The impact of waiting time on satisfaction, experiences, and preferences from metastatic non-small cell lung cancer (NSCLC) patient's perspective

- Including a waiting time analysis (WTA) for PD-L1+ NSCLC patients participating in immunotherapy trials -

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Abbreviations

ALK	Anaplastic Lymphoma Kinase
AVL	Antoni Van Leeuwenhoek
CQI	Consumer Quality Index
CI	Confidence Interval
CT	Chemotherapy
CTT	Chemotherapy Trial
DCE	Discrete Choice Experiment
EGFR	Epidermal Growth Factor Receptor
EHR	Electronic Health Record
IC	Informed Consent
IMT	Immunotherapy Trial
GP	General Practitioner
KRAS	V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog
NKI	Netherlands Cancer Institute
	Nederlands Kanker Instituut
NSCLC	Non-Small Cell Lung Cancer
OR	Odds Ratio
PA	Pathology department
	Pathologist
PD-L1	Programmed Death-Ligand 1
PM	Personalized Medicine
QOL	Quality of Life
RET	REarranged during Transfection
ROS	Reactive Oxygen Species
SD	Standard Deviation
SDM	Shared Decision Making
SE	Standard Error
TT	Targeted therapy
TTT	Targeted therapy Trial
VIKC	Association for Integral Cancer Centres
	Vereniging Integrale KankerCentra
WTA	Waiting Time Analysis

Preface

This paper describes the study I performed for my Master thesis during the period of February until August 2015. In this study the impact of waiting time on satisfaction, experiences, and preferences from non-small cell lung cancer patients' perspective was analyzed. The study was performed by order of the Netherlands Cancer Institute and the University of Twente.

I would like to express my thanks to a number of people who contributed to this study in a direct or indirect way.

Firstly, I want to thank Wim van Harten, Valesca Retèl, Paul Baas and Karin Groothuis. Also, I want to thank the lung physicians and lung-nurses at the outpatient-clinic of the Netherlands Cancer Institute, and other employees who helped me to realise this project.

Finally, I want to thank my parents Elly and Jos, my brother Bastiaan, and my grandmother Stien for their support during this study period.

Christel Spoolder

Amsterdam, August 2015

Abstract

Introduction

Personalized medicine (PM) is a new treatment method for cancer patients. Specific types of PM are targeted therapy, and immunotherapy. Immunotherapy is a treatment method that uses certain parts of a person's immune system to fight diseases such as cancer. Immunotherapy has proven to be effective in stage IV non-small cell lung cancer (NSCLC) patients. Its effectiveness is seen in patients who have an expression of the Programmed Death-Ligand 1 (PD-L1) receptor. Currently, NSCLC patients are only being treated with immunotherapy in clinical trials, where the biomarker PD-L1 is used to select patients. Waiting time before the start of treatment with immunotherapy appeared to be long for unknown reasons in comparison with regular treatment methods as chemotherapy, or targeted therapy. Delay of treatment can have impact on health status and survival of patients. It is important to identify the factors that influence this delay. In addition, the effects of waiting time on patient satisfaction, experiences, and preferences in lung cancer care are yet unclear.

Objectives

1) Analysis of waiting time among NSCLC patients tested for PD-L1, and treated with immunotherapy in clinical trials in the Netherlands Cancer Institute (NKI).
2) Analysis of patient satisfaction, experiences, and preferences among NSCLC patients who have been treated with immunotherapy, targeted therapy, and chemotherapy in the NKI.

Study design

Retrospective descriptive exploratory study.

Patients and methods

Waiting time analysis (WTA) was performed using 4 clinical trials, which enrolled stage IV NSCLC patients for immunotherapy. Data were derived from the electronic health record (EHR). For each step in the process from informed consent (IC) until start of treatment, waiting times were recorded. Patient satisfaction, and experiences were measured by means of a questionnaire sent by post mail based on items from the Consumer Quality Index (CQI) – Outpatient care and Mamma care, and questions about satisfaction regarding the experiences waiting time. Preferences were measured by means of a Discrete Choice Experiment (DCE), including the attributes 1) Waiting time between referral and first consultation, 2) Waiting time between first consultation and diagnosis, 3) Waiting time between diagnosis and initial treatment, 4) Improvement of symptoms, 5) Risk of side effects due to initial treatment, and 6) Average survival after initial treatment, with 2 or 3 levels each.

Results

1) Data of 54 NSCLC patients were included in the WTA. Mean total waiting time before start of immunotherapy was 38.4 days with a standard deviation (SD) of 8.7 days. The procedures within the hospital ("collection time" and "preparation time" before treatment) were most time consuming with 31.7 days (79.8%) of the total of 38.4 days. Trial patients were more satisfied with waiting times than patients treated with standard of care. Knowledge about immunotherapy was relatively higher compared to knowledge about PDL-1 staining tests.

2) Out of 93, 42 patients (response rate 45.2%) returned the questionnaire within 2 weeks. 1 patient was excluded. In general, patients were satisfied with most subjects. They would all recommend the NKI to their family and friends. Patients marked their treatment trajectory in the NKI with a mean value of 8.7 out of 10. Nevertheless, some points of improvement were found.

38 out of 42 patients filled out the second part of the questionnaire (DCE). We excluded results of 4 patients. 17 out of 34 (50%) patients unanimously chose the 12 scenarios with the highest survival. The other 17 (50%) patients did not consequently chose the scenarios with the highest survival (9 months). The choice of a treatment seems to depend on "Average survival after initial treatment', and "Improvement of symptoms" for the second group of patients. Preference for treatment does not depend on the three waiting time attributes as the risk of side effects. The three most important attributes for the second patient group are: 1) "Average survival after initial treatment" (36.8%), 2) "Improvement of symptoms" (31.8%), and 3) "Risk of side

effects from initial treatment" (9.6%). We did not track big differences in patient demographics.

Conclusion and discussion

1) In the most optimistic situation, waiting time could be sped up to 11 days, an improvement of 10 days. The internal processes (collection time and preparation time) are most time consuming.

2) The study results suggested waiting time had no significant influence on satisfaction, experiences and preferences of NSCLC patients. However, we have discovered some differences between trial patients and patients treated with standard of care. Besides, "Survival after initial treatment`' was considered as the most important attributed included in the DCE.

Based on the results of this study, shorter waiting times in clinical practice will not greatly increase in more satisfaction from patients' perspective. However, health care professionals and patients can interpret this as a point of service.

Keywords

- *Personalized medicine (PM)*
- *Immunotherapy*
- *Waiting time analysis (WTA)*
- *Patient satisfaction*
- *Patient experiences*
- *Patient preferences*
- *Discrete Choice Experiment (DCE)*
- *Non-small cell lung cancer (NSCLC)*

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Introduction

Personalized medicine (PM) is a new treatment approach for cancer patients. PM can be defined as "*an emerging approach to patient care in which an individual's characteristics, including their genetic profile, guide clinical decisions, aiming for the right treatment for the right patient at the right time*" (1). This method type focuses on specific mutations in a patient's DNA of the tumor instead of the total organ where the cancer has located itself. These treatments are called 'targeted treatments'. Another type of PM is immunotherapy. This is a treatment method "*that uses certain parts of a person's immune system to fight diseases such as cancer"* (2). It can focus on the circulatory system, the immune system, or the tumor itself (3).

Immunotherapy has proven to be effective in –amongst others– stage IV non-small cell lung cancer (NSCLC) patients. Its effectiveness is expected in patients who have an expression of the programmed death-ligand 1 (PD-L1) receptor (4–7). The expression of this molecule leads to a reduced immune response, which results in poor clinical outcomes. Immunotherapy agents as nivolumab (Opdivo) and prembolizumab (Keytruda) can block the effect of PD-L1 on tumor cells by means of antibodies. (3,8–11). Besides lung cancer, these findings offer important possibilities in the treatment field of several other types of cancer (12–14). Examples of targeted treatments are erlotinib (Tarceva), or Gefitinib (Iressa) for positively tested Epidermal Growth Factor Receptor (EGFR+) NSCLC patients (15) and crizotinib (Xalkori or Pfizer) for positively tested Anaplastic Lymphoma Kinase (ALK+) patients (16).

