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MAYO CLINIC

2026 UPDATE ON MYOCARDITIS MANAGEMENT

Leslie T. Cooper, Jr., MD
Minneapolis Heart Institute Foundation Cardiology Grand Rounds
February 2nd, 2026

2

DISCLOSURE

Relevant Financial Relationship(s)

- Consultant: Moderna, Cardiol Therapeutics, BMS, Foresee Pharmaceuticals
- Board Member: Stromal Therapeutics

Off Label Usage

- Colchicine

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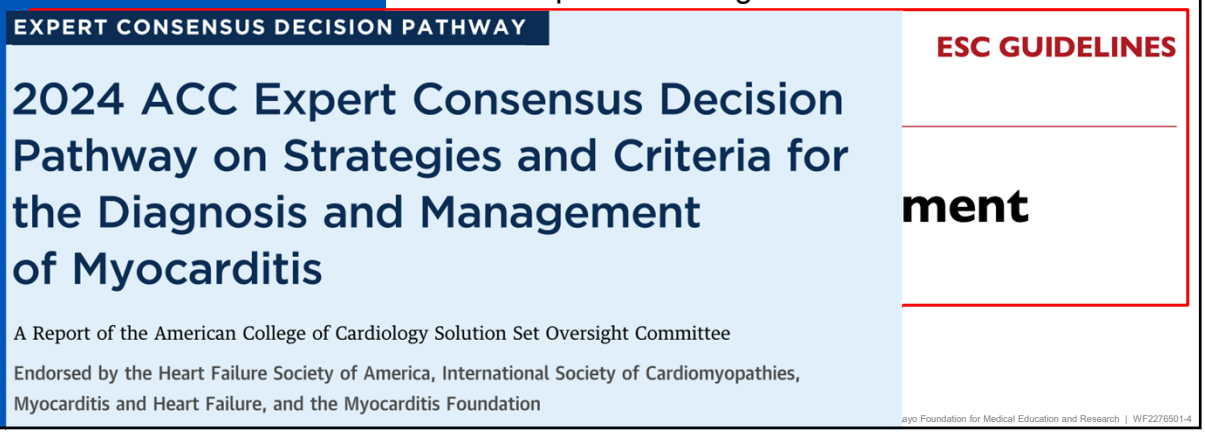
OUTLINE

CURRENT APPROACH TO MANAGEMENT

- 2025 ESC Guideline/2024 ACC ECDP:
  - Epidemiology and Clinical Classification
  - Diagnostic Paradigms
  - Imaging Approaches
  - Therapeutic Strategies



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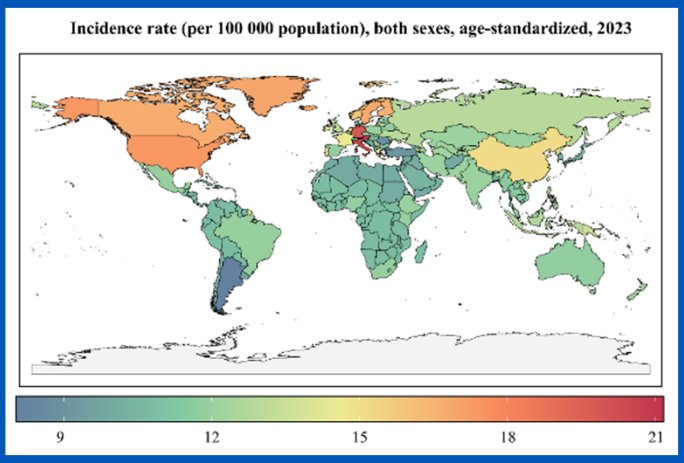
Global age-standardized rates of incidence, prevalence and mortality rates of myocarditis per 100,000 population



Incidence 16.16 (95% UI, 13.11–19.76)
Prevalence 4.83 (95% UI, 5.48–7.44)
Mortality 0.40 (95% UI, 0.32–0.47)

New Myocarditis cases: 1.04 million

Under review, 2026

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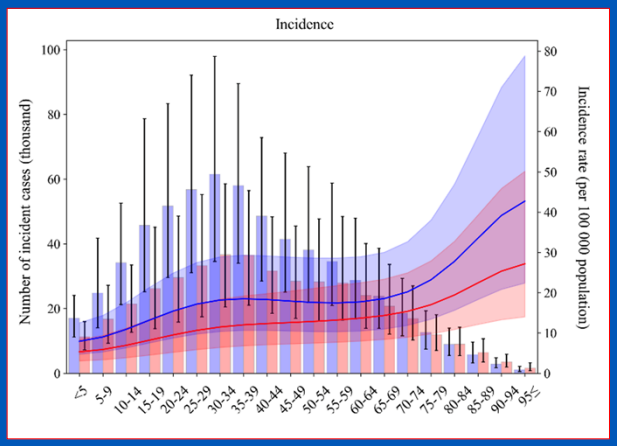
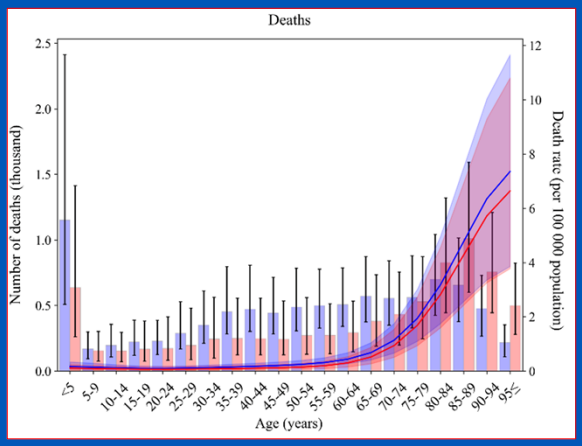
Global age-standardized Incidence and Death numbers and rates of myocarditis per 100,000 population





