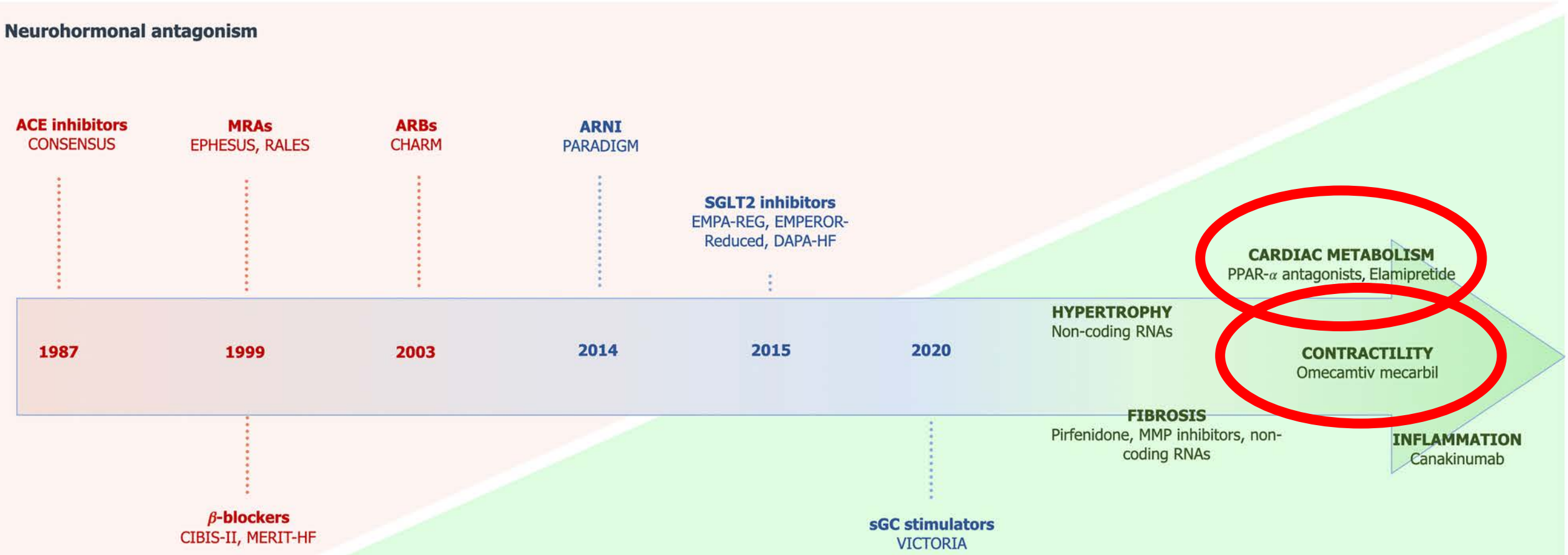
Omecamtiv mecarbil və Elamipretide

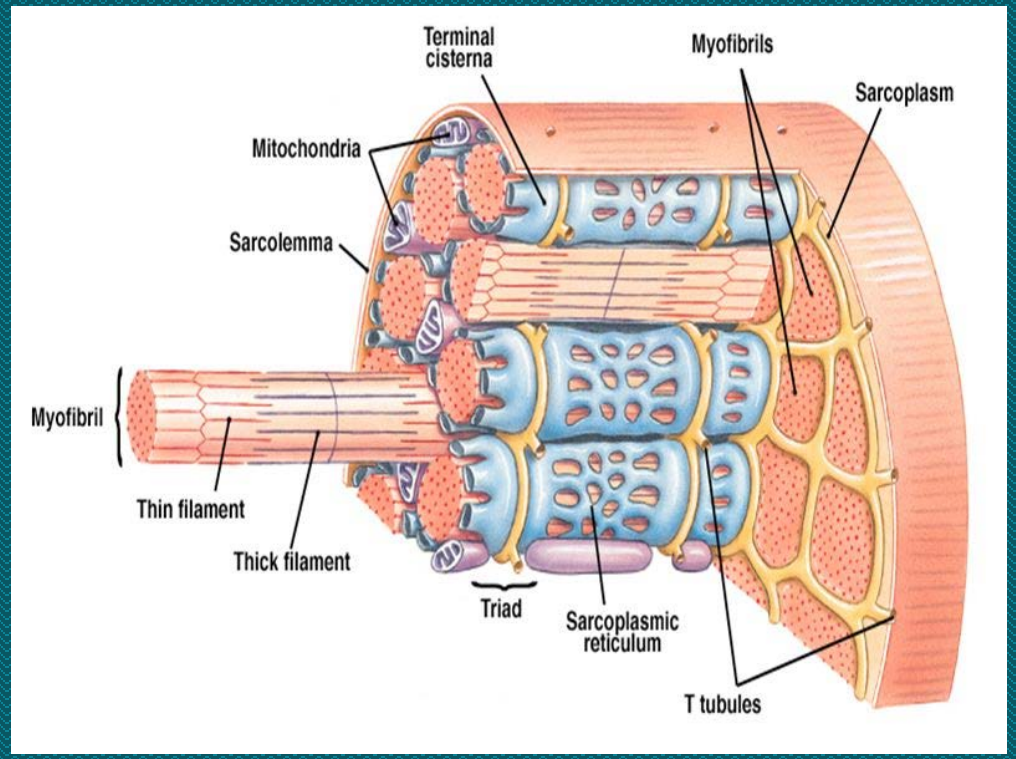
Azərbaycan Kardiologiya Cəmiyyəti

Dr. Cavadov Arif

Hardan hara, nədən nəyə?



Sarkoplazmik retikulum



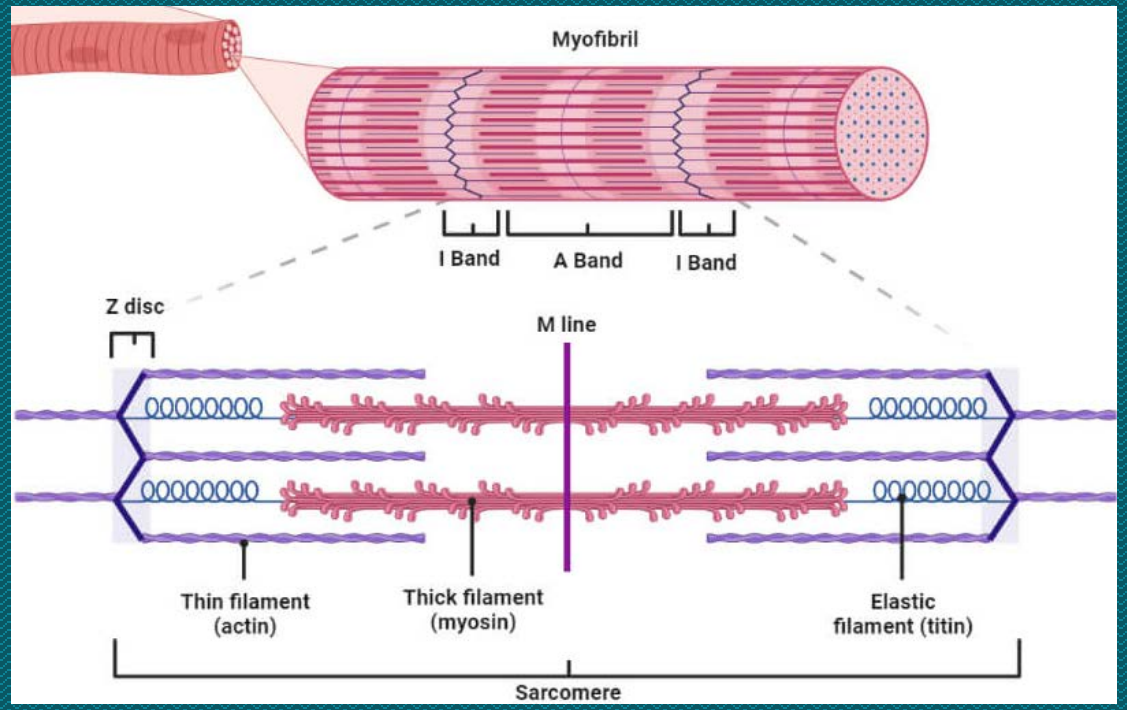
- Miofibrillərin ətrafında
- Ca - toplamaq

