Which treatment aspects matter to patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD)? The development of a patient preference instrument

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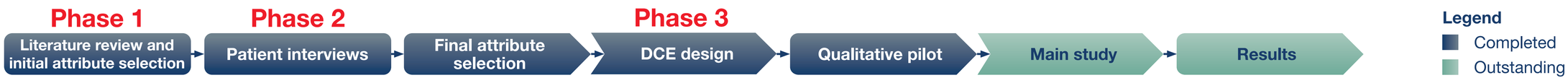
BACKGROUND

- ILD is a frequent complication of SSc, a rare and potentially fatal disease characterised by progressive organ damage; treatment options for SSc-ILD are limited
- Preference elicitation methods are increasingly used in health economics to identify patient healthcare preferences[1,2]
  - Quantitative methods include discrete choice experiments (DCE), where participants are asked to choose between hypothetical treatments characterised by a common set of attributes[2]
  - The resulting preference data can be used to evaluate alternative configurations of current and future treatments for SSc-ILD from patients' perspectives
  - Here, we present the study design and instrument development

OBJECTIVES

- Primary:
  - To elicit patients' preferences for attributes of treatments for SSc-ILD
  - To quantify these preferences in a meaningful and common unit of measurement, such as relative attribute importance and maximum acceptable risk
- Secondary:
  - To compare patients' preferences for alternative treatment configurations

STUDY OVERVIEW



LITERATURE REVIEW

Search conducted: Feb–Mar 2018

Phase 1

METHODS

- A literature search was performed to identify patient-relevant treatment aspects, and targeted clinical evidence, quantitative preference studies, qualitative research and patient-reported outcomes
- 'Treatment Process', 'Adverse events' and 'Symptoms' were identified as key treatment dimensions of potential relevance to patients in DCE instrument development

EXAMPLES OF RELEVANT CONCEPTS

Breathlessness	Coughing frequency	The impact of symptoms on patients' daily life
Skin-related symptoms	The risk of mild-to-severe treatment side effects[a]	The risk of severe treatment side effects[b]

[a]Consisting of diarrhoea, nausea, stomach ache and vomiting
[b]Including infections that may require hospitalisation and the risk of dying from infections or blood cancer

VALUE DIMENSIONS IDENTIFIED FROM THE LITERATURE

Treatment process	Adverse events	Symptoms	
	Severe events	Cough	Further SSc symptoms
– Interaction with HCPs – Treatment frequency – Treatment duration	Mild/moderate events	Symptoms impact – Tiredness – Sleep quality – Communication quality – Chest and stomach pain – Interference with job – Interference with sex life – Interference with social life – Number of 'good days'	Disease progression Breathlessness

- Literature review results were discussed with an SSc-ILD advisory board, including patients from Italy, the UK, China and Mexico. Feedback on symptoms, treatment expectations, and treatment risks further informed the design of the subsequent patient interviews

PATIENT INTERVIEWS

Interviews conducted: Oct–Nov 2018

Phase 2

OBJECTIVE

- To inform attribute selection by identifying important treatment aspects for patients with SSc-ILD and gain patient insights on the symptoms and impacts of SSc-ILD

METHODS

- A semi-structured interview guide was developed based on the literature review and reviewed by two physicians (LAS and MA)
- Included nine patients with SSc-ILD (New Orleans, USA)[c]
- Audio recordings were transcribed, reviewed and personal identifiable information removed; cleaned transcripts underwent a software-driven semantic content analysis to identify treatment and disease aspects relevant to patients (ATLAS.ti)[3]
- Semi-structured interview consisting of two parts:

PART 1: Open-ended questions (accessed by scanning the QR code above) concerned with symptoms and impacts of SSc-ILD, and benefits of and concerns with current treatments

PART 2: Patients were presented with a hypothetical choice between two treatments with different attribute profiles

RESULTS

- Patients suffered from symptoms such as coughing (78%), shortness of breath (56%), and fatigue/dizziness (56%), which affected their social life (100%), physical activity (67%) or work productivity (67%)
  - Fatigue was frequently mentioned as a factor impacting on quality of life
- Beyond the candidate attributes, patients also valued different modes of administration
- Patients indicated their willingness to accept treatment risks in exchange for symptom improvement
- The interviews demonstrated the relevance of identified treatment attributes and patients' willingness to make trade-offs

[c]Patients aged ≥18 years were recruited through EUSTAR, from the EUSTAR registry or based on medical records. Patients provided written and verbal consent to be recorded prior to their interview

