

Comparing 2 eye-injection schedules of aflibercept treatment for people with neovascular (wet) age-related macular degeneration

Date of summary: July 2020

The purpose of this summary is to provide an overview of a research study

- Aflibercept eye injections are approved to treat neovascular age-related macular degeneration.
- Researchers are looking into the optimal schedule to administer this approved medicine.
- This summary reports the results of only 1 study.

How to pronounce medical terms in this summary

Aflibercept <ah-FLIB-er-sept> is also known as Eylea® <EYE-LEE-ah>

Endothelial <EN-doh-THEE-lee-al>

Macula <MACK-you-lah>

Neovascular <KNEE-oh-VAS-cue-LAR>

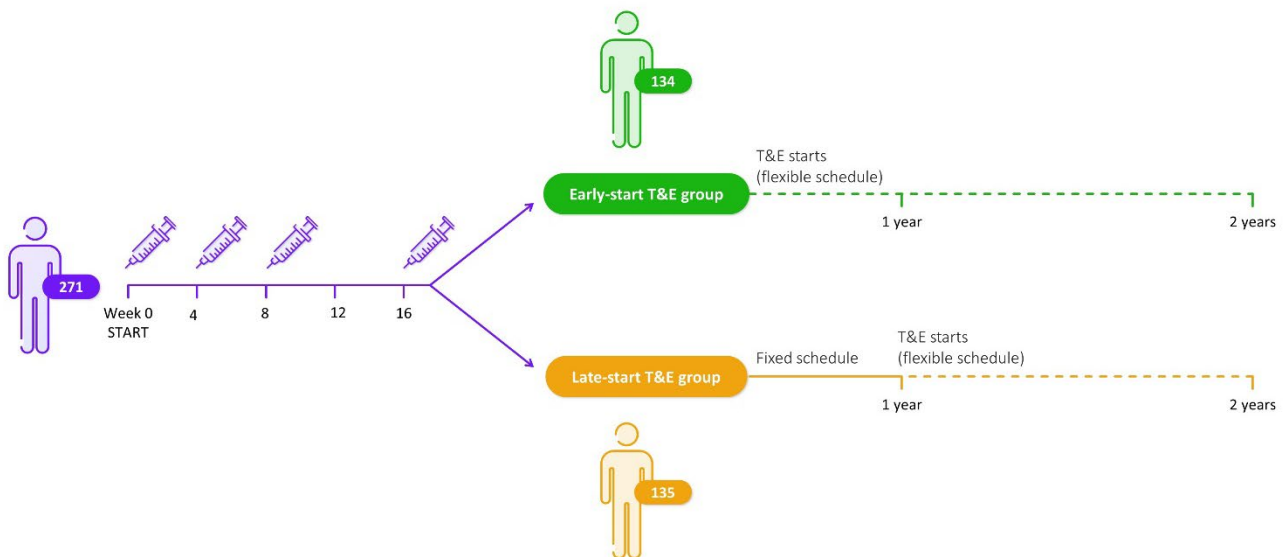
1. What did this study look at?