Under review, 2026

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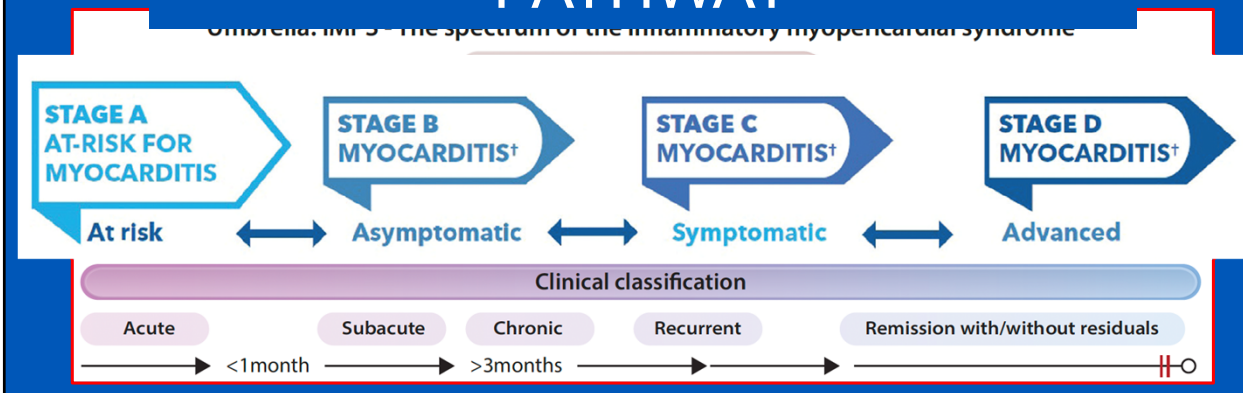
ACC EXPERT CARE DECISION PATHWAY



ESC GUIDELINE EU HEART J. AUG 28TH 2025
ACC ECDP JACC. FEBRUARY 2025

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STAGE A: AT RISK

No clinical syndrome, abnormal biomarkers or structural changes on imaging

- Current immune checkpoint Inhibitor treatment – up to 1%
  - Eg, ipilimumab, nivolumab, pembrolizumab
- Systemic disorders such as sarcoidosis
- Clozapine use for schizophrenia
- Personal history of previous myocarditis or DES gene +?
- SARS-CoV2 mRNA vaccines – males 12-39 years with 2nd dose – 1:10,000

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MAYO CLINIC

Multidisciplinary consensus on prevention, screening and monitoring of clozapine-associated myocarditis and clozapine rechallenge after myocarditis

Elias Wagner, Nicole Korman, Marco Solmi, Matin Mortazavi, Zahra Aminifarsani, Douglas Dubrovin Leão, Matthew K. Burrage, Dan Siskind, Laura McMahon, Oliver D. Howes, Christoph U. Correll, CAM Expert Group* and Alkomiet Hasan

Minimum and enhanced monitoring requirements in weeks 1-4 (clozapine initiation)

	Heart rate	Temperature	SpO_2	ECG	postural BP	hs troponin	CRP	NT-proBNP[1]	FBC[2]
	Clinical			Instrumental			Laboratory parameters		
Parameter									
Minimum	twice weekly	twice weekly	weekly	every 2 weeks	weekly	weekly	weekly	-	weekly
Enhanced	daily	daily	twice weekly	weekly	twice weekly	weekly	weekly	weekly	weekly

THE BRITISH JOURNAL OF PSYCHIATRY (2025)
DOI: 10.1192/BJP.2025.89

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STAGE B: ASYMPTOMATIC

No clinical syndrome but + abnormal biomarkers or structural changes on imaging

- Subjects screened because they are “at risk”: Stage A
- Confirmation needed by CMR/PET, rarely EMB
  e.g. Recent ICI treatment or systemic sarcoidosis
- Management depends on context: e.g. hold ICI therapy

Drazner, Bozkurt, Cooper et al. JACC, 2025

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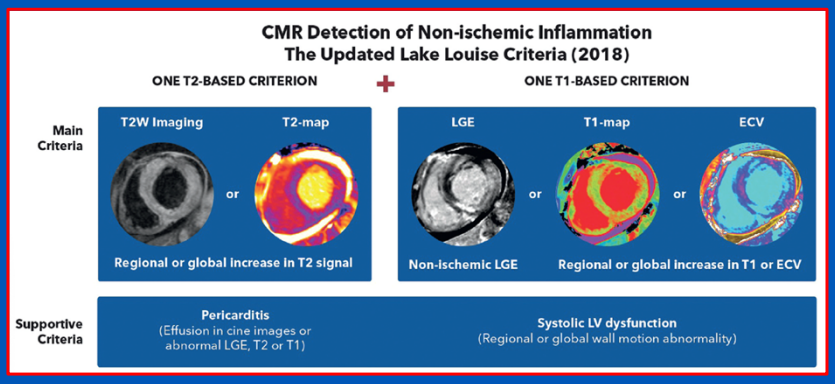
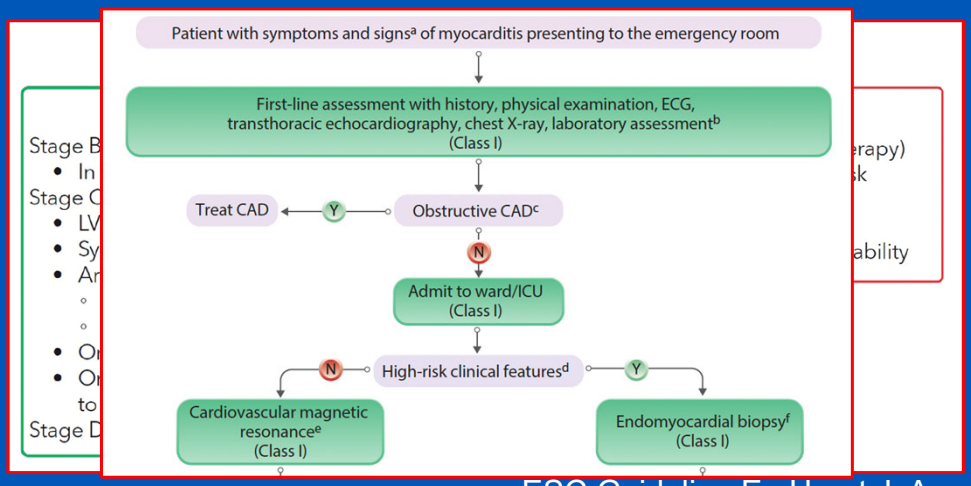
ESC and ACC documents endorse CMR as the noninvasive gold standard for diagnosing acute myocarditis