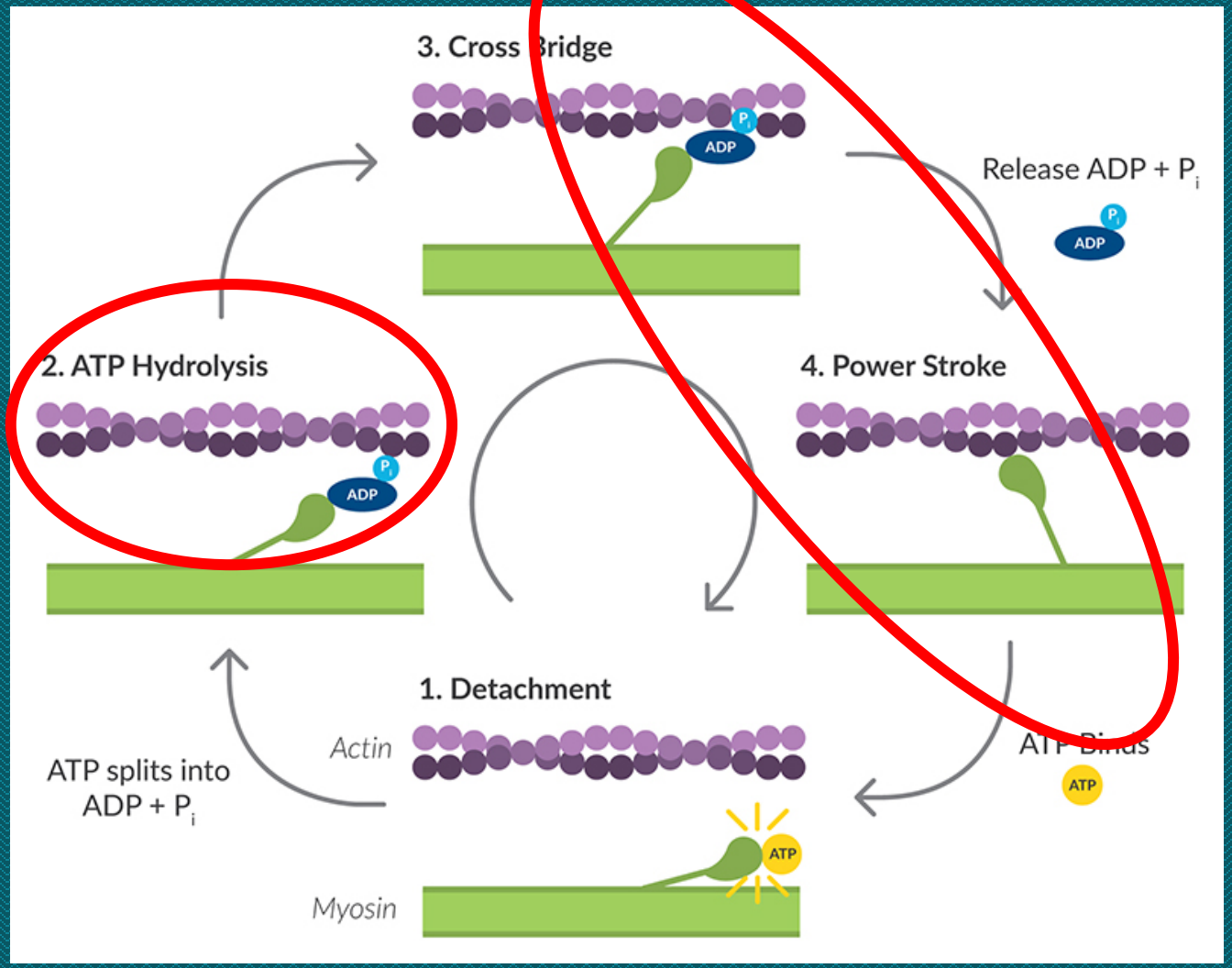
- Levomisendan – Ca reseptor həssaslığını artır
- Dobutamin – Ca hüceyrə daxili toplanmasını
- Milrinon - …
- Və.s

- Ürək vurğuları
- Oksigen tələbatı
- İşemiya
- Aritmiya
- Mortallıq
- Kəskin ÜÇ
- Son mərhələdə

