Clinical trials in advanced stage lung cancer: a survey of patients' opinion about their treatment

Trial clinici nel tumore del polmone in stadio avanzato: un'analisi dell'opinione dei pazienti riguardo al trattamento

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ABSTRACT

Background: **The major aim of this study was to investigate what patients with advanced stage lung cancer, enrolled in a clinical trial, thought about their treatment. We also wanted to investigate if there exist any characteristics that could influence patients' opinion about the clinical trial.**

Patients and methods: **Over the period from June 2008 to June 2009, 59 eligible patients were enrolled in this study. The major inclusion criteria were: participation in a clinical trial, previously treated advanced stage lung cancer, and good performance status (ECOG 0-2). All patients were asked to answer a questionnaire designed to investigate their impressions about participation in a clinical trial. The questionnaire was deposited in a sealed box which was opened at the end of the study. We investigated a possible influence of age, gender, education, lung cancer stage, chemotherapy line and tumor type on the patients' opinion about some aspects of the clinical trial.**

Results: **The majority of the patients were aware they were participating in the clinical trial and a significant number of them were very satisfied with the treatment. Of the investigated factors, only the level of education had a statistically significant influence on some of the questions raised in the questionnaire.**

Conclusions: **Patients participating in clinical trials are satisfied with their treatment, ready to proceed with it and would recommend it to other patients. It depends mainly on health professionals to maintain this level of confidence and justify their trust.**

Keywords: **Chemotherapy, clinical investigation, clinical trial, lung cancer, non small cell lung cancer (NSCLC), small cell lung cancer (SCLC).**

RIASSUNTO

Razionale: **Lo scopo principale di questo studio era valutare ciò che pensano i pazienti con un tumore polmonare in stadio avanzato arruolati in un trial clinico riguardo al trattamento cui sono sottoposti. Desideravamo inoltre valutare se esistesse qualche caratteristica dei pazienti in grado di influenzare la loro opinione sui trial clinici.**

Pazienti e metodi: **Nel periodo tra giugno 2008 e giugno 2009 sono stati inclusi in questo studio 59 pazienti. I principali criteri di inclusione erano la partecipazione ad un trial clinico, essere già stati trattati per un tumore polmonare in stadio avanzato ed avere una buona condizione generale (punteggio 0-2 alla scala Eastern Cooperative Oncology Group). A tutti i pazienti è stato richiesto di compilare un questionario dise-**

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gnato per valutare le loro impressioni sulla partecipazione al trial clinico. Il questionario era depositato in un contenitore sigillato che veniva poi aperto al termine dello studio. Abbiamo ricercato una possibile influenza di età, sesso, scolarità, stadiazione del tumore polmonare, tipologia di chemioterapia e di tumore sull'opinione del paziente riguardo alcuni aspetti del trial clinico.

Risultati: **La maggioranza dei pazienti era consapevole di partecipare ad un trial clinico ed una quota significativa di loro era molto soddisfatta del trattamento. Tra i fattori oggetto di questa ricerca solo il livello di scolarità dimostrava un'influenza statisticamente significativa su alcuni dei punti toccati dal questionario.**

Conclusioni: **I pazienti che partecipano a trial clinici sono soddisfatti del loro trattamento, desiderosi di continuarlo e disposti a raccomandarlo ad altri pazienti. Dipende soprattutto dai professionisti della salute mantenere questo livello di fiducia e giustificare questo credito.**

Parole chiave: **Chemioterapia, studio clinico, tumore polmonare, tumore polmonare non a piccole cellule (NSCLC), tumore polmonare a piccole cellule (SCLC), valutazione clinica.**

INTRODUCTION

Lung cancer still remains one of the deadliest cancer types in the world. Both the incidence and mortality are still high, equally among male and female patients, in practically all parts of the world. Lung cancer is still a leading cause of cancer related mortality, with an overall 5-year survival < 20% in Europe and USA. The estimated number of new cases of lung cancer in USA for 2009 is 219,440. The estimated number of deaths in USA for 2009 is even more discouraging: 159,390 [1-4].