Currently, NSCLC patients are only being treated with immunotherapy in clinical trials. Waiting time before participation in clinical trials – in most cases – takes more time than for most regular treatment methods as chemotherapy. At this moment, there is limited information regarding the reason why waiting times are so long. Several factors can be responsible for this delay: one could think of strict study criteria, freestanding or in combination with (logistical) processes within the hospital the trial takes place, and the dependence of other organizations involved. Shorter waiting periods can help to take more advantage of the possibilities of immunotherapy described above.

The National Working group for Lung Cancer (Landelijke Werkgroep Longtumoren) in the Netherlands has developed a national guideline in cooperation with the Association for Integral Cancer Centres (Vereniging Integrale KankerCentra (VIKC)). The guideline provides recommendations for diagnosis, treatment, follow up and forms. A tolerable waiting time to start treatment is 1 to 28 days. Nevertheless, these maximum tolerable waiting times only have been described as recommendations instead of regulations. It emphasises recommendations for reduction of waiting times in both primary-, and secondary care related to NSCLC. However, these guidelines do not exactly cover waiting times for treatment with targeted therapy or immunotherapy (in the context of clinical trials). (17)

As indicated in the Dutch guideline for NSCLC, it should be clear that it is very important to start personalized treatment as soon as possible to increase the effectiveness of the therapy and the survival chances of NSCLC patients. On top of this, lung tumors in general have a fast doubling time, it is therefore plausible that these patients will be negatively affected by a waiting time in comparison with other tumor types (18). Salomaa et al. contradict this claim. They showed that a longer waiting period is causing less prognostic damage in lung cancer patients with advanced disease. A possible explanation could be slowing growing tumors (19). (In the same article), Salomaa et al, and Gould et al. offered clear indications of diagnostic waiting times and its negative influence on survival in NSCLC patients. (19,20). Despite these assertions, it does not mean that waiting time cannot affect other factors besides the effectiveness and survival of patients. One can think of patient's Quality of Life (QoL) (21), satisfaction (22) and treatment preferences (23,24). Currently, no literature is available about the two last mentioned in NSCLC cancer field regarding to waiting times covering a patients' complete treatment trajectory.

Therefore, the objective was first, to perform a waiting time analysis (WTA) for NSCLC patients treated with immunotherapy in four clinical trials within the Netherlands Cancer Institute (NKI), in order to find reasons for the current waiting times. The second objective was to investigate patient satisfaction, experiences, and preferences in general, and specifically related to waiting times for NSCLC patients treated with immunotherapy, targeted therapy, and chemotherapy, and whether or not participating in a clinical trial.

Methods

Study design

This study is defined as descriptive exploratory study, and is subdivided in two different parts: **1)** A WTA among stage IV NSCLC patients treated with immunotherapy and **2)** An analysis of patient satisfaction, and preferences among stage IV NSCLC patients treated with immunotherapy, targeted therapy, and chemotherapy in the NKI.

1. Analysis of waiting time prior to immunotherapy treatment

1.1 Procedures and data collection

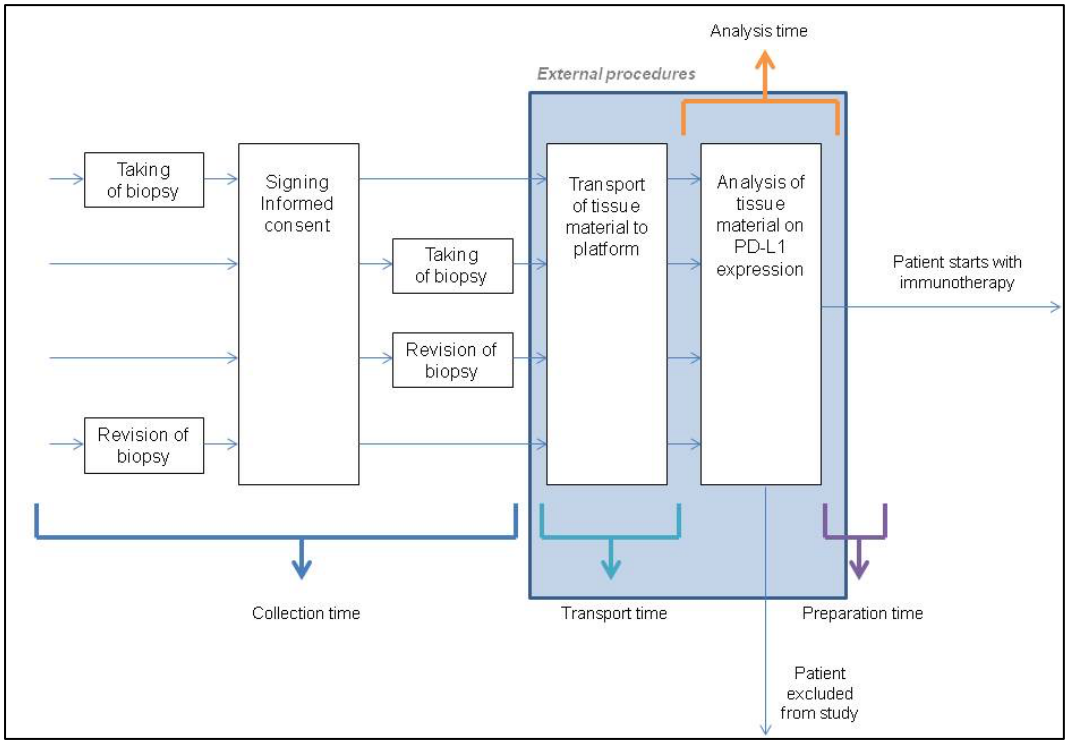
First part of the study is a WTA related to the processes in 4 immunotherapy trials (M13PDL, M14NIV, M13MKD, and M14NGO) for stage IV NSCLC patients. All data was gained by information recorded in the electronic health record called Chipsoft Ezis, and in documents stored at the trial office in the hospital.
Data of waiting times regarding each step in the process, from IC until start of treatment, include internal logistic processes within the NKI, and external analysis of patient's tissue material of PD-L1+ in respectively Belgium, and the United States of America.

No distinction was made between public holidays, weekends, and workdays with the rationale: "Every day counts". Before patients could participate in one or more of the trials described above, various steps and procedures were completed. An overview of the total procedure regarding the internal and external analysis of a patient's tissue material is shown in the **Figure 1**. Patients, participating in more than one trial, were excluded. In this figure, four subgroups are distinguished as well. Details of these subgroups will be explained later. Hypotheses are included in the result section. Definitions of the included time periods are described in **Box 1** and **Box 2**.

1.2 Statistical analysis

Statistical analyses with descriptive statistics (means, medians, minima, maxima, standard deviations (SDs) and standard errors (SEs)) were applied. Besides, we tried to identify subgroups. Calculations were made in Microsoft Excel 2010.

Figure 1: Process flow



Box 1: Definitions of time components

- **Signing informed consent (IC):** The date when the patient signed IC for (potential) participation in one out of the four immunotherapy trials
- **Taking of biopsy:** The date of biopsy or the date when a (re-) biopsy is taken.
- **Revision of biopsy:** The date of observation and approval of biopsy by pathologists at the pathology department (PA) at the NKI.
- **Transport of tissue material**
  - Transport date: The date on which tissue material is transported to the external platform to test for PD-L1 expression.
  - Reception date: The date on which the tissue material is arrived at the external platform.
- Date of report: The date on which the test results are generated.
- **Start with immunotherapy:** the date a patient started his/hers immunotherapy treatment.

Box 2: Definitions of patient's processes

- **Collection time:** Time between the date when a patient had signed informed consent for (potential) participation in one out of the four studies up and including the date of transport
- **Transport time:** Time between the transport date up and including the reception date of tissue material (at the external platform) for testing on PD-L1 expression.
- **Analysis time:** Time between the reception date (definition box 1) and the date of report.
- **Preparation time:** Time between the date of report and a patient's start with his/hers immunotherapy treatment.
- **Total waiting time:** Time between the date when the patient had signed informed consent for (potential) participation in one out of the four studies up and including a patient's start with his/hers immunotherapy treatment.