Emerging Technologies for Heart Diseases, 2020

Sarcomer

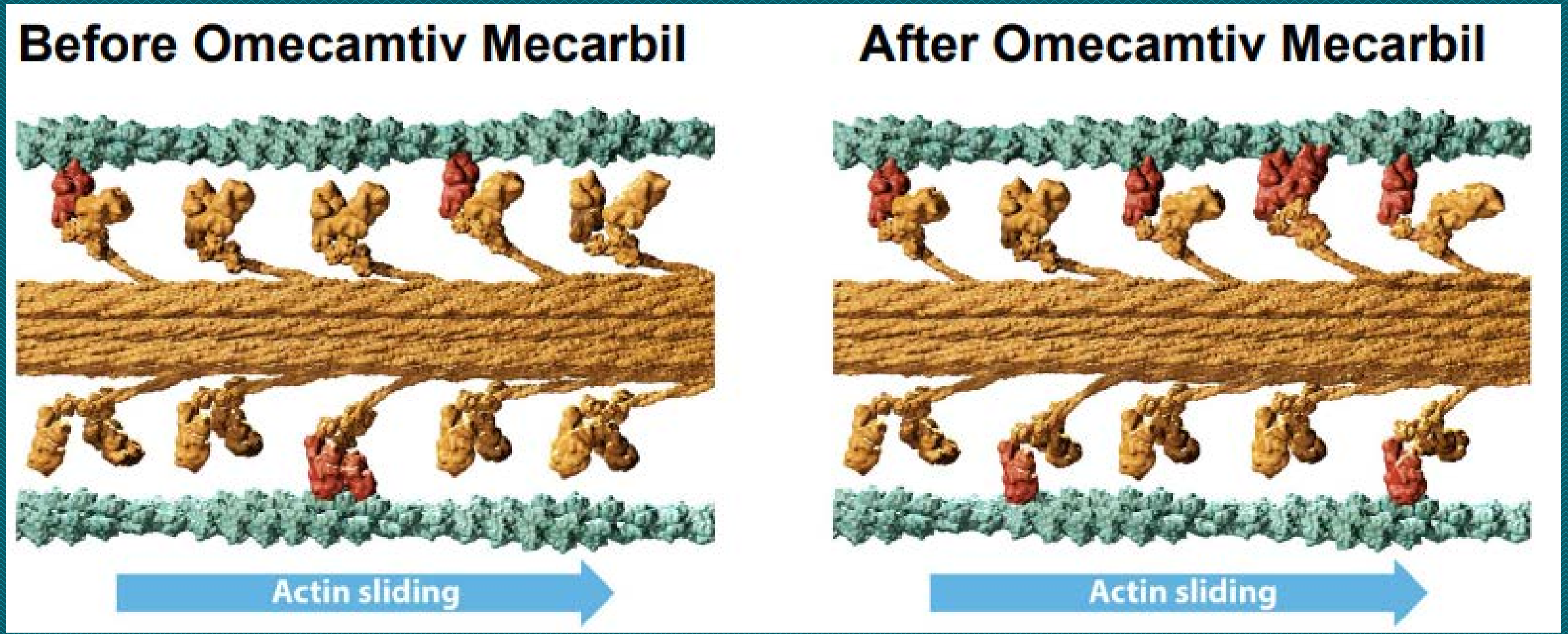




- Omekamtiv mekarbil
- Kardioselektiv miozin activator (S1)
- ATF hidrolizi artırır
- Daha çox miozin başlığı aktivləsir, birləşir
- Cross-bridge mərhələsini uzadır
- Sistola fazası uzanır

Emerging Technologies for Heart Diseases, 2020

Sarcomer



J Am Coll Cardiol HF. 2020 Apr, 8 (4) 329–340

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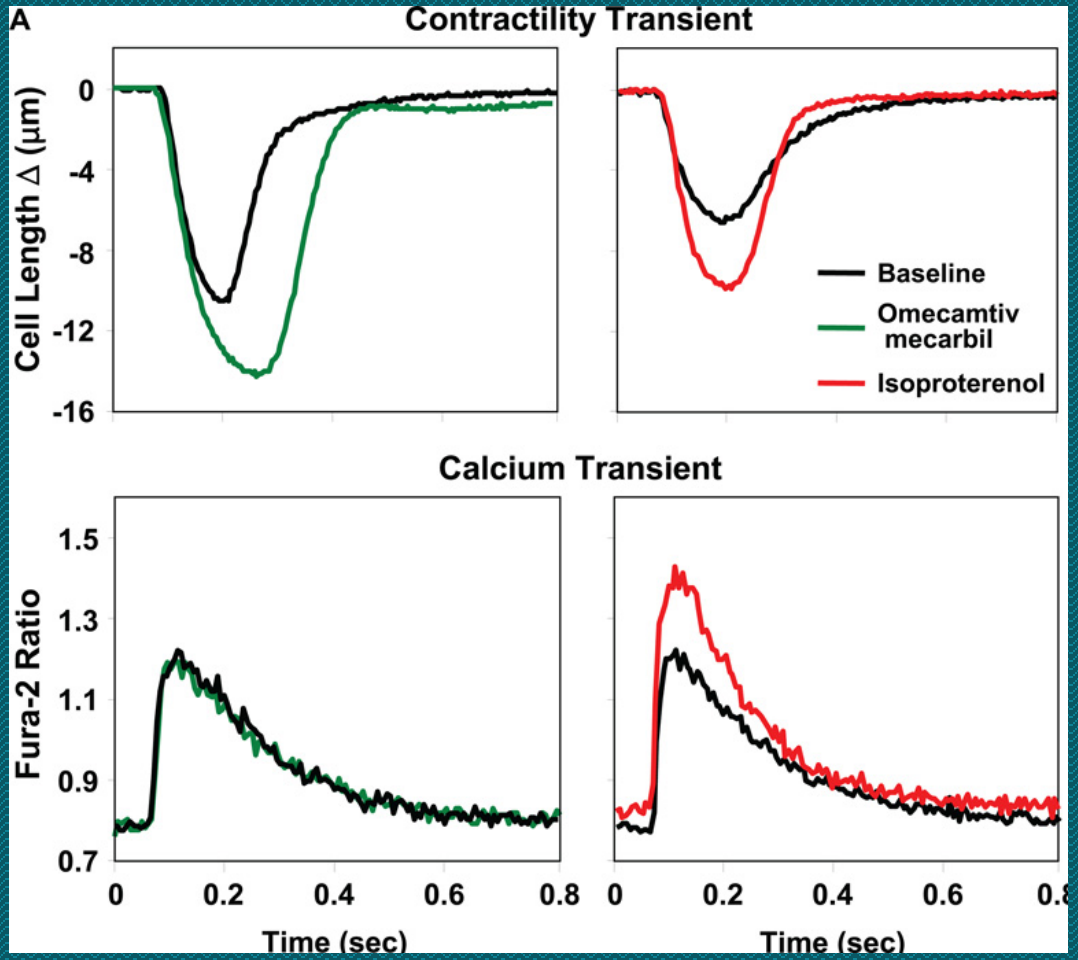
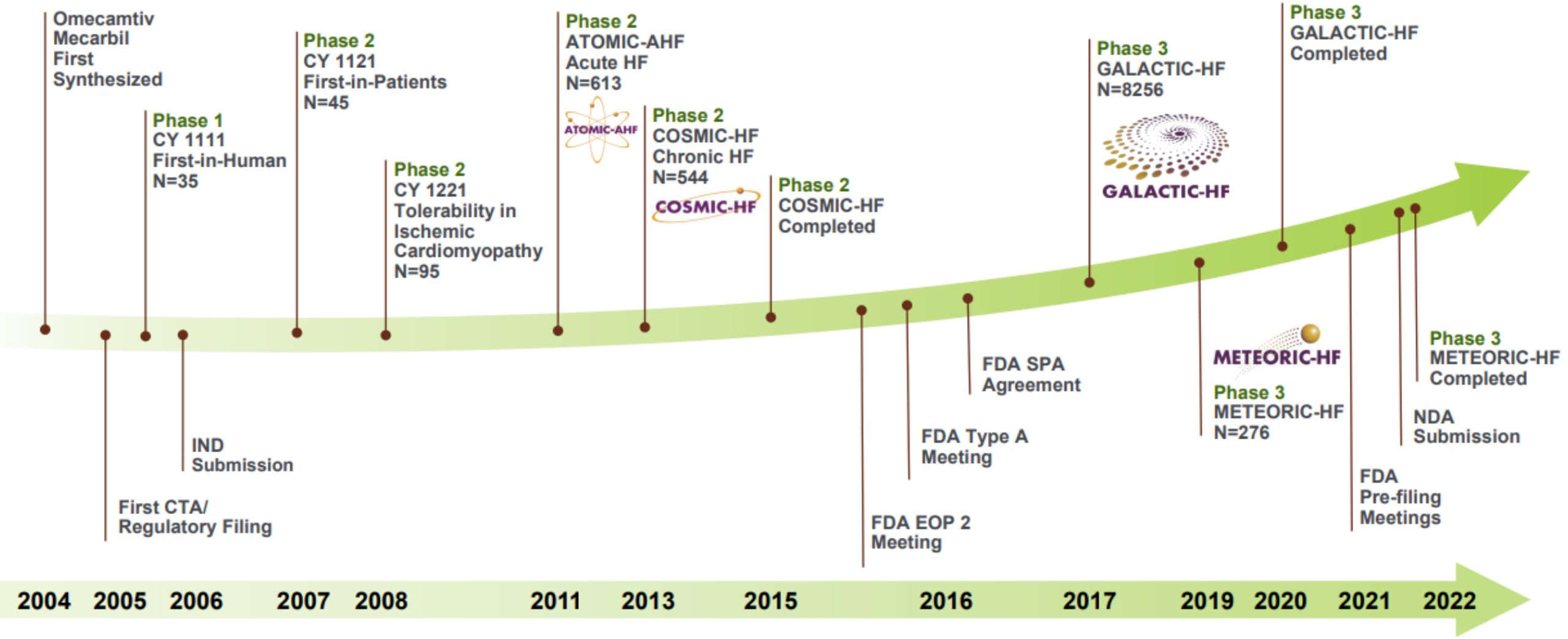
Science. 2011 March 18; 331(6023): 1439–1443. doi:10.1126/science.1200113.

