MYOFLAME-19

International ME/CFS Conference 2026 · Harnack House, Berlin · 7–8 May 2026

MYOFLAME-19

Cardioprotection and immunomodulation with losartan and prednisolone in post-COVID inflammatory cardiac involvement

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Disclosures

- DZHK (German Centre for Cardiovascular Research)
- Significant Research Support Bayer AG (Impression COVID & Heart Study; Myoflame-19 RCT (NCT05619653)
- Patent: Quantitative Imaging of the Heart Muscle (EP4210569A1)
- Co-founder Goethe CVI GmbH (University Spin-off)
- Cardiology Private Practice Frankfurt/Main

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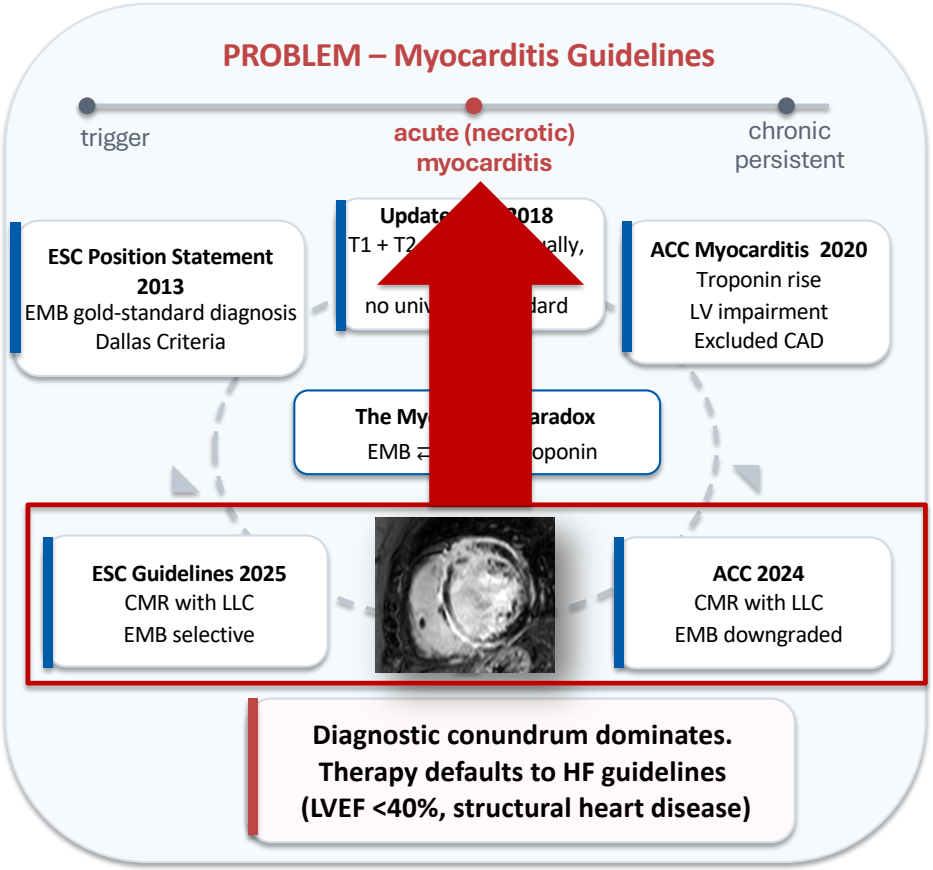
PAIS · Myocarditis · Heart Failure



Caforio EHJ 2013 · Ferreira JCMR 2018 · Kociol Circulation 2020 · Drazner JACC 2024 · Schulz-Menger/Imazio EHJ 2025 · Donagh ESC-HF 2023/24

PAIS · Myocarditis · Heart Failure

SOLUTION - CMR is a means to an end: Therapy

improvement of symptoms and outcome, reducing disability

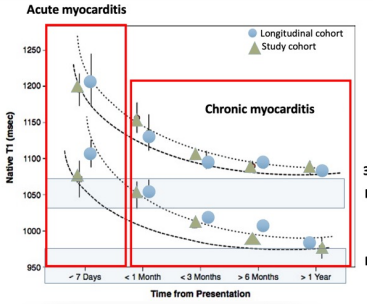
1. **Native T1 / T2 mapping (Goethe CVI® Approaches)**
   Quantitative oedema and diffuse interstitial involvement.
   Sensitive, reproducible, standardised.
   Acute-> subacute-> chronic-> healed (Disease stage)

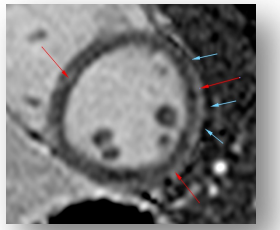
2. **Non-ischaemic (non-necrotic) perimyocardial LGE**
   Central imaging feature of immune-mediated cardiac involvement.