2. Analysis of patient satisfaction, experiences, and preferences among NSCLC patients

2.1 Patient selection

Seven lung-physicians and two lung-nurses employed in the NKI were asked to select patients based on their general health status (in order to not bother the patients who were too ill to participate). The objective was to compare satisfaction with waiting times between different treatment types (immunotherapy, targeted therapy, and chemotherapy) and if patients were participating whether or not in clinical trials (**Table 1**). Both different treatment types (and whether or not participating in a clinical trial) can in potential result in different waiting times and subsequent satisfaction.

Table 1: Selected patients

	Clinical trial	Standard of care
Immunotherapy	12	-
Targeted therapy	1	9
Chemotherapy	3	16

Patients treated with immunotherapy had been tested positive for PD-L1 expression and participated in the period of 1 January 2012 until 1 April 2015 in one of the immunotherapy trials. Patients treated with chemotherapy in clinical trials participated from April 2014 until April 2015. The only patient participating in the targeted therapy trial signed IC at February 2015. Patients treated with chemotherapy in standard care signed IC in the period of October 2012 up and including April 2015. Patients treated with targeted therapy in standard care were informed during the period of December 2013 up and including March 2015.

Patients who participated in the current study were at least 18 years old and were able to speak and read Dutch. Patients who were physically not able to participate in this study (evaluated by seven physicians) were excluded. In addition, patients were able to fill out the questionnaire independently.

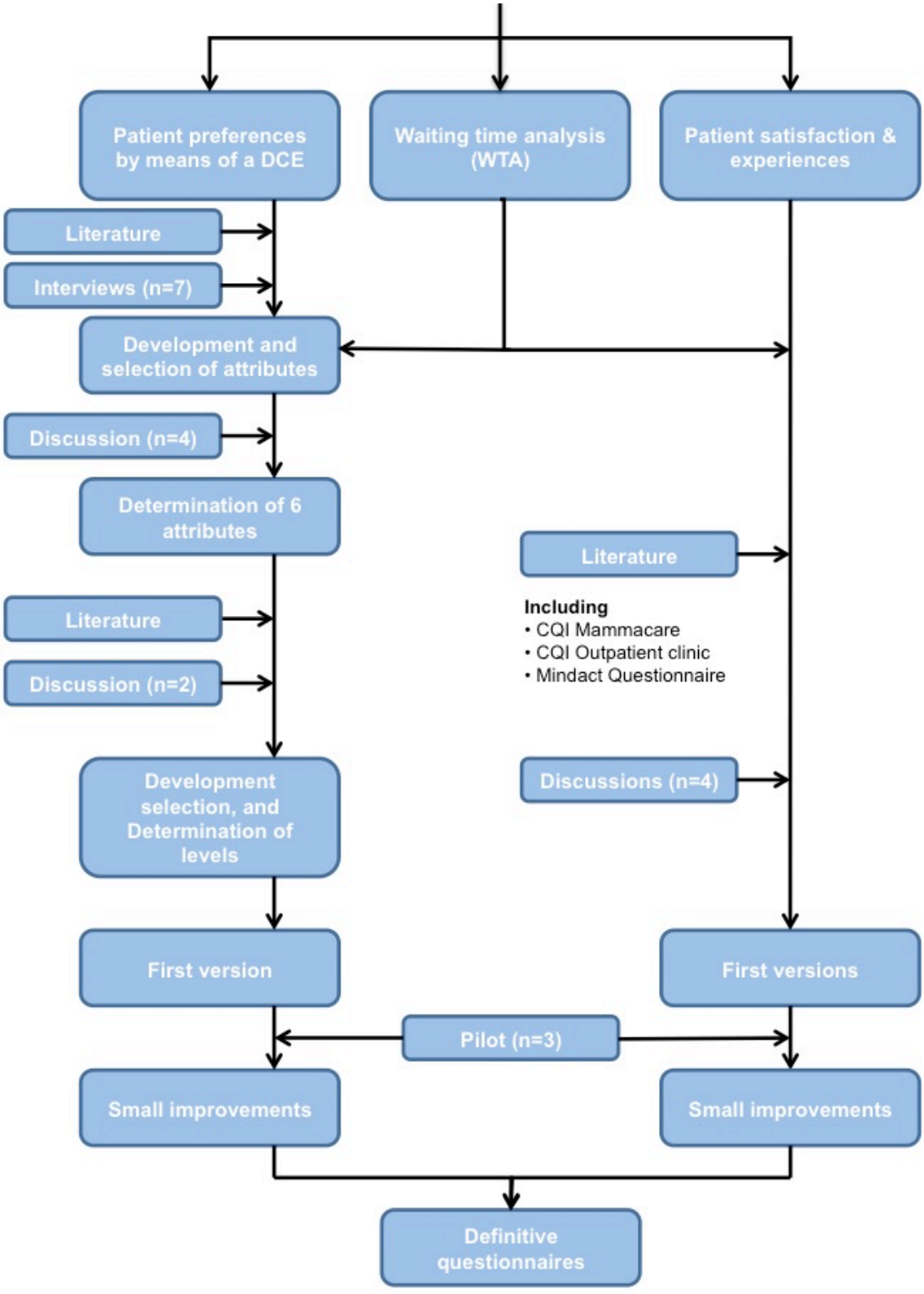
2.2 Procedures and data collection

2.2.1 Patient satisfaction, and experiences

Patient satisfaction, and experiences related to current waiting times were tested by means of a questionnaire. The scales and questions were based on different parts of a patient's care pathway from first outpatient clinic visit to start of treatment in the hospital. The questionnaire consisted of closed questions and was partly based on the Consumer Quality Index (CQI) – Outpatient care (Version 2.1) (25), the Consumer Quality Index – Mamma care (version 2.3) (26), and the Mindact Questionnaire (27). We included questions from the previously mentioned questionnaires because of the importance of these subjects for our purposes (analysis of patient satisfaction at the outpatient clinic in general) combined with the questionnaires' proven validity. The Mindact questionnaire gave the idea to include knowledge statements about PDL-1 staining tests and immunotherapy treatment. Questions copied or derived from the CQI's are marked with "*". Further, we used 2 point-scales (no-yes), 3-point scales (no problem-small problem-big problem), and 4-point likert scales (no, completely not-a little-mostly-absolutely yes and never-sometimes-mostly-always).

In addition, input of experts and literature were imputed in this renewed questionnaire (**Figure 2**). Patient's knowledge about immunotherapy and body material tests was tested by true-false-"I don't know" questions. Questions about different parts of a patient's pathway in the hospital, and patient satisfaction related to current waiting times were included as well. Two different versions were developed: one for patients who participated in clinical trials, and one for patients who did not participate in clinical trials. The questionnaires were filled out once by every participating patient after a patients' treatment with one of the three treatment methods described above. The questionnaires were sent by postal mail. Patients could return the questionnaires at the next appointment with their treating physician or they could send the questionnaires in the enclosed return envelope. An example of this questionnaire is included in Appendix 1. In addition, we did not make the distinction between trial patients and patients treated with standard of care for the majority of the included questions, because most questions affected every patient in general. This is in contrast to the questions concerning waiting times at the NKI. These last mentioned questions were analyzed in detail, because of the possible distinction between the trial patients and patients treated with standard of care related to our main research question.

Figure 2: Methods



2.2.2 Patient preferences (Discrete Choice Experiment)

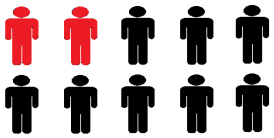
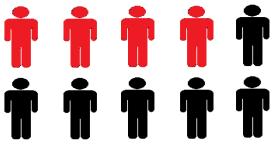
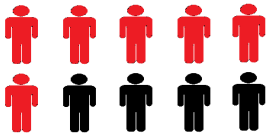
Patient preferences were tested by means of a Discrete Choice Experiment (DCE), which provides opportunities for the evaluation of process effects. This method can be used to investigate individual's preferences. The technique is an attributed measure of benefit, based on assumptions. Alternatives can be described followed by an individual's valuation, which depends on the levels of these alternatives. (28) This technique was chosen because of the appropriateness in this setting related to the stage of the study problem: Little is known about patient preferences related to waiting time. In addition, DCEs have the potential to contribute more directly to outcome measurement when it will be used in cost-utility analysis, and cost-benefit analysis. (29)

2.2.2.1 Attributes, levels and design

A detailed overview of the total procedure that is described in this section is shown in **Figure 2.** Literature, interviews, and discussions with 5 (clinical) experts, 2 patient representatives, and the 4 supervisors provided the basis for the definitive set of attributes and levels. We asked these experts what kind of factors would be important for our patient population in the NKI based on literature, which resulted in the first three attributes. Subsequently, we included three concrete attributes related to waiting time or delay for patients. This approach led to the following 6 attributes with 2 or 3 levels each: 1) Waiting time between referral and first consultation, 2) Waiting time between first consultation and diagnosis, 3) Waiting time between diagnosis and initial treatment, 4) Improvement of symptoms, 5) Risk of side effects from initial treatment, and 6) Average survival after initial treatment. Levels are based on literature and discussion with 2 supervisors (**Table 2**).

