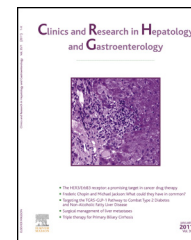




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ORIGINAL ARTICLE

Patient-reported tolerance in treatments approved in neuroendocrine tumors: A national survey from the French Group of Endocrine Tumors

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KEYWORDS

Neuroendocrine tumors;
Survey;
Tolerance;
Patient-reported

Summary

Background: Patients with advanced neuroendocrine tumors (NETs) benefit from an increasing number of treatments. The patient's preference could help physicians to choose among these options. Our patient-reported survey aims to compare the perceived tolerance of NETs treatments.

Methods: Patients treated by at least three different therapeutic options have evaluated their perceived tolerance from one (very good) to five (very poor) for each single treatment. Referent physician confirmed the type and ranking over time of each treatment.

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Results: Two hundred and forty two treatments have been evaluated by 54 patients. Among patients and NETs characteristics, only a female gender was associated with poor perceived tolerance. Median perceived tolerance increased from 1 (somatostatin analogs, peptide receptor radionuclide therapy (PRRT)), 2 (surgery, radiofrequency ablation and oral chemotherapy), 3 (interferon and everolimus), to 4 (liver embolization, sunitinib and intravenous chemotherapy). In taking somatostatin analogs as reference, the odd ratios for poor perceived tolerance were 1.7 [0.6–5.1] for oral chemotherapy, 2.2 [0.9–5.3] for surgery of the primary tumor, 2.4 [0.6–9.5] for radiofrequency ablation, 2.8 [1.1–7.3] for surgery of metastasis, 3.4 [1.4–7.9] for everolimus, 3.7 [1.6–8.5] for liver embolization, 4.9 [2.2–10.7] for intravenous chemotherapy and 5.9 [2.6–13.1] for sunitinib. Only PRRT had negative odd ratio.

Conclusion: Our retrospective analysis suggests that perceived tolerance differ in between therapeutic options and may help physicians to sequence the therapeutic strategy.

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Introduction

Many treatments are now available for advanced neuroendocrine tumors (NETs), either loco-regional (surgery, radiofrequency ablation or transarterial liver embolization) or systemic (somatostatin analogs, interferon, everolimus, sunitinib, intravenous or oral cytotoxic chemotherapy, and peptide receptor radionuclide therapy, PRRT) [1]. Currently, no head to head comparison or predictors of response are available allowing the determination of the best strategy. Therefore, the best strategy is decided on a case-by-case during a multidisciplinary meeting, based on factors such as presence of symptoms, patient comorbidities (kidney, heart and liver failure), prognostic factors (mainly tumor grade, morphological progression, and tumor burden), uptake on somatostatin receptor scintigraphy, expected treatment efficiency and side effects. The possibilities are proposed to patients and the final treatment is decided together with the patient.

Toxicity is well reported in clinical trials, mainly assessed by Common Terminology Criteria of Adverse Events (CTCAE), but not by the patients themselves. Quality of life studies are also reported in most clinical trials, but the questionnaires are often too fastidious for NET patients [2]. Studies focusing on patients themselves, such as patient-reported outcome studies and patient treatment experience, are becoming increasingly important endpoints in oncology [3–5]. Their goals are to assess disease symptoms, adverse effects of received treatments, quality of life, as well as physical and mental health. Recent studies have been reported in NET patients, but these only rated the impact of the disease not the impact of the treatments [3,6]. Thus, we designed a national survey on patient-reported tolerance of treatments approved in NETs. The main objective was to evaluate and compare treatments toxicities based on patient perception. Secondly, we explored the association between poor perceived tolerance and patient/tumor characteristics.

Material and methods

Patients

This was a French multicenter survey, financed by a grant from APTED (*Association de patients porteurs de tumeurs*

endocrines diverses), an association of patients with NET. Patients were included between December 2014 and December 2015. To be eligible, patients were required to have:

- an advanced well-differentiated NET;
- received at least three anti-tumoural treatments;
- an access to the internet;
- and have given their written informed consent.

If the patient had received the same treatment twice or several times, only the first period of prescription was evaluated.

Patients were informed and invited to participate by their physician or the patient association. They received a flyer with a unique access code and the URL of the website created for the survey. The code allowed a self-inclusion of patients who wanted to participate.

Survey

The survey website was approved by the regional medical ethics committee (*Région Sud-Est France*). Information for consent to the survey was printable from the website. Physicians and webmaster contacts were available for any questions. The survey was tested and approved by ten members of the patient association (APTED) before implementation. Patients could be helped by a nurse or a research assistant, unrelated to their oncologist, in order to complete questionnaires.

The following clinical data were recorded by patients: date of birth, gender, name/center of his/her referent oncologist, presence of pain at the time of the survey, and treatments they had received in chronological order, from a multiple choice list including surgery of primary tumor, surgery of metastasis, radiofrequency ablation (RFA), transarterial embolization (TAE) or chemoembolization (TACE), somatostatin analogs (SSA), interferon, everolimus, sunitinib, temozolomide ± capecitabine, intravenous chemotherapy (oxaliplatin-based (GEMOX, FOLFOX, or XELOX), dacarbazine-based, streptozotocine-based, and FOLFIRI). Patients could also add a treatment not listed. Each treatment was evaluated using a perceived tolerance score scaled from one to five (1: very good, 2: good, 3:

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