Many prevention and political measures, such as prohibition of smoking in public places or the banning of cigarette commercials, might contribute to a decrease in morbidity and mortality. However, these measures need time to show their true potential. In the past decade, we have observed a drop in morbidity (mostly in squamous cell lung cancer) due to the public measures and increased public awareness, but mortality still remains alarmingly high [5-8].

The introduction of novel chemotherapeutic agents, the development of targeted therapy, the combination of standard chemotherapy with molecular targeted therapy, and combinations with various radiotherapy regimens, might result in a better survival of lung cancer patients. Indeed, some clinical trials with novel targeted therapy agents, or their combinations with chemotherapy, have shown a significant improvement in the disease free survival, or even the overall survival. On the other hand, we should always be cautious about the results of clinical studies and wait for more data, or meta-analyses before implementing these results in the clinical practice [4,9-12]. Nevertheless, in the light of the current situation regarding lung cancer mortality, it is true that the most appropriate treatment for a patient is his/her inclusion in a clinical trial. Practically all cancer societies, dealing with the problem of lung cancer, recommend treatment in a clinical trial setting [12-16].

However, in the hunt for a better survival and better results, with a substantial number of patients in clinical trials, what do we actually know about our patients' thoughts and feelings? What do they themselves know about their own condition and the treatment itself? The regulations and rules for the clinical trials are strict and defined, and all physicians investigating the treatment of lung cancer adhere to these rules and regulations [14-18]. But still, what do patients think and know about it? Many patients receive therapeutic benefits from participating in clinical trials, even moreso than they are aware, and in some cases these benefits exceed those that standard care could provide. However, the patients participating in clinical trials contribute not only to their own and future patients' treatment benefits, but also to the benefits of medicine and to science itself. The physicians are aware of this fact, but are the patients aware of the same fact, too?

The major aim of the study we conducted was to investigate what patients knew and thought about their disease, about the options for their current and future treatment, as well as about the clinical trial they participated in. We wanted to investigate how satisfied they were with the treatment in the clinical trial (this is why we included only previously treated patients), and what they thought and knew about the novel chemotherapy they were treated with. We designed a short questionnaire in order to obtain the answers to some of these questions. The secondary aim of the study was to investigate the influence of age, gender, education, lung cancer type and stage, chemotherapy duration and chemotherapy line on the patients' opinion about the disease, treatment, and clinical trial.

PATIENTS AND METHODS

This was a prospective trial conducted at the Clinic for Pulmonary Oncology of the Institute for Pulmonary Diseases of Vojvodina, Serbia. The study was carried out over a 1-year period, from July 2008 to July 2009, and it was approved by the institutional review and ethical board. All the patients who agreed to participate in the study and answer the questionnaire were informed about the study and signed the informed consent form.

Of 86 patients who at the time participated in clinical trials on administration of novel chemotherapeutic agents, 59 met all the inclusion criteria and were eligible for the study. The inclusion criteria were: current participation in a phase II or III clinical trial on non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC), the treatment including targeted molecular therapy, chemotherapy or their combination, advanced stage (IIIB, IV) NSCLC or extensive SCLC, second or third line chemotherapy, good performance status graded by Eastern Cooperative Oncology Group (ECOG) 0-2, and willingness to participate in the study. The exclusion criteria were: the first line chemotherapy, stage I – IIIA NSCLC, limited SCLC, current or concurrent radiotherapy, ECOG ≥ 3, inability or refusal to par-

ticipate in the study.

A specially designed questionnaire (Figure 1) was given to each patient enrolled. The patients were asked to answer the questionnaire after the third course of the second or third line chemotherapy regimen. All of the patients had sufficient time to answer the questions and to place the questionnaires in the "answer box". The "answer box" was a sealed carton container placed in the main hall of the clinic, enabling the patients to keep their privacy and anonymity after completing the questionnaire. This approach provided privacy to the patients, and ensured true and honest answers. It was explained to the patients that they should write their

FIGURE 1: *AD-HOC* QUESTIONNAIRE TO INVESTIGATE PATIENTS' IMPRESSIONS ABOUT PARTICIPATION IN A CLINICAL TRIAL

QUESTIONNAIRE

The main purpose of this investigation is explained to you in the informed consent form you read and signed. If you wish, you can answer the questions in this questionnaire. Answer the questions by simply circling the answer you think is appropriate. When you finish, please put the questionnaire in the answer box located in the main lobby of the clinic.