Cardiac Myosin Activation: A Potential Therapeutic Approach for Systolic Heart Failure



Completed studies enrolling over 10,300 participants



ATOMIC-AHF

- Kəski
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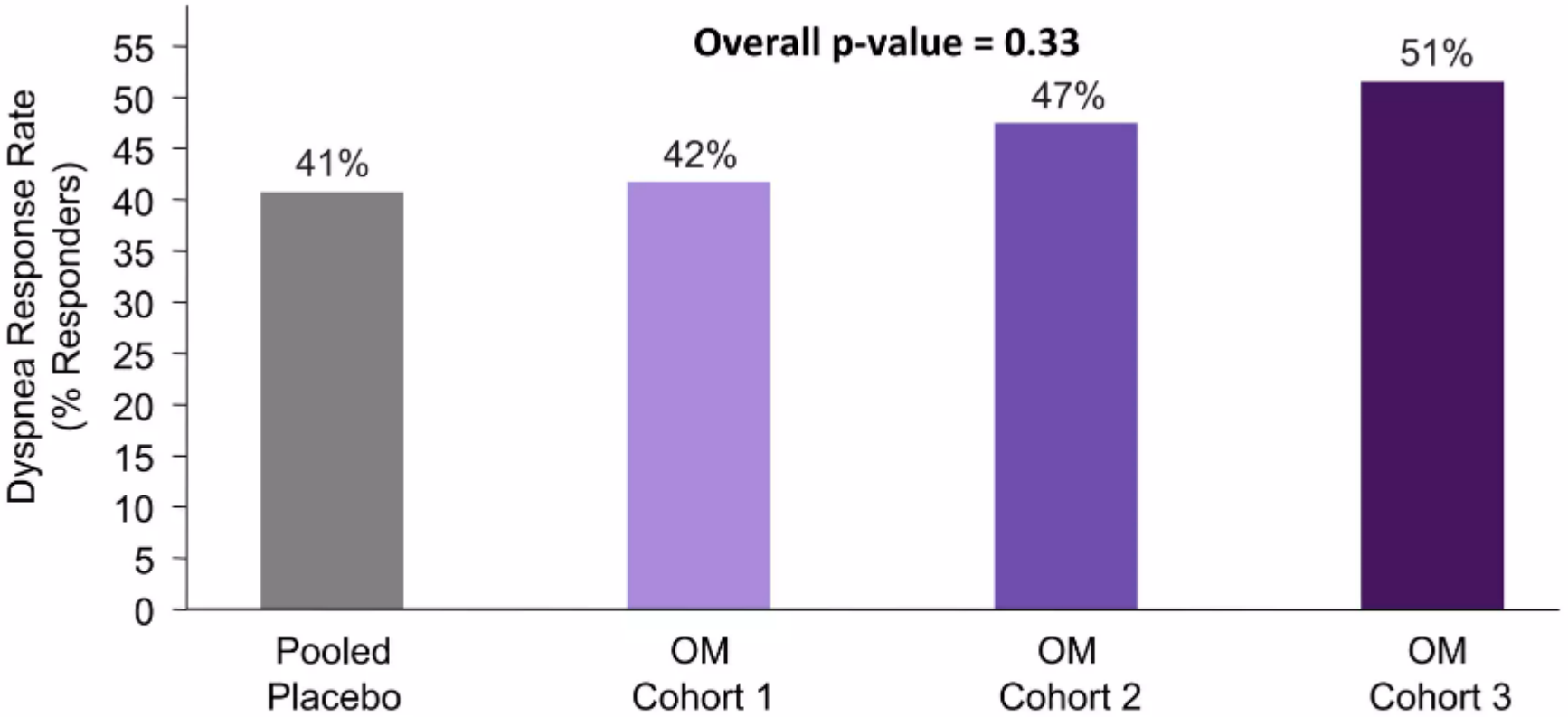
- 606 x
  - 10
  - 99
  - 10
  - 30
- Birinc

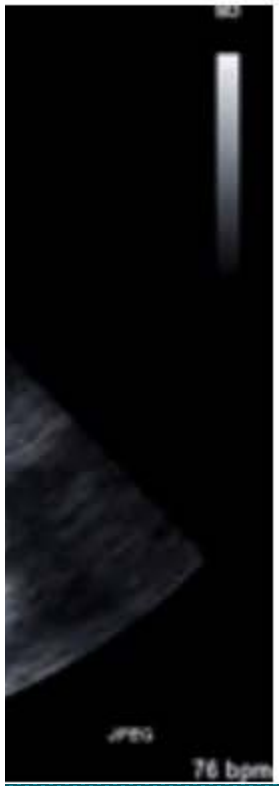


Response Rate Ratio*	**1.03**	**1.15**	**1.23**
95% CI	**(0.79, 1.35)**	**(0.90, 1.47)**	**(0.97, 1.55)**

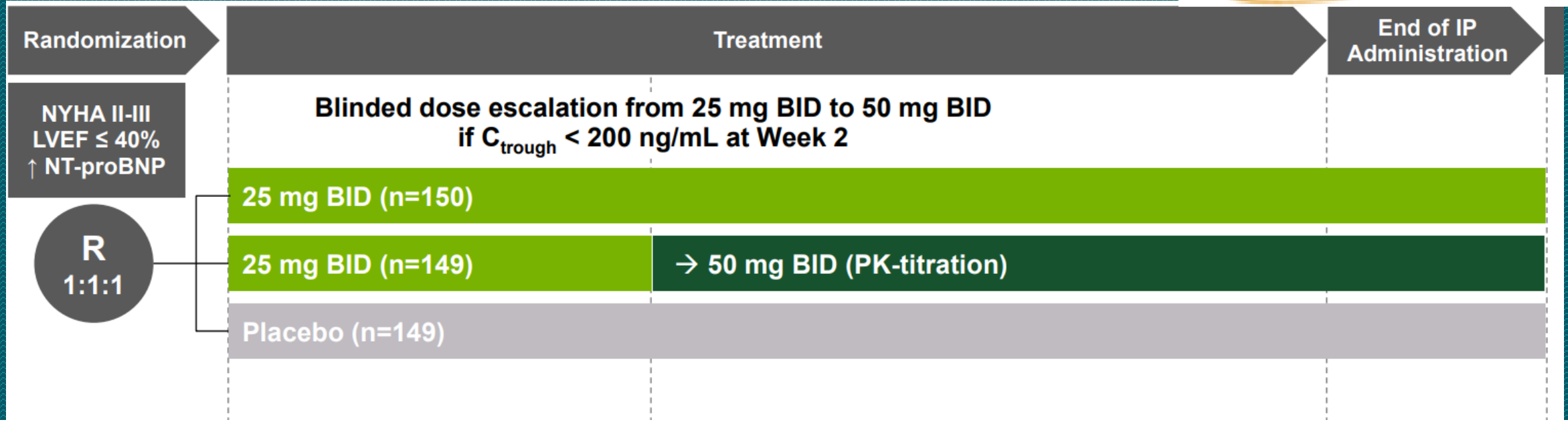
*Ratio of response rate to Pooled Placebo
p-value of a CMH test among all 3 Placebo arms = 0.32