A draft questionnaire (including part 1+2) was individually pilot tested on 3 patients of the targeted trialnpopulation to ensure they correctly understood the questions. Patients were asked to mark every question or answering category they did not understand and/or was to difficult. They were asked then to provide suggestions for improvement. No changes in the attributes or levels were necessary based on the results of the pilot study. Small changes were implemented in the first part of the questionnaire mainly based on simplification of the Dutch language.

Table 2: Included attributes and levels

Attributes	Level 1	Level 2	Level 3
Waiting time between referral and first consultation			
	1 week	2 weeks	
Waiting time between first consultation and diagnosis			
	1.5 weeks	2 weeks	3 weeks
Waiting time between diagnosis and initial treatment			
	No waiting time. On the day of diagnosis treatment starts	1 week	2 weeks
Improvement of symptoms			
	After 2 weeks	After 2 months	No improvement. Complaints will not reduce or will remain the same as a result of initial treatment patients
Risk of side effects from initial treatment			
	≤ 20 % (2 out of 20 patients or less) 	40% (4 out of 10 patients) 	60% (6 out of 10 patients) 
Average survival after initial treatment			
	3 months	9 months	

2.3 Statistical analysis

For the analysis of satisfaction and experiences, an analysis of descriptive statistics was used. We described the answers of all respondents (n=41) in percentages and tried to split up the results per patient category. However, a sample size of at least 63 patients was estimated by the "Rule-of-thumb", in order to get reliable results. Based on this rule, at least 63 patients had to fill out the DCE. All calculations for this analysis were done in SPSS (version 22.0). The impact of waiting time on satisfaction was measured with the Pearson Correlation coefficient.

For the DCE, Ngene (version 1.0) by ChoiceMetrics was used to create a design with 100% D-optimality. A fractional factional design was created, consisting of a carefully chosen subset (also called fraction) derived from a full factorial design consisting of (4^3 x 2^2) 256 scenarios. Finally, 36 unique choice tasks were divided into 3 different blocks (also called sets). All three sets were randomly disseminated among the study population, so that every patient had to fill out 12 scenarios. The choice sets in this DCE were unlabelled: Patients could only choose between treatment A and treatment B in every choice set. We asked every patient to fill out not more than 12 scenarios to avoid a low response rate and overloading patients. An example of block 1 can be found in Appendix 2. Patients who indicated they did not understand the DCE were excluded. Calculations related to the DCE were made in SPSS (version 22.0) as well. Preferences related to the attributes and its levels included in the DCE were analyzed by means of logistic regression. Relative importance of all six attributes was measured as well.

Results

1. Analysis of waiting time before treatment with immunotherapy

54 patients (including 30 male (55.6%) and 24 (44.%) women) with a mean age and SD of 61 ± 9.6 years were included in the final analysis. The youngest patient had an age of 36. The eldest patient was 79 years old. At April 1st 2015, 34 out of 54 (64.8%) patients were still alive. Two patients were excluded to prevent bias of results: these patients participated in two or more out of the four trials, which could have an impact on their personal waiting times. Waiting times for each step in the process from five patients were not found in detail in the EHR.

A general overview of all throughput times is shown in **Table 3**. The colours used in this table are corresponding with the colours in the graphs. Missing data and outliers were excluded. Based on the results in this table, the steps "collection time" and "preparation time" were most time consuming. In addition, this was accompanied with large SDs, which means that there were a lot of fluctuations in time or dispersion related to these process components. "Transport times" and "analysis times" resulted in shorter mean times and smaller SDs. Those time components were considered as more constant because of its little fluctuations. The associated lower SEs indicated higher accuracy for these components as well.

Table 3: Throughput times

Throughput	N 54	Mean ± SD (days)	SE	Min.	Q1	Median (days)	Q3	Max.
Collection time	53	11.2 ± 8.5	1.2	2	5	8	17	33
Transport time	48	2.7 ± 1.7	0.2	1	1	3	3	7
Analysis time	48	4.9 ± 3.1	0.5	1	3	6	6	13
Preparation time	46	19.0 ± 6.6	1.0	7	14.3	18.5	24	33
Total waiting time	49	38.4 ± 8.7	1.2	21	32	39	45	56

1.1 Time distribution concerning the different process steps (per patient)

Based on the results relating to the "collection times" shown in **Figure 3A**, it took 7 days or less for 25 out of 54 (46.3%) patients to collect and prepare tissue material for transport to an external platform. The number of patients per category per week decreased with approximately factor 2.0 as time (per week) increased.

Figure 3A: Distribution of collection times (n=54)

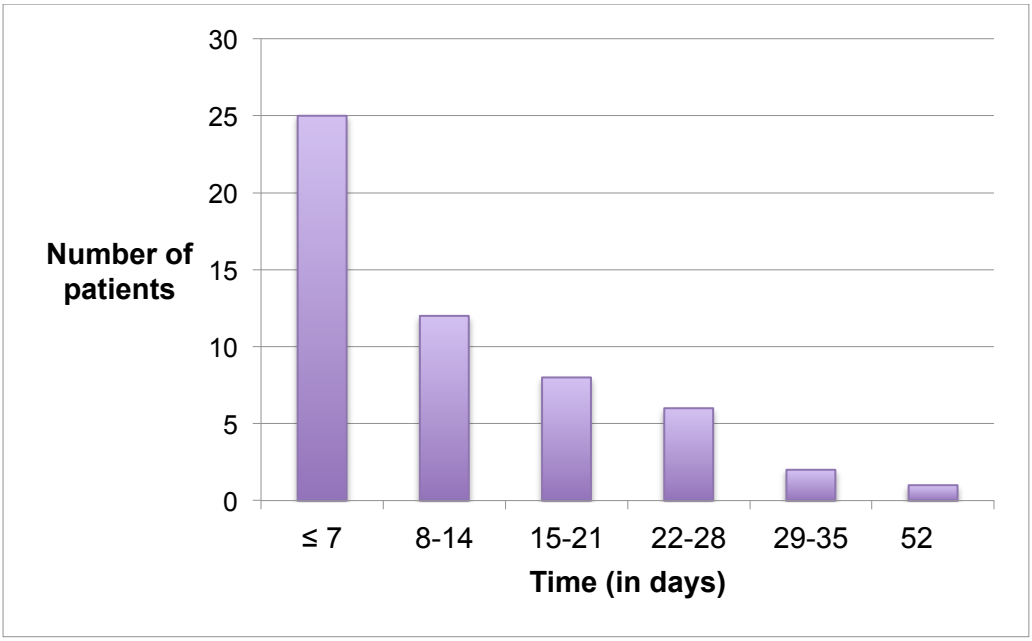
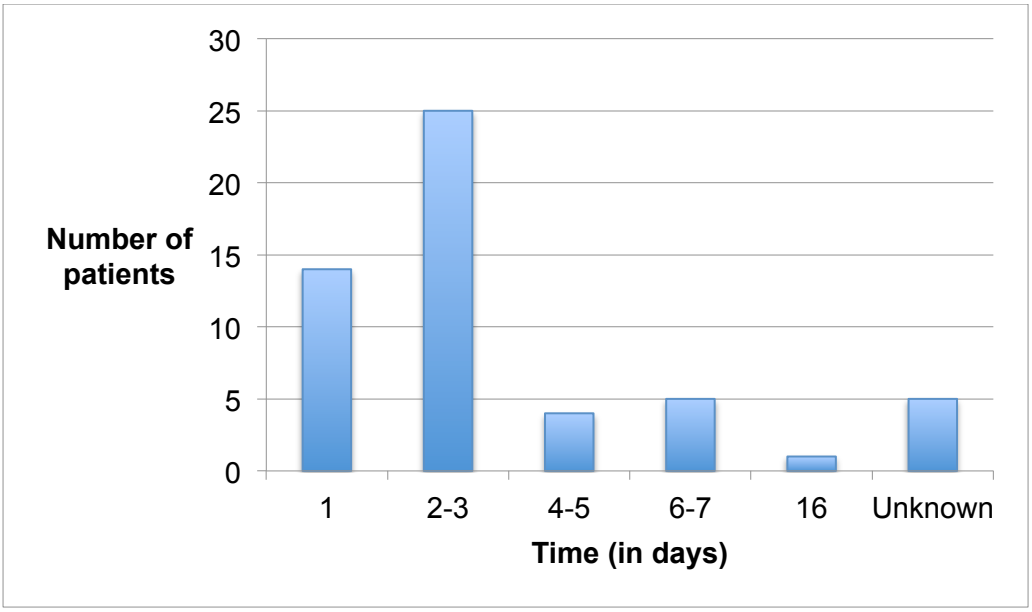


