Development and Evaluation of a Real-World Outcomes-Based Tool to Support Informed Clinical Decision Making in the Palliative Treatment of Patients With Metastatic NSCLC

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PURPOSE To develop and evaluate a tool for patients with stage IV non–small-cell lung cancer and their thoracic oncologists (TOs) that provides insight into real-world effectiveness of systemic treatments to support informed clinical decision making in the palliative setting.

METHODS A participatory design approach was used to acquire insights from patients and TOs into preferences regarding the content and design of the web-based tool. Implementation was investigated by means of an adoption and usage rate. The appreciation of the tool was evaluated through a telephone survey with patients and a questionnaire for TOs.

RESULTS From clinical data of 2,989 patients with stage IV non–small-cell lung cancer diagnosed in one of the Santeon hospitals, an interface was developed to show treatments plus both real-world outcomes and clinical trial results after selecting patient characteristics (patients like me). This prototype of the tool was finalized after discussion in a focus group with four TOs and semi-structured interviews with six patients. The tool was implemented and used by TOs in three of six Santeon hospitals (50% adoption rate). The tool was used in 48 patients (29% usage rate), of which 17 participated in the telephone survey. Ten TOs responded to the questionnaire. The responses varied from positive reactions on the clear overview of treatment outcomes to statements that the tool rarely changed treatment decisions. Overall, the majority of patients and TOs scored the tool as of added value (71% and 83%, respectively).

CONCLUSION Our real-world data tool in metastatic lung cancer was appreciated in clinical practice by both patients and TOs. However, the efficacy of the implementation can be improved.

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INTRODUCTION

Most oncologists use survival and toxicity data from clinical trials to counsel patients, inform decision making, and obtain consent for treatment. The same applies to the creation of treatment guidelines. It is known, however, that patients treated in everyday practice tend to be older and more frail, have poorer performance status, and have more comorbidities and less social support than those selected to participate in clinical trials. This makes the translation of outcomes data from clinical trials to regular practice complex.

Previously, we found that survival of patients with metastatic non–small-cell lung cancer (NSCLC) treated with systemic therapy in real-world practice is 23% shorter than for patients included in clinical trials, and stopping treatment for toxicity is more frequent in real world. Patients’ performance status, earlier discontinuation, and fewer subsequent lines of treatment partly explained this difference.

From these findings, we considered that, in addition to clinical trial efficacy data, data about clinical effectiveness of systemic treatment options in metastatic NSCLC from real-world settings can be useful to provide to patients an overview of what can be expected from different treatment options. Such information is known to be appreciated by patients and could help patients to consider their options from a personal view (eg, how important the possible benefits and harms are to them) and could help them to be involved in making a decision together with their health practitioner. Additionally, real-world data can assist thoracic oncologists (TOs) in formulating treatment options with enough gain in overall survival to be worthwhile for patients, as research has shown that oncologists tend to overestimate life expectancy of patients and that they could benefit from using tools providing individual survival estimates.

The potential added value of providing real-world outcomes data through a tool has not been studied...
CONTEXT

Key Objective
To develop and evaluate a tool for patients with stage IV non–small-cell lung cancer and their thoracic oncologists (TOs) that provides insight into real-world effectiveness of systemic treatments to support well-informed treatment decisions in the palliative setting and to evaluate the appreciation of the tool in routine clinical practice.

Knowledge Generated
The developed web-based tool provided insight on both real-world treatment outcomes from patients resembling selected characteristics and trial efficacy data for reference. The majority of patients and TOs reported an added value in terms of usefulness and appreciation of the web-based tool when used in clinical practice.

Relevance
Our tool fulfilled the wished-for function of integrating knowledge from clinical trials and real-world outcomes data. Our evaluation learned that for adaptation by TOs, tooling must evolve and reflect advances in treatment strategies. Furthermore, more effort should be invested in guiding implementation coupled with training in shared-decision making.

before in patients with metastatic NSCLC. A review by Revesz et al on available decision support systems (DSS) for incurable patients with metastatic NSCLC reported that all DSS were based on statistical models that make use of probabilities (eg, prediction models or nomograms) but lacked recent clinical data. Furthermore, there is no DSS that gives an overview of all treatments relevant to consider in patients with incurable NSCLC or that offers information about intensive treatment versus best supportive care. Additionally, Revesz et al examined the needs and preferences of TOs with regard to future DSS in the treatment of metastatic NSCLC and reported that 77% would welcome new DSS for their own decision making and/or for shared decision making.