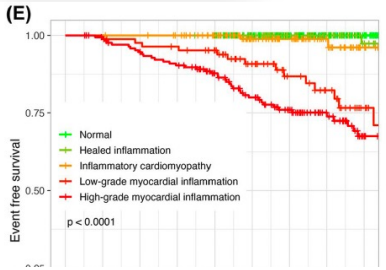
3. **Longitudinal assessment**
   Track the spectrum from hyperacute to mild chronic inflammation. Measure change, not just presence.

4. **Prognostic Evidence**
   Native T1 and ECV predict all-cause mortality
   Native T1 and T2, LGE predict MACE

From diagnostic classification → treatment selection → response
CMR-defined Cardiac Inflammation Endotype







Puntmann Circ Cvi 2013 Hinojar JACC CVI 2015 · Puntmann JACC CVI 2016 · Puntmann Radiology 2017 · Winai ARD 2018, Puntmann JACC 2018 Haslbauer Int J Card 2019 DeLeuw JACC CVI 2020
Zainal JCMR 2025 · Nagel Int JCVI 2026 PostCOVID: Puntmann JAMA Cardiol 2020 · Puntmann Nat Med 2022·Shchendrygina Sci Rep 2025 · Rozewicz-Juraszek JCMR 2026

Post-COVID Cardiac Inflammation Endotype: diagnostic window to Long COVID

POST-COVID CARDIAC INFLAMMATION ENDOTYPE

- **↑ Native T1** myocardial fibrosis
- **↑ Native T2** myocardial oedema
- **Perimyocardial LGE** non-ischaemic, immune-med. LGE
- **LVEF low-normal 45-50%** preserved, yet abnormal

A reproducible signature of chronic persistent immune-mediated myocardial inflammation

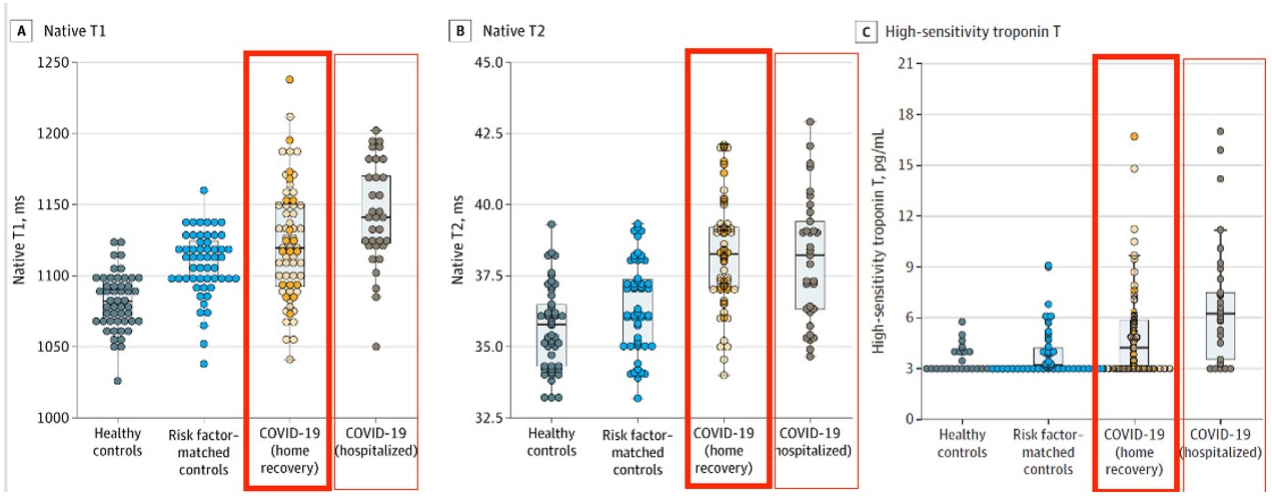
IMPRESSION COVID & HEART
Puntmann JAMA Cardiol 2020 ·
Puntmann Nat Med 2022
Shchendrygina Sci Rep 2025 ·
Rozewicz-Juraszek JCMR 2026