Thank you for your participation.

1. Are you familiar with the nature of the disease you suffer from?
   a) Yes b) No c) I am not sure
2. Do you know the type of lung cancer you suffer from?
   a) Yes b) No c) I am not sure
3. Do you know what kind of chemotherapy for lung cancer you have so far received?
   a) Yes b) No c) I am not sure
4. Are you aware in what stage your condition (lung cancer) currently is?
   a) Yes b) No c) I am not sure
5. Have you received your previous chemotherapy in a regional hospital or at the Institute for Pulmonary Diseases of Vojvodina (IPBV)?
   a) Regional hospital b) IPBV c) I am not sure
6. Do you understand that you are participating in the clinical trial with novel chemotherapy or targeted therapy drug?
   a) Yes b) No c) I am not sure
7. Do you understand what a clinical trial is?
   a) Yes b) No c) I am not sure
8. Have you read the entire Informed Consent Form (ICF) your physician gave you before you entered the clinical trial?
   a)Yes b) No c) I am not sure
9. How satisfied are you with the information about the clinical trial you obtained from your physician or from the ICF?
   a) Very satisfied b) Satisfied c) Not satisfied d) I am not sure
10. Do you think that during the clinical trial period you will need additional information about the study treatment?
    a) Yes b) No c) I am not sure
11. Do you think that by participating in a clinical trial you have a better chance for surviving the lung cancer?
    a) Yes b) No c) I am not sure
12. Do you think that chemotherapy given within the clinical trial is better than the chemotherapy patients usually get?
    a) Yes b) No c) I am not sure
13. Are you aware of the fact that you might not be treated with the investigational product in the clinical trial you are currently participating?
    a) Yes b) No c) I am not sure
14. Do you think the investigational product (chemotherapy) given in the clinical trial you are currently participating in has fewer side effects than the chemotherapy you were previously treated with?
    a) Yes b) No c) I am not sure
15. Do you think that the medical personnel (physicians and nurses) conducting this clinical trial have sufficient knowledge and training?
    a) Yes b) No c) I am not sure
16. Do you think the physicians and nurses are more easily accessible to you because you are participaring in the clinical trial?
    a) Yes b) No c) I am not sure
17. Do you think that your treatment within the clinical trial is better than the treatment of patients who are not participating in clinical trials?
    a) Yes b) No c) I am not sure
18. How would you assess your treatment in the clinical trial so far?
    a) Excellent b) Very good c) Good d) Neither good nor bad e) Bad
19. If there were an opportunity to join another clinical trial, after you finish the current one, would you join?
    a) Yes b) No c) I am not sure
20. Would you recommend to other patients to join the clinical trial you have been participating in?
    a) Yes b) No c) I am not sure

initials and date of birth in order to enable obtaining other relevant data from their medical charts needed for evaluation of the results to be performed later.

Descriptive statistics were generated for all study variables, including the mean and standard deviation for continuous variables and relative frequencies for categorical variables.

The variables concerning 'the patients' satisfaction' were treated as the data in nominal category. In order to compare these answers according to gender, cancer type, cancer stage, education level of patients and line of chemotherapy, we used Pearson's χ^2 test with $p < 0.05$ as a significant level of probability. All statistical analyses were performed using the SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL) software.

RESULTS

Fifty-nine patients were included in this study. The average age of the patients was 56 ± 10 years (range 36-73). The average chemotherapy duration was 11 ± 4 months (range 3-19). There were 48 (81.4%) male patients and 11 (18.6%) females included in this study. Most patients (n = 32, 54.2%) had squamous cell lung cancer diagnosed; small cell lung cancer was diagnosed in 16 (27.1%) patients, and adenocarcinoma in 11 (18.6%) patients. The majority of the patients (30/59, 50.8%) had an advanced stage IV NSCLC. Thirteen patients (22%) had stage IIIB NSCLC. Extensive SCLC was investigated in 16 patients (27.2%). There were 17 patients (28.8%) enrolled in phase II clinical trials versus 42 (71.2%) in phase III clinical trials. The majority of the patients (32 or 54.2%) were high school graduates; 16 (27.1%) patients had a university degree, while 11 patients (18.6%) had elementary school education.