The aim of the present study was to develop a tool for patients with stage IV NSCLC and their TOs that provides insight into the real-world effectiveness of systemic treatments (patients like me concept) to support well-informed treatment decisions in the palliative setting and to evaluate the appreciation of the tool in routine clinical practice.

METHODS

Figure 1 shows the steps conducted in the development and evaluation phases of the tool. A participatory design approach was used to acquire insights from patients and TOs into preferences regarding the content and design of the web-based tool.8

Development of the Tool

From our aforementioned systematic evaluation study on the efficacy-effectiveness gap of systemic treatments in metastatic NSCLC (cohort of N = 2,989 patients with stage IV NSCLC),3 data on patient characteristics, types of treatment received (including best supportive care), survival, and toxicity-related outcomes were extracted per patient. In short, this cohort includes all patients with stage IV NSCLC diagnosed between 2008 and 2014 in the Santeon hospitals, the Netherlands. For every treated patient, overall survival was calculated on the basis of the time between start date of systemic treatment and date of death. Patients still alive at January 31, 2017 were given this end of follow-up date as imputed date of death (n = 54). Besides survival, toxicity was assessed using percentage of dose reductions (≤80% of the initial dose) and early discontinuation (fewer than four cycles or tyrosine kinase inhibitor use <1 month) as proxy. These data were collated in a spreadsheet that formed the base for the present project.

Step 1: prototype on the basis of available data. On the basis of the first-line treatment regimens in the spreadsheet, a prototype of the tool was designed that included three parts: (A) drop-down menus for all available patient characteristics (eg, age, sex, Eastern Cooperative Oncology Group performance status [ECOG PS], and comorbidities), to be entered by the TO; (B) graphical representation of individual survival times of prior real-world patients resembling the patient characteristics within a selection; and (C) graphical representation of treatment outcomes (eg, proxies for toxicity such as percentage of the resembling patients with dose reduction and most common side effects of the systemic treatments shown).

Step 2: focus group and meetings with TOs. To ensure a good understanding of the complex data to be presented in the tool, the exact layout of the interface and how the data should be presented was determined in close collaboration with TOs from three Santeon hospitals in the Netherlands (St Antonius Hospital Nieuwegein/Utrecht; OLVG Hospital Amsterdam; and Canisius-Wilhelmina Hospital, Nijmegen). The prototype of the tool (step 1) was discussed in a focus group with four TOs, using a question route moving from general to more specific issues, focusing on their perceptions of applying the tool (positive features, changes needed, relevance, and timing of use).

Because of novel treatment options emerging during the development period of the tool (eg, immunotherapy),
individual conversations and three group meetings (with two to four participants) were organized to discuss the feasibility for processing these novel treatments into the tool.

**Step 3: interviews with patients.** Individual semi-structured interviews with six patients who were recently diagnosed with stage IV NSCLC in the St Antonius Hospital were organized to discuss and further develop the content and layout of the tool as designed in step 1 and 2. Patients were asked about their recent process of acquiring information about their diagnosis and treatment options and the idea of obtaining information through a web-based tool. The prototype of the tool was shown and discussed, including questions about interpretation of the information as shown in the tool, lacking information, suggestions for usability, timing of use, and the added value of such a tool in their decision-making process.

The development of the tool was finalized by adjusting the three parts of the tool as mentioned in step 1, as a result of step 2 and 3.

