Hereditary Transthyretin Amyloidosis (hATTR): Burden of Disease and Treatment Perspectives

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BACKGROUND

- Hereditary transthyretin-mediated amyloidosis (hATTR) is a severe, progressive, and life-threatening disease characterized by the accumulation of misfolded proteins (amyloid) in tissues and organs
- hATTR is caused my mutations in the gene encoding transthyretin. More than 120 mutations have been identified; Val30Met is predominant in Portugal, Spain, France, Japan, and Sweden
- Val30Met is most common, generally associated with early onset, and is also known as familial amyloid polyneuropathy (ATTR-FAP)
- Liver transplant is an established treatment modality; tafamidis is licensed in Brazil; and new treatment options are in development
- More information is needed to better understand the impact of hATTR and treatment preferences at the patient- and caregiver-level

OBJECTIVE

- Obtain patient and caregiver perspectives on disease burden and treatment approaches associated with hATTR

METHODS

- The Amyloidosis Research Consortium developed two online surveys with input from patients, caregivers, and Health Technology Assessment (HTA) bodies
- Participants were recruited from patient support groups or through social media/websites; the survey portal was open July – October 2018

RESULTS

Table 1. Demographics

	Patients (N=113) n (%)	Caregivers (N=60) n (%)
Place of residence	n= 113	n = 60
Brazil	71 (62.8%)	53 (88.3%)
Portugal	39 (34.5%)	7 (11.6%)
Other	VEN, FRA, GBR (2.6%)	0
Age of respondent	n = 112	n = 59
≤ 39 y.o	30 (26.8%)	19 (32.2%)
40 – 59 y.o	63 (56.3%)	28 (50.0%)
60 – 79 y.o	18 (16.1%)	12 (20.3%)
≥ 80 y.o	1 (0.9%)	0
Time since patient diagnosis	n = 113	n = 60
>1 yr	16 (14.2%)	7 (11.7%)
1 – 2 yrs	14 (12.4%)	13 (21.7%)
2 – 5 yrs	24 (21.2%)	13 (21.7%)
>5 yrs	59 (52.2%)	27 (45.0%)
Genetic mutation of patient	n = 113	n = 51
Val30Met	65 (57.5%)	24 (47.0%)
Thr60Ala	1 (0.9%)	2 (3.9%)
Val122Ile	1 (0.9%)	0
Ile68Leu	0	1 (2.0%)
Other	11 (9.7%)	30 (58.8%)
Not sure/not typed	35 (31.0%)	3 (5.9%)
Employment status	n = 113	n = 59
Employed full-time	40 (35.4%)	27 (45.6%)
Employed part-time	6 (5.3%)	6 (10.2%)
Not employed, looking	7 (6.2%)	7 (11.9%)
Not employed, unable	21 (18.6%)	9 (15.3%)
Retired	39 (34.5%)	10 (16.9%)

- Participants (N=173 valid responses) consisted of adults with hATTR (n=113; 28 - 80 y.o) and caregivers (n=60; 24 - 78 y.o)
- Nearly all respondents resided in Brazil (n=124) or Portugal (n=46)
- The majority of patients were diagnosed >5 years ago; Val30Met was the most common known mutation

Table 2. Disease-targeting Treatment for hATTR

Medication (no. respondents)	Receiving n (%)	Discontinued n (%)	Never Used n (%)	Not Sure n (%)
Diflunisal (n=111)	2 (1.8%)	4 (3.6%)	98 (88.3%)	5 (4.5%)
Doxycycline (n = 109)	2 (1.8%)	1 (0.9%)	94 (86.2%)	12 (11.0%)
Tafamidis (n = 109)	29 (26.6%)	18 (16.5%)	59 (54.1%)	3 (2.8%)
Patisiran (n = 108)	4 (3.7%)	0	99 (91.7%)	5 (4.6%)
Inotersen (n = 108)	8 (7.4%)	0	95 (88.0%)	5 (4.6%)

- Many patients (41/111; 36.9%) received a liver transplant
- Most never used, or were not currently taking disease-targeting medications
- Patients also reported a range of treatments or strategies to manage symptoms, including use for:
  - reduction of neuropathic pain (39%)
  - relief of gastrointestinal symptoms (32%)
  - management of blood pressure (19%)
  - management of cardiac function (19%)

Figure 1. Patient-reported Multi-systemic Burden

- Respondents selected symptoms experienced in the last 12 months (n = 113)