An overview of the questions, and frequency and percentage of the answers is presented in Table I. The questions marked with an asterisk are explained further in the text. It is clear from the table that all the patients who participated in both clinical trials and our study were familiar with the nature of their disease. A significant number of patients knew the type of lung cancer they suffered from. There was also a significant number of patients who knew what kind of chemotherapy they received prior to the enrollment in the clinical trial. The majority of the patients were aware of their current lung cancer stage. Question 5 addressed the place or institution where the patients received previous chemotherapy. Most patients were previously treated in our institution (44/59 or 74.6%); 14 (23.7%) patients were treated in the regional hospital, while one patient did not know where he was treated. Almost all patients (58/59 or 98.3%) knew that they were participating in a clinical trial; the remaining patient responded that he did not know he was participating in a clinical study. The large majority of patients (47/59 or 79.7%) said they understood what "a clinical trial" was, but 12 patients (20.3%) were not sure what "a clinical trial" means. One of the most interesting results shows that 5 patients (8.5%) did not read the entire informed consent form (ICF). However, a significant number of patients (54/59 or 91.5%) had read the entire ICF. Question 9 addressed the level of satisfaction with the information about the treatment within the clinical trial. Forty-three patients (72.9%) were very satisfied with the information given by the investigators or provided in the ICF and 16 patients were satisfied. There were no patients who were not satisfied or who were unable to answer question 9. Practically equal numbers of patients thought they would/would not require additional information during the clinical trial period, i.e. 47.5% and 49.2% of the patients, respectively.

One of the most important findings obtained in the study was the opinion of patients that the chemotherapy given in the clinical trial would give them a better chance for survival. A significant number of patients (93.2%) thought they had a better chance of survival in the clinical trial, and 6.8% of the patients were not sure about it. There was also a large number of patients who answered that chemotherapy given in the clinical trial was better than the therapy used previously. Forty-eight patients (81.4%) thought that chemotherapy in the clinical trial was better than the "usual" chemotherapy, 2 patients thought it was not better, while 9 patients (15.3%) were not sure. A majority of patients (98.3%) understood that during the clinical trial they might not receive the investigational product. There were 38 patients (64.4%) who thought that chemotherapy given in the clinical trial had fewer side effects, 16 who thought the contrary (that chemotherapy given in the clinical trial did not have fewer side effects), and 5 (8.5%) who were not sure. There were 57/59 (96.6%) patients who thought that the medical personnel conducting the clinical trial had sufficient knowledge and skills. This shows that a majority of patients believe that their doctors and nurses are adequately trained. All the patients enrolled in the study expressed the opinion that the physicians and nurses were more easily accessible to them because they participated in the study. A significant number of patients (57/59 or 96.6%) believed the treatment within a clinical trial was better than the treatment given to patients not included in trials. Two remaining patients were not sure about this issue. A majority of the patients (89.8%) graded their overall treatment in the clinical trial as excellent. Five patients (8.5%) assessed their treatment as very good, while one patient assessed it as good. There were no patients who assessed their treatment as "neither good nor bad" or "bad". Interestingly, 88.1% of the patients answered that they would participate in future clinical trials when they finished the treatment in the current one. This means that a significant number of patients would like to continue the treatment within the clinical trial. On the other hand, two patients (3.4%) would not any more participate in clinical trials, while 5 patients (8.5%) were not sure about it. The majority of patients (56/59 or 94.9%) would recommend the clin-