Ferreria, V., e al. JACC 2018

11

SELECTIVE USE OF EMB IN SUSPECTED MYOCARDITIS



ESC Guideline Eu Heart J. Aug 28th 2025

ACC ECDP JACC. February 2025

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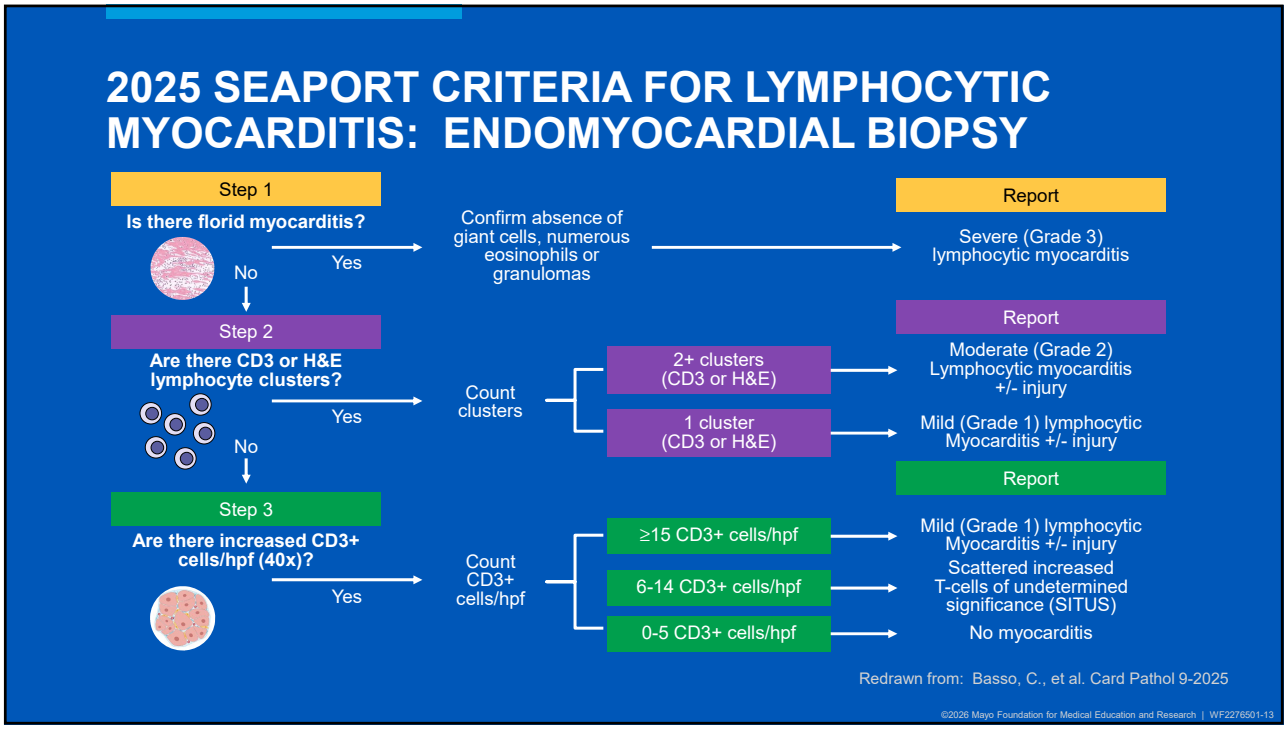

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Summary: 2024 ACC Expert Consensus Decision Pathway

On strategies and criteria for the diagnosis and management of myocarditis

STEP 1 Recognize clinical syndromes compatible with acute myocarditis
- Initial workup: CBC with differential, biomarkers (hs-cTn), ECG, and echocardiography
- Exclude obstructive coronary artery disease as clinically appropriate

STEP 2 Triage

Assess needs for:
- Hospitalization
- Urgent referral to advanced heart failure center
- Emergent arrhythmia management or circulatory support

STEP 3 Pivotal diagnostic tests
- CMR with T1 and T2 parametric mapping
- Endomyocardial biopsy

STEP 4 Treatment
- Pharmacologic
- Withdraw inciting agent when present
- Temporary pacemaker or ventricular arrhythmia management (if now needed)
- Temporary circulatory support (if now needed) followed by durable LVAD or transplant (if no recovery and suitable candidate)
- Temporary restriction of strenuous physical activities including competitive sports

STEP 5 Longitudinal surveillance
- Biomarkers
- Echocardiography
- CME with T1 and T2 parametric mapping
- Outpatient genetic counseling and testing
- Assessment for return to strenuous physical activity including competitive sports

Clinical deterioration

Drazner, Bozkurt, Cooper, et al. JACC 2025

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Recent Myocarditis Registries
Most recover with 6-20% Recurrence

ITAMY Study (Aquaro 2017)	2006-2013 10 Italian centers	374	Mean 35y 73% Male	CMR Lake Louise II criteria (definite AM) all LVEF≥50%	4.3y	Low event rates; anteroseptal mid-wall LGE has worse prognosis
Lombardy Registry (Ammirati, 2018)	2001–2017 19 Italian centers	443	Median 34y 80% Male	EMB/CMR + biomarkers 27% LVEF<50%	2.9y	5-year cardiac death/HTx ~4.1% overall; complicated AM (27% of cohort) ~14.7%
Sheba Medical Center (Younis 2020)	2005–2017 Single-center	322	Mean 37y 84% Male	Clinically Dx AM 19% LVEF<50%, 73% CMR	Up to 1y	4.3-fold higher in-hospital mortality with low LVEF; higher 1-y outcomes stratified by LVEF

