

# Supplementary materials

## Supplemental Methods

All data, including diagnoses and treatments, were self-reported and could not be verified by cross-checks with medical records. In terms of the anticipated sample size for this survey, we estimated that 180–240 patients would complete this exploratory survey for Cohort 1 and 100 for Cohort 2. No power analysis or sample size calculation was done.

The main questionnaire (**Supplemental Tables 2 and 3**) was assessed and validated internally via face-to-face interviews with six nAMD patients individually (four who had discontinued anti-VEGF therapy and two continuing anti-VEGF therapy). Following these interviews, the pre-defined reasons were modified in terms of the clarity of the wording, avoiding duplicated meanings, and inclusion of the most expected reasons.-

All respondents were also asked to complete validated Japanese versions of the EQ-5D-5L to assess health-related quality of life and the PAM-13 to measure patient activation levels [1]. The PAM-13 is a 13-item questionnaire designed to assess the patient's knowledge, skill, and confidence with self-managing their health or disease [2-4]. Each item comprises four possible responses (disagree strongly/disagree/agree/agree strongly/not applicable), which are converted to a scale of 0–100, where higher levels indicate more proactive attitudes towards managing own health.

## References

1. Herdman, M.; Gudex, C.; Lloyd, A.; Janssen, M.; Kind, P.; Parkin, D.; Bonnel, G.; Badia, X. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* **2011**, *20*, 1727-1736, doi:10.1007/s11136-011-9903-x.
2. Fujita, E.; Kuno, E.; Kato, D.; Kokochi, M.; Uehara, K. Development and validation of the Japanese version of the Patient Activation Measure 13 for Mental Health. *Seishin Igaku* **2010**, *52*, 765-772 (in Japanese).
3. Hibbard, J.H.; Mahoney, E.R.; Stockard, J.; Tusler, M. Development and testing of a short form of the patient activation measure. *Health Serv Res* **2005**, *40*, 1918-1930, doi:10.1111/j.1475-6773.2005.00438.x.
4. Hibbard, J.H.; Stockard, J.; Mahoney, E.R.; Tusler, M. Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. *Health Serv Res* **2004**, *39*, 1005-1026, doi:10.1111/j.1475-6773.2004.00269.x.

**Table S1.** Patient questionnaire.

<b>Questions</b>	<b>Responses</b>
<b>Screening questions</b>	
Have you been diagnosed with age-related macular degeneration (AMD) by a physician?	<ul style="list-style-type: none"> <li>• Yes</li> <li>• No</li> <li>• Not sure</li> </ul>
Have you received anti-VEGF therapy to treat your AMD?	<ul style="list-style-type: none"> <li>• Yes</li> <li>• No</li> <li>• Not sure</li> </ul>
Has it been 6 months or longer since you last received anti-VEGF therapy?	<ul style="list-style-type: none"> <li>• Yes (Cohort 1)</li> <li>• No (Cohort 2)</li> </ul>
If Cohort 1: Was it your doctor's decision to not have anti-VEGF therapy in the last few months?	<ul style="list-style-type: none"> <li>• Yes (Cohort 1-1)</li> <li>• No (Cohort 1-2)</li> </ul>
If Cohort 1-1: How would you describe your current situation regarding anti-VEGF therapy?	<ul style="list-style-type: none"> <li>• I completed treatment</li> <li>• I am still continuing follow-up visits</li> </ul>
Sex	<ul style="list-style-type: none"> <li>• Male</li> <li>• Female</li> </ul>
Age	<ul style="list-style-type: none"> <li>• &lt;50 years</li> <li>• 50–59 years</li> <li>• 60–69 years</li> <li>• 70–79 years</li> <li>• ≥80 years</li> </ul>
Place of residence	<ul style="list-style-type: none"> <li>• Japan scale</li> </ul>
<b>General questions</b>	
Are you living with family?	<ul style="list-style-type: none"> <li>• Yes</li> <li>• No</li> </ul>
Who are they?	<ul style="list-style-type: none"> <li>• Spouse/partner</li> <li>• Children</li> <li>• Other</li> </ul>
Are you currently employed?	<ul style="list-style-type: none"> <li>• Yes</li> <li>• No</li> </ul>
What is your highest level of education?	<ul style="list-style-type: none"> <li>• Middle school</li> <li>• High school</li> <li>• Vocational school</li> <li>• Junior college</li> <li>• University</li> <li>• Post-graduate school</li> </ul>
How often do you smoke?	<ul style="list-style-type: none"> <li>• Everyday</li> <li>• Sometimes</li> <li>• Used to smoke</li> <li>• Never smoked</li> </ul>
<b>Comorbidities</b>	
Other than AMD, what illnesses do you have? (multiple choice)	<ul style="list-style-type: none"> <li>• Glaucoma</li> <li>• Cataract</li> <li>• Cerebrovascular disease</li> <li>• Heart disease</li> <li>• Diabetes mellitus</li> <li>• Hypertension</li> <li>• Hyperlipidemia</li> <li>• Cancer</li> <li>• Other</li> <li>• None</li> </ul>
<b>Eye-related questions</b>	

