To treat or watch? Identifying drivers of decisions for patients with GEP-NET using reflective Multi-Criteria Decision Analysis

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ABSTRACT

BACKGROUND: GEP-NET are slow-growing tumors with heterogeneous presentation. Somatostatin analogs (SSAs) or watchful waiting are recommended for management of unresectable, well- or moderately-differentiated non-functioning GEP-NET. This study aimed to develop a comprehensive shared-decisionmaking MCDA framework, and explore drivers of decision.

METHODS: A decision support tool was designed using a holistic MCDA framework (EVIDEM), literature review and insights from a Chatham-house panel of US physicians and patients with GEP-NET. A second extended panel (5 patients, 6 physicians) explored drivers of decision using two scenarios (SSA [reference case lanreotide] versus watchful waiting; lanreotide versus octreotide). Evidence was synthesized from a comprehensive literature review. Participants assigned weights through two techniques. For each criterion, participants were prompted to share experiential insights and knowledge, and assign a score (+5 [Much in favor of option 1] to -5 [Much in favor of option 2]). Contributions to relative benefit-risk balance (RBRB) and modulated RBRB (NormWeight X Score) were calculated for each criterion. Sensitivity analyses were performed.

RESULTS: At group level, when exploring treatment over watchful waiting, Type of therapeutic benefit, Disease severity, Effectiveness (mainly due to Progression-free survival and Disease symptoms) and Quality of evidence favored treatment (mean contribution: 0.08 ± SD 0.06, 0.07 ± 0.09, 0.07 ± 0.09 and 0.06 ± 0.06 respectively) whereas Costs aspects (interventions, medical and non-medical) favored watchful waiting. When comparing two treatment options, the majority of criteria did not favor one option over another. System capacity (0.02 ± 0.02) and Non-medical costs and constraints (0.02 ± 0.03) tip the scale in favor of lanreotide and Cost of intervention in favor of octreotide (0.08 ± 0.12). Sub-criteria Impact on autonomy and Impact on dignity favored lanreotide. Wide SDs reflect variability of drivers of decision across participants.

CONCLUSIONS: Exploration of scenarios identified drivers of decision for GEP-NET management and revealed the diversity of participants' perspectives. Holistic MCDA embedded with evidence supports individual reflection and informed shared-decisionmaking.

OBJECTIVES

- To explore the preferences and underlying criteria that patients and clinicians use in making their decisions on the treatment options of unresectable, well- or moderately differentiated nonfunctioning GEP-NET, by elucidating which criteria are considered and how they are considered using an MCDA approach. The study aims to develop a comprehensive decision framework and identify preferences of patients and clinicians.

BACKGROUND

- Neuroendocrine tumors (NETs) are rare slow-growing tumors arising in the endocrine system. In the United States, the prevalence is estimated to be 103,312 cases or 35 per 100,000.[1] GEP-NET symptoms are often nonspecific and mimic a variety of disorders, obstructing and delaying diagnosis. Diagnosis typically occurs at an advanced stage, often inadvertently and after metastases have developed.[2,3]

BACKGROUND (cont.)

- For patients with unresectable, well- or moderately differentiated nonfunctioning GEP-NET with asymptomatic stable disease and mild tumor burden, treatment options include watchful waiting or systemic therapy with somatostatin analogues (SSAs) such as octreotide or lanreotide.

- The open-source EVIDEM MCDA framework was designed to stimulate structured reflection and pragmatic collection of insights on the true value of interventions from all stakeholders, through a broad set of quantitative and qualitative criteria, each explicitly rooted in ethical aspects inherent to fair and accountable decisionmaking.[4-7]

- The EVIDEM framework was selected for this study as a comprehensive platform to explore decision criteria and preferences underlying treatment options for patients with GEP-NET.

METHODS

Development of the decision support tool

- A decision support tool was designed using the EVIDEM framework. Decision criteria were identified from the framework, the literature review and insights of patients and physicians collected as part of a Criteria workshop held in March 2016.