ATTRIBUTE SELECTION

- A dedicated attribute selection workshop reviewed the Literature Review results with clinicians (OD and MA) to select the attributes and levels for inclusion in the DCE
- The following final attributes were selected: mode of administration, shortness of breath, skin tightness, coughing, tiredness, risk of diarrhoea, nausea and/or vomiting, and risk of infections. The final attributes and levels (after qualitative pre-testing) may be accessed by scanning the QR code above
- Levels of the risk attributes were informed by clinical performance data of different treatments,[d] to capture the risk levels observed for SSc-ILD regimens

[d]Cyclophosphamide, mycophenolate mofetil, nintedanib, rituximab and tocilizumab

EXAMPLE DCE QUESTION

	Treatment A	Treatment B
Mode of administration	**Oral** (twice daily)	**Infusion** (every 6–12 months at hospital or local clinic)
Skin tightness	Tightness in your **hands or arms is present, but *does not limit* daily activities**	Tightness in your **hands or arms is present and *limits* daily activities**
Shortness of breath	You are short of breath when **walking up hills or stairs** *(no problems with breathlessness)*	You are short of breath when **sitting or lying still** *(severe breathlessness)*
Tiredness	You feel tired **some days** a week and **complete most** usual activities	You feel tired **most days** a week and **complete few** usual activities
Coughing	You have a **persistent** cough that is **easy** to tolerate	You have an **occasional** cough that is **easy** to tolerate
Risk of diarrhoea, nausea and/or vomiting	20 have diarrhoea, nausea or vomiting 80 do not have diarrhoea, nausea or vomiting	60 have diarrhoea, nausea or vomiting 40 do not have diarrhoea, nausea or vomiting
Infections	30 have non-serious infections 10 have serious infections 60 have no infections	5 have non-serious infections 0 have serious infections 95 have no infections

DCE DESIGN

Phase 3

- A design was generated for the DCE that had the following properties:
  - Respondents repeatedly chose between two hypothetical treatments for SSc-ILD
  - A D-efficient design that minimised the covariance matrix of a multinomial logit model was generated assuming directional priors
  - The design had 24 experimental choice tasks that were split into two equal blocks and each respondent completed one randomly assigned block; the order of choice tasks was randomised to minimise the risk of ordering effects
- To assess internal validity:
  - Two choice sets will be repeated to explore whether participant preferences are complete or formed during the project due to acquired learning
    - The 3rd and 10th choice task (as presented to respondents) will be repeated after the last DCE question; this will allow for the assessment of consistency of the participants' answers and potential learning effects or fatigue
  - A dominant alternative will be presented as the last DCE question to test for the monotonicity of preferences; the dominant alternative will be described by the most favourable levels of attributes with a natural ordering (e.g. risk)
- The DCE design and survey structure, recruitment approach and ethical considerations were described in detail in the study protocol, which was reviewed by participating clinicians (LAS, CB, OD and MA)

SURVEY STRUCTURE

DCE QUESTIONNAIRE

- The online survey lasted for 25–30 minutes and included five sections
- Patients were introduced to the survey with information about SSc-ILD and symptoms, including a video about SSc-ILD
- Attributes were introduced interactively with rating and ranking questions

1. Symptoms and clinical background
2. Introduction of attributes and DCE
3. DCE and internal validity
4. Debriefing questions
5. Sociodemographic questions

QUALITATIVE PILOT

METHODS

- The DCE, integrated into a structured feedback questionnaire, was pre-tested in English with three patients with SSc-ILD (USA, Italy and UK)
- One patient was asked to think aloud when choosing their preferred treatment (to explore if all attributes are considered in a compensatory choice process); two patients in Europe completed the survey and provided feedback in the form of a short questionnaire

RESULTS

- Overall, patients understood the survey and choice tasks
  - Patients were able to identify their treatment priorities and make trade-offs
  - Patients found the survey accessible and patient-centred
- Patient feedback to improve the wording of the questionnaire was included in the final version of the survey

Patients could distinguish between the relative importance of attributes and made trade-offs. For example, one patient stated:

"[It] became obvious to me that I did not mind the method of administration, but the impact on breathlessness and tiredness were a top priority. I was more concerned about the risk [of] infection than diarrhoea"

CONCLUSION

- The interviews demonstrated the relevance of identified treatment attributes and patients' willingness to make trade-offs
- DCE pre-testing suggested that the preference elicitation survey was accessible to patients
- There were several limitations:
  - The number of patients participating in the qualitative pilot was small
  - The qualitative research recruited patients from New Orleans only, which may limit the generalisability; however, patient input was also collected at a diverse patient advisory board meeting (attended by both caregivers [one each from Spain and Portugal] and patients [two from the USA, Belgium and Canada; one each from China, Ireland, Spain, Portugal, the UK, Italy, Croatia, Mexico and Germany])
  - The survey translations were not checked by full backwards translations, but native speakers reviewed all translations to ensure consistency with the English protocol and cultural appropriateness
- Next steps are fielding >200 patients with confirmed diagnosis via physician referral across the USA, UK, France, Germany, Italy, Norway and Switzerland, who will be referred for participation in the main project