Fulminant Myocarditis Case Series

FULLMOON (Huang 2023)	2008-2020 36 centers in 15 countries	419	Median 40y 47% Male	Fulminant AM, by CMR 23%, EMB 77%	1y	77% requires temporary mechanical circulatory support, 65% transplant-free survival; early EMB group had better transplant free survival (63% vs 40%)
European Multicenter (Majunke 2025)	2012-2022 25 centers in Europe	271	Median 43y 58% Male	Fulminant AM, by CMR/ Clinical 29%, EMB 72%	1y	31% in-hospital mortality. GCM, older age and lower pH were associated with in hospital and 1 year mortality

Tang and Cooper, JCF in Press 2026

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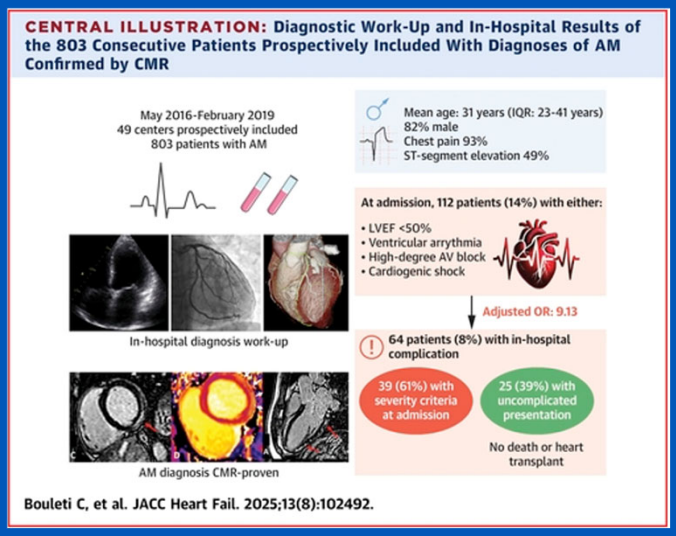
MyocarditIRM French Registry
49 center with Non-ICU Myocarditis

N = 803
82% male; age 31 yr
93% with chest pain

691 (86%) had an uncomplicated presentation and 3.6% risk of progression



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MANAGEMENT OF ACUTE MYOCARDITIS: ESC GUIDELINE AND ACC ECDP ALIGNED

- GDMT for Heart Failure and Arrhythmias
- Colchicine often with aspirin or NSAIDS for concomitant pericarditis in the absence of heart failure
- Avoid NSAIDS in symptomatic Stage C and D with heart failure
- Immunosuppression for select cases of giant cell, ICI, eosinophilic, granulomatous or other autoimmune myocarditis per expert consensus statements
- Consider viral genome assessment on endomyocardial biopsy tissue where feasible to identify active viral infections

Schulz-Menger., et al 2025; Drazner, et al 2025

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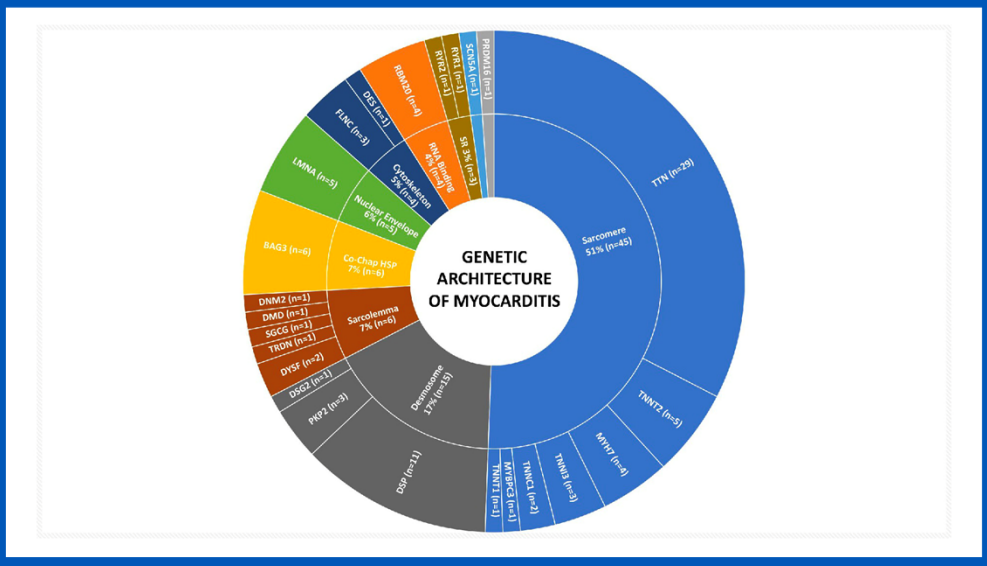
Colchicine in Myopericarditis and Myocarditis

Recommendation Table 9 — Recommendations for medical therapy in myocarditis (see Evidence Table 9)

Recommendations	Class[a]	Level[b]
Management of symptoms		
NSAIDs (together with proton pump inhibition) should be considered in patients with associated symptoms of pericarditis to reduce symptoms.	IIa	C
Colchicine should be considered in patients with myopericarditis to reduce recurrences.[263]	IIa	B

Schulz-Menger., et al 2025

18



4% of uncomplicated, 22% of complicated; 44% pediatric myocarditis

Monda, et al. JACC Heart Fail. Apr 03, 2024.

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ORIGINAL RESEARCH ARTICLE

Prognostic Role of Myocarditis-Like Episodes and Their Treatment in Patients With Pathogenic Desmoplakin Variants

1014 patients with P/LP DSP variants
177 (17.5%) experienced ≥1 documented myocarditis-like episode
Immunosuppression was associated with a reduced risk of ventricular arrhythmia and heart failure outcomes (HR 0.18; *P*<0.001)

