Clinician Preferences for Transthyretin Amyloidosis Treatment: Results from a Discrete-Choice Experiment

For US HCPs Only

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Conclusions

- **Of the non-clinical attributes of ATTR treatments tested, speed of TTR knockdown was found to be the dominant driver of treatment choice among 200 U.S. neurologists and cardiologists**
- **Clinicians equated speed of TTR knockdown with impact on improving clinical outcomes and halting clinical progression and valued it higher than attributes relating to medication administration (location and by whom) and dosing frequency.**

Background

- Patients with Transthyretin amyloidosis (ATTR) typically present with cardiomyopathy or with polyneuropathy, or both.[1-4] Those with cardiomyopathy are treated by cardiologists and those with polyneuropathy, by neurologists, and those with mixed phenotype, by both specialties.
- Multiple disease-specific treatments are approved for Transthyretin amyloidosis (ATTR), to treat cardiomyopathy and/or polyneuropathy manifestations of the disease.[5-16] Of interest are the subcutaneous, 'gene silencer' class of treatments.
- Since these treatments differ in administration characteristics and dosing and pharmacodynamic profiles, such non-clinical attributes of treatment may factor into treatment decision making, in addition to clinical efficacy and safety.
- The objective of this study was to elicit clinicians' preferences for non-clinical attributes of treatments for ATTR.

Methods

- A two-phased mixed methods study was conducted:
  - **Phase 1** included 26 interviews in total: 18 qualitative interviews using concept elicitation and cognitive debriefing related to key survey components (e.g., treatment attribute descriptions, patient profiles, and example choice scenarios), and 8 pre-test interviews based on the findings from these qualitative interviews. The three non-clinical attributes included in the survey as preference drivers based on the qualitative interviews were (see **Table 1** for details on attribute levels)
    - Speed of TTR knockdown
    - Medication administration approach (where and by whom medications are administered)
    - Dosing frequency
  - **Phase 2** included the final online quantitative survey preference study (conducted as a discrete choice experiment [DCE*]) among 200 clinician respondents in the U.S. The study sought to elicit clinicians' treatment preferences for hypothetical patient profiles representing patients with 'mild' (PND 1 or NYHA ≤ II) or 'severe' (PND ≥ II and NYHA ≥ III) disease.

Table 1. Attributes and Levels Used in the Discrete-Choice Experiment

Technical label	Clinician-facing label	Attribute levels
Speed of TTR knockdown	Time until reaching a 60% reduction in serum TTR concentration	. 3 weeks . 7 weeks . 9 weeks
Medication administration (location and by whom)	Who administers the medication and where it is administered	. Administration by patient (self-administration) or caregiver at home . HCP administration at medical facility
Dosing frequency	Dosing frequency	. Injection once every month . Injection once every 3 months

TTR: transthyretin; HCP: Healthcare professional

- Respondents were presented pairs of hypothetical treatments defined by different attribute combinations and then asked to choose their preferred treatment from the pair, for specified hypothetical patient profiles. This allowed estimation of preference weights for each attribute level
- The final survey instrument included 6 DCE choice questions and 1 direct elicitation question (that represented real-world treatment profiles)

Results

Descriptive statistics

- 100 neurologists and 100 cardiologists, in the US, completed the DCE survey.
  - –Mean age was 51 years, 17.5% identified as female and 55% as white
  - –55% practiced in a private setting, 35.5% in an academic setting and 9.5% in a hospital setting
  - –Respondents had experience treating ATTR on average for 11.8 years (Std. Dev=8.4 years), with approximately 39 patients treated each year

