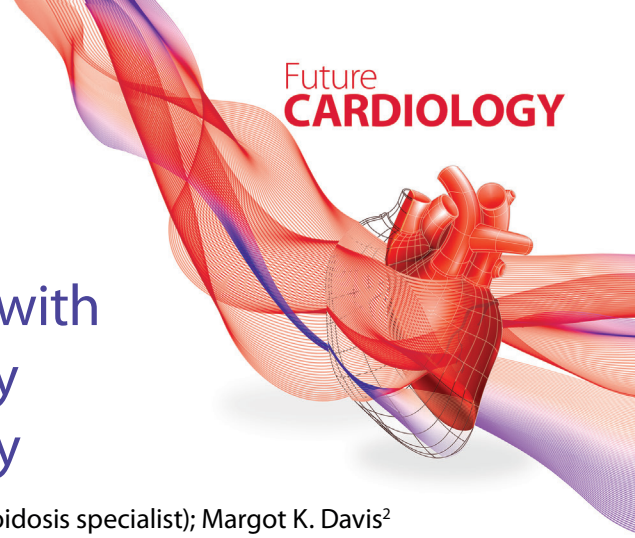
Future CARDIOLOGY

Plain Language Summary of Publication

The effect of long-term tafamidis treatment on quality of life in people with transthyretin amyloid cardiomyopathy (ATTR-CM): A plain language summary



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Where can I find the original article on which this summary is based?

This summary is based on an original article published in the *European Journal of Heart Failure*. You can read the original article for free at: https://onlinelibrary.wiley.com/doi/10.1002/ejhf.3190. It is called 'Effect of long-term tafamidis treatment on health-related quality of life in patients with transthyretin amyloid cardiomyopathy.'

Summary

How to say (double click sound icon to play sound)...

- **Amyloid:** A-muh-loyd
- **Amyloidosis:** A-muh-loy-DO-sis
- **ATTR-ACT:** uh-TRAKT
- **Cardiomyopathy:** KAR-dee-oh-my-OP-uh-thee
- **Placebo:** pluh-SEE-boh
- **Tafamidis:** tah-FAM-ah-dis
- **Transthyretin:** trans-thy-REH-tin

What is this summary about?

This summary explains some results of a study called ATTR-ACT and its ongoing long-term extension study that were published in the *European Journal of Heart Failure*. The purpose of ATTR-ACT was to find out if a drug called tafamidis is an effective treatment for people with a heart condition called transthyretin amyloid cardiomyopathy (ATTR-CM). People took tafamidis or placebo for up to 2.5 years in ATTR-ACT (the initial study). A placebo looks like the study medicine but does not contain any active ingredients. After people completed the initial study, they could take part in the extension study. An extension study allows people to continue receiving treatment after the original clinical study ends and helps researchers understand how well a treatment works over a longer time period. This extension study allows people to receive tafamidis for up to an additional 5 years. People who took placebo in the initial study now receive tafamidis. People who took tafamidis in the initial study continue tafamidis treatment. Researchers looked at changes in peoples' ability to enjoy life ('quality of life') and heart failure symptoms since they started ATTR-ACT. Results are available for the first 2.5 years of the extension study.

What are the key takeaways?

During the initial study, there was less worsening of quality of life and heart failure symptoms in people who took tafamidis compared to people who took placebo. In the extension study, quality of life and heart failure symptoms were maintained or nearly maintained in people who took tafamidis in the initial study. In people who started tafamidis in the extension study, quality of life and heart failure symptoms continued to worsen, but the worsening slowed down.

What were the main conclusions reported by the researchers?

Tafamidis slows the worsening of quality of life and heart failure symptoms in people with ATTR-CM. People with ATTR-CM should start treatment early to receive the most benefit.

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10.1080/14796678.2024.2391250.

What is the purpose of this plain language summary?

