Title: Evaluating patients' preferences regarding treatment options for Waldenström's Macroglobulinemia, a Discrete-Choice-Experiment

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Abstract

Introduction
The number of available treatment options for Waldenström's Macroglobulinemia (WM) has expanded in the last decades. However, there is no consensus on a preferred regimen. The currently available treatment options have varying properties in terms of efficacy, toxicity profile, duration (fixed-duration vs long-term maintenance), administration (oral vs intravenous/subcutaneous (IV/SC)), and type of agent (immuno-chemotherapy vs targeted therapy). Therefore, patient preferences become increasingly important in making an individualized treatment plan and for the design of future clinical trials. Still, little is known about WM patients' priorities and perspectives regarding their treatment options. We evaluated treatment preferences of Dutch WM patients by means of a discrete choice experiment (DCE).

Methods
A mixed-method approach, consisting of a literature review, qualitative interviews and expert discussions was utilized for identification and selection of attributes of different therapies and corresponding levels. The DCE questionnaire included 5 attributes: 5-year progression-free survival (PFS), frequency/route of administration(IV/SC vs oral)/setting (clinic vs home) of treatment, adverse events (nausea & vomiting and fatigue, neuropathy and atrial fibrillation), risk of future secondary malignancies (low vs high), and type of treatment agent (immuno-chemotherapy vs targeted therapy). Each respondent was presented with 16 choice cards and was asked to choose between two hypothetical but realistic treatment options (see **Figure 1A** for an example).
Data were collected via a nationwide online questionnaire via the patient organizations' website and via paper-based questionnaires sent to the participants known at the outpatient clinic of Amsterdam UMC. An orthogonal design was used to construct the choice tasks and a mixed logit panel data model was used to assess patients' preferences and trade-offs between attributes/levels.

Results
A total of 330 online questionnaires and 17 paper-based questionnaires were returned. In total, 214 (65%) complete questionnaires were included for data analysis, respondents characteristics are presented in **Table 1**. The 5-year PFS followed by the risk of secondary malignancies were the most important attributes for making treatment decisions. The probability of choosing a treatment option increased with 26% if the 5-year PFS increased

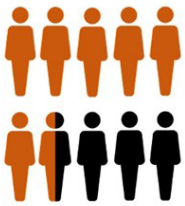
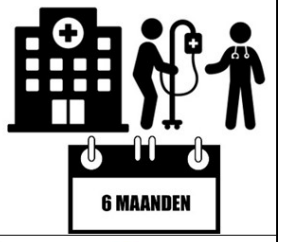
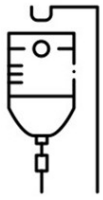
from 50% to 70% and increased 22% if the chance of future secondary malignancies was “low risk” instead of “high risk”. Of the adverse events, patients wanted to avoid neuropathy the most and were willing to give up 7,2% treatment efficacy to avoid neuropathy. The probability of choosing a treatment option increased with 8% for a fixed-duration treatment with IV/SC administration at the hospital compared to an ongoing daily oral regimen at home. Treatment with targeted therapy as opposed to chemotherapy also resulted in 8% increased probability of choosing this treatment option (**Figure 1B**).

Conclusion

These are the first systematic data on WM patient preferences on treatment. These results may help discussions with individual patients about their treatment choices. Also, based on these data, future clinical trials in WM should focus on effective fixed duration regimens with non-cytotoxic and non-neurotoxic drugs since such a regimen is currently not available.

Figure 1A. Example of a choice task

Scenario 6

	Treatment A	**Treatment B**
How effective is the treatment?	After 5 years, the disease is still suppressed in 65% of the patients. 	After 5 years, the disease is still suppressed in 70% of the patients. 
What does the treatment look like?	Long-term treatment; maintenance treatment in which the medicine has to be taken daily and orally until ineffective or excess symptoms occur. This treatment will be at home. 	Fixed duration treatment; every 3 weeks for 6 months in the outpatient hospital after which the treatment comes to an end. The administration can be subcutaneous, intravenous or a combination of the two. 
Adverse events	One in 5 patients suffer from damage to the nerve endings leading to pain and numbness in the hands and feet. 	One in 10 patients experience cardiac arrhythmias and/or an increased tendency to bleed. 
Risk of other cancers in the future	Not or hardly increased 	Not or hardly increased 
Type of agents in the treatment regimen	Does not contain chemotherapy but "targeted" therapy 	Contains chemotherapy 

Which treatment would you prefer? (*There are no right or wrong answers, it's your personal preference.*)

Treatment A ☐ Treatment B ☐

Figure 1B. Average marginal effects indicating the change in probability of choosing a treatment option if the attribute level was changed from the reference category. The references categories are depicted with *. The error bars represent the 95% confidence intervals about the point estimate. *P <.05, **P<.01, ***P<.001, ****P<.0001.