**Implementation for Pilot Study**

The final tool was implemented in clinical practice after an instruction to all possible users in the participating hospitals (eg, TOs, oncology nurses, pulmonologists, and lung or oncology doctors in training) about how to login, how to use the drop-down menus, and how to interpret the displayed outcomes about survival and treatment and about integration in the outpatient department (eg, informed consent procedure). These implementation meetings were provided in a tailored manner, with a certain degree of local adaptation allowed for each hospital, with respect to the course of events as usual in their clinical practice.

The tool was offered to all newly diagnosed patients with stage IV NSCLC in the participating Santeon hospitals.
(stepwise introduction) starting August 1, 2019. Eligible patients were identified at the multidisciplinary tumor board (MTB) meetings of the lung cancer oncology team. Non-eligible were patients with no fluency in speaking and reading Dutch and/or only best supportive care as the possible treatment option (no treatment decision to be made). The TO revealing the cancer diagnosis to the patient offered the tool during the first outpatient visit of the patient after the MTB meeting and asked for consent toward the evaluation. If desired, the tool could also be used in a potential follow-up visit with the oncology nurse.

**Evaluation and Measures**

The primary evaluation parameter was the added value of the tool for both patients and TOs, measured by the percentage of patients and TOs who reported availability of tooling as useful and appreciated. The added value of the tool was predefined as satisfying when reported by $\geq 50\%$ of the patients or $\geq 50\%$ of the TOs. The tool was evaluated through a structured telephone survey with patients (Data Supplement) within 2 weeks after using the tool in clinical practice and a study-specific questionnaire for TOs at the end of the pilot period. Information about age, sex, and ECOG PS of the patient was anonymously collected from the values entered in the tool.

Secondary parameters were as follows: (1) the adoption rate (intention to use the tool) and usage rate (actual use) of the tool in six Santeon hospitals and (2) decisional roles of patients and TOs when using the tool in clinical practice, as reported with the Control Preferences Scale (CPS<sub>post</sub>,<sup>10</sup> and CPS,<sup>11</sup> respectively). The adoption rate was calculated as the percentage of hospitals in which the tool was implemented with the TOs and the usage rate as the percentage of patients for whom the tool was actually used, on the basis of logging data of the application. The tool was predefined as feasible for patients and TOs in case of an adoption rate and usage rate of more than 50\%, on the basis of those rates reported in previous studies on patients like me.
web-based applications.\textsuperscript{9,12} From the CPS and CPS\textsubscript{post}, the percentage of patients and TOs with a preferred or used active, collaborative, or passive decisional role was calculated.

The evaluation study was approved by a medical research ethics committee (CMO region Arnhem-Nijmegen registration number 2018-4337). All participants provided their written consent before participation in the telephone survey.

### Statistical Analyses
Descriptive statistics were used. To present an overview of baseline characteristics for all patients in the pilot study, frequencies (proportions) were calculated for categorical variables and the median (with range) was provided for nonnormal distributed continuous data (age). Primary and secondary parameters were presented as percentages.

### RESULTS

#### Development of the Tool

The focus group and meetings with TOs and the semi-structured interviews with patients yielded several adjustments to the prototype of the tool. Besides a reduced number of drop-down menus with patient characteristics in part A of the tool (restricted to age, sex, and ECOG PS), drop-down menus about clinical information (type of histology, programmed death ligand-1 expression, and epidermal growth factor receptor mutation status) were added for adequate selection of possible treatments to be shown. Second, adjustments were made to the graphical

#### SURVIVAL

<table>
<thead>
<tr>
<th>Patients with early discontinuation of treatment</th>
<th>Patients with dose reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>46%</td>
</tr>
<tr>
<td>Immuno+chemotherapy</td>
<td>16%</td>
</tr>
<tr>
<td>Immunotherapy</td>
<td>18% (from clinical trials)</td>
</tr>
<tr>
<td>No data available</td>
<td>no data available</td>
</tr>
</tbody>
</table>

#### TREATMENT

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Chemotherapy</th>
<th>Immuno+chemotherapy</th>
<th>Immunotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in blood count</td>
<td>39% patients with 1-year survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>63% patients with 1-year survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal complaints</td>
<td>61% patients with 1-year survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appetite changes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