ATOMIC-AHF

Characteristic	Omecamtiv Mecarbil	Placebo
LVOT SV (mL)		
Baseline	**23**	**26**
24 hrs	**54**	**24**
EF (%)		
Baseline	**18**	**18**
24 hrs	**23**	**18**
HR (bpm) – supine ECG		
Baseline	**88**	**85**
24 hrs	**57**	**86**



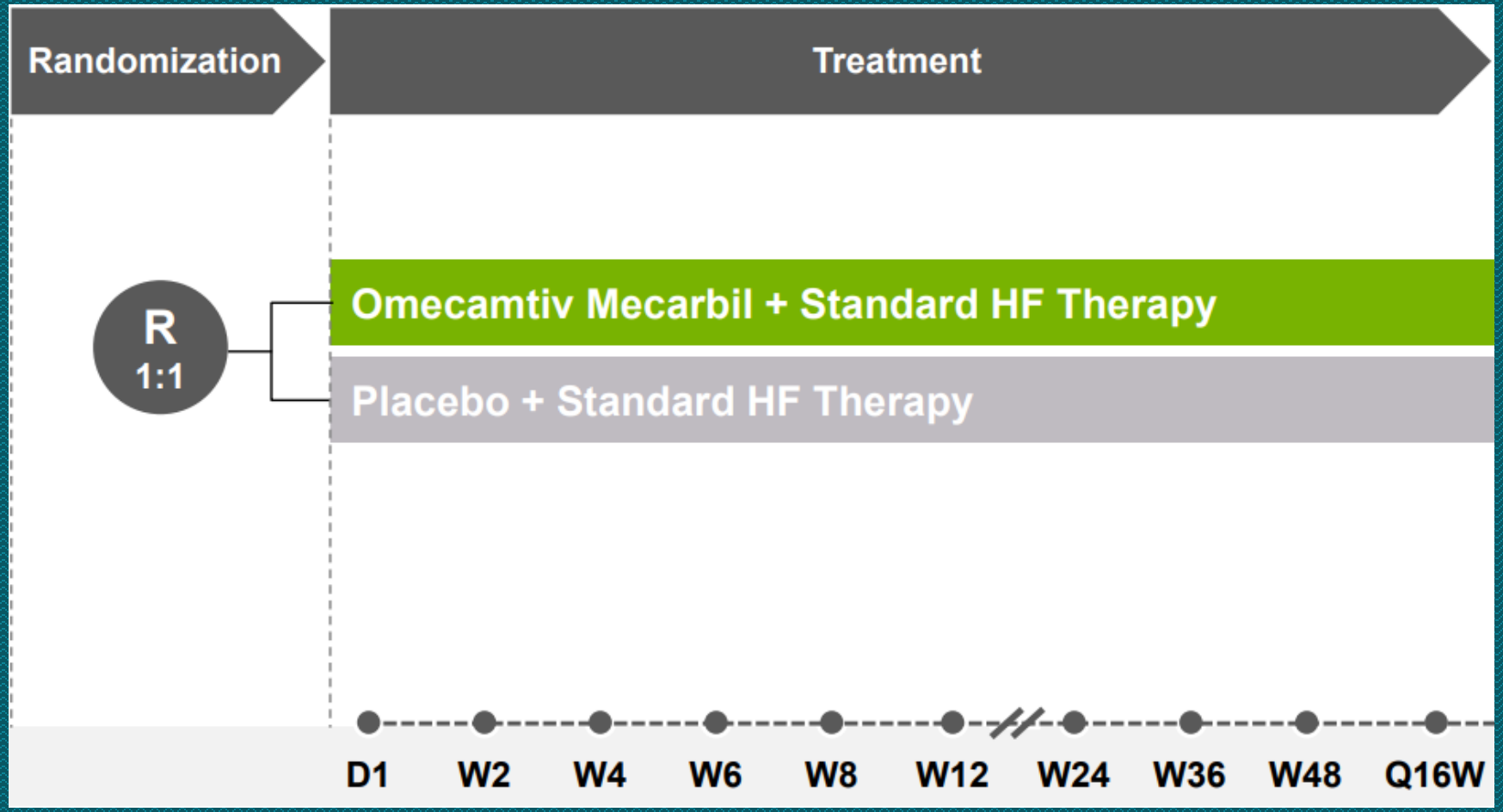
COSMIC-HF



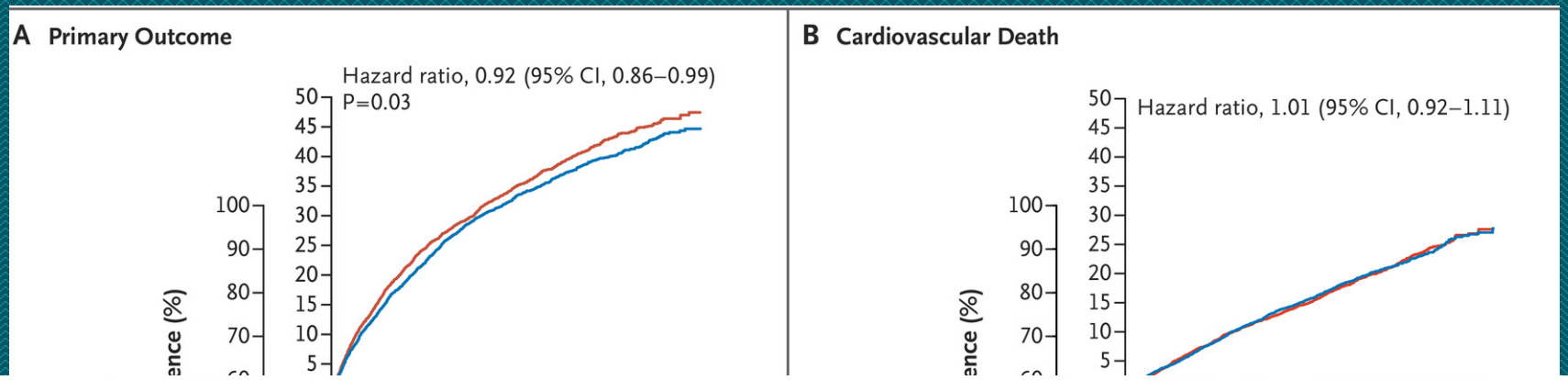
Findings: From March 17, 2014, to March 5, 2015, we enrolled 150 patients in the fixed-dose omecamtiv mecarbil group and 149 in the pharmacokinetic-titration and placebo groups. Mean maximum concentration of omecamtiv mecarbil at 12 weeks was 200 (SD 71) ng/mL in the fixed-dose group and 318 (129) ng/mL in the pharmacokinetic-titration group. For the pharmacokinetic-titration group versus placebo group at 20 weeks, least square mean differences were as follows: systolic ejection time 25 ms (95% CI 18-32, p<0·0001), stroke volume 3·6 mL (0·5-6·7, p=0·0217), left ventricular end-systolic diameter -1·8 mm (-2·9 to -0·6, p=0·0027), left ventricular end-diastolic diameter -1·3 mm, (-2·3 to 0·3, p=0·0128), heart rate -3·0 beats per min (-5·1 to -0·8, p=0·0070), and N-terminal pro B-type natriuretic peptide concentration in plasma -970 pg/mL (-1672 to -268, p=0·0069). The frequency of adverse clinical events did not differ between groups.