The purpose of this plain language summary is to help you understand the findings from recent research. When reading this summary, it is important to understand the following:

- Tafamidis is approved to treat the condition under study that is discussed in this summary.
- This summary reports the results of more than one study. The results of these studies may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence.
- This summary includes the results of a planned interim analysis of the long-term extension study that followed ATTR-ACT. This means that the extension study has not yet been completed.
- The long-term extension study described is still ongoing; therefore, the final outcomes of the extension study may differ from the outcomes described in this summary.

Who is this article for?

This summary may help people with ATTR-CM and their caregivers understand the results of this study. This summary may also be useful for healthcare providers who treat people with ATTR-CM.

Who sponsored these studies?

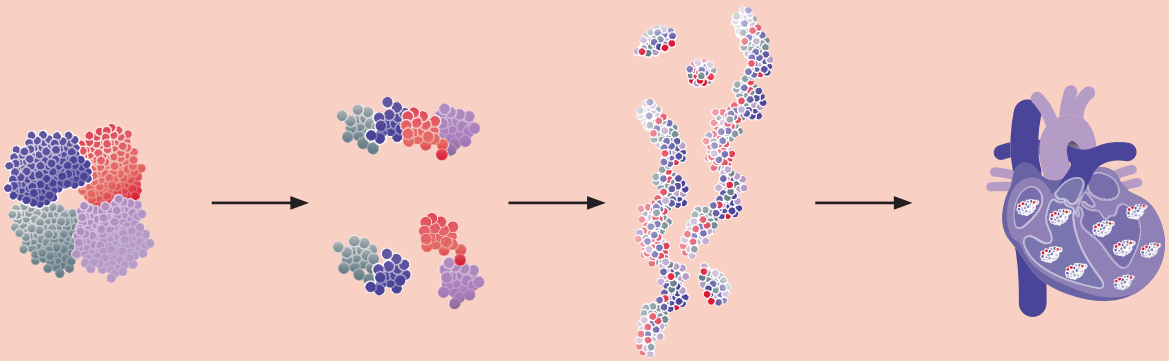
ATTR-ACT and the extension study were **sponsored** by Pfizer.

Sponsor: A company or organisation that oversees and pays for a clinical research study. The sponsor also collects and analyses the information that was generated during the study.

What is transthyretin amyloid cardiomyopathy?

Transthyretin amyloid cardiomyopathy (ATTR-CM) is a disease that affects a person's heart.

People with ATTR-CM see their overall health get worse over time. They become less able to enjoy their lives ('quality of life').



Transthyretin is a protein made in the liver. Proteins are building blocks of the body. They make up body structures and are needed for the body to function.

Sometimes the transthyretin protein breaks into pieces and forms abnormal shapes.

Abnormally shaped transthyretin protein can form clumps called amyloid.

In ATTR-CM, transthyretin amyloid builds up in the heart. This build-up causes the heart to become thick and stiff, making it harder for the heart to pump enough blood to the body. This is called heart failure.

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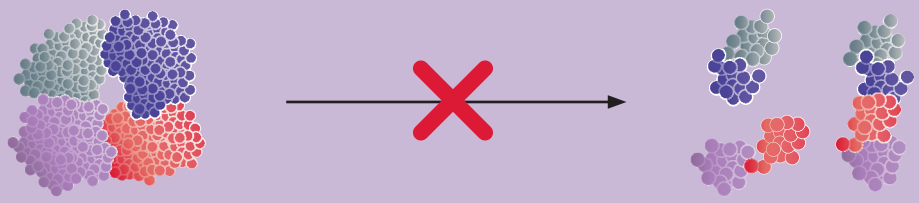
What is tafamidis and how does it work?

Tafamidis is a medicine approved by the US FDA and in several other countries to treat people with ATTR-CM.

Tafamidis helps prevent transthyretin from breaking into pieces and forming abnormal shapes.

- This means that transthyretin amyloid is less likely to build up in the heart and cause heart failure.



Why were ATTR-ACT and its long-term extension study needed?

Before tafamidis was developed, there were no medicines approved to treat ATTR-CM.

The purpose of ATTR-ACT (the initial study) was to find out whether tafamidis helped people with ATTR-CM compared to placebo.

