Understanding the patient voice in hereditary transthyretin-mediated amyloidosis (ATTR amyloidosis)
Summary of the patient voice survey

- The survey ran from September 4–30, 2015
- Only patients with hereditary ATTR amyloidosis were eligible to complete the survey
- Patients were classified according to whether the primary involvement was neuropathy, cardiomyopathy, or both
- 64 patients completed the survey
- The survey was supported by the Amyloidosis Foundation and the Amyloidosis Support Groups
Survey objectives and patient demographics

- The objective of the survey was to collect data to help raise awareness of the patient journey for hereditary ATTR amyloidosis.
- The survey was an online, interactive tool, completed by patients or caregivers on behalf of patients.

<table>
<thead>
<tr>
<th></th>
<th>N=64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>57.9</td>
</tr>
<tr>
<td>Male/female, n (%)</td>
<td>43 (67)/ 21 (33)</td>
</tr>
<tr>
<td>Patient/caregiver, n (%)</td>
<td>60 (94)/ 4 (6)</td>
</tr>
<tr>
<td>Organ involvement, n (%)</td>
<td></td>
</tr>
<tr>
<td>Neuropathy</td>
<td>28 (44)</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>9 (14)</td>
</tr>
<tr>
<td>Both (neuropathy+cardiomyopathy)</td>
<td>27 (42)</td>
</tr>
<tr>
<td>Family history of disease, n (%)</td>
<td>49 (77)</td>
</tr>
<tr>
<td>Receiving amyloidosis-specific medication, n (%)</td>
<td>43 (67)</td>
</tr>
</tbody>
</table>
Patient journey

Most patients have a family history of disease

- A constellation of symptoms were initially observed, which seriously impacted QoL
- Progressive symptoms imparted heavy burden of disease
- Many specialists were seen, and a delay in diagnosis and/or misdiagnosis were reported
- Family history did not always expedite diagnosis
- Most patients were seeing a specialist
- Yet many patients were not on treatment, or receiving investigational therapies

QoL, quality of life
Almost three-quarters of patients were at least 50 years of age.

- <50 years old: 26.6%
- ≥50 years old: 73.4%

N=64

Mean age = 57.9 (range, 28–77) years
Majority of patients have neuropathy, and 77% have a family history of disease.

Cardiomyopathy is present in over half of the patients (56%).

- **Neuropathy (n=28):**
  - With family history: 44 patients (39.1%)
  - Without family history: 7.8 patients (6.3%)

- **Cardiomyopathy (n=9):**
  - With family history: 14 patients (12.5%)

- **Both (N+C) (n=27):**
  - With family history: 29.7 patients (29.7%)

**QS1.** What type of amyloidosis do you have?
**QS10.** Do you have a family history of amyloidosis TTR-FAP and/or TTR-FAC?
Initial symptoms of disease were multi-systemic

- Dizziness/lightheadedness = 3% of patients
- Stomach/intestines = 17%
- Chest = 23%
- Hand/arm = 39%
- Leg = 25%
- Foot/toes = 48%
- Eyes = 5%
- Genital area = 2%

N=64

Foot/toe symptoms were typically the first symptoms experienced

However, hand/arm symptoms were initially observed in nearly 40% of patients
Symptoms impact a number of facets of patient functioning

Patients had at least some difficulty with:

**Fine motor skills**
- 55%
- 33%
- 39%
- 22%

**Bathroom/self-care**
- 31%
- 14%
- 31%
- 31%

**Movement/mobility**
- 72%
- 52%
- 34%

**Acts of daily living**
- 31%
- 22%
- 27%

N=64

QB3. How does amyloidosis affect your daily life?
At completion of the survey, ~1 in 5 patients (11/64) were unable to take care of themselves most of the time/at all.

There was a heavy disease burden for patients and caregivers.

Mental health/outlook on life is affected in 35/64 (55%) of patients:
- Anxiety = 25/35 (71%) patients
- Stress = 22/35 (62%) patients
- Depression = 15/35 (43%) patients

Some quotes on how amyloidosis has impacted mental health:
- "Preparing myself and children for the inevitable"
- "Physical limitations stop me doing things I love"
- "Anger, impatience"
Patient mobility was impacted by the disease

Almost half of patients (45%) have suffered falls

6% of patients had broken or fractured a bone as a result of an amyloidosis-related fall

QB1_2. Do you need help with walking?
QB1_3. Do you ever need to use a walking stick?
QB_4. Do you ever need to use a wheelchair?
QB1_5. Have you fallen over?
QB1A1_1. Have you ever broken or fractured a bone as a result of an amyloidosis-related fall?
A range of specialists were consulted before patients were correctly diagnosed.

N=64
(41 patients [64%] saw >1 type of specialist clinician)

Prior to diagnosis, primary care physicians and neurologists were the most common clinician that provided consultation.

*Other specialists seen include: genetic counselor, nephrologist, hematologist, ophthalmologist, rheumatologist, urologist, oncologist, surgeon, pulmonologist
Disease misdiagnosis was not uncommon

Was your amyloidosis misdiagnosed as another disorder?