GALACTIC-HF

- Randomizə, ikili-kor, plasebo-kontrollu
- 35 ölkə
- 8256 xəstə
- HFrEF (<35%)
- Birincili sonlanım: kardiovaskular ölüm və ÜÇ hadisəsi



GALACTIC-HF



Subgroup (cont.)	Hazard Ratio (95% CI)
Atrial fibrillation or flutter	
No	0.86 (0.79–0.94)
Yes	1.05 (0.93–1.18)
LVEF	
≤Median (28%)	0.84 (0.77–0.92)
>Median (28%)	1.04 (0.94–1.16)
Systolic BP level	
<100 mm Hg	0.89 (0.76–1.05)
≥100 mm Hg	0.92 (0.86–1.00)

METEORIC-HF

Effect of Omecamtiv Mecarbil on Exercise Capacity in Chronic Heart Failure With Reduced Ejection Fraction

The METEORIC-HF Randomized Clinical Trial

Conclusions and Relevance In patients with chronic HFrEF, omecamtiv mecarbil did not significantly improve exercise capacity over 20 weeks compared with placebo. These findings do not support the use of omecamtiv mecarbil for treatment of HFrEF for improvement of exercise capacity.

5ci ürək çatışmazlığı dərmanı?

News > Medscape Medical News

FDA Panel Votes No on Omecamtiv Mecarbil for Heart Failure

Megan Brooks, December 14, 2022

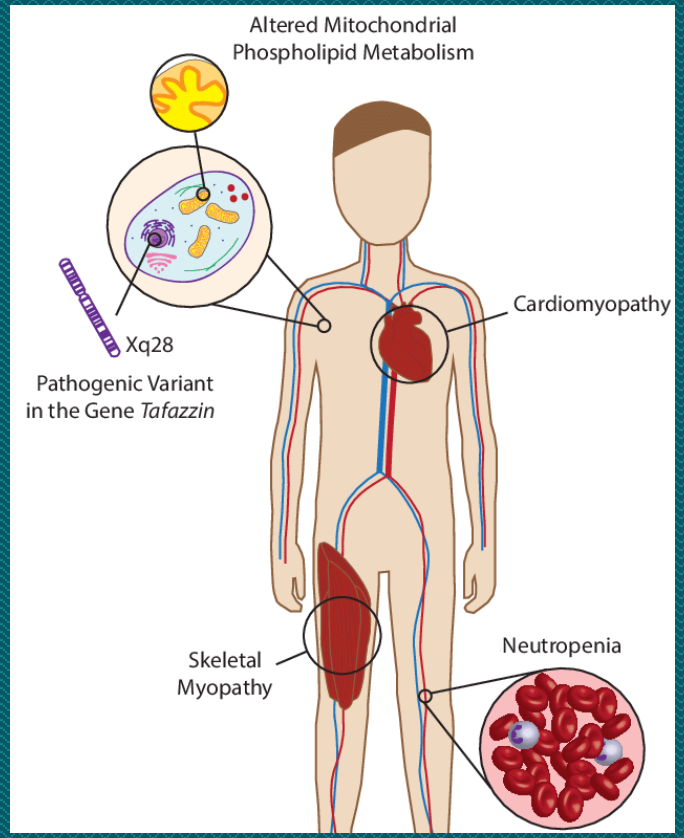
- 8 səs üzərindən 3 səs qazandı
- Həyat keyfiyyətini artırmadı
- Təkrari hospitalizasiya və mortallığı azaltmada əhəmiyətli fərq olmadı
- EF<28% - effektivdir, >28 % effektivliyi azdır

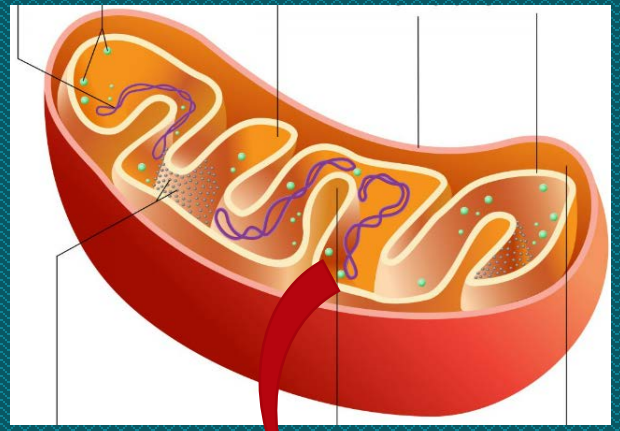
ESC 2021-də Omecamtiv mecarbil

Cardiac myosin activator

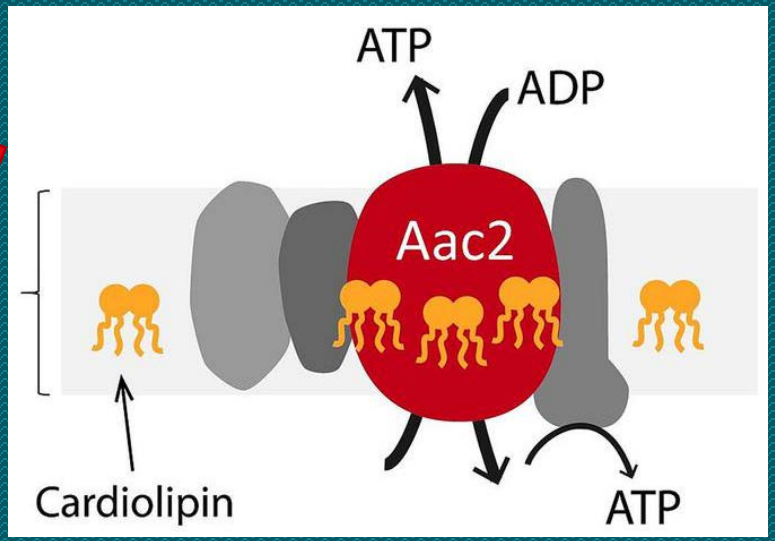
The GALACTIC-HF study assessed the efficacy and safety of the cardiac myosin activator, omecamtiv mecarbil, in HFrEF patients, enrolling patients in both the inpatient and outpatient settings. The primary endpoint of a first HF event or CV death was reduced by 8%. There was no significant reduction in CV mortality. Currently, this drug is not licensed for use in HF. However, in the future it may be able to be considered, in addition to standard therapy for HFrEF to reduce the risk of CV mortality and hospitalization for HF.[159]