- An extended panel (5 patients, 6 physicians) explored drivers of decision using two scenarios (SSA [reference case lanreotide] versus watchful waiting; lanreotide versus octreotide).

- Participants assigned weights using two techniques (Hierarchical Point Allocation and Direct Weighting Scale).[4,8]

- For each criterion, participants shared experiential insights and knowledge, and assigned a score (+5 [Much in favor of option 1] to -5 [Much in favor of option 2]). Participants were allowed to provide a single score or a range of scores, according to the degree of uncertainty regarding their judgment.

- For qualitative criteria, participants were asked to identify whether a criterion was considered and if it impacted their decision in favor of option 1, in favor of option 2 or not impacted.

- Using a linear aggregation model, the RBRB and the modulated RBRB (sum of NormWeights X Scores) were calculated, and presented as means ± SD.

- Sensitivity analyses were performed.

RESULTS

- At group level, an overall mean modulated RBRB of 0.12 (±0.4) favored treatment with lanreotide over watchful waiting (see Figure 1).

- Type of therapeutic benefit (mean contribution, 0.08 ± 0.06), Comparative effectiveness (0.07 ± 0.09) Disease severity (0.07 ± 0.12), and Quality of evidence (0.06 ± 0.10) favored treatment with lanreotide over watchful waiting.

RESULTS (cont.)

- The criteria with the highest contributions to RBRB in favor of treatment with lanreotide were Progression-free survival (0.1 ± 0.13) and Disease symptoms (0.05 ± 0.06). Watchful waiting was favored with respect to the criteria Non-fatal non-serious adverse events (-0.02 ± 0.03), Non-fatal serious adverse events (-0.01 ± 0.02) and Convenience (-0.01 ± 0.01). Costs considerations, namely Cost of intervention, Other medical costs and constraints and Non-medical cost and constraints favored watchful waiting (mean contributions: -0.14 ± 0.12; -0.05 ± 0.07; -0.03 ± 0.07, respectively).

- Among patients, Comparative effectiveness obtained the highest mean contribution (0.12 ± 0.11), favoring treatment with lanreotide, whereas the criterion Cost of the intervention favored watchful waiting (mean -0.12 ± 0.1).

- Among clinicians, Disease severity (0.10 ± 0.15 and Type of therapeutic benefit (0.10 ± 0.07) obtained the highest mean contributions favoring treatment with lanreotide. The criterion Cost of the intervention favored watchful waiting (-0.15 score ± 0.15).

Figure 1. Mean Modulated RBRB contributions* of each quantitative criterion and overall Modulated RBRB† for treatment (using lanreotide as reference case) vs. watchful waiting
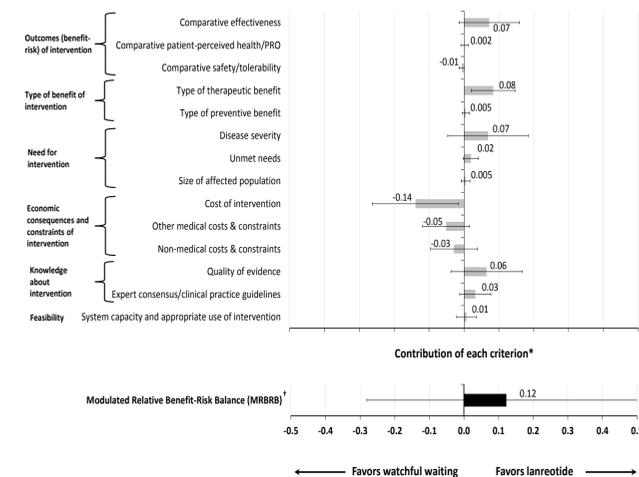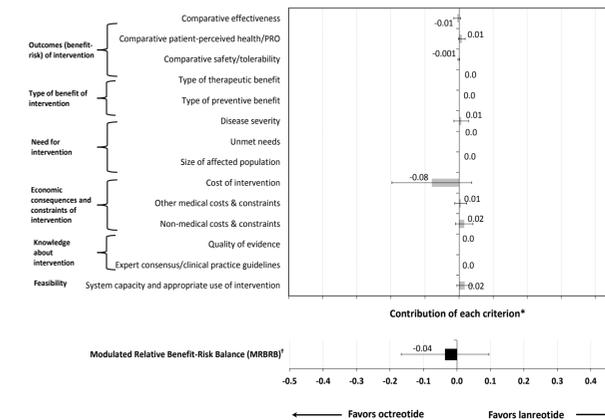