Figure 3B: Distribution of transport times (n=54)



In **Figure 3B,** transport times of tissue material are shown per patient. For approximately 39 out of 54 (72.2%) patients, it took a maximum of three days to deliver the tissue material at the external platform. Results of 5 out of 54 patients were unknown. A maximum of 16 days was registered. This result can be explained by new tissue material, which was send after.

Based on the "analysis times" shown in **Figure 3C**, it took 7 days or less to generate the PD-L1 results of 39 out of 54 (72.2%) of the patients. One outlier of 17 days for unknown reason was registered. Results of 5 out of 54 (9.2%) patients are unknown.

Figure 3C: Distribution of analysis times (n=54)

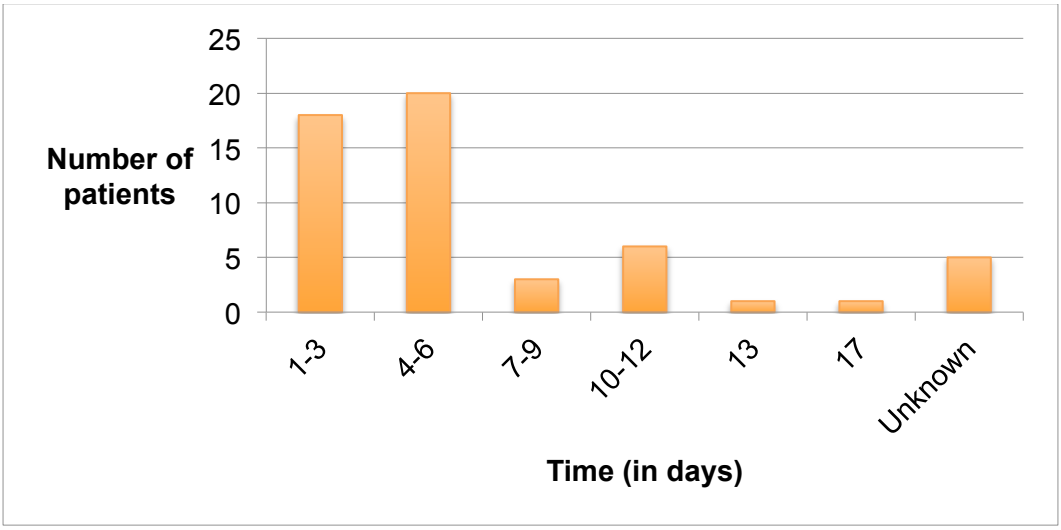
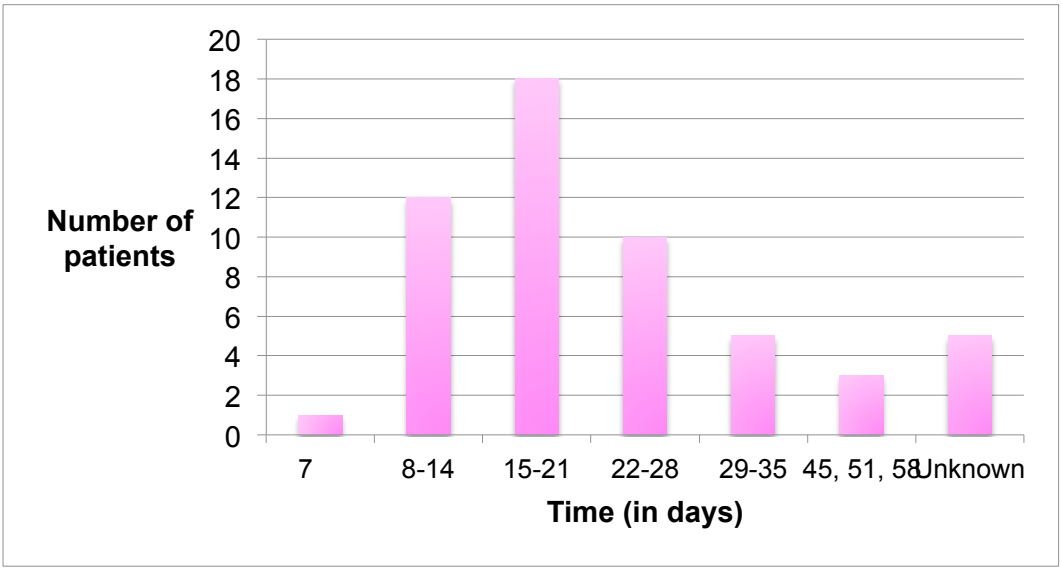


Figure 3D: Distribution of preparation times (n=54)

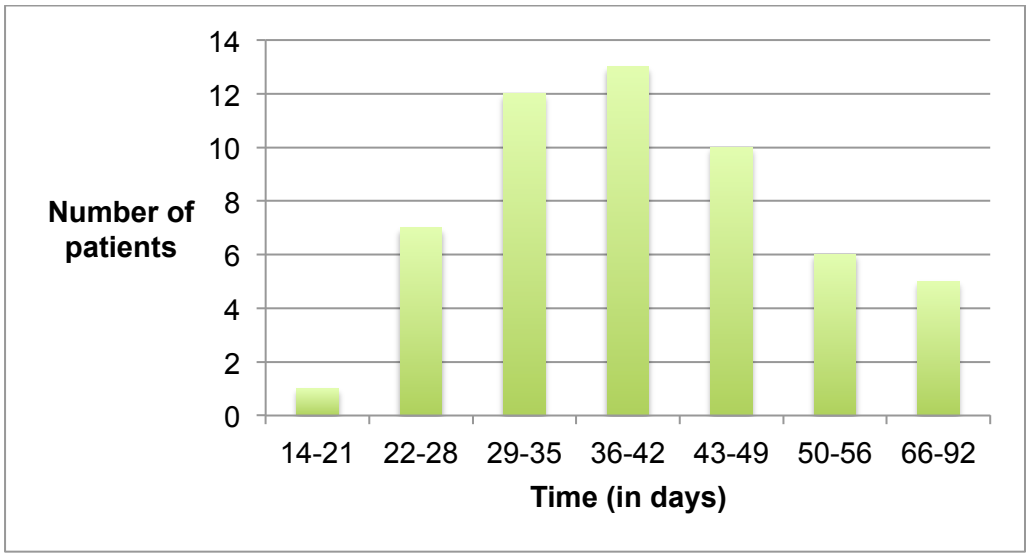


From **Figure 3D**, it can be seen that "preparation time" took between 8 to 28 days for more than half of all patients. The most optimal registered "preparation time" of one patient took 7 days. Results of 5 patients were unknown. Furthermore, we registered three outliers of 45, 51 and 58 days. These cases could be explained by hospitalization and screening failure. An overview of all screening failures selected for participation in one or more out the four trials is shown in **Figures 4A** and **4B** in Appendix 3. Because this subject falls outside this study scope, details related to these screening failures will not be further discussed.