- ATTR-ACT was a Phase 3 study.
- In a Phase 3 study, researchers test how safe a new treatment is and how well it works when a large group of people take it.

In the initial study, people took tafamidis or placebo by mouth for up to 2.5 years.

- A placebo does not contain any active medicine. It looks the same as the study medicine. People do not know if they are taking the study medicine or a placebo.
- People who took tafamidis could receive the currently approved amount of tafamidis ('dose') for ATTR-CM (80 mg) or a lower dose (20 mg).

In a previous report, researchers found that people who took tafamidis rather than placebo:

- Were less likely to die or be admitted to the hospital for heart problems.
- Were able to maintain a better quality of life.

Tafamidis was approved by the US FDA to treat adults with ATTR-CM based on results from the initial study.

After people completed the initial study, they could take part in a long-term extension study.

- The purpose of the extension study is to find out if tafamidis works over a longer period of time. This extension study is still ongoing.
- All people receive tafamidis for up to an additional 5 years in the extension study.

What did this study look at?

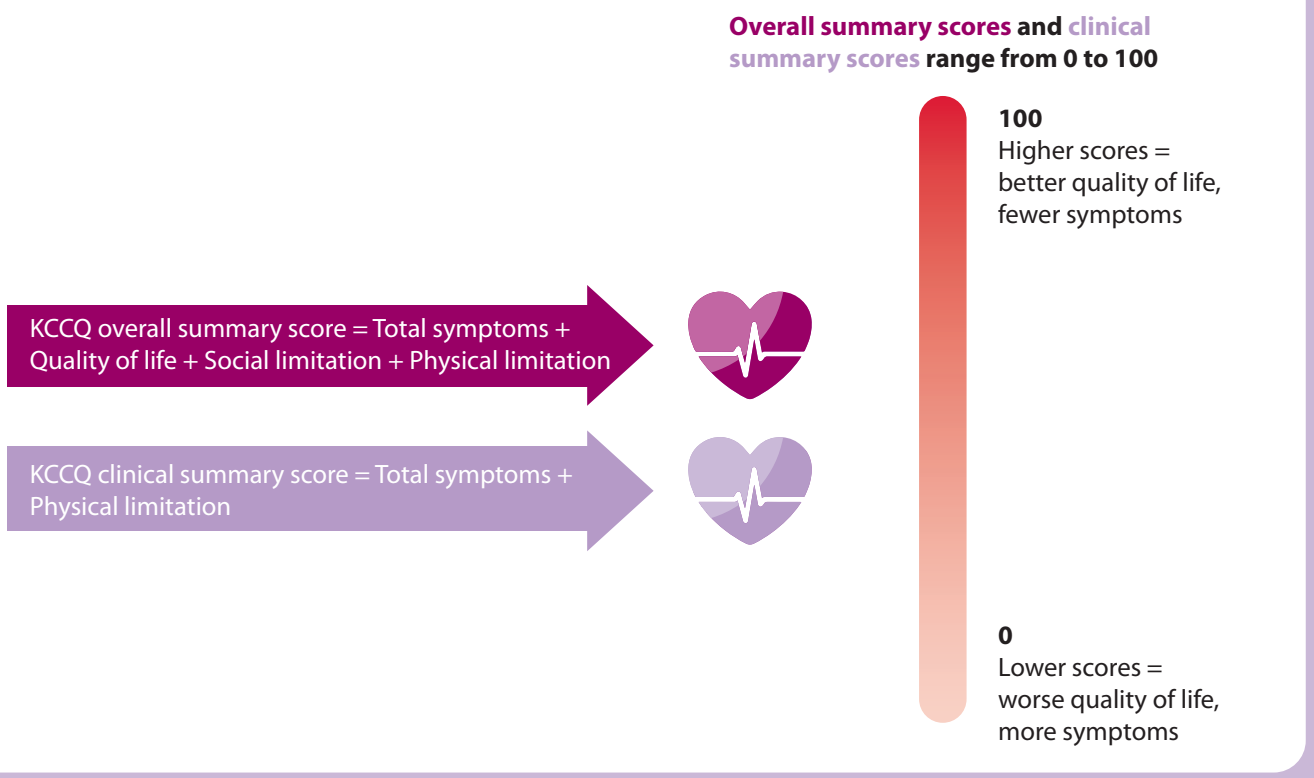
Researchers looked at changes in people's quality of life and heart failure symptoms since they started the initial study.
Researchers measured people's quality of life and symptoms using the Kansas City Cardiomyopathy Questionnaire (KCCQ for short).