Regarding your eye condition, what do you find difficult in daily life?  
(multiple choice)

- To recognize people's faces or objects
- To read books or newspapers
- To drive
- To go out alone
- Other
- No particular difficulties
- 0.01–0.1
- 0.2–0.3
- 0.4–0.6
- 0.7–1.0
- $\geq 1.2$
- Not sure

What is your current visual acuity?

### Diagnosis-related questions

When were you diagnosed with AMD?

- Within 1 year
- Within 3 years
- Within 5 years
- Within 10 years
- $\geq 10$  years
- One eye
- Both eyes
- Good
- Quite good
- Not quite good
- Not good at all

Do you have AMD in one eye or both eyes?

What was your level of understanding of AMD at the beginning of your diagnosis/treatment?

### Anti-VEGF therapy related questions

Type of hospital

- Eye clinic (primary care)
- Eye hospital with referral
- Eye hospital without referral (personal choice of secondary care)

Time to get to hospital

- $< 30$  minutes
- $\geq 30$  minutes
- $\geq 1$  hour
- $\geq 1.5$  hours

How did (do) you travel to hospital

- By car
- By taxi
- By public transport (train, bus, etc.)
- By bicycle
- On foot

Did (does) someone accompany you to hospital?

- Yes
- No
- $< 3$  months
- $\geq 3$  months
- $\geq 1$  year
- $\geq 3$  years
- $\geq 5$  years

How long have you continued anti-VEGF therapy?  
(approximate time from the first to last injection)

Frequency of visits

- Every month
- Every 2 months
- Every 3 months
- Every 6 months
- Neither applies

Frequency of injections

- Every month
- Every 2 months
- Every 3 months
- Every 6 months
- Neither applies

What was the cost per visit when you had (have) an injection?	<ul style="list-style-type: none"> <li>• &lt;10,000 JPY</li> <li>• 10,000–29,999 JPY</li> <li>• 30,000–49,999 JPY</li> <li>• ≥50,000 JPY</li> </ul>
What is your relationship with your doctor?	<ul style="list-style-type: none"> <li>• Very good</li> <li>• Good</li> <li>• Neither good nor bad</li> <li>• Not good</li> <li>• Not good at all</li> </ul>
What is your current level of understanding of AMD?	<ul style="list-style-type: none"> <li>• Good</li> <li>• Quite good</li> <li>• Not quite good</li> <li>• Not good at all</li> </ul>

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AMD, age-related macular degeneration; VEGF, vascular endothelial growth factor.