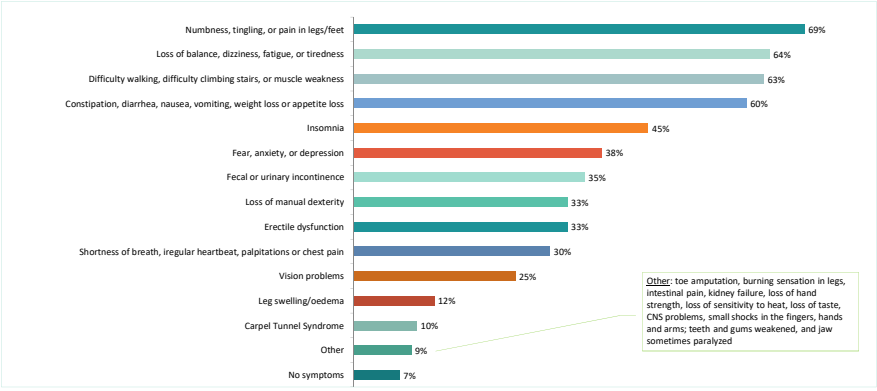
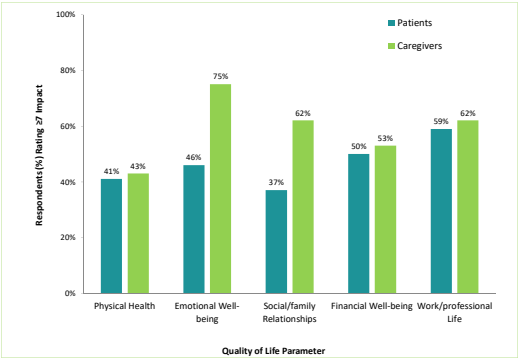


Figure 2. Disease Burden on Patients and Caregivers

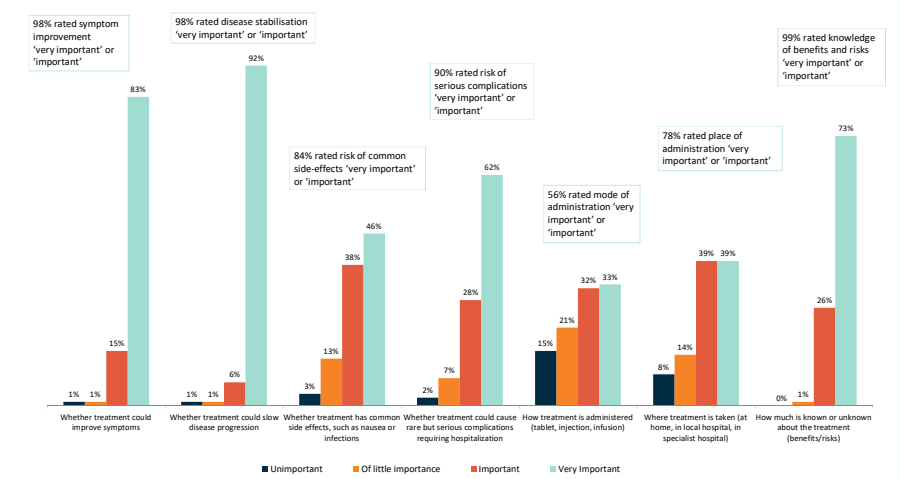
- Respondents rated the impact of hATTR on aspects of their life over the last 12 months using a scale of 0 (no impact) to 10 (extreme impact)



- hATTR severely impacts many quality of life parameters for patients and caregivers alike
- For patients (n=93), financial well-being and work/professional life were most impacted; 24% and 38% reported extreme impact (score of 10), respectively
- For caregivers (n=48), emotional well-being and work/professional life were most impacted; 33% and 38% reported extreme impact (score of 10), respectively
- Caregivers reported a higher degree of impact than patients in the areas of emotional well-being and social/family relationships
- Free-text responses suggest the impact on QoL domains is inextricably linked and caregivers experience significant practical and emotional burden

Figure 3. Treatment Goals

- Respondents rated the relative importance of treatment goals and concerns (n=95)



- Patients placed importance on efficacy as primary treatment goal; 64% ranked impact on disease progression as the most important factor. Mode (41%) and location (33%) of treatment administration were ranked least important factors.
- Caregivers rated the importance of most treatment factors similarly to patient responses (data not shown)

CONCLUSIONS

- hATTR is a multi-systemic disease and affects all aspects of life.
- hATTR significantly impacts patients' independence and sense of normality: their ability to work, participate in family and social life, be mobile and undertake daily activities and hobbies
- hATTR considerably impacts caregivers: the emotional burden of 'knowing what's to come', practical caring burden and the effect on their own ability to work
- Patients and caregivers value multiple factors as important for treatment, including efficacy, risk of side-effects, and knowledge of benefits-risks
- New treatments specifically for hATTR offer significant hope to patients and their families, especially in the context of the disease being hereditary, high impact on quality of life, and no/few alternatives

REFERENCES

Ando Y, Coelho T, Berk JL, et al. Guideline of transthyretin-related hereditary amyloidosis for clinicians. Orphanet J Rare Dis. 2013;8:31.