TABLE I: PATIENTS' RESPONSES PER RESPONSE CATEGORY (NUMBER AND %) TO EACH ITEM OF THE QUESTIONNAIRE

Question	Answers		
	Yes n/%	No n/%	I am not sure n/%
1. Are you familiar with the nature of disease you suffer from?	59/100	0/0	0/0
2. Do you know the type of lung cancer you suffer from?	50/84.7	0/0	9/15.3
3. Do you know what kind of chemotherapy for lung cancer you received so far?	58/98.3	0/0	1/1.7
4. Are you aware at what stage your condition (lung cancer) currently is?	44/74.6	1/1.7	14/23.7
5. Have you received your previous chemotherapy in a regional hospital or at the Institute for Pulmonary Diseases of Vojvodina (IPBV)?*			
6. Do you understand that you are participating in a clinical trial with novel chemotherapy or a targeted therapy drug?	58/98.3	0/0	1/1.7
7. Do you understand what a clinical trial is?	47/79.7	0/0	12/20.3
8. Have you read the entire Informed Consent Form (ICF) your physician gave before you entered the clinical trial?	54/91.5	5/8.5	0/0
9. How satisfied are you with the information about the clinical trial you obtained from your physician or from the ICF?*			
10. Do you think that during the clinical trial period you will need additional information about the study treatment?	28/47.5	29/49.2	2/3.4
11. Do you think that by participating in a clinical trial you have a better chance for surviving the lung cancer?	55/93.2	0/0	4/6.8
12. Do you think that chemotherapy given within the clinical trial is better than the chemotherapy patients usually get?	48/81.4	2/3.4	9/15.3
13. Are you aware of the fact that you might not be treated with the investigational product in the clinical trial you are currently participating?	58/98.3	0/0	1/1.7
14. Do you think that the investigational product (chemotherapy) given in the clinical trial you are currently participating in has fewer side effects than the chemotherapy you were previously treated with?	38/64.4	16/27.1	5/8.5
15. Do you think that medical personnel (physicians and nurses) conducting this clinical trial have sufficient knowledge and training?	57/96.6	1/1.7	1/1.7
16. Do you think that physicians and nurses are more easily accessible to you because you are participating in the clinical trial?	59/100	0/0	0/0
17. Do you think that your treatment within the clinical trial is better than the treatment of patients who are not participating in clinical trials?	57/96.6	0/0	2/3.4
18. How would you assess your treatment in the clinical trial so far?*			
19. If there would be an opportunity to join another clinical trial, after you finish the current one, would you join?	52/88.1	2/3.4	5/8.5
20. Would you recommend to other patients to join the clinical trial you have been participating in?	56/94.9	1/1.7	2/3.4

Answers on questions marked with asterisk are explained in the text.
Questions are consecutively stated in Figure 1.

ical trial treatment to other patients. One of the patients would not recommend it, while two were not sure about it.

Several factors that could potentially influence the patients' answers were evaluated in the multivariate analysis, including age, gender, lung cancer type, current lung cancer stage, chemotherapy line, patients' education level, and duration of chemotherapy treatment. However, only one factor proved influential on the patient's answers on specific questions: and that factor was the patients' education level. A statistically significant higher number of patients ($p = 0.008$) with university education knew the exact type of lung cancer they suffered from compared to patients with high or elementary school level of education. There was also a statistically significant number of patients with a university degree ($p < 0.001$) who knew the exact stage of their disease, a significant number of them ($p = 0.004$) understood what the "clinical trial" was. There was also a significant number of patients with university degree who had read the entire informed consent form ($p = 0.02$) and a significant number of them thought that they would require additional information regarding the trial ($p = 0.001$). On the other hand, there was a statistically significant number of patients with high school education level who believed that the investigational product given in the chemotherapy trial caused less side effects ($p = 0.04$). There was also a statistically significant number of patients with a lower education level than university degree (high school) who would join another clinical trial after completion of the current one ($p = 0.01$).

DISCUSSION

The findings of this study reveal that the majority of the patients included in the study had an advanced stage NSCLC, primarily the squamous cell lung cancer. This is due to the fact that squamous cell lung cancer is the most prevalent type of lung cancer in our country, but selection bias also played a significant role: most of the studies from which our patients were drawn were examining chemotherapy in squamous cell lung cancer. That is the main reason why the distribution of lung cancer types does not correlate with the general distribution of lung cancer types in most published studies. Lung cancer is usually diagnosed in its late or advanced stage; in our country almost 80% of patients with NSCLC are diagnosed with an advanced stage lung cancer. The majority of patients with SCLC are also diagnosed in an extensive disease stage. In most countries there are no clear screening programs for lung cancer. The same is true for Serbia, but here we are also facing low public health awareness. The political measures for prevention of lung cancer are still in their infancy in Serbia, as in many developing countries, and it is too early to expect the results until in the next few years.