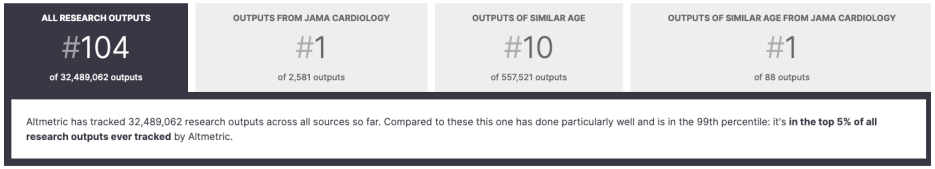
Research

JAMA Cardiology | Original Investigation

Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19)

Valentina O. Puntmann, MD, PhD; M. Ludovica Carerj, MD; Imke Wieters, MD; Masia Fahim; Christophe Arendt, MD; Jedrzej Hoffmann, MD; Anastasia Shchendrygina, MD, PhD; Felicitas Escher, MD; Mariuca Vasa-Nicotera, MD; Andreas M. Zeiher, MD; Maria Vehreschild, MD; Eike Nagel, MD





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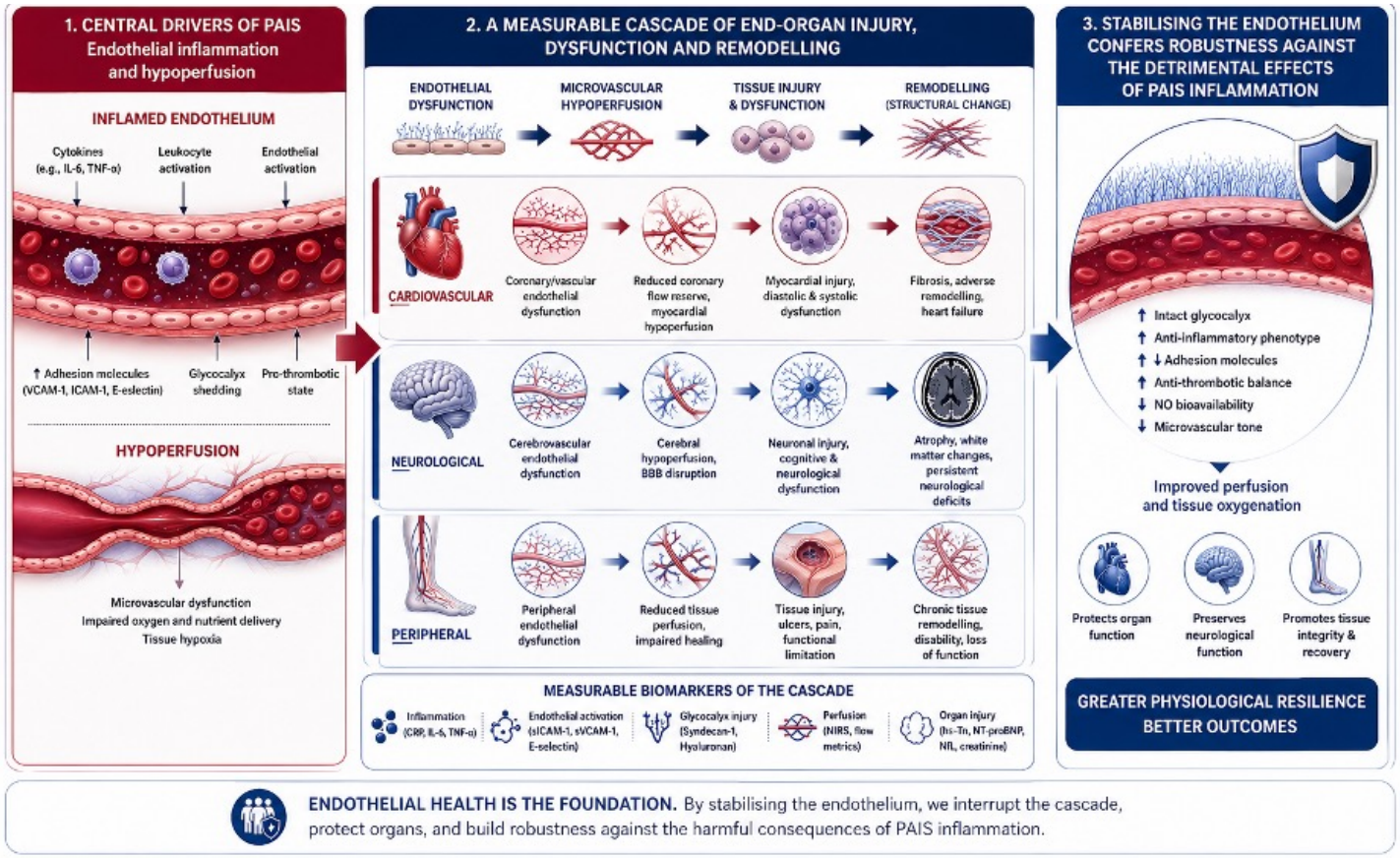