- People completed the KCCQ at the start of the initial study and then every 6 months while in the study.

On the KCCQ, people answered 23 questions about:

- Their heart failure symptoms:
  - ➜ How frequent and bothersome are the symptoms? (Total symptoms)
- The effect of their symptoms on their:
  - ➜ Overall enjoyment of life and well-being (Quality of life)
  - ➜ Social activities such as visiting friends and family outside the home (Social limitation)
  - ➜ Everyday activities such as dressing, showering, doing yardwork, and carrying groceries (Physical limitation)

Based on people's responses to the KCCQ, researchers calculated an overall summary score and a clinical summary score:



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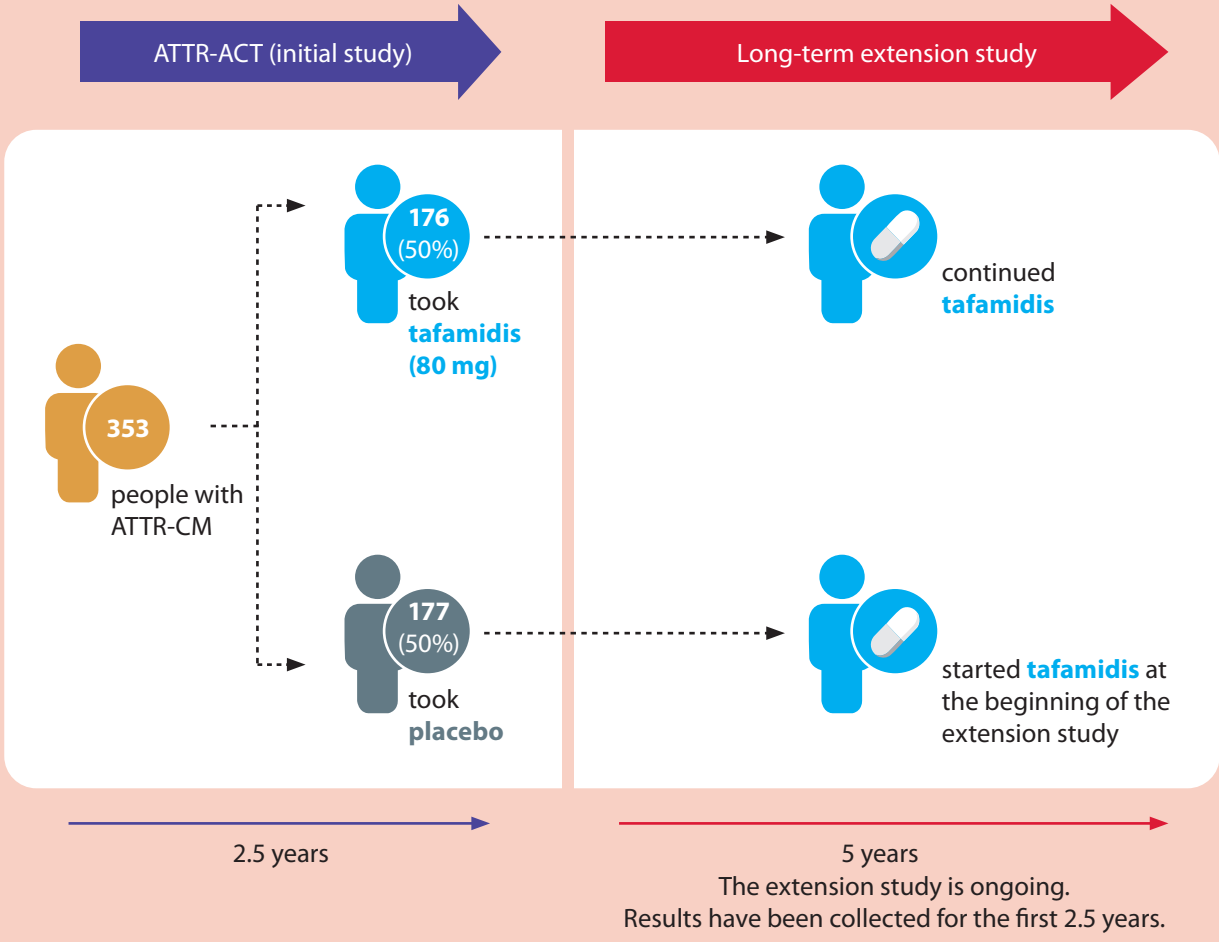
Who took part in this study?