Our patients were asked to answer the questionnaire after the third cycle of the clinical trial chemotherapy regimen in order to be able to compare their previous experience with the current one. The patients included in this study were receiving second or third line chemotherapy within the clinical trial in which they were participating, so they already had substantial experience with chemotherapy. The results show that most patients know the true nature of their disease and even the type of lung cancer they suffer from, suggesting that patients are well informed about their condition and disease. A frank approach to a patient, giving him/her a thorough explanation of the disease characteristics and the treatment, is a cornerstone for gaining the patient's trust. It can also create a relationship in which it is easier to explain to the patient the significance of participation in the clinical trial, if the patient qualifies for it. This is particularly important in low income countries where clinical trial therapy, even for control groups, is a big step forward with respect to the therapy patients would usually get. We often have the situation that the physicians are highly interested in the clinical trial, not from the financial standpoint, but because it is the only way for patients to be treated as recommended by the guidelines. This is probably one of the reasons why we are often among the sites with the highest enrollment in many clinical trials.

The adequate approach to the patient with lung cancer can also be observed through a significant number of the patients who knew what type of chemotherapy they received prior to the enrollment in the clinical trial. However, this may be related to the fact that the majority of the patients received that therapy in our institution where the institutional policy is to explain to patients what kind of therapy they will receive. One of the most important results showed that the majority of the patients knew that they were participating in the clinical trial, except for one patient. One of the reasons might be insufficient engagement of the physician or inability to completely understand the informed consent form (ICF). The ICF is usually too robust for a patient to read it completely, and without significant help from the physician the patient can hardly understand all that is written in the document. Whatever the reason for that one negative answer is, it stands as a warning. We must pay due attention to all patients in clinical trials all the time they are under our treatment. The fact that 8.5% of the patients did not read the entire ICF represents also an alarming finding. As stated before, ICFs usually provide more detailed information about the trial than an investigator can give during the interview with a patient. The multivariate analysis showed that a significant number of the patients with a university degree read the entire ICF. This suggests we should pay more attention to less educated patients, especially when providing information and ICF documentation. On the other hand, the scientific management and study protocol teams should pay more attention to the concept of the ICF, taking into consideration its length and the patients' ability to understand what is written. Too extensive ICFs exceeding a certain

number of pages, with complicated explanations and medical terms are usually not understandable for the patient. No matter how a patient may be motivated to read the entire document, 20 pages of text are a bit too much. One factor is also very important - the translation from English to native languages. These translations are usually made by professional translators and not medical professionals, leading to a literary translation which is sometimes hard to understand even for physicians.

The overall satisfaction with the level of information provided was significantly high in our group, suggesting that our study teams provided sufficient and relevant information. We tried to avoid potential biases by providing a level of anonymity to the patients who dispatched their answers in a sealed carton box placed in the clinic lobby. We also explained to the patients that the sincerity of their answers was of major importance, and that whatever answers they gave, it would not have any influence on their further treatment. The level of education influenced the requirement of the patients for additional information although the number of patients who answered that they would require additional information and those who answered that they wouldn't was practically equal. This is related to the fact that more educated patients expect a more detailed update on their condition. The patients' belief and trust in the treatment is also reflected by a significant number of patients who answered that they believed that chemotherapy given in the clinical trial is better than the "usual" chemotherapy. The answer might be biased by an excessive explanation of the advantages for participation in the clinical trial given by the physician. However there were two patients with university degree who gave a negative answer, and 9 patients who were not sure, and they represent almost 20% of the patients included in the study. These results suggest that the possible bias could be minimal, and that the patients really believed the trial chemotherapy was better. The important issue is that chemotherapy given in the clinical trial protocol in developing countries is more advanced, from the medical point of view, and patients are able to recognize this fact.