![Fig 3. Screenshot of web-based tool for patients with stage IV non–small-cell lung cancer—part C.](image-url)

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representation of survival outcomes in part B, to be able to display outcomes of novel treatment options emerging during the development period of the tool. Screenshots of part B and C are given in Figures 2 and 3, respectively (the original Dutch interface is provided in the Data Supplement). The minimal required sample to display part B and C after the selections in part A was set on 10 patients, and for understandability for patients, it was decided not to show confidence intervals with frequencies. Finally, a print option for patients was added where all three parts can be printed together to take home, with the possibility to discuss the information with other caregivers and family. The Data Supplement describes the development of part B and C of the tool in greater detail.

Implementation for Pilot Study
The meetings revealed that information that was normally provided to the patient by the TO and/or the oncology nurse about the different treatment options (eg, information about the method of administration for the different drugs and the number of times the patient would need to come to hospital) should be given the same way as without using the tool. Accordingly, the tool was used as source of information alongside the standard procedures and provision of information during a consultation.

The tool was implemented and used by TOs in three of six Santeon hospitals (50% adoption rate). The main reason for not adopting was the current COVID-19 pandemic. The total number of potential patients for whom the tool could have been used was 166 (eligible and noneligible patients), on the basis of the number of patients in MTB meetings in the respective pilot study periods per hospital. Eventually, the tool was used in 48 of these patients (29% usage rate), of whom 21 were reached for the telephone survey and 17 patients actually answered the questions (Fig 4). The majority of the latter patients were male (71%), the median age was 66 years, and 88% had an ECOG PS of 0-1 (Table 1).

Added Value of the Tool (usefulness and appreciation) in Pilot Study

**Added value of the tool according to patients.** The results of the telephone survey showed that for most of the patients the information in the web-based tool was clear (94%) and almost two-third (65%) reported that this information was important for them. Patients were positive about the overview of the different outcomes for various treatment options, for example, “It was impressive seeing the differences of the treatment options for which I was eligible.” Furthermore, 71% of the patients reported an added value of the web-based tool when used in clinical practice. However, some patients stated that the tool was not useful to them, because “most of the information was already explained by the thoracic oncologist.” Overall, eight of 17 patients (47%) stated the tool was useful in decision making. Several patients reported that they already had made a treatment decision, varying from “Actually, I already
TABLE 1. Characteristics of Participants in Telephone Survey

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participants in Telephone Survey (n = 17), No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12 (71)</td>
</tr>
<tr>
<td>Female</td>
<td>5 (29)</td>
</tr>
<tr>
<td>Age, median (range), years</td>
<td>66 (51-80)</td>
</tr>
<tr>
<td>ECOG PS</td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>15 (88)</td>
</tr>
<tr>
<td>≥ 2</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Squamous</td>
<td>4 (24)</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>12 (71)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (6)</td>
</tr>
<tr>
<td>PD-L1 expression, %</td>
<td></td>
</tr>
<tr>
<td>&lt; 1</td>
<td>9 (53)</td>
</tr>
<tr>
<td>1-49</td>
<td>3 (18)</td>
</tr>
<tr>
<td>≥ 50</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (12)</td>
</tr>
</tbody>
</table>

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death ligand-1.

made the decision myself. Doing nothing is not an option. I’ll go for it!” to “I don’t want chemotherapy and there are no treatment options for me which give curative.” From some, it seemed that the tool still helped in confirming their treatment decision.

Two patients mentioned areas for improvement: adding reasons for early discontinuation on the tab about toxicities and side effects (part C of the tool), adding real-world outcomes for novel treatment options (ie, immunotherapy), and some visual challenges when using the print option.

*Added value of the tool according to TOs.* The concept of the web-based tool seemed to be supported by TOs; however, a limited amount of time was spent for actual use of the tool in clinical practice. One TO noted that “I used the tool less often in clinical practice than expected/hoped,” which seems to confirm the general tendency observed in our study. The questionnaire for TOs, which was completed by 10 respondents, revealed some barriers for use of the tool during consultation of patients. The most given reason was that the information in the web-based tool was considered alarming and confronting to patients. Additionally, TOs reported that patients declined to look into the information as displayed in the web-based tool. Furthermore, TOs stated that the tool rarely changed treatment advice. Last, the lack of real-world outcomes about immunotherapy was often mentioned as a barrier for using the tool in clinical practice.