- Neovascular age-related macular degeneration (nAMD for short) is a condition that affects central vision. It is also known as wet AMD. It usually affects people in their 70s, but can appear as early as 50s and 60s.
 - nAMD happens when abnormal blood vessels grow at the back of the eye and bleed or leak fluid into the layer of sensory cells called the retina.
 - The centre of the retina is called the macula. It is responsible for precise vision, necessary for reading, driving or recognising faces, especially from a distance.
- Aflibercept (also known as Eylea®) is an approved treatment for nAMD. People receive aflibercept as an injection directly into the eye.
 - It blocks a substance called vascular endothelial growth factor (VEGF for short).
 - This prevents blood vessels from growing abnormally and leaking fluid in the retina. This helps to improve vision.
- The greatest improvements in vision usually occur during the first few months of aflibercept treatment. Researchers are now looking at injection schedules that could help maintain these vision improvements and be more convenient for people with nAMD.
- One of the ways to schedule injections is called treat and extend (T&E for short). With T&E, people receive treatment at every visit. In the initial phase, people receive injections at regular intervals. After this, the interval between injections may be increased gradually as long as the condition remains stable. In this way, the frequency of injections is adapted to each person's individual needs.
 - For some people, the condition can be kept under control with less frequent injections. Other people need more frequent injections.
 - Previous studies have shown that the frequency of injections stays similar for each person, although it may need adjusting over time.
- In this study, researchers looked at 2 different types of T&E schedules. After 16 weeks of following the same fixed dosing schedule, people were randomly selected to:
 - Extend treatment intervals immediately (early-start T&E group).
 - Continue with injections every 8 weeks to the end of the year, and then extend treatment intervals during the second year (late-start T&E group).
- The researchers measured changes in vision using a specially designed chart called an ETDRS chart. ETDRS stands for Early Treatment Diabetic Retinopathy Study.
 - The ETDRS chart shows a series of 5 letters on each row, with each row decreasing in size. People read the chart from the top until they can no longer identify 3 of the 5 letters on a row.
 - Vision is considered to be maintained if fewer than 15 letters are lost.
- This summary looks at whether early-start T&E worked as well as late-start T&E. The researchers looked at:
 - How many letters people could read on the ETDRS chart.

- The amount of fluid and swelling at the back of the eye, based on the thickness of the retina. This was measured using a special OCT camera. OCT stands for optical coherence tomography.
- How many injections people received overall.

2. Who took part in this study?

- 271 people with nAMD took part in this study.
 - They were aged 50 years or older.
 - They had not received treatment for nAMD before.
- The people were from 8 different countries: Australia, Canada, France, Germany, Hungary, Italy, Spain and the United Kingdom.

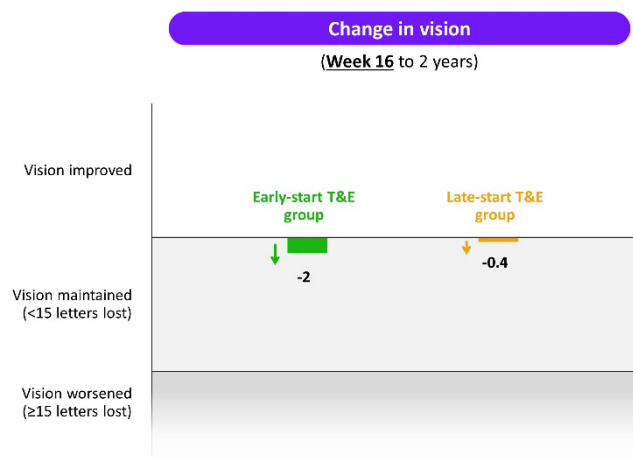


- Once people started T&E, the time between their injections could be increased by 2 weeks at a time. This was based on lack of swelling of their retina, measured at each visit. The longest time allowed between injections in this study was 16 weeks.

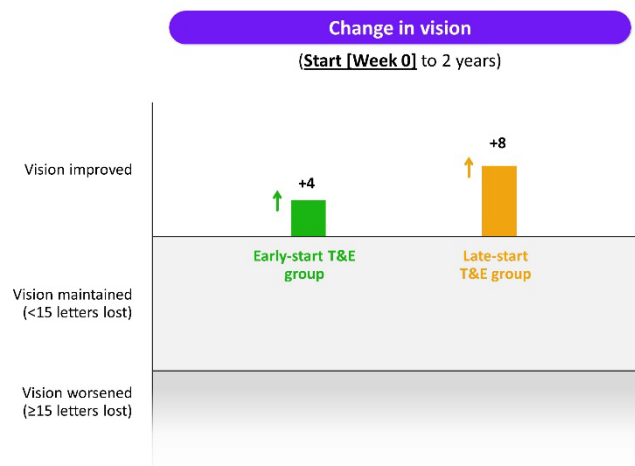
3. What were the results of the study?