People who completed the initial study and chose to continue in the long-term extension study.

- Only people who took the currently approved dose for ATTR-CM (80 mg) are included.
- People who took a lower dose (20 mg) in the initial study are not included.

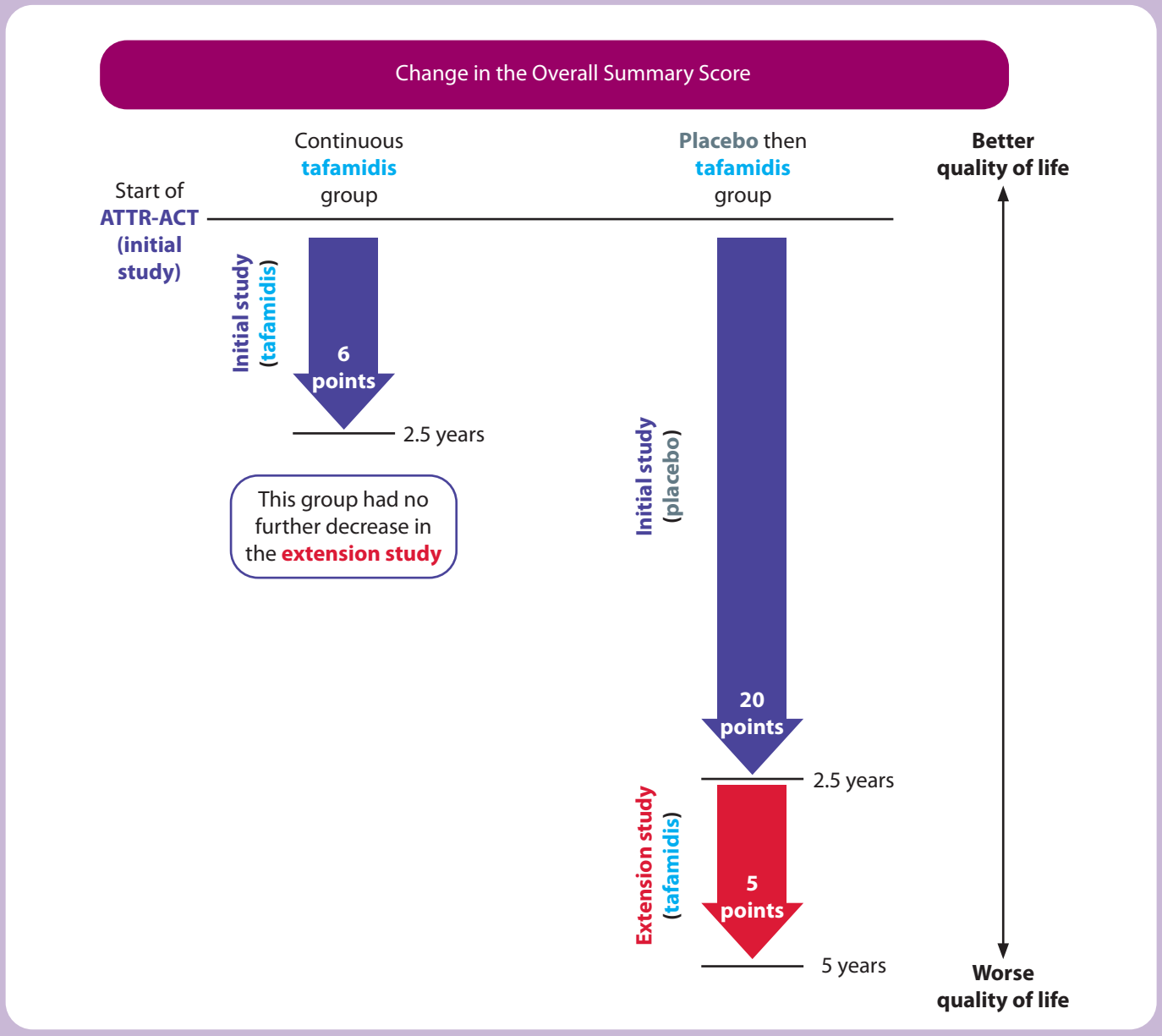
People in this study were an average of 75 years old, and 9 in 10 (90%) were men.