Despite all barriers, 83% of the TOs reported an added value of using the web-based tool in clinical practice, because “the tool gives transparent and less abstract information on treatment outcomes for patients” and “the tool serves as a proper framework for giving information to patients.” According to the TOs, this contributes to realistic expectations about the pros and cons of a treatment and enables informed decision making.

**DISCUSSION**

We developed a web-based tool for patients with stage IV NSCLC and their TOs that provides real-world outcomes data from available treatment options. The tool provided insight on both treatment outcomes from patients resembling selected characteristics and trial efficacy data for reference. The majority of patients and TOs reported an added value in terms of usefulness and appreciation of the web-based tool when used in clinical practice.

To our knowledge, this is the first study that developed and evaluated a tool that provides real-world outcomes data to patients with metastatic NSCLC and their oncologists. Other tools we know of are constructed on the basis of trial efficacy data solely. In contrast, we constructed a unique interface wherein individual real-world outcomes are shown together with an aggregated trial efficacy result so that patients and TOs can observe how an individual patient fits into the population in the trial. Besides this, the tool provided data about how frequent and what treatment (or best supportive care) was started in past patients.

Although our tool fulfilled the wished-for function of integrating knowledge from clinical trials and real-world
outcomes data, the tool was still infrequently used in clinical practice. Explanations from our evaluation are that real-world outcomes of recently introduced treatment options (immunotherapy) were lacking and that the information was considered confronting to patients. Additionally, preferred and used roles regarding treatment decisions during consultation were different according to patients and TOs. Besides strengths, our study also has limitations. First, the evaluation can be considered limited because of suboptimal implementation in clinical practice, reflected in the 50% adoption rate and 29% usage rate. This hampers generalizability of statements about the added value of the tool. Although TOs were strongly involved in the design of the web-based tool, actually making use of the tool in clinical practice was considered complex. In an observational study on communication about life expectancy with patients with advanced cancer, Henselmanns et al. found that oncologists did not initiate talk about life expectancy easily as they were generally not trained or encouraged regarding prognostic communication. Education on skills, knowledge, and attitudes toward well-informed decision making in combination with how to use the tool in clinical practice might be a way to improve this.

Second, real-world data from recently introduced treatment options (mono-immunotherapy and chemo-immunotherapy combinations) were not yet available from the hospitals. As a solution for this, in the tool, we predicted these outcomes by multiplying aggregated trial efficacy data from these novel treatments by the mean efficacy-effectiveness factor from the patients resembling the selected criteria. We acknowledge, however, that this is suboptimal and has caused some TOs to be less convinced to use the tool with patients.

Third, bias may have been introduced by the fact that less than half of the patients who experienced the tool participated in the telephone survey. It is not inconceivable that our evaluation is driven by patients being above average–positive about well-informed decision making. On the other hand, the mean age and distribution of sex, ECOG PS, and histology in our sample were comparable with patients not being interviewed and also with patients from a large unsellected population of patients with metastatic NSCLC.

Despite the abovementioned limitations, our study provides important results upon which to base further work to improve well-informed treatment decisions on the basis of real-world data. First, our evaluation learned that for adaptation by TOs, tooling must evolve and reflect advances in treatment strategies. A way to organize this is to incorporate DSS in electronic health records in combination with smart algorithms such that continuous updating and rapid adaptation of these instruments are ensured. Second, more effort should be invested in guiding implementation coupled with training in shared decision making.

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COLLECTION AND ASSEMBLY OF DATA: Christine M. Cramer-van der Welle, Elisabeth A. Kastelijn, Bram C. Plouvier, Franz M. N. H. Schramel


MANUSCRIPT WRITING: All authors

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ACCOUNTABLE FOR ALL ASPECTS OF THE WORK: All authors

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REFERENCES