IMPRESSION COVID & HEART
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MYOFLAME-19 RCT DESIGN

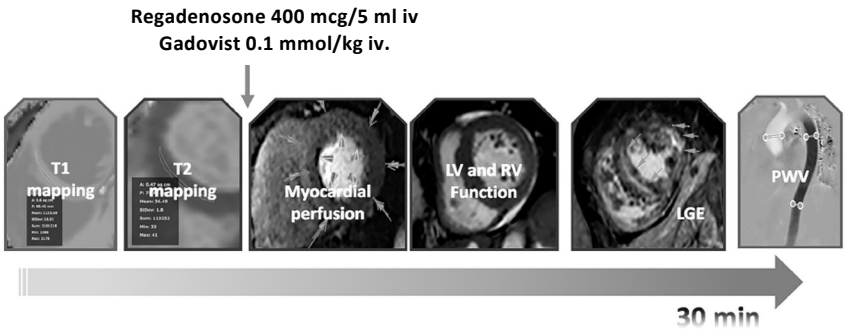
Hypothesis: targeting inflammatory endothelial dysfunction improve end-organ impairment?

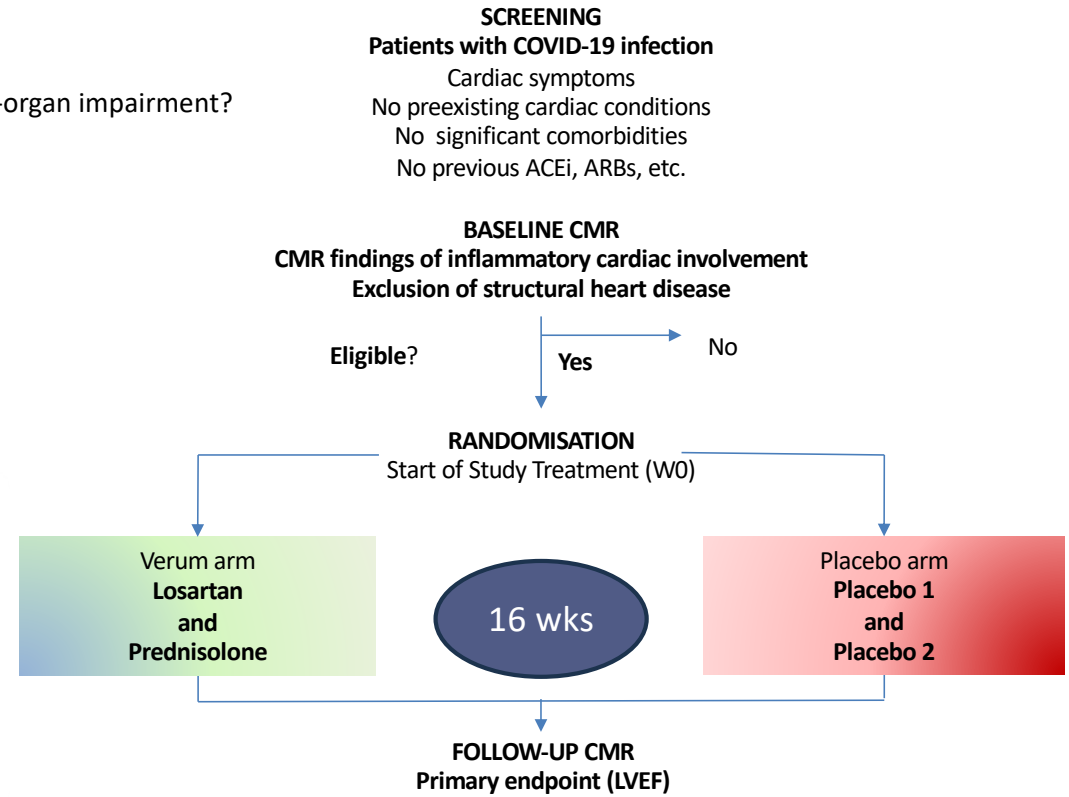
Multicentre randomised double-blind clinical trial:

➔Primary endpoint = ΔLVEF by CMR by Core lab

N= 280 subjects

4 centres (3 Germany, 1 Austria; active recruitment): Frankfurt (DE), Kiel (DE), Greifswald (DE), Vienna (AT)





Puntmann et al. Design and rationale of MYOFLAME-19 randomised controlled trial. JCMR 2024

MYOFLAME-19 POPULATION

Previously fit adults with PostCOVID Syndrome & CMR-defined endotype of cardiac inflammation.