Gasperetti, A. et.al. Circulation. 8/20/2025

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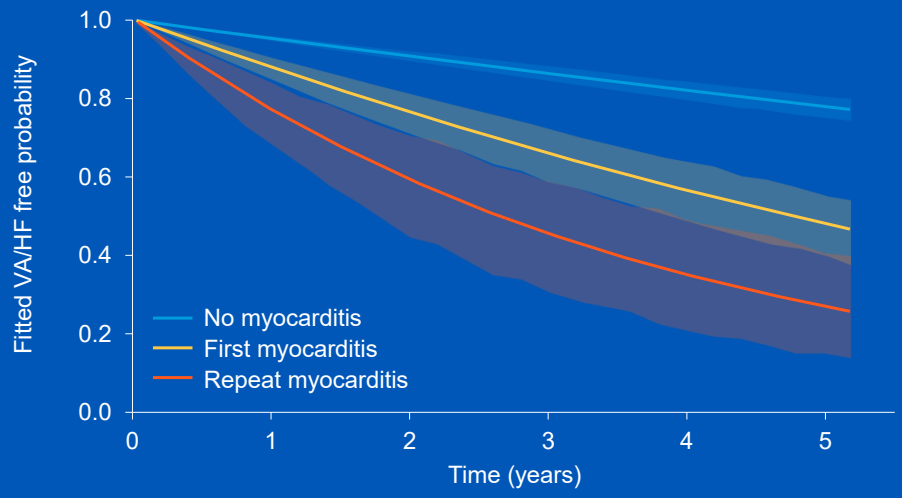
FITTED PROBABILITY OF VA OR HF OCCURRENCE



Redrawn from: Gasperetti, A. et.al. Circulation. 2025

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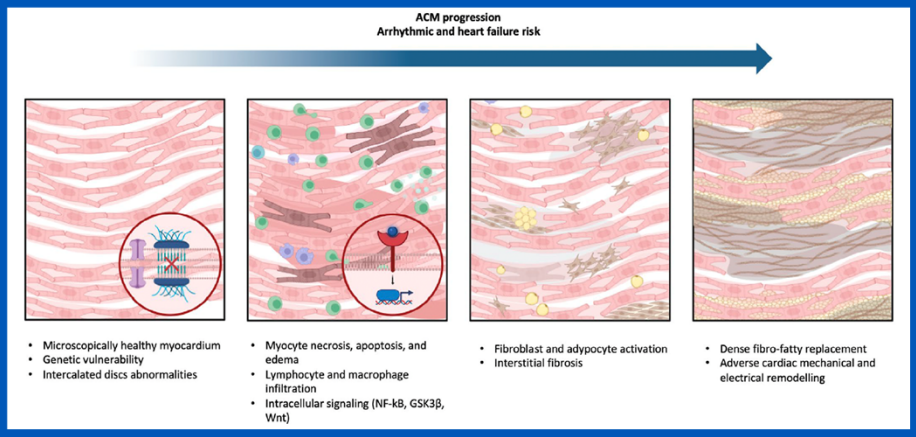
Histological Progression of ACM is associated with different early and Late Ventricular Arrhythmia Mechanisms



Peretto…Cooper, LT. Immunological Reviews February 2026

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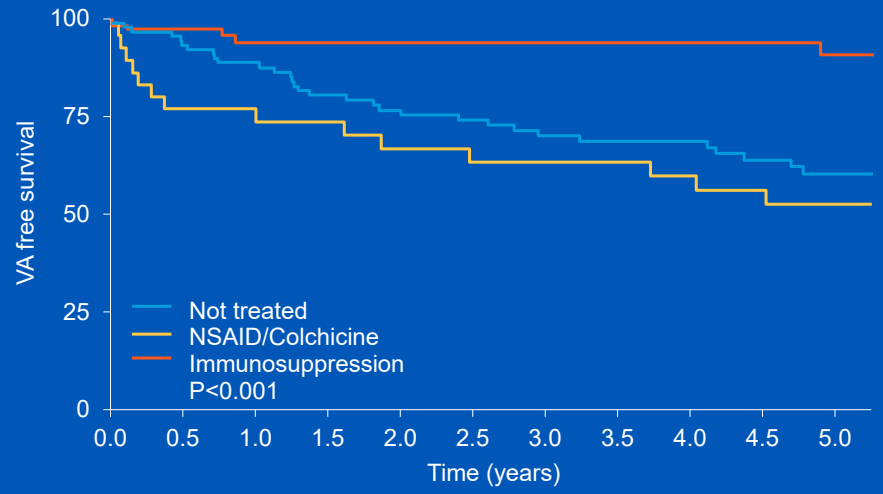
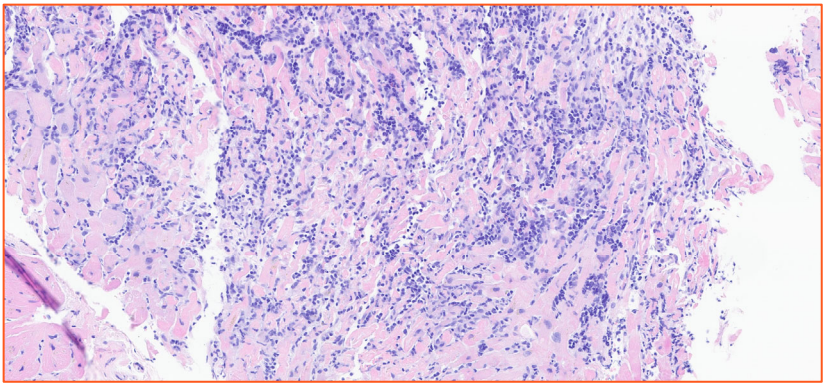
ASSOCIATION OF TREATMENT OF MYOCARDITIS ON VENTRICULAR ARRHYTHMIA



