Treatment History, Tolerability, and Impact on Health-Related Quality of Life in AL Amyloidosis

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BACKGROUND

- Amyloid light chain (AL) amyloidosis is a complex, rare disease characterized by systemic amyloid deposits, composed of misfolded light chain protein, in tissue and vital organs
- Accumulation of amyloid deposits in the body can lead to organ toxicity, irreversible organ damage, and death, but patients' experiences of the disease vary broadly because of the wide heterogeneity in organ involvement and dysfunction[1,2]
- Although no medications to treat patients with AL amyloidosis have yet been approved by the United States Food and Drug Administration or the European Medicines Agency, chemotherapy, stem cell transplantation (SCT), and immunomodulatory drugs are used off-label
- All existing regimens are associated with tolerability problems and treatment-emergent symptoms,[3,4] but little is known about the impact of these treatments on health-related quality of life (HRQoL) in patients with AL amyloidosis[5,6]

OBJECTIVE

- To describe the history of treatments and tolerability experiences and their impact on HRQoL in a diverse group of adult patients with AL amyloidosis

METHODS

Data Sources

- An online, noninterventional, longitudinal study of adults (≥18 years of age) with self-reported AL amyloidosis (N = 341)
- These analyses were based on cross-sectional patient response data from the baseline survey collected in 2015
- Two patient advocacy groups helped to support recruitment efforts using social media postings and e-mail messages that highlighted this study participation opportunity
- Patients' responses were collected online using the Optum Smart Measurement® System

SF-36v2® Health Survey

- The SF-36v2® Health Survey is a 36-item, self-report measure of generic HRQoL; the standard (4-week recall) version was used for this study[7]
- The survey allows for the calculation of 8 domains of functional health and well-being and 2 summary scores, shown here
  - Physical functioning (PF)
  - Role limitations due to physical health (RP)
  - Bodily pain (BP)
  - General health (GH)
  - Vitality (VT)
  - Social functioning (SF)
  - Role limitations due to emotional health (RE)
  - Mental health (MH)
  - Physical Component Summary (PCS)
  - Mental Component Summary (MCS)
- Each scale/summary measure is calculated and standardized to 50 ± 10 (mean ± standard deviation); thresholds for clinically meaningful differences on the scales range from 2 to 4
- For all scales, a score of 50 is the average in the US general population; higher scores represent better functioning
  - MCS scores <42 can be used to predict clinical depression[7]
- US general population averages are based on data from a 2009 Internet-based HRQoL-norming study (n = 4024). Study participants were recruited from the Knowledge Panel® (maintained by Knowledge Networks, Burnaby, BC, Canada [now GfK Custom Research, LLC]), a probability-based sample of US noninstitutionalized adults

Statistical Analysis

- Patients reported their current and previous treatments for AL amyloidosis
- Aspects of tolerability were captured based on the following
  - Lifetime history of treatment-emergent symptoms (dichotomous variable)
  - Consequences of treatment-emergent symptoms, including discontinuation, reduction, or maintenance despite symptoms
  - Ability to tolerate the current or most recent AL amyloidosis treatment (based on a 4-point scale [range, 1-4] from "extremely poorly" to "very well," where higher scores indicate better tolerability)
- The prevalence of each treatment type and each treatment-emergent symptom was calculated for the sample of patients
- The association between ability to tolerate current or most recent treatment and HRQoL, measured by PCS and MCS scores, was evaluated using analysis of variance. Given the response distribution, a 3-level version of the ability to tolerate current treatment measure was derived such that "extremely poorly" and "not very well" were collapsed into the same category
  - The relationship between tolerability and HRQoL was evaluated with and without controlling for measures of disease severity, including number of organs affected, cardiac involvement, and Patient Global Impression–Severity, a 5-point, self-report assessment of disease severity[8]

RESULTS

- Characteristics of the patients are detailed in **Table 1**

Table 1. Demographic and Disease Characteristics of Patients With AL Amyloidosis

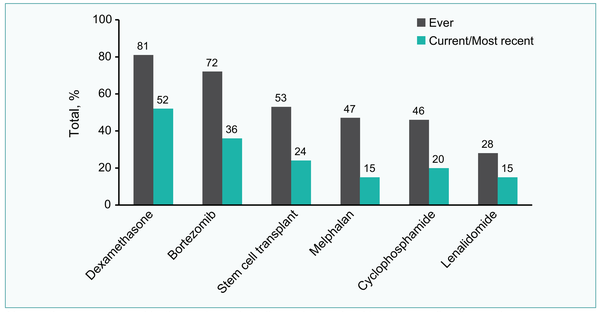
Characteristic	Patients N = 341	
	n	%
Age, years		
Mean (SD)	60.6 (10.2)	
Range (median)	23–85 (61)	
Gender (n = 340)[a]		
Male	160	47.1
Female	180	52.9
Race/Ethnicity		
White	304	89.1
Other	37	10.9
Education (n = 322)[a]		
≤High school diploma or GED	26	8.1
Some college (<4 years; associate's or technical degree)	99	30.7
Bachelor's degree	109	33.9
Graduate degree	88	27.3
Marital status (n = 330)[a]		
Married	271	82.1
Other	59	17.9
Employment status (n = 300)[a]		
Currently employed	115	38.3
Time since diagnosis		
Mean (SD)	4.5 (4.0) years	
Range (median)	1 month–28 years (3.5 years)	
Organs/systems affected[b]		
Heart (cardiac)	178	52.2
Kidney	214	62.8
Liver	49	14.4
Nervous system	126	37.0
Gastrointestinal	148	43.4
Other	117	34.3
Number of organs involved		
1	95	27.9
2	89	26.1
≥3	157	46.0
Most recent hematologic response status		
No response to treatment	23	6.7
Partial hematologic response or partial remission	126	37.0
Complete hematologic response or complete remission	141	41.3
Do not know	51	15.0

[a]Subtotals <341 were attributed to missing data; percentages were based on available data.
[b]Multiple response options were allowed.