People had similar changes in their vision whether they started T&E early or late

- The researchers looked at how many letters people could read on the ETDRS chart at 16 weeks (when they were randomly selected to start T&E early or late) compared with 2 years. This allowed researchers to check how well their vision was being maintained on the different schedules.
 - People who started T&E early could read around 2 fewer letters on average (vision was maintained: a difference of 2 letters is not considered meaningful).
 - People who started T&E late could read about the same number of letters on average (vision was maintained).



- The researchers also compared how many letters people could read on an eye chart at the start of the study (Week 0) compared with 2 years.
 - People who started T&E early could read around 4 more letters, on average.
 - People who started T&E late could read around 8 more letters, on average.



- Between the start of the study (Week 0) and 2 years, almost everyone maintained their vision.
 - Around 9 in 10 people (94%) who started T&E early maintained their vision.
 - Around 9 in 10 people (96%) who started T&E late maintained their vision.

People had similar changes in swelling at the back of the eye, whether they started T&E early or late

- Researchers compared retinal thickness between the start of the study (Week 0) and 2 years. They measured this in one-millionths of a metre (micrometres or μm).
 - On average, retinal thickness decreased by 162 μm for people who started T&E early and 159 μm for people who started T&E late.
 - Retinal thickness at the end of the study was around 300 μm , so a difference of 3 μm between the 2 groups is insignificant.

People who started T&E early had 1 fewer injection overall than people who started T&E late

- On average, people who started T&E early had 12 injections over the 2-year study. People who started T&E late had 13 injections.

People had similar times between injections by the end of the study

- The average time between injections by the end of the study (2 years) was:
 - 11.5 weeks for people who started T&E early.
 - 11.4 weeks for people who started T&E late.

The researchers did not find any new or unexpected adverse events in this study. The adverse events were similar to those reported in other studies of aflibercept. All adverse events that appeared during the study are reported but not all adverse events were caused by aflibercept. Serious adverse events are those that may require hospitalisation, be considered as life threatening or may cause lasting problems

- Around 8 in 10 people had adverse events, whether they started T&E early or late.
 - For most people in each group, these adverse events were mild or moderate.
 - Around 2 in 10 people (22%) who started T&E early had a serious adverse event.
 - Around 2 in 10 people (26%) who started T&E late had a serious adverse event.

- Only 4 people in total (1.4%) had a serious adverse event that was likely to be related to aflibercept.
 - 2 people who started T&E late and 2 people who started treatment but had not yet been put into a group had a serious adverse event that was likely to be related to aflibercept.
- Around 5 in 10 people had adverse events related to the eye, whether they started T&E early or late.
 - Nobody (0%) who started T&E early had a serious eye adverse event.
 - Fewer than 1 in 10 people (3%) who started T&E late had a serious eye adverse event.
 - None of these serious eye adverse events were likely to be related to aflibercept.

4. What were the main conclusions reported by the researchers?

- In this study, people with nAMD had similar outcomes regardless of whether they started T&E treatment with aflibercept early or late.
- People who started T&E early had 1 fewer injection overall than people who started T&E late.
- Allowing people to start T&E earlier could help their treatment to be individualised.
 - Extending the time between injections could make treatment more convenient for some people with nAMD receiving aflibercept injections.
 - Reducing the number of appointments for some people could also reduce the pressure on clinics.

5. Are there any plans for further studies?

- This study is completed.
- There is another study ongoing that is looking at the effects of flexible dosing schedules on vision for people with nAMD who are receiving aflibercept.
 - This study is called XTEND.
 - The study ID number is NCT03939767.

6. Who sponsored this study?

Bayer Consumer Care AG, Switzerland

Bayer would like to thank everyone who took part in this study.

Further information

- Study ID number: NCT02581891
Study start date: November 2015
Study end date: April 2019
- The full title of this article is: Efficacy and safety of intravitreal aflibercept using a treat-and-extend regimen for neovascular age-related macular degeneration: the ARIES study
 - You can find the full article here: <https://doi.org/10.1097/iae.0000000000003128>
 - You can access the full article for free.

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