An overview of total waiting times per registered patient is shown in **Figure 3E**. The graph appeares to be a "normal distribution". This means that, most people scored around the specific average score. However, a mild right skewed distribution can be observed, with a tendency towards shorter waiting times.

For almost 75% of the patients it took 3 up and including 7 weeks time, to start initial treatment with immunotherapy, calculated from first moment of informed consent related to its specific trial. 5 outliers with waiting times of 66 up and including 92 days were excluded from the calculations in table 2 as well. Hospitalization, rescreening, and a missing biopsy can explain these outliers. The other two outliers were unaccountable because of missing data.

Figure 3E: Distribution of total waiting times (n=54)



Based on the various components and the results shown in **Table 4** and **5**, the impact of the following aspects on total waiting time was studied:

- *Moment of biopsy or revision*
- *Variation between the locations of the three platforms*
- *Variation between the four trial logistics/ processes/ criteria.*

Underlying hypothesises related to the aspects above are:

- *Material retrieved from other hospitals followed by revision in the NKI results in longer waiting times compared to biopsies directly taken in the NKI.*
- *Platforms located at a great distance from the NKI provide longer waiting times relative to platforms located close to the NKI.*
- *Criteria and process differences related to the four immunotherapy trials result in differences in (and possibly longer) waiting times.*

1.2 Moment of biopsy or revision

Four subgroups can be defined, based on moment of biopsy, and the revision of tissue material per patient:

- Group 1: Performance of biopsy before IC
- Group 2: Revision of tissue material by PA before IC
- Group 3: Performance of biopsy after IC
- Group 4: Revision of tissue material by PA after IC

Table 4: Impact of moment of biopsy or revision on total waiting time

	N	Total waiting time ± SD	SE	P-value
Biopsy or revision **before** IC (Group 1 & 2)	20	38.1 ± 10.5	2.4	0.249
Biopsy or revision **after** IC (Group 3 & 4)	24	41.7 ± 9.8	2.0	

Table 5: Impact of biopsy/ revision on total waiting time

	N	Total waiting time ± SD	SE	P-value
Biopsy (Group 1 & 3)	18	39.3 ± 8.4	2.0	0.067
Revision by PA (Group 2 & 4)	34	44.9 ± 12.9	2.2	

In 4 out of 54 patients biopsies were taken at the same day when informed consent was signed. For that reason, these results were excluded. The differences in moment of biopsy or revision by PA after, or before informed consent are shown in Table **4**. It took a mean time of 31.3 days with a SD of 11.5 days (n=16) until moment of informed consent **before** biopsy had been taken or revision by PA had been done. For the other group it took a mean time of 8.1 days with a SD of 7.2 days (n=26) **after** biopsy had been taken or revision by PA had been done. Based on the results in **Table 5**, it can be concluded that moment of biopsy or revision before or after informed consent has no significant influence on total waiting time, however a small difference in total waiting time was observed. The results in this table show that there is difference in time between biopsies (mean total waiting time of 39.3 days (n=18)) compared to revisions by PA (mean total waiting time of 44.9 days (n=34)) with a mean value of approximately 6 days. Nevertheless, these results were not significant (p=0.067).

In **Table 6**, details of the four subgroups are shown. Waiting times related to biopsies before and after IC, and waiting times related to revision before and after IC were compared. Biopsies before IC took a mean time of 12.2 days (n=9) until moment of IC. This subgroup indicated the shortest waiting time of all subgroups with a mean time of 37.3 days (n=9). Revision after signing IC took a mean time of 7.7 days corresponding with a mean total waiting time of 44.1 days (n=16). Moment of revision, and biopsy are not significant in both cases. Remarkably, the moment of revision before informed consent corresponded with the highest mean of the total waiting time of 52.6 days (n=10) for all subgroups. Moment of biopsy or revision has no significant influence on total waiting time.

Table 6: Impact per subgroup on total waiting time

	N	Time until IC or biopsy/ reception PA ± SD	SE	N	Total waiting time ± SD	SE	p-value
Biopsy before	9	12.2 ± 7.3	3.0	9	37.3 ± 9.2	3.1	0.327
Biopsy after	9	8.9 ± 6.5	2.2	9	41.3 ± 7.5	2.5	
Revision before	10	14 ± 13.8	4.4	10	52.6 ± 16.6	5.2	0.553
Revision after	17	7.7 ± 7.7	1.9	16	44.1 ± 13.9	3.5	

1.3 Variation between the locations of the three platforms

The results per platform are shown in **Table 7**. Two platforms were located in the United States and one in Belgium. To begin with the "transport times": Ventana (USA) had a mean "transport time" of 4.8 days (n=4). This could be expressed in the SD and SE.

It took 3.3 days to transport the tissue material to Labcorp. It took approximately 1.3 days to transport the tissue material to Histogenex located in Belgium.

The impact of the "transport times" and the analyses per trial by the three platforms on total waiting time will be further explained in the next section.

Table 7: Details per platform

	Ventana, U.S.A.	**Labcorp, U.S.A.**	**HistoGenex, Belgium**
N = 51	4	35	13
Mean transport time ± SD (transport date – reception date)	4.8 ± 7.5	3.3 ± 1.5	1.3 ± 0.8
SE	3.8	0.3	0.2
N = 48	4	31	13
Mean analysis time ± SD (reception date - report date)	9.8 ± 3.0	5.2 ± 2.8	2.7 ± 1.5
SE	1.5	0.5	0.4
N = 52	4	35	13
Mean total waiting time ± SD (Informed consent – start with initial treatment)	52.8 ± 10.6	41.6 ± 11.6	33.2 ± 6.3
SE	5.3	2.0	1.7

1.4 Variation between the four trials/ logistics/ processes/ criteria

The results per trial are shown in **Table 8**. The M14NGO trial had the shortest "collection time" with a mean value of 7.8 days. In addition, the trial had the lowest SE of all four trials. Notwithstanding, most biopsies and revisions took place after informed consent. Only one outlier in the M14NGO trial was excluded. Most dispersion occurred in the M14NIV trial regarding the collection of a patient's tissue material. The M13PDL trial had the highest mean "collection time" with 17.5 days. However, only four dates were included. Moment of revision could cause this high mean "collection time": In 3 out of 4 cases revision took place after patients had signed informed consent.

Mean "transport times" of the M14NIV trial and the M13MKD trial were close to each other. Nevertheless, the "analysis times" of both trials were different. Tissue material in the M14NIV trial was only tested on PD-L1 expression while tissue material in the M13MKD trial was tested on PD-L1 expression and EGFR, V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS), and ALK mutations as well. In addition, this platform operates on a large scale. Other factors as holiday seasons and demand peaks can result in longer process times as well. This could be a reason why it took more time to collect complete results.

"Preparation times" of all trials are practically the same and are most time consuming. Likewise as shown in Table 5, total waiting times of the M14NIV trials and the M13MKD trials are near to 40 days. Excluded outliers cause the discrepancy between the results of total waiting times in Table 4 and 5. Details related to time occupation per process will be explained in the next section.

Table 8: Details per trials

	M13PDL	M14NIV	M13MKD	M14NGO
N = 52	4	14	22	12
Collection time ± SD (signing IC – transport date)	17.5 ± 4.8	12.1 ± 11.0	10.7 ± 7.7	7.8 ± 5.1
SE	2.4	2.9	1.6	1.5
N = 51	4	13	22	13
Transport time ± SD (transport date – reception date)	4.8 ± 7.5	3.1 ± 1.0	3.5 ± 1.8	1.3 ± 0.8
SE	3.8	0.7	0,4	0.2
N = 49	4	13	19	13
Analysis time ± SD (reception date - report date)	9.8 ± 3.0	4.5 ± 1.8	6.3 ± 4.2	2.7 ± 1.5
SE	1.5	0.5	1.0	0.4
N = 47	4	11	19	13
Preparation time ± SD (report date – start with treatment)	21.5 ± 2.4	18.1 ± 6.9	20.0 ± 9.8	19.8 ± 5.5
SE	1.2	2.1	2.2	1.5
N = 50	4	12	21	13
Total waiting time ± SD (IC – start with initial treatment)	52.8 ± 10.6	37.8 ± 10.7	40.7 ± 7.1	33.2 ± 6.3
SE	5.3	3.1	1.6	1.7

1.5 Throughput times

Based on the results shown in **Figure 5A** up and including **5E**, it can be concluded that "preparation time" was the most time consuming part of the whole process. In **Table 9,** the differences between internal and external procedures were made. The greater part of the whole waiting time process (72.5% to 87.3%) took place in the NKI.