4 centres (Frankfurt · Kiel · Greifswald · Vienna) ·· Dec 2022 – Mar 2025

INTERVENTION or PLACEBO
Losartan 12.5- > 50 mg + Prednisolone 20→5 mg

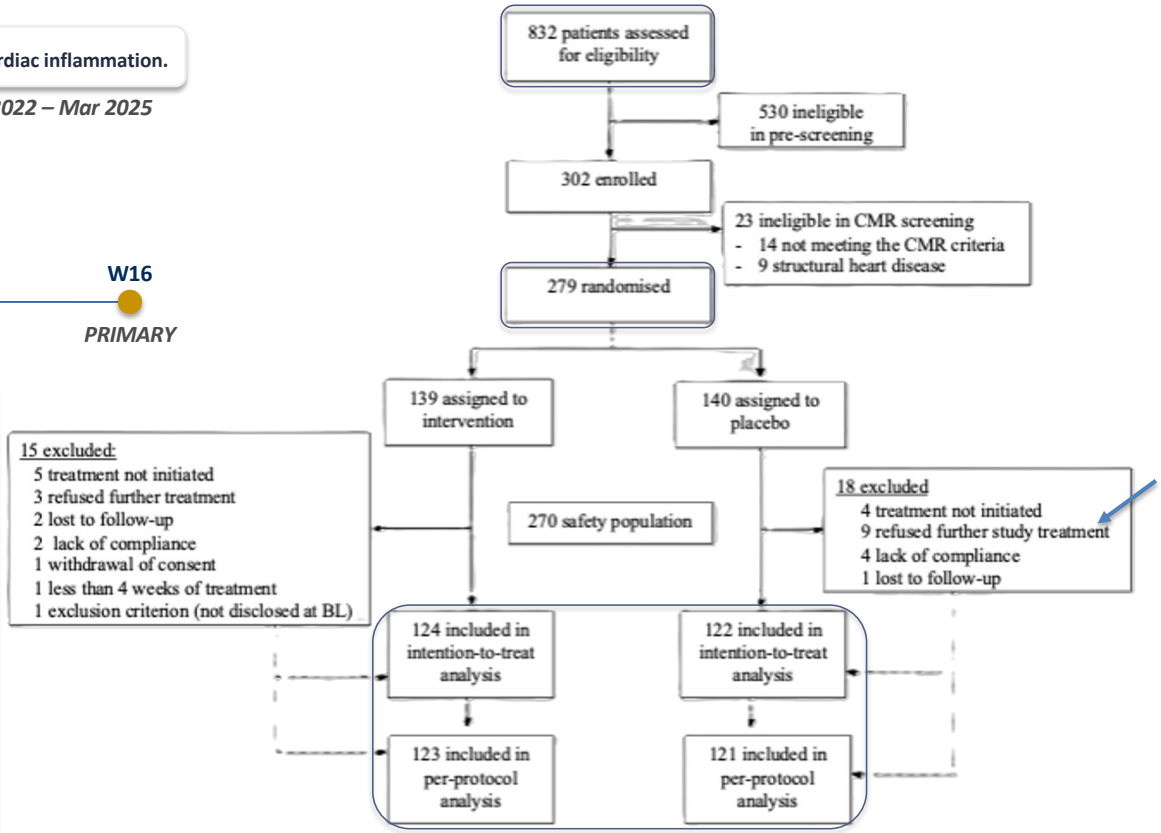
BL — *CMR · labs · QoL*
W2 — *safety*
W6 — *titration*
W12 — *safety*
W16 — *PRIMARY*

WHO WE LOST ON THE WAY

Attrition:
- **33 / 279 (12 %)** non-evaluable for the primary endpoint
- balanced across arms (12.2 % vs 11.4 %)
- but above the 8 % planned.

Dominant reasons:
- compliance issues (n=6)
- treatment not initiated (n=9),
- refusal to complete W16-Tx (n=12),

— > reflecting the lived heterogeneity of the post-COVID population.