Treatment History

- The most commonly reported treatments were dexamethasone (81%) and bortezomib (72%) (**Figure 1**)
- 53% of participants underwent SCT
- 51% of participants received ≥3 different treatments

Figure 1. Rates of treatments for AL amyloidosis by treatment type.[a,b]



[a]Many patients reported combination treatment, including cyclophosphamide + bortezomib + dexamethasone (CyBorD; 17% current or most recent).
[b]Sample size for each survey item ranged from 337 to 341 because of missing data.

Treatment Tolerability

Lifetime History of Tolerability Problems

- Nearly three-quarters (71%; n = 226) of treated patients reported ever having problems tolerating treatment for AL amyloidosis (**Table 2**)

Consequences of Treatment-Emergent Symptoms

- Of patients who experienced any tolerability problems, nearly half (47%; n = 107) discontinued, slightly more than half (51%; n = 116) reduced the dosage for ≥1 medication, and more than one-third (36%; n = 83) continued with the treatment regimen despite problems

Tolerability of Current or Most Recent Treatment

- Nearly half (46%) of treated patients reported some tolerability issue (less than very good tolerability). Tolerability varied among the common treatments from a low of 3.22 (SD, 0.90) for cyclophosphamide to a high of 3.61 (SD, 0.52) for SCT

Table 2. Treatment Tolerability Among Patients With a Treatment History

Tolerability	Patients N = 321	
	n	%
Lifetime history of treatment-emergent symptoms[a]		
Ever had problems tolerating any treatment	226	71.3
Have not experienced problems tolerating any treatment	91	28.7
Ability to tolerate current or most recent treatment regimen[a]		
Very well	154	53.7
Moderately well	99	34.5
Not very well	28	9.7
Extremely poorly	6	2.1
Mean score (SD)	3.40 (0.75)	
Consequences of treatment-emergent symptoms (among patients with a history of tolerating treatments, n = 226)[b]		
Discontinued ≥1 medication/treatment	107	46.9
Reduced dosage for ≥1 medication/treatment	116	50.9
Experienced difficulty tolerating ≥1 medication/treatment but made no changes	83	36.4

[a]Subtotals <321 were attributed to missing data; percentages were based on available data.
[b]Multiple response options were allowed.

Tolerability and HRQoL

- Any problems tolerating current or most recent medications corresponded with decrements in HRQoL (both PCS and MCS; $P < 0.001$) (**Figure 2**)
- Differences in PCS and MCS scores across tolerability categories were statistically significant and clinically meaningful. Significant associations between current tolerability and PCS or MCS persisted even after adjusting for markers of disease severity

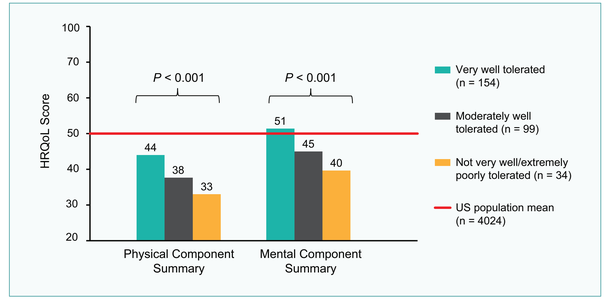
Physical Health

- Even patients who could tolerate their current or most recent medication "very well" reported HRQoL scores much lower than the US population average score of 50 on PCS. Any further tolerability problems were associated with PCS scores >1 SD to <2 SD below normal, a level of functioning associated with severe impairment

Mental Health

- Patients who could tolerate their current or most recent medication "very well" had MCS scores in the normal range. Mean MCS scores among patients who reported the worst tolerability levels were at or below the threshold for clinical depression

Figure 2. HRQoL scores as a function of tolerability of current or most recent treatment for AL amyloidosis.



CONCLUSIONS

- Lifetime history of tolerability problems was high among patients with AL amyloidosis, and discontinuation of AL amyloidosis treatments was fairly common. The high prevalence of treatment discontinuation and the history of multiple AL amyloidosis treatments suggests that physicians and patients try a variety of treatments to balance tolerability and efficacy
- Having problems tolerating treatment was associated with decrements in HRQoL over and above the previously reported burden of AL amyloidosis.[9] Both physical and mental HRQoL diminished noticeably in patients who experienced tolerability problems with the current or most recent treatment
- These findings highlight the importance of assessing HRQoL during AL amyloidosis treatment to better understand the tradeoffs between treatment effectiveness and treatment tolerability. The prevalence of tolerability problems and treatment discontinuation underscore the need for more treatment options for AL amyloidosis

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