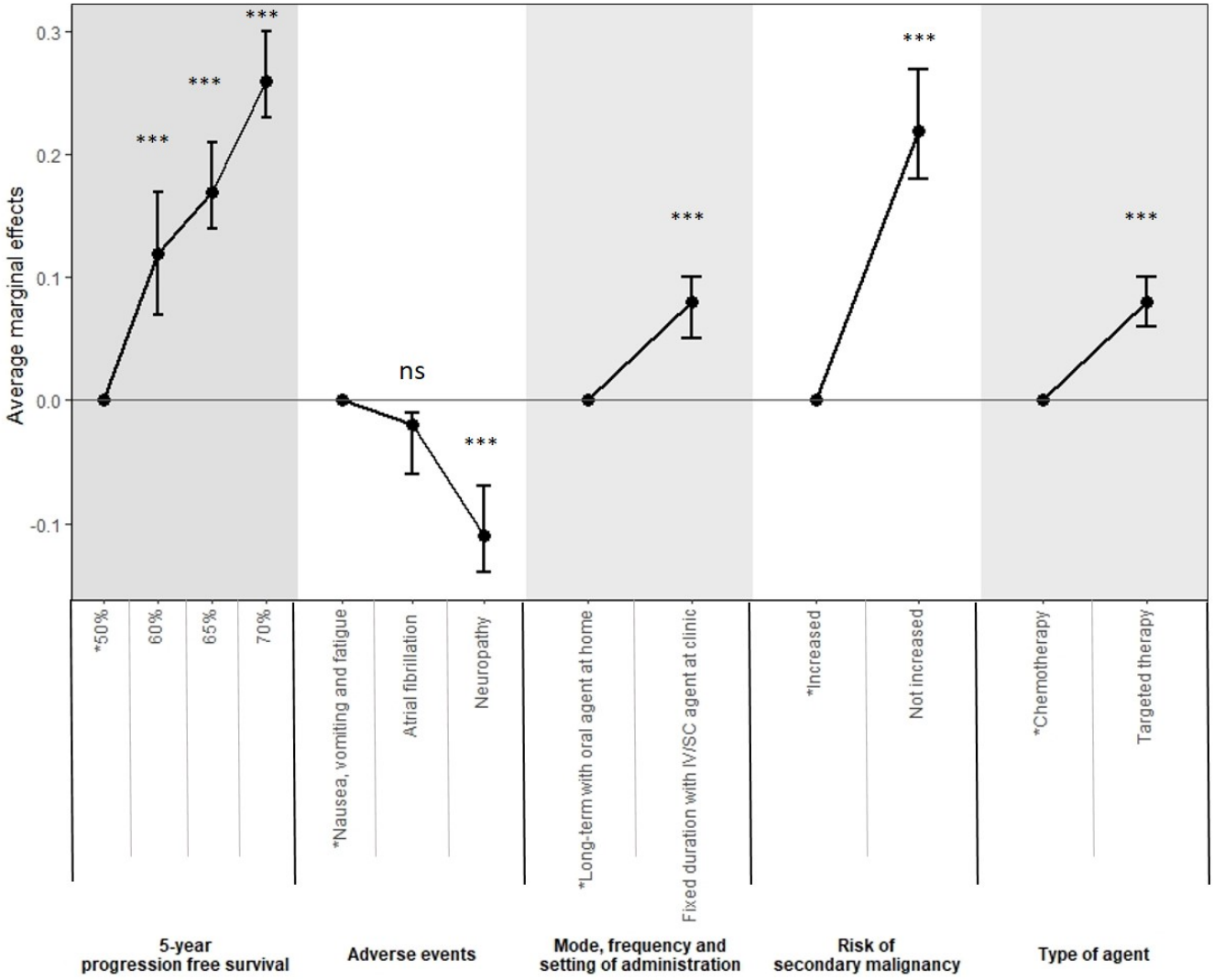


Table 1. Socio-demographics and clinical characteristics of the respondents

	Patients who completed DCE (n=214)	*Patients who completed only demographic questions but not DCE (n=41)*	*P value*
Age (years, median (SD; min-max))	67 (9.8; 29-91)	63 (14.2; 29-91)	0.09
Males, n (%)	35/65 (54%)[a]	8/17 (47%)[b]	0.82
Time since diagnosis (years, min-max)	6.9 (0.1-48)	4.3 (0-20.1)	
High educational level*, n (%)	115/209 (55%)	16/40 (40%)	0.12
Disease status			0.38
Wait & see	66/211 (31%)	17/37 (46%)	
Remission	83/211 (39%)	11/37 (30%)	
Progression	20/211 (10%)	3/37 (8%)	
Currently treated	42/211 (20%)	6/37 (16%)	
Previously treated at time of completion of the questionnaire			0.31
Yes	122/212 (58%)	17/38 (45%)	
No	60/212 (28%)	15/38 (40%)	

**High educational level defined as completed HBO (Higher Vocational Education) or University; [a]Missing: 149; [b]Missing: 24*