Figure 5A: Throughput M13PDL trial

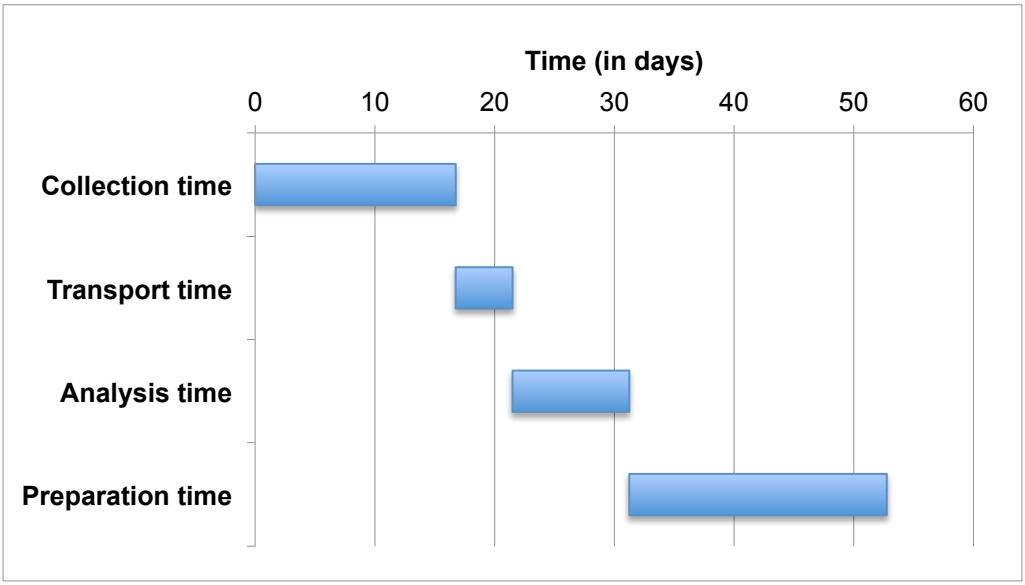


Figure 5B: Throughput M14NIV trial

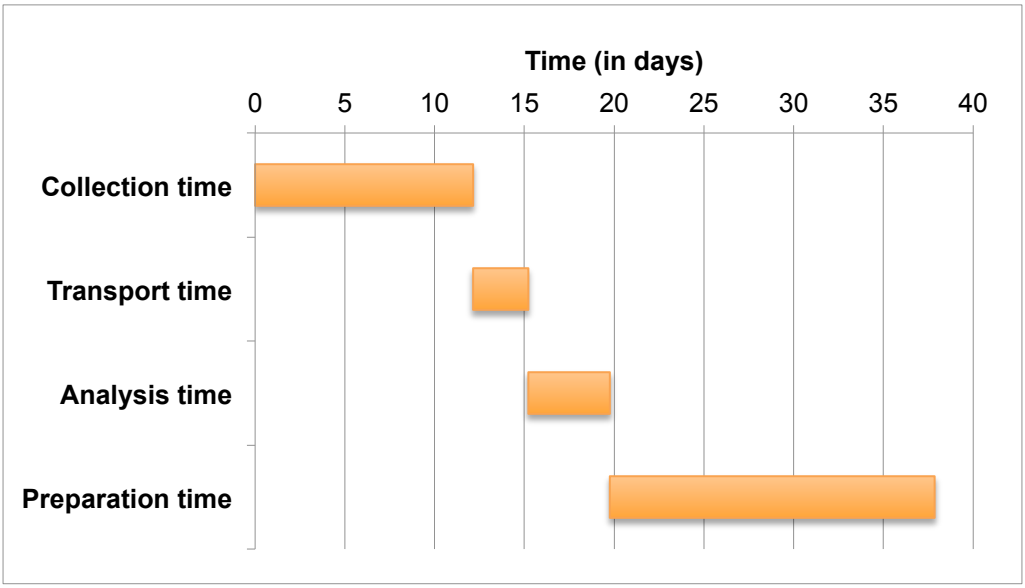


Figure 5C: Throughput M13MKD trial

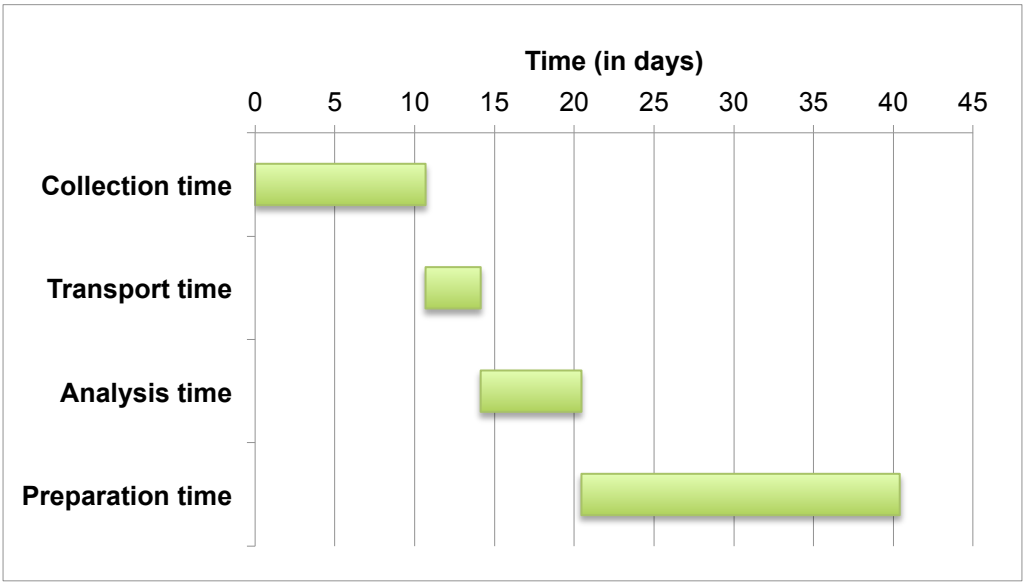


Figure 5D: Throughput M14NGO trial

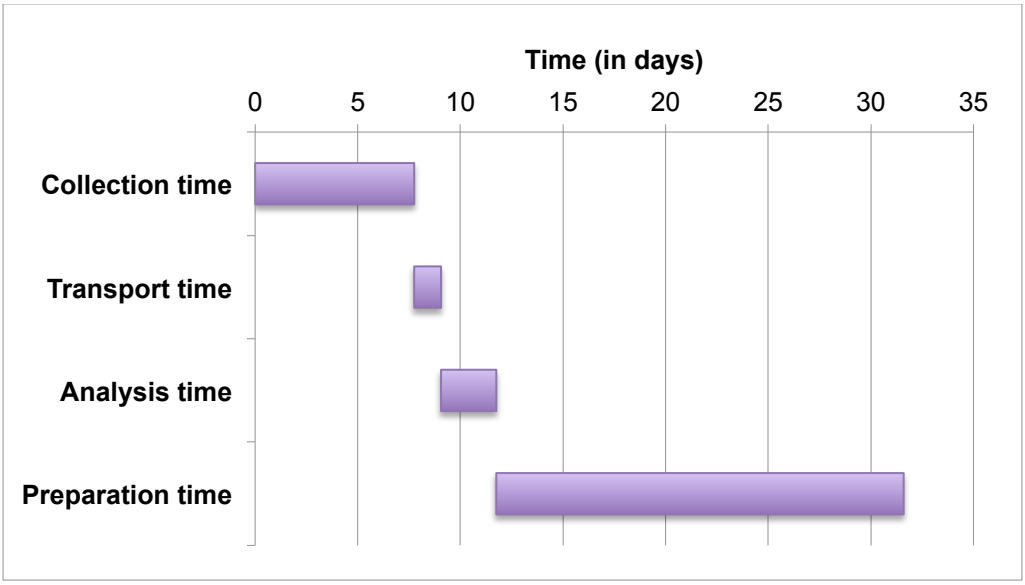


Figure 5E: Mean throughput time

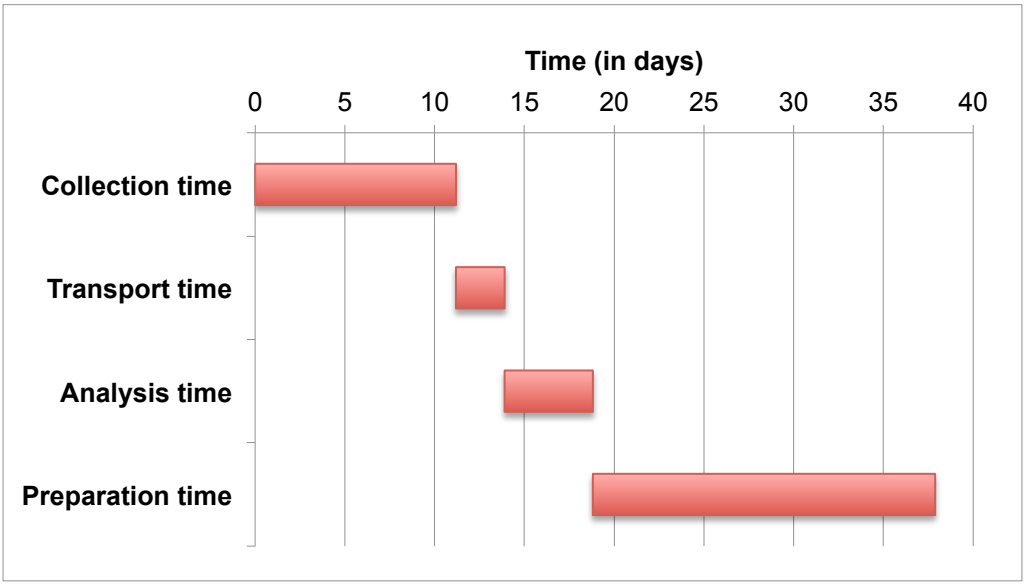


Table 9: Throughput time per trial

	M13PDL		M14NIV		M13MKD		M14NGO		Mean	
	days	%	days	%	days	%	days	%	days	%
Internal	38.3	72.5	30.2	79.9	30.6	75.8	27.6	87.3	31.7	79.8
External	10.8	18.5	7.6	20.1	9.8	24.2	4.0	12.7	8.0	20.2

1.6 Sub conclusion

Firstly, a total waiting time of 38.4 days was analyzed consisting of four steps. The first step called “collection time” had a mean total waiting time of 11.2 days, followed by a mean “transport time” of 2.7 days. “Analysis time” took 4.9 days, and “Preparation time” took 19.0 days. We analyzed a minimum “collection time” of 2 days and a maximum “collection time” of 33 days, and a minimum “preparation time” of 21 days and a maximum “preparation time” of 56 days. These last two mentioned steps had the highest SDs.

In addition, we analyzed the impact of several possible factors that could have an impact on total waiting time. Moment of biopsy or revision before IC resulted in a shorter total waiting time in comparison with moment of biopsy after IC. In addition, the mean total waiting time for patients from whom biopsies had been taken directly at the NKI indicated a shorter total waiting time compared to patients from whom biopsies were only under revision at the NKI. But, both results were not significant. Biopsies taken before moment of IC indicated the shortest total waiting time of all four groups. These results were not significant as well. Because of the non-significance of the results described above, we could not reject the first zero hypotheses mentioned in the methods.
Based on the results per platform, it can be concluded that the mean “transport time”, and mean “analysis time” related to Histogenex (located in Belgium) were shortest in comparison with the mean “transport time” and mean “analysis time” of the two platforms located in the U.S.A. Process steps of the M14NGO trial were less time consuming in comparison with the three other trials, which resulted in the shortest mean total waiting time of all four trials. We could not measure the impact of the study criteria and related processes based on the avalaible information.

Finally, it can be concluded that the internal processes in the NKI were most time consuming related to the external process (PDL-1 testing on tissue material). “Preparation times” took most time of the total waiting times per trial.
Because of the insignificant results related to the hypothesizes, the hypothesizes can also not be rejected.

2. Analysis of patient satisfaction, experiences, and preferences among NSCLC patients

2.1 Patient satisfaction and experiences

We selected 93 NSCLC patients to participate in this study. In total, 42 (response rate 45.2%) patients filled out the questionnaire in 2.5 weeks time. 1 patient was excluded because of treatment in another hospital (second opinion). Finally, 41 patients were enrolled (**Table 10** and **Figure 8**) Demographics of these patients are shown in **Table 11.** Completion of the questionnaire constituted individual's consent to participate. No ethics statement was required for this specific study since the questionnaire does not impact on the health of participants. The results are presented per theme or scale. An overview of all answers can be found in Appendix 4. To explore any relation with waiting times, for the specific questions, patients were subdivided into subgroups namely: 1) immunotherapy, 2) targeted therapy (in trial or standard care), and 3) chemotherapy (in trial or standard care).