**Table S2.** Main questionnaire: reasons for discontinuing anti-VEGF therapy in Cohort 1.

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Topic	<p><b><i>CI-1: Other than the doctor’s decision, please specify whether each of the statements below is true in explaining your reason for discontinuing anti-VEGF therapy.</i></b></p> <p><b><i>CI-2: Please specify whether each of the statements below is true in explaining your reason for discontinuing anti-VEGF therapy.</i></b></p>
Efficacy	<ul style="list-style-type: none"> <li>• Because the treatment was ineffective</li> <li>• Because there was no deterioration in vision</li> </ul>
Finance	<ul style="list-style-type: none"> <li>• Because of financial burden</li> </ul>
Understanding	<ul style="list-style-type: none"> <li>• Because I was not sure why I should continue the treatment</li> </ul>
Visits	<ul style="list-style-type: none"> <li>• Because I had to visit hospital too often</li> <li>• Because transport to hospital was inconvenient</li> <li>• Because treatment was time-consuming including long wait times</li> <li>• <i>If you were in need of a companion</i>, because it was hard to find someone who could take me to hospital</li> </ul>
Treatment	<ul style="list-style-type: none"> <li>• Because treatment required injections too many times</li> <li>• Because it was scary to have an injection in the eye</li> <li>• Because the feeling of the injection was unpleasant</li> <li>• Because I was dissatisfied with the doctor</li> </ul>
Etc.	<ul style="list-style-type: none"> <li>• Because I had another disease I had to prioritize over AMD</li> <li>• Because I was concerned about side effects</li> </ul>

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All reasons were presented in a random order, and had four possible responses: definitely true, mostly true, mostly false, definitely false. AMD, age-related macular degeneration; VEGF, vascular endothelial growth factor.

**Table S4.** Reasons for treatment discontinuation in Cohort 1.

	Cohort 1-1 (discontinued due to doctor's decision) ( <i>n</i> = 185)					Cohort 1-2 (discontinued due to their own decision) ( <i>n</i> = 22)				
	<b>True</b> (= Definitely true + Mostly true)	Definitely true	Mostly true	Mostly false	Definitely false	<b>True</b> (= Definitely true + Mostly true)	Definitely true	Mostly true	Mostly false	Definitely false
There was no deterioration in vision	<b>65 (35.1)</b>	36 (19.5)	29 (15.7)	26 (14.1)	94 (50.8)	<b>15 (68.2)</b>	7 (31.8)	8 (36.4)	3 (13.6)	4 (18.2)
The treatment was ineffective	<b>36 (19.5)</b>	10 (5.4)	26 (14.1)	34 (18.4)	115 (62.2)	<b>10 (45.5)</b>	7 (31.8)	3 (13.6)	5 (22.7)	7 (31.8)
Financial burden	<b>24 (13.0)</b>	3 (1.6)	21 (11.4)	33 (17.8)	128 (69.2)	<b>12 (54.5)</b>	6 (27.3)	6 (27.3)	2 (9.1)	8 (36.4)
It was scary to have an injection in the eye	<b>21 (11.4)</b>	4 (2.2)	17 (9.2)	34 (18.4)	130 (70.3)	<b>8 (36.4)</b>	4 (18.2)	4 (18.2)	4 (18.2)	10 (45.5)
Treatment was time-consuming including long waiting times	<b>20 (10.8)</b>	4 (2.2)	16 (8.6)	33 (17.8)	132 (71.4)	<b>9 (40.9)</b>	2 (9.1)	7 (31.8)	7 (31.8)	6 (27.3)
The feeling of the injection was unpleasant	<b>18 (9.7)</b>	6 (3.2)	12 (6.5)	31 (16.8)	136 (73.5)	<b>5 (22.7)</b>	2 (9.1)	3 (13.6)	5 (22.7)	12 (54.5)
I was not sure why I should continue the treatment	<b>16 (8.6)</b>	5 (2.7)	11 (5.9)	33 (17.8)	136 (73.5)	<b>10 (45.5)</b>	7 (31.8)	3 (13.6)	5 (22.7)	7 (31.8)
I had to visit hospital too often	<b>12 (6.5)</b>	1 (0.5)	11 (5.9)	39 (21.1)	134 (72.4)	<b>4 (18.2)</b>	0	4 (18.2)	11 (50.0)	7 (31.8)
Treatment required injections too many times	<b>12 (6.5)</b>	0	12 (6.5)	38 (20.5)	135 (73.0)	<b>5 (22.7)</b>	0	5 (22.7)	4 (18.2)	13 (59.1)
I was dissatisfied with the doctor	<b>10 (5.4)</b>	2 (1.1)	8 (4.3)	29 (15.7)	146 (78.9)	<b>4 (18.2)</b>	2 (9.1)	2 (9.1)	9 (40.9)	9 (40.9)
Transport to hospital was inconvenient	<b>8 (4.3)</b>	0	8 (4.3)	28 (15.1)	149 (80.5)	<b>7 (31.8)</b>	1 (4.5)	6 (27.3)	6 (27.3)	9 (40.9)
I had another disease I had to prioritize over AMD	<b>8 (4.3)</b>	2 (1.1)	6 (3.2)	23 (12.4)	154 (83.2)	<b>3 (13.6)</b>	0	3 (13.6)	4 (18.2)	15 (68.2)
I was concerned with side effects	<b>7 (3.8)</b>	1 (0.5)	6 (3.2)	37 (20.0)	141 (76.2)	<b>3 (13.6)</b>	0	3 (13.6)	6 (27.3)	13 (59.1)
<i>If you were in need of a companion, it was hard to find someone who could take me to hospital</i>	<b>4 (2.2)</b>	1 (0.5)	3 (1.6)	24 (13.0)	157 (84.9)	<b>0</b>	0	0	7 (31.8)	15 (68.2)