Redrawn from: Gasperetti, A. et.al. Circulation. 2025

23

78 YEAR OLD MAN WITH ACUTE HEART FAILURE 4 WEEKS AFTER STARTING AN IMMUNE CHECKPOINT INHIBITOR



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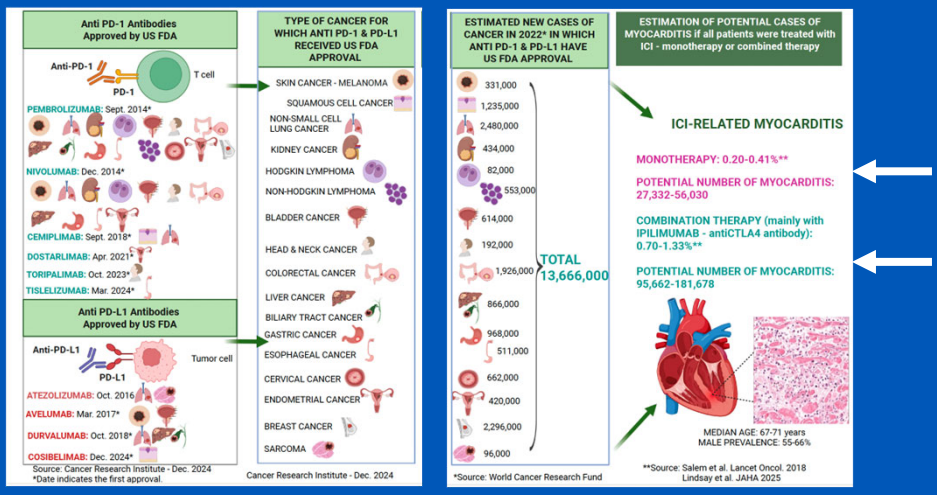
ESTIMATED NUMBER OF ICI MYOCARDITIS CASES WORLDWIDE

13 ICI approved for 17 cancers as of 12/2024

Myocarditis: 27-56,000 w/mono Tx 95-181,000 w/combo Tx



Klingel, et al. Nature CV Medicine In Press

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MANAGEMENT OF CARDIAC INJURY IN PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS

RISK: 1:200

Grade	Management
Abnormal Cardiac Biomarkers	Hold ICPi
Grade 1 and mild symptoms	1-2 mg/kg/d prednisone
Moderate symptoms and/or conduction delay	CCU level care
Moderate to severe symptoms	Consider abatacept or alemtuzumab

Schultz-Menger, J., et al 2025
Redrawn from: ASCO Guideline Update. Schneider, et al. J Clin Oncology 2021

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TREATMENT OF ICI MYOCARDITIS: 2025 ESC MYOCARDITIS GUIDELINE

Recommendation Table 18 — Recommendations for immune checkpoint inhibitor-associated myocarditis (see Evidence Table 18)

Recommendations	Class[a]	Level[b]
ICI-induced myocarditis		
1st line therapy	Withdraw ICI, reassess Non-severe: methylprednisolone 500–1000 mg/day × 3 days, then taper with oral prednisone Severe: i.v. methylprednisolone 7–14 mg/kg/day × 3 days, then 1 mg/kg/day	
2nd line therapy	If no response in 24–48 h: mycophenolate mofetil[b], ATG[g] abatacept[l], alemtuzumab[m]	
3rd line therapy	Infliximab[j] or adalimumab[k], rituximab[i]	
patient.		
Second-line immunosuppression treatment should be considered in patients with steroid-refractory ICI-associated myocarditis.[501,504]	IIa	C
Second-line immunosuppression treatment may be considered in patients with fulminant/severe ICI-associated myocarditis.[501,504]	IIb	C

© ESC 2025

Eur Heart J. August 29th, 2025.

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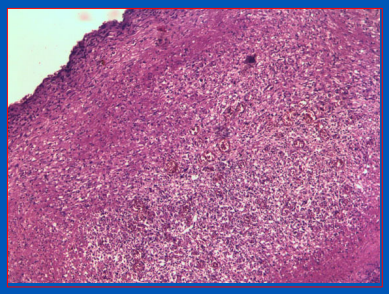
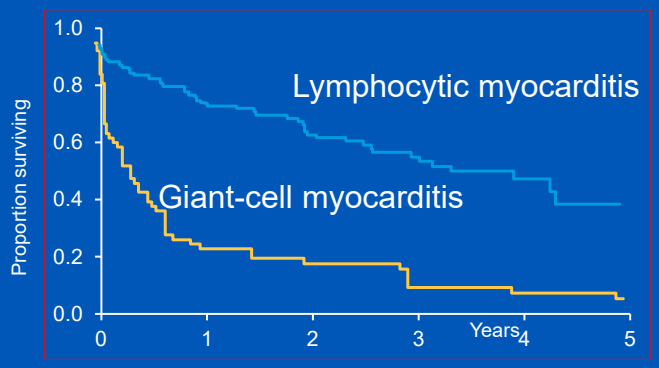
PROGNOSIS IN GCM IS WORSE THAN IN LYMPHOCYTIC MYOCARDITIS





P<0.0001

Cooper, et al: N Engl J Med 1997 336:1860-66

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MAYO CLINIC

Fulminant myocarditis: outcome predictors in an international cohort study

Nicolas Majunke, Franz Haertel, Leonhard Binzenhöfer, Natalie Fischer, Julia Höpler,

- N=26 or 13% with GCM
- GCM had a 54% 1 year mortality

Eu Heart J Published 10Sept 2025

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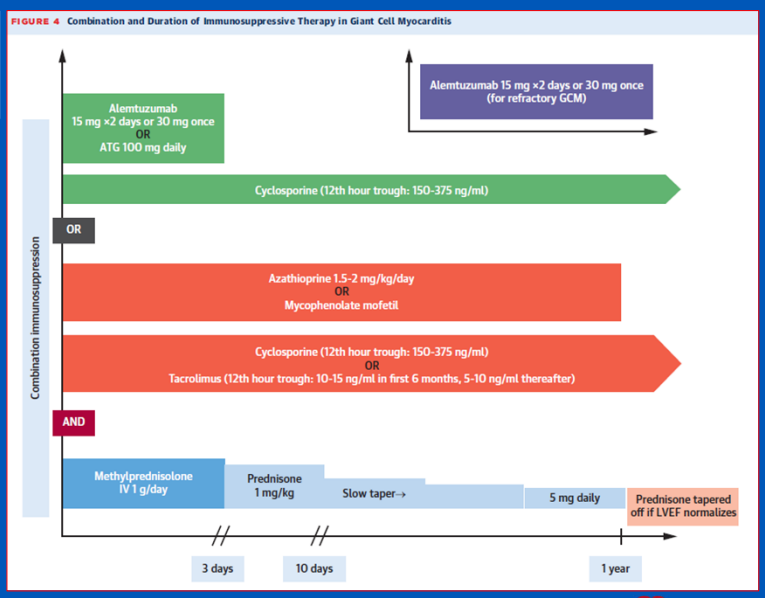
Management of Patients With Giant Cell Myocarditis