INTERACTIVE

www.globalmedcomms.com/respiratory/SSWC2020/

https://www.globalmedcomms.com/respiratory/SSWC2020/Saketkoo/

Disclosures

LAS receives research funding or has a consultancy relationship with Boehringer Ingelheim, CSL Behring, Mallinckrodt Pharmaceuticals, Eicos Sciences and United Therapeutics. CB received consulting fees from Actelion and Eli Lilly. NS and MA are employees of Boehringer Ingelheim. SH and AD are employees of Evidera. A-MH-V received research funding and/or consulting fees or other remuneration from Actelion, Boehringer Ingelheim, GSK and Roche. OD had a consultancy relationship and/or has received research funding from Abbvie, Actelion, Acceleron Pharma, Amgen, AnaMar, Beacon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, Catenion, Competitive Drug Development International Ltd, CSL Behring, ChemomAb, Curzion Pharmaceuticals, Ergonex, Galapagos NV, Glenmark Pharmaceuticals, GSK, Inventiva, Italfarmaco, iQone, iQvia, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Target Bio Science and UCB in the area of potential treatments of scleroderma and its complications. In addition, OD has a patent mir-29 for the treatment of systemic sclerosis issued (US8247389, EP2331143).

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Abbreviations

DCE, discrete choice experiment; EUSTAR, European Scleroderma Trials and Research Group; HCP, healthcare practitioner; ILD, interstitial lung disease; SSc, systemic sclerosis.

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Boehringer Ingelheim

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Supplementary: Which treatment aspects matter to patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD)? The development of a patient preference instrument

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Example questions for Part 1 of the semi-structured interview included:
"Let's begin with discussing how you would describe SSc-ILD in your own words. What are typical symptoms and how do you think they affect patients' daily life?"
"From your perspective, how can SSc-ILD patients know if their treatment is working?"
"What aspects of SSc-ILD treatment concern you?"
"What are the positive aspects of current SSC-ILD treatments?"
"What is the burden that SSC-ILD patients are experiencing due to current treatments? Is there anything you would change about current treatments?"

FINAL ATTRIBUTES AND LEVELS (AFTER QUALITATIVE PRE-TESTING)

Attributes	Possible levels
Mode of administration	**(1) Oral** (twice a day) **(2) Infusion** (every 6–12 months at hospital or local clinic) **(3) Infusion** (every month at hospital or local clinic) **(4) Injection** into the skin by yourself (once every week at home)
Shortness of breath	**(1)** You are short of breath when **sitting or lying still** *(severe breathlessness)* **(2)** You are short of breath when **getting washed or dressed** *(moderate breathlessness)* **(3)** You are short of breath when **walking on level ground** *(mild breathlessness)* **(4)** You are short of breath when **walking up hills or stairs** *(no problems with breathlessness)*
Skin tightness	**(1) No skin tightness** is present **(2)** Tightness in your **hands or arms is present, but *does not limit* daily activities** **(3)** Tightness in your **hands or arms is present and *limits* daily activities** **(4)** Tightness in your **face *limits* your facial expressions, oral hygiene or speech**
Coughing	**(1)** You have an **occasional** cough that is **easy** to tolerate **(2)** You have an **occasional** cough that is **difficult** to tolerate **(3)** You have a **persistent** cough that is **easy** to tolerate **(4)** You have a **persistent** cough that is **difficult** to tolerate
Tiredness	**(1)** You feel tired ***some* days** a week and **complete *most*** usual activities **(2)** You feel tired ***some* days** a week and **complete *some*** usual activities **(3)** You feel tired ***most* days** a week and **complete *some*** usual activities **(4)** You feel tired ***most* days** a week and **complete *few*** usual activities
Risk of diarrhoea, nausea and/or vomiting	**(1) 20 out of 100** (20%) **(2) 40 out of 100** (40%) **(3) 60 out of 100** (60%) **(4) 80 out of 100** (80%)
Risk of infections	**(1) 5% (5 out of 100):** 5% are non-serious, 0% are serious **(2) 20% (20 out of 100):** 20% are non-serious, 0% are serious **(3) 20% (20 out of 100):** 15% are non-serious, 5% are serious **(4) 40% (40 out of 100):** 30% are non-serious, 10% are serious