Puntmann et al. Myoflame-19 manuscript (Nat Comm-accepted) · CONSORT Figure 1
Puntmann et al. Design and rationale of MYOFLAME-19 randomised controlled trial. JCMR 2024

RESULTS · PRIMARY ENDPOINT

Primary endpoint — change in LVEF at week 16

ANALYTICAL STRATEGY	Δ LVEF (95 % CI)
Pre-specified confirmatory **Unpaired t-test** *Between-group mean difference at W16*	**+0.74 pp** 95 % CI −0.14 to 1.62 p = 0.10 — NEUTRAL
Pre-specified supportive **Baseline-adjusted ANCOVA** *Quantitative endpoint is a change — analysis must calibrate for each participant's starting point.*	**+0.99 pp** 95 % CI 0.15 to 1.83 p = 0.021 · +1.69 % relative

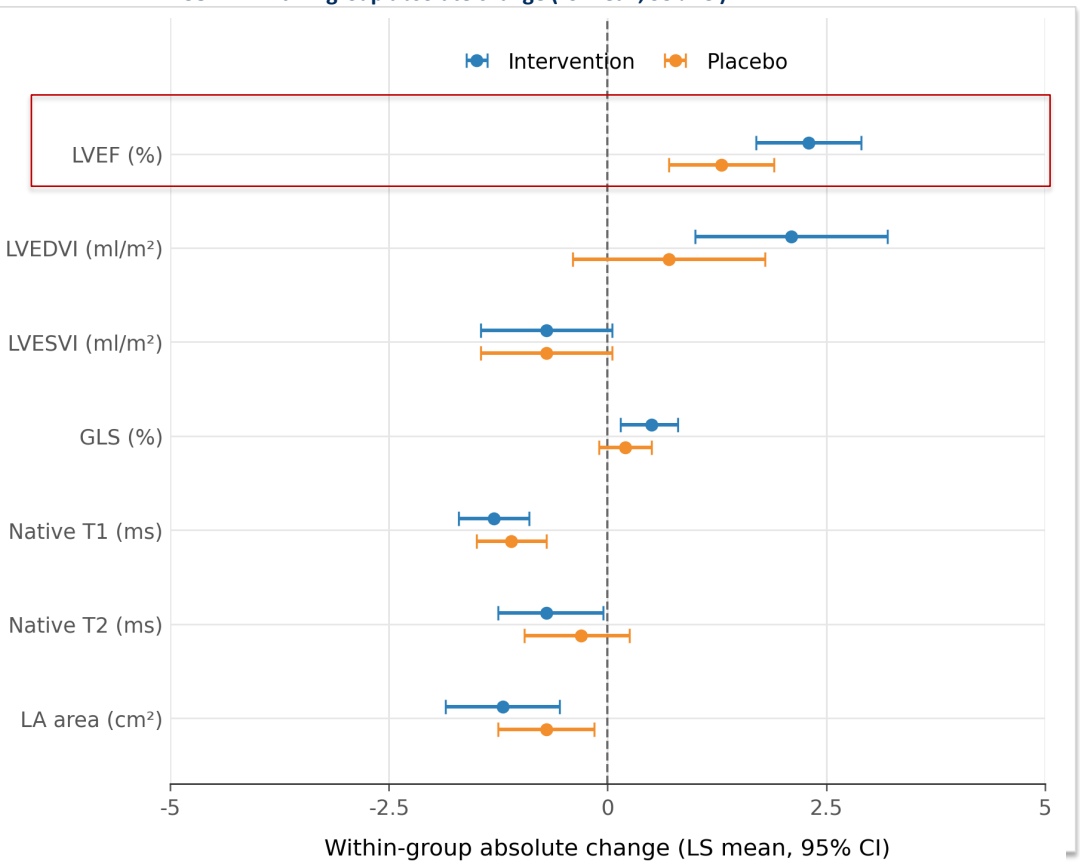
DIRECTIONAL PROOF OF CONCEPT

Parallel improvements across axes:

- cardiac functional markers (↑LVEF, GLS, LVEDVI, RVEF; ↓LA size)
- tissue inflammation markers (native T1 and T2 ↓, perimyo-LGE % ↓)
- systemic inflammation (Lymphocytes ↓, CRP ↓, D-dimer ↓)

All inferential statements are exploratory and contextual.