*Values shown represent the contribution of criteria to Modulated relative benefit risk balance calculated as normalized weight (summing to 1) multiplied by score for each criterion (theoretical range from −1 to +1).
†Relative benefit risk balance is the sum of contributions from all criteria (theoretical range from −1 to +1)
Error bars show standard deviations across 11 participants.

RESULTS (cont.)

- When comparing two treatment options (lanreotide vs. octreotide), the majority of criteria did not favor one option over another and the overall mean RBRB was -0.04 ± 0.13 in favor of octreotide (see Figure 2). System capacity (0.02 ± 0.02) and Non-medical costs and constraints (0.02 ± 0.03) tip the scale in favor of lanreotide, and Cost of intervention in favor of octreotide (-0.08 ± 0.12).

- Among patients and clinicians, most of the modulating criteria did not favor one option over the other. Other medical costs obtained the highest value in favor of lanreotide by patients (0.02 ± 0.02).

- Clinicians indicated System capacity (0.03 ± 0.03), Non-medical costs (0.02 ± 0.03), Disease severity (0.01 ± 0.03) and Patient-perceived health/PRO (0.008 ± 0.01) favored lanreotide whereas Cost of intervention obtained the highest mean in favor of octreotide by both patients and physicians (0.04 ± 0.06 and -0.1 ± 0.14, respectively).

- Four of 11 participants indicated that the criterion Opportunity costs and affordability is in favor of watchful waiting in the first scenario and of octreotide in the second scenario. None of the qualitative criteria favored lanreotide.

Figure 2. Mean Modulated RBRB contributions* of each quantitative criterion and overall Modulated RBRB† in the scenario comparing lanreotide vs. octreotide

*Values shown represent the contribution of criteria to Modulated relative benefit risk balance calculated as normalized weight (summing to 1) multiplied by score for each criterion (theoretical range from −1 to +1).
†Relative benefit risk balance is the sum of contributions from all criteria (theoretical range from −1 to +1)
Error bars show standard deviations across 11 participants.

CONCLUSIONS

- The MCDA EVIDEM framework was selected as it allows evidence, values, perspectives and trade-offs to be incorporated into a comprehensive and pragmatic approach combining both quantitative and qualitative insights when making decisions regarding treatment options for patients with unresectable, well- or moderately differentiated nonfunctioning GEP-NET.

- Most participants deemed that all criteria of the EVIDEM MCDA framework are relevant to engage in a discussion around treatment initiation.

- Through the exploration of two scenarios (watchful waiting vs. treatment with lanreotide, and lanreotide vs. octreotide), applying the MCDA process allowed the in-depth exploration of what matters and how it matters in the shared decisionmaking process.

- Scenarios comparing watchful waiting to treatment with lanreotide at a group and subgroup level indicate that patients and clinicians prefer to opt for treatment, whereas scenarios comparing SSAs did not seem to favor one treatment option over the other, despite a trend observed in favor of lanreotide.

- Holistic MCDA embedded with evidence supports individual reflection and informed shared-decisionmaking. This exploration highlights the importance of identifying what matters to patients and conveying, to patients and their caregivers, the available evidence and relevant information.

ACKNOWLEDGEMENTS

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