JACC Review Topic of the Week



Bang., et al., JACC, February, 2021

ESC Myocardial & Pericardial Diseases

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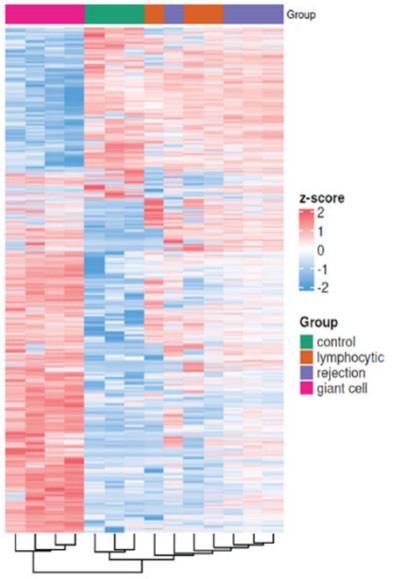
RNA-Sequencing Reveals a Distinct Transcriptomic Signature for Giant Cell Myocarditis and Identifies Novel Druggable Targets

Kaushik Amancherla, Juan Qin, Yu Wang, Margaret L. Axelrod, Justin M. Balko, Kelly H. Schlendorf, Robert D. Hoffman, Yaomin Xu, JoAnn Lindenfeld, Javid Moslehi

Pathway enrichment analysis in GCM showed that upregulated pathways were enriched for neutrophil degranulation, multiple cytokine signaling pathways, and phagocytosis



Unsupervised Hierarchical Clustering

Circ Research, June 21st, 2021

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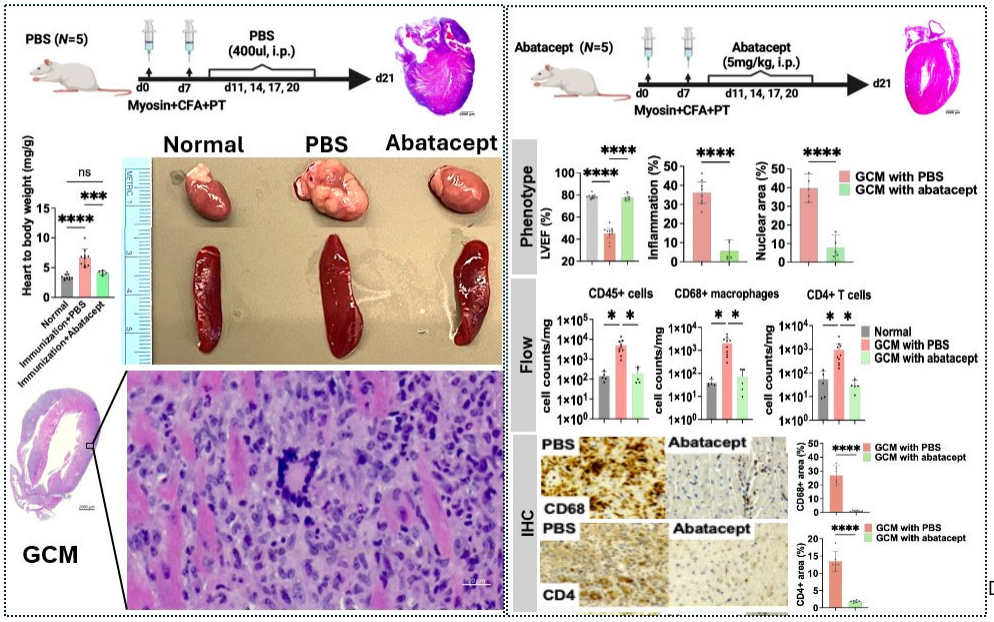
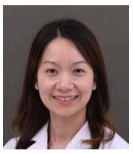
Rat model of GCM

Treatment Efficacy with abatacept





Yingxian Grace Liu, M.D.
Post-doc, UCSF
Cardiologist, PUMCH

Javid Moslehi, Professor
Director of Cardio-Oncology & Immunology section
Department of Cardiology, UCSF

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Cardiac Sarcoidosis Scientific Statements

Recommendations	Class[a]	Level[b]
Electro-anatomical mapping should be considered in cases of suspected myocarditis (especially cardiac sarcoidosis) to guide endomyocardial biopsy.[218,220,221,253,256–258]	IIa	C

Rakesh

Richard K. C
David H. Bir
Kristen K. P
and Transpla

...ledge,
Challenges, and Future Perspectives State-of-the-Art Review

NISHA A. GILOTRA, MD,[1] JAN M. GRIFFIN, MD,[2] NOELLE PAVLOVIC, MSN, RN,[3] BRIAN A. HOUSTON, MD,[4]
JESSICA CHASLER, PharmD, MPH,[5] COLLEEN GOETZ, CRNP,[6] JONATHAN CHRISPIN, MD,[7] MICHELLE SHARP, MD, MHS,[8]
EDWARD K. KASPER, MD,[1] EDWARD S. CHEN, MD,[8] RON BLANKSTEIN, MD,[9] LESLIE T. COOPER, MD,[10]
EMER JOYCE, MBBCh, PhD,[11] AND FAROOQ H. SHEIKH, MD[6]

Sharma, R. et al. Eu Heart J 2024; Cheng, R et al. Circulation 2024

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Fragmented Intracardiac Electrograms at the Basal Septum Normal voltages elsewhere in a man with Suspected Sarcoidosis