Barth sindromu



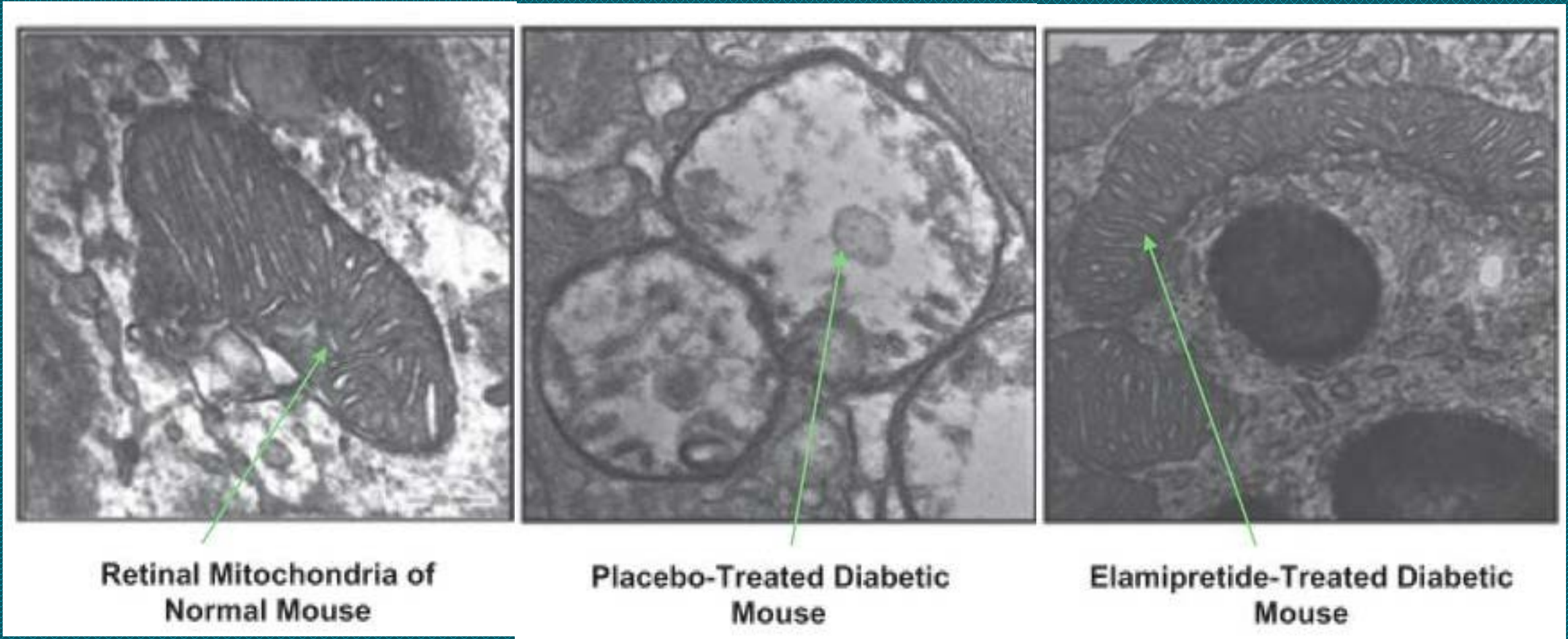


Elamipretid



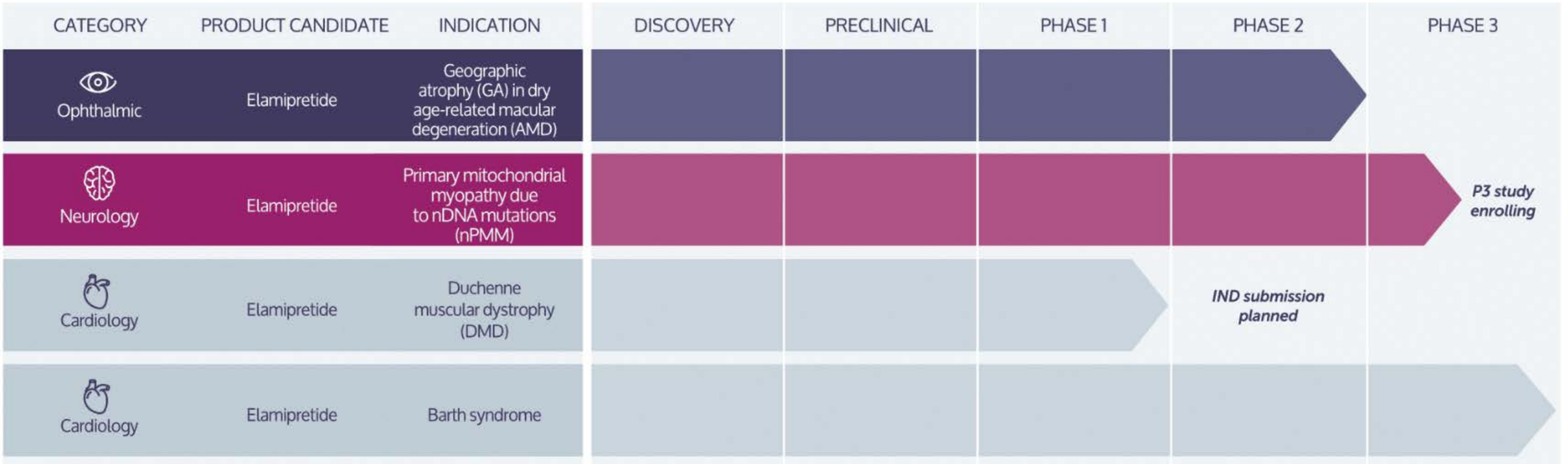
JIMD Rep. 2023 Jan; 64(1): 65–70. Published online 2022 Sep 21. doi: 10.1002/jmd2.12335

Elamipretidin effektivliyi



Clin Pharmacol Ther . 2014 Dec;96(6):672-83. doi: 10.1038/clpt.2014.174. Epub 2014 Sep 4.

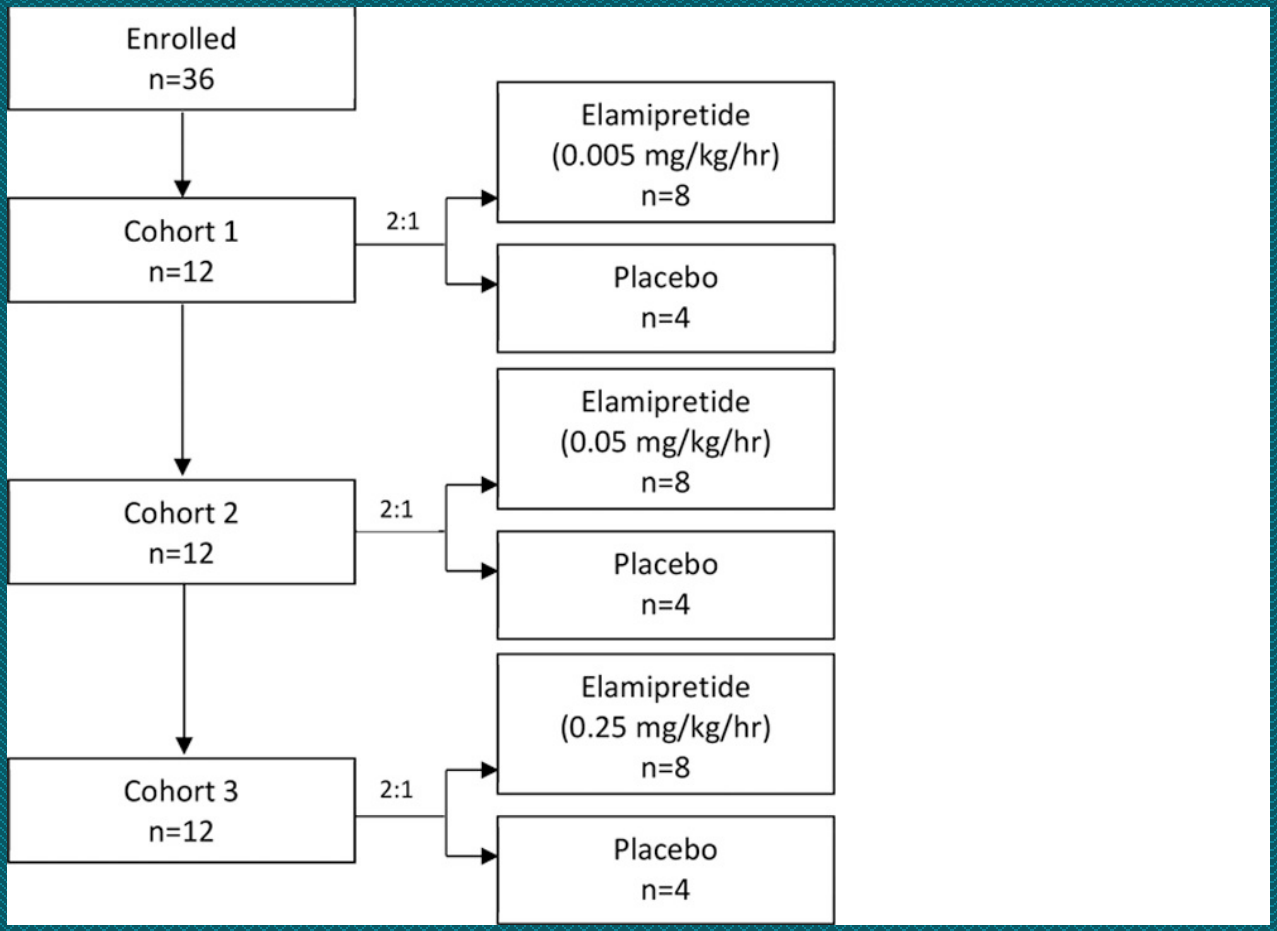
Elamipretid hansı sahələrdə?