Values are *n* (%). AMD, age-related macular degeneration.

**Table S5.** Reasons for dissatisfaction with treatment in Cohort 2 ( $n = 65$ ).

	<b>True</b> (= Definitely true + Mostly true)	Definitely true	Mostly true	Mostly false	Definitely false
Treatment is time-consuming with long waiting times	<b>50 (76.9)</b>	20 (30.8)	30 (46.2)	8 (12.3)	7 (10.8)
Financial burden	<b>46 (70.8)</b>	22 (33.8)	24 (36.9)	9 (13.8)	10 (15.4)
Treatment is ineffective	<b>38 (58.5)</b>	9 (13.8)	29 (44.6)	20 (30.8)	7 (10.8)
Feeling of the injection is unpleasant	<b>34 (52.3)</b>	10 (15.4)	24 (36.9)	25 (38.5)	6 (9.2)
I am scared of having an injection in the eye	<b>33 (50.8)</b>	9 (13.8)	24 (36.9)	24 (36.9)	8 (12.3)
Injections are required too often	<b>31 (47.7)</b>	7 (10.8)	24 (36.9)	24 (36.9)	10 (15.4)
I have to visit the hospital too often	<b>27 (41.5)</b>	5 (7.7)	22 (33.8)	27 (41.5)	11 (16.9)
Transport to hospital is inconvenient	<b>22 (33.8)</b>	4 (6.2)	18 (27.7)	26 (40.0)	17 (26.2)
I am concerned about side effects	<b>20 (30.8)</b>	2 (3.1)	18 (27.7)	27 (41.5)	18 (27.7)
It is unclear why I should continue treatment	<b>19 (29.2)</b>	4 (6.2)	15 (23.1)	32 (49.2)	14 (21.5)
I have another disease more severe than AMD	<b>15 (23.1)</b>	5 (7.7)	10 (15.4)	22 (33.8)	28 (43.1)
I am dissatisfied with the doctor	<b>12 (18.5)</b>	0	12 (18.5)	29 (44.6)	24 (36.9)
<i>If you are in need of a companion, it is hard to find someone who can take me to hospital</i>	<b>9 (13.8)</b>	3 (4.6)	6 (9.2)	13 (20.0)	43 (66.2)

Values are  $n$  (%). AMD, age-related macular degeneration.