ANCOVA · Within-group absolute change (LS mean, 95 % CI)



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SECONDARY RESULTS

Secondary endpoints: symptoms and QoL change at week 16

SYMPTOMS

−7.7 pp

proportion reporting > 5 symptoms

(95 % CI −18.9 to 3.6)

FATIGUE

−6.3 pp

participants reporting fatigue

(95 % CI −14.0 to 1.3)

QUALITY OF LIFE

no change

SF-36 PCS / MCS

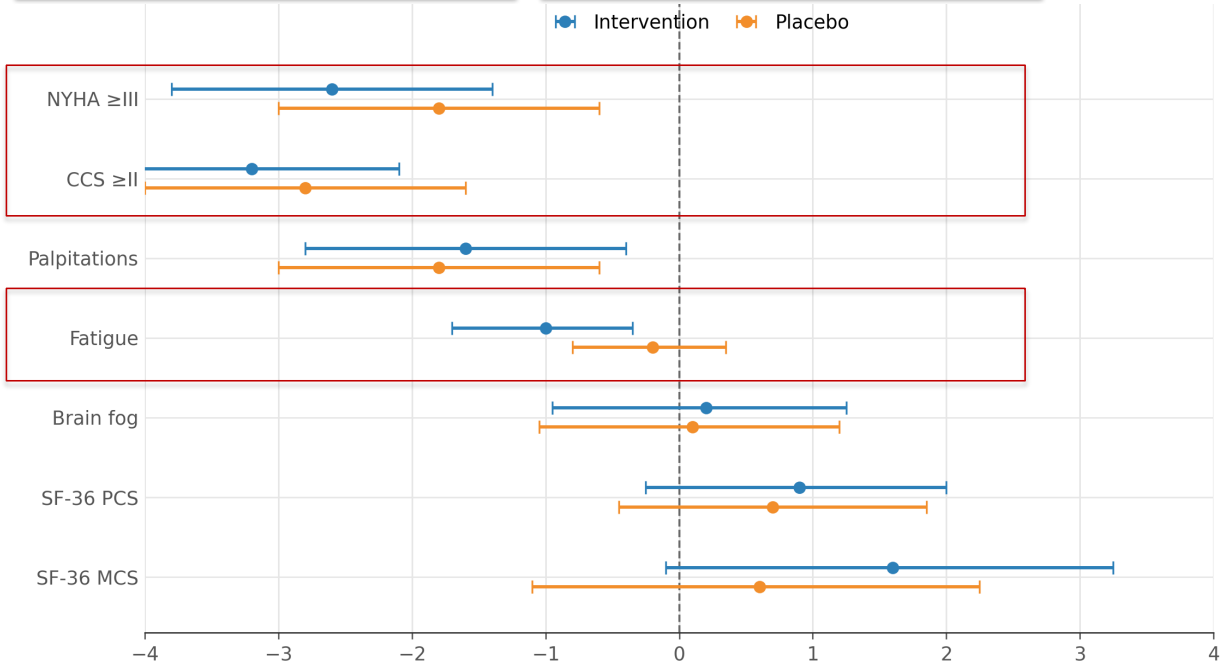
unchanged in either arm

Improvements in symptoms did not translate into QoL gains

— The pre-illness baseline remains the reference point.

STRUCTURED LIFESTYLE SUPPORT APPLIED TO BOTH ARMS

1. **Pacing**
   graded activity, avoid PEM
2. **Hydration**
   adequate fluid intake
3. **Regeneration**
   energy conservation, sleep



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Conclusions -1

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DIRECTIONAL PROOF OF CONCEPT

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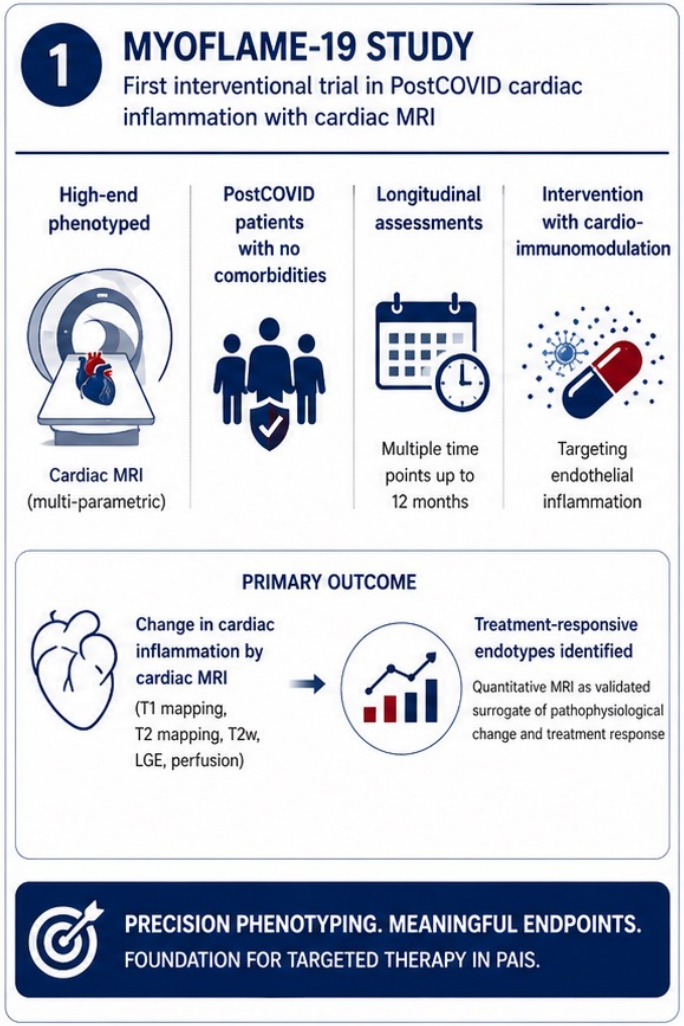
- **systemic inflammation (Lymphocytes ↓, CRP ↓, D-dimer ↓)**