Novel Mitochondria-Targeting Peptide in Heart Failure Treatment

A Randomized, Placebo-Controlled Trial of Elamipretide

Originally published 7 Dec 2017 | https://doi.org/10.1161/CIRCHEARTFAILURE.117.004389 | Circulation: Heart Failure. 2017;10:e004389



Conclusions

This is the first study to evaluate elamipretide in heart failure with reduced ejection fraction and demonstrates that a single infusion of elamipretide is safe and well tolerated. High-dose elamipretide resulted in favorable changes in left ventricular volumes that correlated with peak plasma concentrations, supporting a temporal association and dose–effect relationship. Further study of elamipretide is needed to determine long-term safety and efficacy.

Clinical Trial > J Card Fail. 2020 May;26(5):429-437. doi: 10.1016/j.cardfail.2020.02.001. Epub 2020 Feb 14.

Effects of Elamipretide on Left Ventricular Function in Patients With Heart Failure With Reduced Ejection Fraction: The PROGRESS-HF Phase 2 Trial

- 71 xəstə
- HFrEF ≤ 40%
- 28 gün, Elamipretid 4mg və ya 40mg, 1x1

Results: The mean age (standard deviation) of the study population was 65 ± 10 years, 24% were females, and the mean EF was 31% ± 7%. The change in LVESV from baseline to week 4 was not significantly different between elamipretide 4 mg (89.4 mL to 85 mL; difference, -4.4 mL) or 40 mg (77.9 mL to 76.6 mL; difference, -1.2 mL) compared with placebo (77.7 mL to 74.6 mL; difference, -3.8 mL) (4 mg vs placebo: difference of means, -0.3; 95% CI, -4.6 to 4.0; P = 0.90; and 40 mg vs placebo: difference of means, 2.3; 95% CI, -1.9 to 6.5; P = 0.28). Also, no significant differences in change in LVESV and LVEF were observed between placebo and either of the elamipretide groups. Rates of any study drug-related adverse events were similar in the 3 groups.

5ci ürək çatışmazlığı dərmanı?

Search

elamipretide

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FDA issues refuse-to-file letter for application for Barth syndrome

https://www.fda.gov/drugs/drug-safety-and-availability/fda-issues-refuse-file-letter-application-barth-syndrome

… the company's new drug application for Forzinity (**elamipretide** HCl) to treat Barth syndrome, a rare and serious … the company's new drug application for

02-Jim Carr, Stealth Biotherapeutics

https://www.fda.gov/media/131586/download

… Insights from the Clinical Development of **Elamipretide** for Primary Mitochondrial Disorders Jim Carr, … dysfunction as a new frontier Our lead product can
an evolving frontier. We are evaluating **elamipretide** in Barth syndrome, primary mitochondrial …

10-Bruce Cohen, Akron Children's Hospital

https://www.fda.gov/media/131583/download

… modifying agents, biologics, gene editing; EPI-743, **elamipretide**, RTA-408 New Drug Development (not yet …

01-Robert Naviaux, UCSD

https://www.fda.gov/media/131574/download

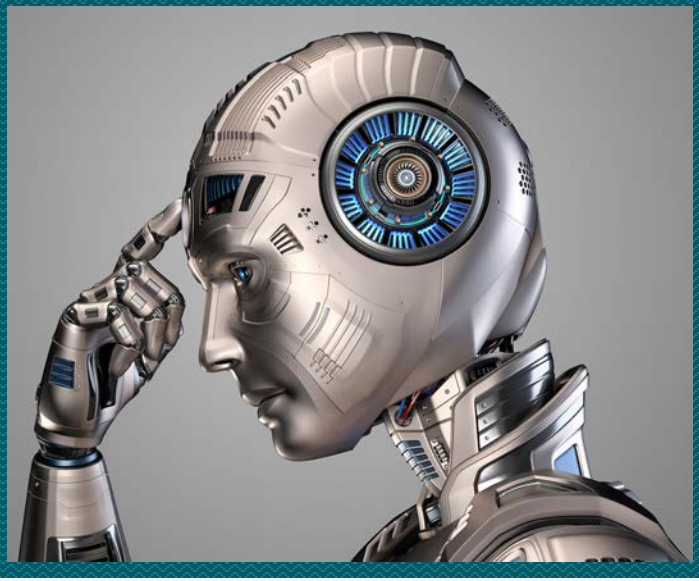
… NR Leigh II Vitamin E-like NPMDS NCT03323749 NR **Elamipretide** Myopathy II Cardiolipin+ 6MWT, PMMSA …

EL-PFDD Meeting on Barth Syndrome Voice of the Patient Report

https://www.fda.gov/media/130562/download

… that target different disease pathways, including **elamipretide** and bezafibrate, there is also considerable …

Bard Google AI



Has the FDA approved elamipretide for heart failure?

No, the FDA has not approved elamipretide for heart failure. However, it is currently under investigation for the treatment of Barth syndrome, a rare genetic disorder that causes heart muscle disease. In a clinical trial, elamipretide was shown to improve exercise capacity and quality of life in people with Barth syndrome. The FDA is still reviewing the data from this trial, and it is not yet clear when or if elamipretide will be approved for the treatment of heart failure.

Here are some of the reasons why the FDA has not yet approved elamipretide for heart failure:

- The clinical trial that showed the benefits of elamipretide for Barth syndrome was small and short-term.
- Elamipretide has not been shown to be effective in other types of heart failure.

Azərbaycan
Kardiologiya
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Təşəkkürlər