It is very important that a significant majority of the patients know that they might not receive the investigational product during the trial. That shows that the patients are aware of the study design, its benefits and pitfalls and they still want to participate, even though they have the opportunity to withdraw from the trial whenever they want. Still, they are satisfied with the treatment and consider their physicians as trustworthy, well educated and knowledgeable. The patients enrolled in the clinical trial think that because of their participation in the trial, nurses and physicians are more easily accessible to them. This might be true - it is a fact that more time and special care is provided to the patients in the clinical trial. It is sometimes required by the protocol of the trial itself (to perform more examinations or more detailed examinations, more lab tests, to check the patients' condition several times a day). All this creates an impression of special care received, so the patients usually feel more comfortable and more appreciated. This might be also one of the reasons why the majority of the patients expressed the opinion that their treatment was better than the treatment of the patients not included in the trial. A significant number of our patients qualified their overall treatment in the clinical trial as excellent. This is a direct consequence of the number and quality of provided services. Certainly, the quality and engagement of the sponsors who provided travel reimbursement and refreshments could play a significant role in such assessment of the treatment. On the other hand, the fact is that the combination of drugs in the clinical trials in advanced stage lung cancer nowadays includes targeted therapy alone or in combination with chemotherapy. This results in fewer side effects and better clinical improvement compared to standard chemotherapy available in developing countries. The patients can observe and feel the improvement and they usually feel satisfied with the treatment. The physicians are eager to monitor the patients more carefully, ready to dedicate more time and attention to them in order to detect a result of the treatment and record the patients' current condition. The physician's interest is generated on one side by scientific and, on the other, by financial reasons. But, no matter what generates it, a higher physicians' vigilance results in better care for the patients and this is what matters most. This of course is the case in developing countries; the situation in more developed economies could be substantially different.

The overall success of the treatment in the clinical trials in our study is testified by the fact that a statistically significant number of patients would join another trial after they finish the current one, and a significant majority of the patients would recommend the treatment in clinical trials to other patients. That should be one of the goals of clinical trials in advanced lung cancer. The majority of the published guidelines suggest that the best treatment for patients with advanced stage lung cancer is in a clinical trial. But if one patient recommends the trial to another, the trial itself gains popularity and importance among the patients. There is no better motivation for a patient to join a trial than the recommendation of a friend or a fellow patient. We encountered situations in which a significant number of patients were interested in joining the study because they had heard about it form other patients. However, this implies a huge responsibility for the physicians: a very selective choice of the trials with special concern for a full ethical discolsure of the study, taking of course into consideration the medical justification.

A major disadvantage of this study is that the questionnaire was developed by our own study team that included medical physicians and non-medical staff (pulmonologists and medical oncologists, nurses, statisticians and IT engineers). The questionnaire did not undergo all the testing phases in concor-

dance with the guidelines for questionnaires in clinical trials. However, our intent was to make a survey of the patients' opinion, not to measure their satisfaction, because that would require a fully developed and tested questionnaire, which is not available in that form. With the form of the questionnaire we created, we tried to minimize the biases and maximize the quality of the answers used for the analysis.

CONCLUSION

Clinical trials in advanced stage lung cancer are currently the best option for the treatment of patients with that condition. Our study showed that the patients included in several clinical trials have a very positive attitude toward the current trial and clinical trials in general. The overall satisfaction with the treatment was very high, suggesting that the patients think they received the best possible care, and probably they think so because they are enrolled in a clinical trial. The patients' confidence and trust in their physicians and nurses is very firm and the majority of patients completely trusted their physicians. The major conclusion of this study could be that not only do the physicians have high hopes from the trials, but that patients understand what the trial is and have high hopes too. This study showed that the patients would recommend the trial to other patients, proving that they are aware of the fact that they could, with their opinion and experience, help others, too.

The only factor identified in this study that possibly influences the patients' opinion about the treatment is the level of education. We should adjust our approach to each individual patient with a special concern about the level of education. Our recommendation to study teams and protocol writers would be to pay special attention to the ICF, its length and amount of information provided by it. In conclusion, our patients do believe in clinical trials and they do believe in us. It is difficult to say how much effort we must additionally invest to obtain better results and longer survival of patients with lung cancer. One thing is sure: we must give our best to justify the confidence and the hope our patients place in us.

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