People in the initial study were from Belgium, Brazil, Canada, the Czech Republic, France, Germany, Italy, Japan, the Netherlands, Spain, Sweden, the United Kingdom, or the United States.



What were the results of the study?

- People who took tafamidis or placebo had similar KCCQ scores at the start of ATTR-ACT.
- On average, people who took tafamidis in the initial study and the extension study ('continuous tafamidis group') had a 6-point decrease in the overall summary score during the initial study. There was no further decrease in score in the extension study.
- On average, people who took placebo in the initial study then tafamidis in the extension study ('placebo then tafamidis group') had a 20-point decrease during the initial study and a 5-point decrease during the extension study.
- A decrease of 5 or more points means the person's quality of life has worsened enough to be noticeable ('clinically meaningful').



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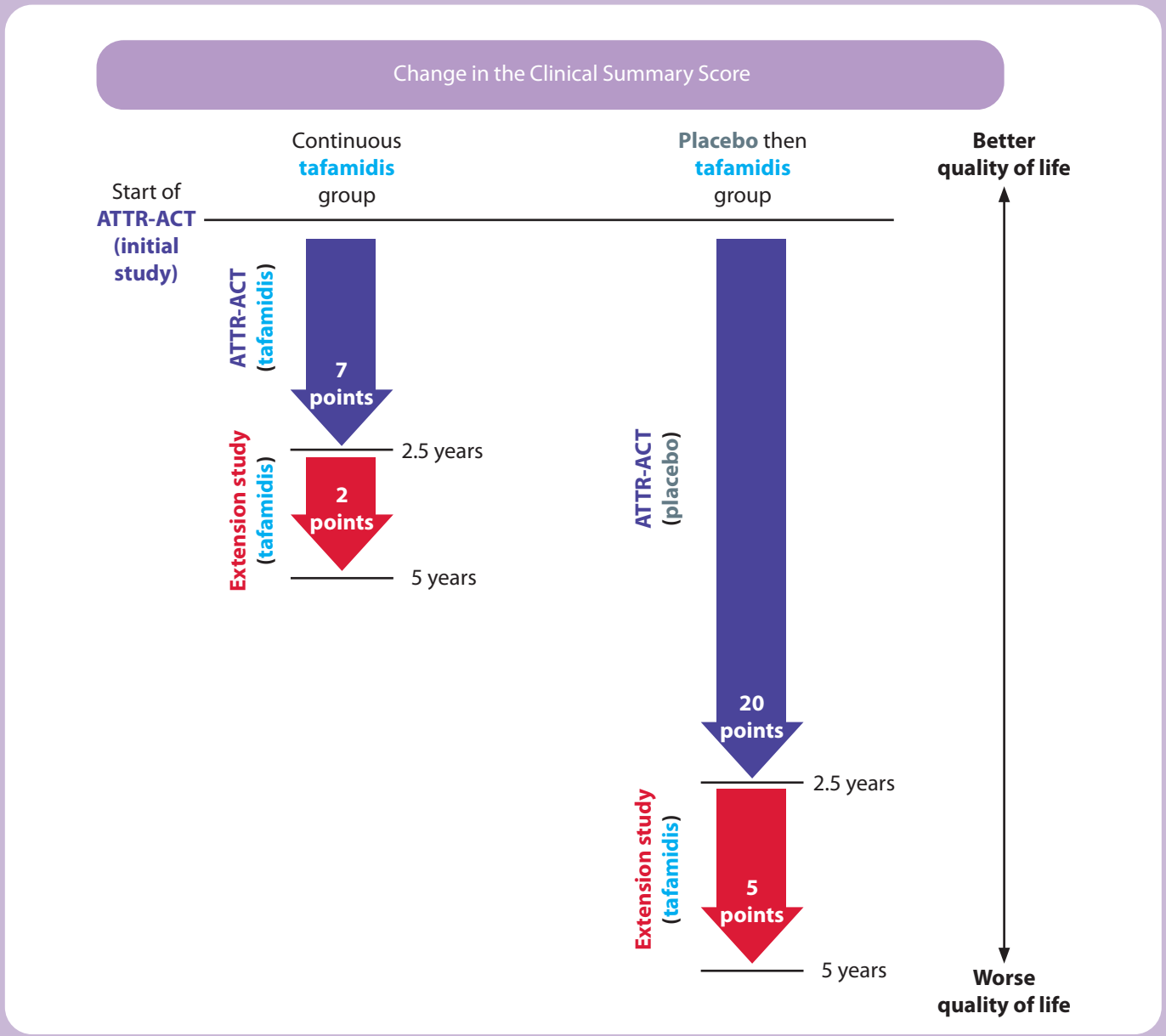
- On average, people in the continuous tafamidis group had a 7-point decrease in the clinical summary score during the initial study and a 2-point decrease during the extension study.
- On average, people in the placebo then tafamidis group had a 20-point decrease during the initial study and a 5-point decrease during the extension study.
- A decrease of 5 or more points is clinically meaningful.