Yes 45%

No 55%

N=64

Misdiagnosed conditions:

- Ocular herpes
- Spinal problem
- IBS
- CHF
- COPD
- Plantar fasciitis
- Fibromyalgia
- Idiopathic PN
- Bronchitis GERD
- Asthma
- Gastroparesis
- Sjogren’s syndrome
- NSAID-induced constipation

Carpal tunnel syndrome (6/64) was the most common misdiagnosis
The majority of patients required numerous specialist visits before correct diagnosis.

For 1 in 5 patients, 1 visit to see a doctor was sufficient, but a large proportion required up to 10 doctors’ visits before diagnosis.

Some patients even required >20 doctors’ visits prior to diagnosis.

N=64
(Specialty/specialist may have been visited more than once)
Time to diagnosis was similar irrespective of family history of disease

With or without family history, the majority of patients were diagnosed within 2–3 years of symptom onset.

However, delayed diagnosis (>10 years after symptom onset) was observed in patients with a family history of disease.

QS5. What was the duration of time between you first experiencing symptoms of amyloidosis and your confirmed diagnosis of amyloidosis?
The majority of patients were seen at an amyloidosis center

A little over one-quarter of patients have not been to an amyloidosis center

QK1. Are you currently seeing a doctor at an amyloidosis specialist center?
1 in 5 patients have had a liver transplant

Following liver transplant, 4/13 patients (31%) reported no improvement in symptoms; Slowing/halt of symptom progression post-transplant was not measured

2/13 patients have received amyloidosis-specific medication after liver transplant

QK3. Are you currently receiving any amyloidosis-specific medication?
QK4. What medication are you currently receiving?
The majority of patients are receiving amyloidosis-specific or investigational drug Diflunisal (44%) Not taking a TTR stabilizer (54%) (5 patients are taking >1 medication)

67% are receiving an amyloidosis treatment*

<table>
<thead>
<tr>
<th>Therapy, n (%)</th>
<th>(n=43)</th>
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<tbody>
<tr>
<td>Diflunisal</td>
<td>19 (44)</td>
</tr>
<tr>
<td>ISIS-TTR&lt;sub&gt;Rx&lt;/sub&gt;</td>
<td>15 (35)</td>
</tr>
<tr>
<td>Patisiran</td>
<td>5 (12)</td>
</tr>
<tr>
<td>Doxy/TUDCA</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Revusiran</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Doxy only</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Tafamidis</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

*Patients may have received medication during participation in a clinical trial

Approximately half of the patients (47%) prescribed amyloidosis-specific therapy are taking a TTR stabilizer

QK3. Are you currently receiving any amyloidosis-specific medication? QK4. What medication are you currently receiving?

Doxy, doxycycline; TUDCA, tauroursodeoxycholic acid
Patient education and support

58% of patients requested additional support/information

Further support requested included:
- More disease information (11/64)
- More information on trials (11/64)
- Emotional support (5/64)

QK5. Do you think you were given enough information about amyloidosis when you were first diagnosed?

QS6.2. Do you feel knowledgeable about clinical trials in amyloidosis?
Summary

- The pathway to diagnosis can be complex, involving many specialists, and can be prolonged if disease is not recognized early after symptom onset
  - Family history does not always reduce delay in diagnosis
- Fine motor skills are commonly affected by the disease, difficulty is also observed in performing more common tasks (e.g., walking up stairs)
  - Disease also creates a burden for caregivers
- Mobility is impacted by the disease, with >25% of patients dependent on a cane or wheelchair most/all of the time
- Approximately 2 in 3 patients (67%) are taking an amyloidosis directed treatment or investigational therapy
  - The most common medication taken is diflunisal (19/64), although a variety of investigational agents are being used
  - Liver transplantation was performed in 20% of patients
Thank you to all patients and caregivers who have completed this survey. Your answers have provided genuine insight into the burden of ATTR amyloidosis.
Initial symptoms differed according to disease type

- Initial foot/toe and leg symptoms were more common in patients with neuropathy only.
- As expected, chest symptoms were frequently observed first in patients with cardiomyopathy only.
- Initial hand/arm symptoms occurred more frequently in patients with both cardiomyopathy and neuropathy vs neuropathy alone.

N=64

QS2: First experienced symptoms of amyloidosis
The number of visits before diagnosis was similar regardless of family history of disease. However, even with a family history, >20 visits were required before diagnosis for some patients.

A slightly higher proportion of patients with family history were diagnosed on the first visit to a doctor.
Patients with a family history were most frequently diagnosed by a neurologist.

65% (32/49) of patients with family history of disease saw >1 type of specialist ahead of correct diagnosis vs 80% (12/15) without family history.
There was a heavy disease burden for patients and caregivers

At completion of the survey ~1 in 5 patients (11/64) were unable to take care of themselves most of the time/at all

Greater than 10% (≥7/64) of patients were unable to:

- Push shopping cart around: 13%
- Catch a small object: 22%
- Bend to pick up a small object: 11%
- Walk up a flight of stairs: 23%
- Walk in busy street: 20%
- Travel on bus/train: 11%
- Walk ~0.5 miles: 19%
- Carry a heavy object: 19%
- Dance: 25%
- Drive a car: 11%

N=64

QB1.1. Are you able to take care of yourself?
QB3. How does amyloidosis affect your daily life?
Many patients are diagnosed shortly after symptom onset, but those who are not may wait a number of years before correct diagnosis.

For ~1 in 10 patients, diagnosis took >6 years after onset of symptoms.