Mechanistically coherent and biologically plausible.

1 · Real endotype of condition
CMR-defined, symptom-linked, biologically plausible endotype of endothelial dysfunction.

2 · Treatable signal
Directional coherent biological signal in response to cardioprotection + immunomodulation.



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Conclusions - 2

MYOFLAME-19

Randomized trials in post-COVID condition remain challenging

- population heterogeneity,
- evolving pathophysiology,
- the absence of validated endpoints;

Within this landscape, **the Myoflame-19 trial contributes a methodological and mechanistic foundation for subsequent investigations.**

WHAT'S NEXT — MYOFLAME 2.0

A confirmatory, adequately powered, adaptive trial with pre-specified multi-organ sub-studies.

Sample size	Adaptive design	Core lab	Multi-organ
Based on Myoflame-19 variance/ attrition	baseline-calibrated quantitative endpoints	standardised CMR analysis	cardiometabolic · neuromuscular · immunomodulatory · pain

Post-COVID / ME-CFS is multi-system. Cardiac imaging is one window onto a shared pathophysiology — do not create silos.

Acknowledgment

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Statisticians: Christine Windemuth-Kieselbach; Sebastian Eckhardt (Alcedis GmbH)

Steering Committee
Colin Berry (Chair), Biykem Bozkurt; Juan Carlos Kaski; Gernot Rohde; Philipp DeLeuw;

Data Safety and Monitoring Committee
Peter C Taylor (Chair); Erica Spatz; Eva Herrmann

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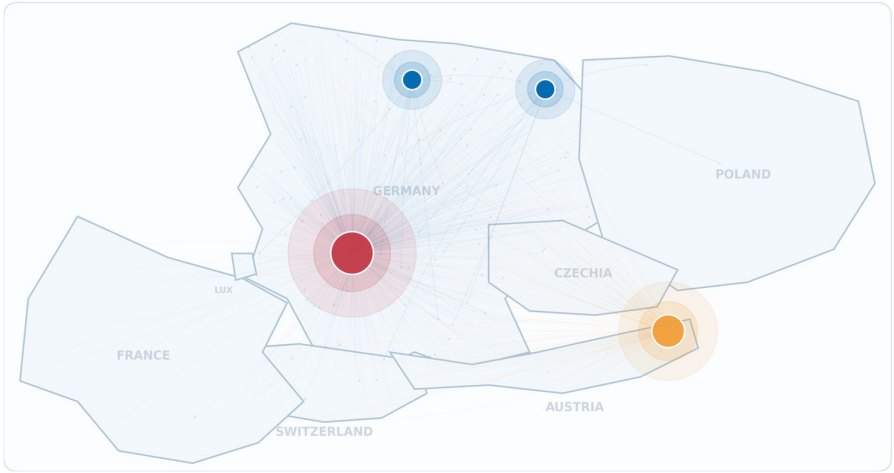
Clinical Research Organization: Alcedis GmbH

Acknowledgment

MYOFLAME-19 Participants



UNITE TO FIGHT

LONG COVID DEUTSCHLAND

Long Covid Austria

LONG COVID EUROPE

LONG COVID SCHWEIZ SUISSE SVIZZERA SWITZERLAND

Fatigatio e.V. Bundesverband ME/CFS

LONG COVID KIDS

Long COVID PLATTFORM

NICHT GENESEN KIDS