What were the main conclusions reported by the study authors?

- Tafamidis slowed the worsening of quality of life and heart failure symptoms in people with ATTR-CM compared to placebo.
- People who took tafamidis for 5 years were eventually able to maintain, or nearly maintain, their quality of life and heart failure symptoms.
- When people switched from placebo to tafamidis, the worsening of quality of life and heart failure symptoms slowed down.
- Early treatment is important for people with ATTR-CM to receive the most benefit.

Are there any plans for future studies?

The full findings from the long-term extension study will be reported when the study is complete.

Where can I find more information?

Original article citation: Grogan M, Davis MK, Crespo-Leiro MG, et al. Effect of long-term tafamidis treatment on health-related quality of life in patients with transthyretin amyloid cardiomyopathy. *Eur J Heart Fail.* 2024; 26(3): 612-615. You can read the original article at the following website: https://onlinelibrary.wiley.com/doi/10.1002/ejhf.3190

ATTR-ACT start date: December 2013
ATTR-ACT end date: February 2018
Extension study start date: June 2016
Extension study end date: Ongoing at the time of this analysis.

You can read more about ATTR-ACT at the following websites:

- https://clinicaltrials.gov/ct2/show/NCT01994889
- https://www.nejm.org/doi/full/10.1056/NEJMoa1805689

You can read more about the long-term extension at the following websites:

- https://clinicaltrials.gov/ct2/show/NCT02791230
- https://www.tandfonline.com/doi/10.2217/fCA-2022-0096

For more information on clinical studies in general, please visit:

- https://www.clinicaltrials.gov/ct2/about-studies/learn

For more information on amyloidosis, including patient support groups, please visit:

- https://amyloidosis.org (the Amyloidosis Foundation)
- https://arci.org (the Amyloidosis Research Consortium)
- https://www.amyloidosissupport.org (Amyloidosis Support Groups)
- https://mm713.org (Mackenzie's Mission)
- https://rarediseases.org (National Organization for Rare Disorders)
- https://www.myamyloidosispathfinder.org (My Amyloidosis Pathfinder)

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Competing interests disclosure

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript.

Writing disclosure

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