq 1000$  pg/mL or BNP  $\geq 250$  pg/mL for patients without AF; elevated NT-proBNP  $\geq 2000$  pg/mL or BNP  $\geq 500$  pg/mL for patients with AF AF, atrial fibrillation; BNP, B-type natriuretic peptide; CV, cardiovascular; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide Colorado Prevention Center. NCT06008197. Available at: <https://clinicaltrials.gov/study/NCT06008197> (accessed April 2024)

CV, cardiovascular; HF, heart failure; HFF, hospitalisation for heart failure; HFpEF, heart failure with preserved ejection fraction; hsCRP, high-sensitivity C-reactive protein; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; s.c., subcutaneous; SOC, standard of care  
1. Novo Nordisk A/S.NCT05636176 Available at: <https://clinicaltrials.gov/ct2/show/NCT05636176> (accessed April 2024); 2. Novo Nordisk A/S. Data on file

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**What proportion of patients with  
HFmrEF and HFpEF have  
hs-CRP  $\geq 2$  ?**

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**Dr. Sharma,**

# **Can lifestyle changes influence inflammation in ASCVD and in HF?**

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# Q&A Period

All panelists

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# Take-home Messages

Dr. Zieroth

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# THANK YOU!

*Please remember to  
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**Next Up! Please proceed back to the Ballroom for lunch and the co-sponsored symposia *Evolving Perspectives: Optimizing Diagnosis and Management of Hypertrophic Cardiomyopathy* and *Shot to the Heart: CV Risk Reduction Through Vaccination***

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