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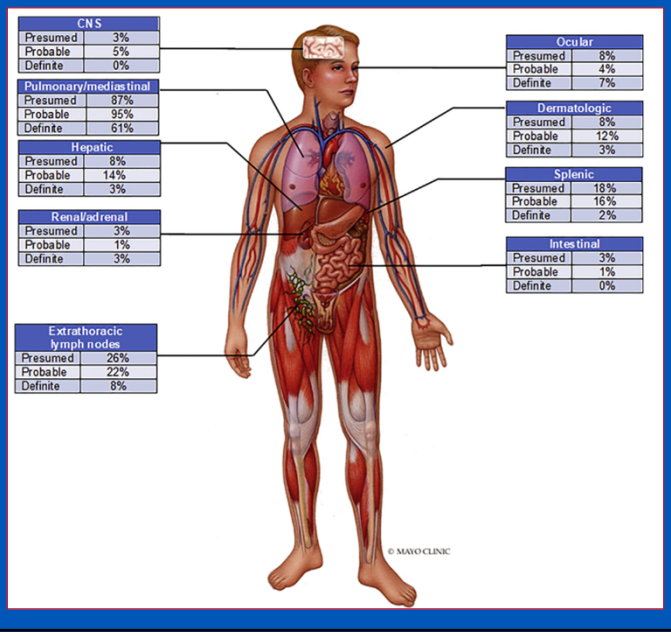
EXTRACARDIAC MANIFESTATIONS OF SARCOIDOSIS



Rosenbaum, A, et al.
Int J Cardiol. April 17th, 2021

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SCIENTIFIC STATEMENT

Clinical Considerations for Competitive Sports Participation for Athletes With Cardiovascular Abnormalities

Recommendation Table 26 — Recommendations for physical activity and myocarditis/pericarditis (see Evidence Table 26)

Recommendation	Class[a]	Level[b]
Restriction of physical exercise until remission, for at least 1 month, is recommended in athletes and non-athletes after IMPS using an individualized approach to accelerate recovery.	I	C

Kim, et al. JACC February 2025

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ARCHER TRIAL: IMPACT OF CANNIBIDIOL ON MYOCARDIAL RECOVERY

Presentation November 29th

Clinical diagnosis of acute myocarditis (Lake Louise Criteria)
Cardiac Magentic Resonance (CMR) or Endomyocardial biopsy

RANDOMIZED 1:1 DOUBLE-BLIND

Pharmaceutically produced Cannabidiol Formulation
2.5 mg/kg 10 10 mg/kg b.i.d

Matching PLACEBO

Primary Endpoint: Improvement in Extracellular Volume (ECV) and Global longitudinal Strain (GLS), measured by CMR after 12 weeks

Secondary Endpoint: Improved in Left Ventricular Ejection Fraction (LVEF), measured by CMR after 12 weeks

McNamara, D et al., ESC Heart Failure: October 2024

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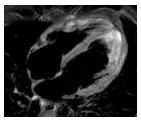
Trial Population
n=109
Clinically suspected acute myocarditis



Confirmed by CMR

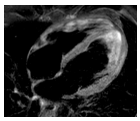
Intervention
Randomization

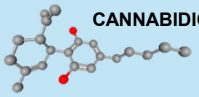
12 weeks of pharmaceutically manufactured cannabidiol

12 weeks of placebo

Repeat CMR at 12 weeks

Morphology, function, tissue pathology



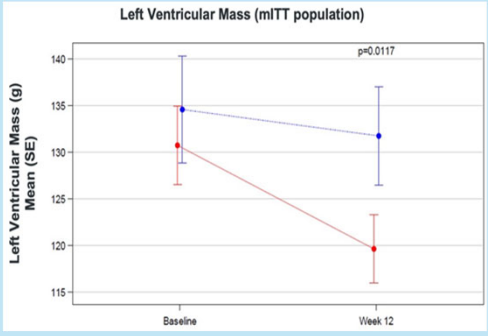


Pharmaceutically manufactured cannabidiol oral solution modulates pathways involved in NF-κB-mediated inflammasome priming and NLRP3 inflammasome activation.

Results

Oral cannabidiol treatment was associated with significantly greater reduction (versus placebo) in LV mass, driven by reductions in ECV and ICV.

No treatment-dependent changes in LVEF or GLS were evident.



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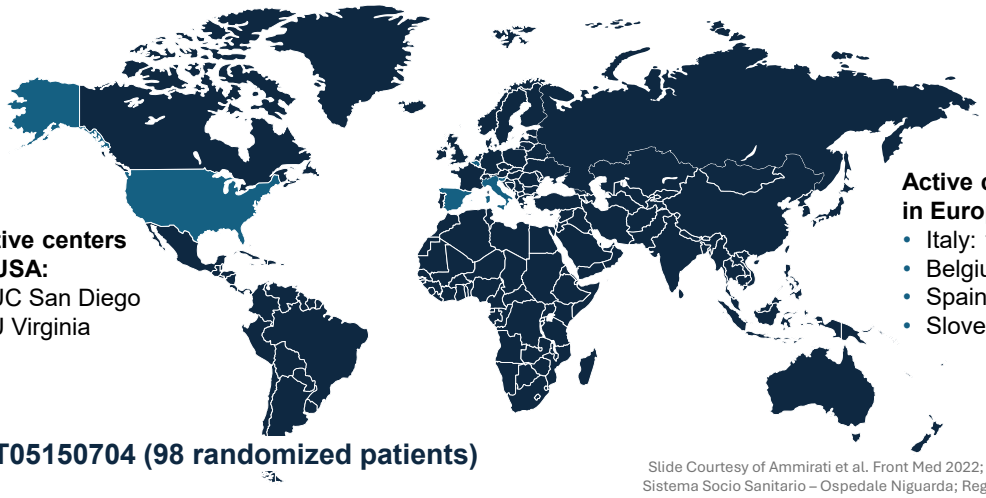
MYTHS Trial

IV Methylprednisolone in Fulminant Myocarditis

Active centers = 33 – Planned centers = 45



Active centers in USA:
- UC San Diego
- U Virginia

Active centers in Europe:
- Italy: 19
- Belgium: 3
- Spain: 8
- Slovenia: 1

NCT05150704 (98 randomized patients)

Slide Courtesy of Ammirati et al. Front Med 2022; Mar 7:9:838564
Sistema Socio Sanitario – Ospedale Niguarda; Regione Lombardia.

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QUESTIONS & ANSWERS

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