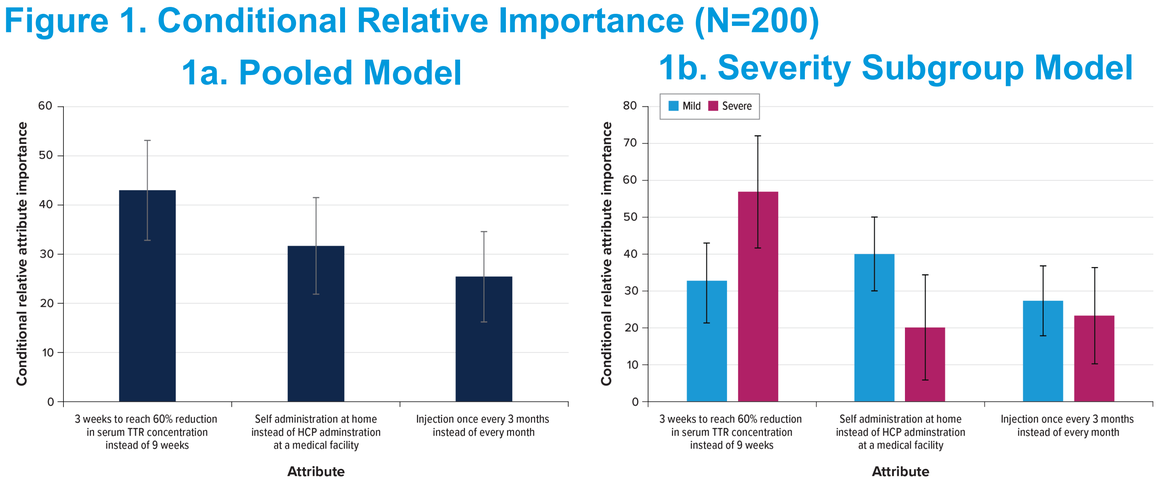
Preference analysis

- Attribute preferences did not differ between neurologists and cardiologists systematically (p=0.366), while attribute preferences differed systematically when considering the treatment of patients with mild vs. severe disease (p<0.001).
- In the pooled analysis across disease severity levels, respondents preferred a treatment
  - –That lowers the serum TTR concentration faster
  - –With a less-frequent dosing schedule
  - –That is administered by the patient (self-administration) or their caregiver at the patient's home

Conditional relative importance (CRI)

- The CRI, which is the importance of the different attributes (and levels) tested, relative to one another, in driving clinician preference, showed that in the pooled model (**Figure 1a**),
  - –Speed of TTR knockdown had the greatest relative influence on treatment choice, with the highest CRI, accounting for 42.9% of the total change in utility that would occur in moving from the least-preferred to the most-preferred treatment profile (considering all tested attribute levels across all attributes tested).
  - –Medication administration approach (where and by whom medications are administered) and Dosing frequency had CRIs of 31.7% and 25.4%, respectively

Figure 1. Conditional Relative Importance (N=200)



TTR: transthyretin; HCP: Healthcare professional

- Attributes are presented in the order in which they appeared in the DCE questions. For each attribute, the CRI is the difference between the preference weight on the most-preferred attribute level and the least-preferred attribute level, with scaling so that the sum of CRI estimates across attributes equals 100. 95% CIs for the CRIs were calculated using the Delta method and represented by the black vertical bars on top of the blue bars.
- Preference weights were estimated based on physicians' DCE responses for two distinct patient profiles: one for the mild patient profile and one for the severe patient profile. Therefore, the total number of observations is 400 (for the clinician sample of 200).

- In the subgroup model (**Figure 1b**)
  - –For 'mild' patients, Medication administration approach (where and by whom medications are administered) had the highest CRI (40.0%), followed by Speed of TTR Knockdown (CRI=32.8%) and Dosing Frequency (CRI=27.2%).
  - –For 'severe' patients, Speed of TTR Knockdown had the highest CRI (56.7%), followed by Dosing Frequency (CRI=23.3%) and Medication administration approach (where and by whom medications are administered) (CRI=20.0%).

***A DCE is a quantitative research method in which participants make a preferred choice from a set of hypothetical alternatives, each of which is defined by a set of attributes. The purpose of a DCE is to elicit preferences and understand trade-offs that individuals make when evaluating and choosing between alternatives.**

Funding: This study was funded by Alnylam Pharmaceuticals.

Disclosures: FC reports consulting fees from Alnylam Pharmaceuticals, AstraZeneca, Bayer, BridgeBio, and Pfizer; **AS** reports consulting fees and honoraria from Alnylam Pharmaceuticals, AstraZeneca, and Pfizer; **CC** reports consulting fees and honoraria from Alnylam Pharmaceuticals, AstraZeneca, Bayer, CVRM Connect, and Pfizer; **CP, RM, CB** are employees of RTI Health Solutions, which received funding for the analysis from Alnylam Pharmaceuticals; **MD** was a fellow at Alnylam Pharmaceuticals; **DD** was an employees of Alnylam Pharmaceuticals and owns shares in Alnylam Pharmaceuticals. **VK** is an employee of Alnylam Pharmaceuticals and owns shares in Alnylam Pharmaceuticals; **JF** reports travel support from Alnylam Pharmaceuticals.

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Presented at: **EU-ATTR, 2025. Baveno, Italy**

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