Table 10: Number of enrolled patients

	Clinical trial	Standard of care	Total
Immunotherapy	12	-	12
Targeted therapy	1	9	10
Chemotherapy	3	16	19

Question 1 - Referral (N=41)

38 patients answered this question. 3 (7.3%) patients did not answer this question. Referral on "own request" was selected by 15 out of 41 (36.6%) patients, and "referral by another specialist" was selected by 16 (39.0%) patients. 1 (2.4%) patient was tipped by "another patient", and 1 patient (2.4%) was referred by the "General Practitioner (GP)". 3 patients (7.3%) were referred by "someone else", and 2 patients indicated they were referred by more than one person (a combination of possible answers).

Question 2 – Contactibility (N=41)

All 41 patients answered this question. 25 patients (61.0%) answered it was “totally not a problem” to get in touch with the assistants at the policlinic by phone. 13 (31.7%) patients answered this question with “a little”. 2 (4.8%) patients answered with “mostly”. 1 patient answered this question with “not applicable”.

Table 11: Patient demographics

	N = 41	Percentage (%)
Gender		
Male	18	43.9
Female	23	56.1
Age groups (years)		
54 years and younger	7	17.1
55 – 64 years	14	34.1
65 years and older	20	48.8
Nationality		
Dutch	41	100
Marital status		
Married/living together	37	90.2
Widowed	3	7.3
Divorced	1	2.4
Single	0	0
Children		
Yes	34	82.9
No	7	17.1
Educational level		
Primary school	0	0
Secondary school	13	31.7
Secondary vocational education	9	22
Higher vocational education	14	34.1
University	5	12.2

Question 3 – 6 First consultation at the NKI (N=41)

Partners assisted 22 out of 41 (53.7%) patients during their first visit at the NKI. 4 out of 41 (9.8%) patients were assisted by their children. 12 out of 41 (29.3%) patients were assisted by their “partner and one or more of his/her children or family/friends”. 1 (2.4%) patient was assisted by “Nobody”

In retrospect, 34 out of 41 (92.9%) patients indicated they wanted to be assisted by the “same person(s)” at their first consultation. Subsequently, 4 (9.8%) patients

indicated they wanted to be assisted by “nobody”. Partners and/or children assisted 3 of those patients. 1 (2.4%) patient was assisted by nobody.

15 out of 41 patients (36.6%) had to wait less than 1 week before their first consultation at the NKI. 19 out of 41 (46.3%) patients had to wait 1 to 2 weeks before their first consultation at the NKI. 6 out of 41 patients (14.6%) had to wait 2 to 3 weeks. 1 (2.4%) patient had to wait more than 3 weeks. 1 (2.4%) patient did not fill out this question.

In addition, we asked patients to what extent they experienced the waiting time until first consultation as a problem. 30 out of 41 (73.2%) patients filled out that waiting time until first consultation was “no problem”. The only patient who had a waiting time of more than 3 weeks before his/her first consultation assessed a waiting period of more than 3 weeks as “a big problem”. 3 (7.3%) other patients with a waiting time less than 3 weeks assessed their personal waiting time as “a big problem” as well. 2 of these patients had a waiting time between 1 to 2 weeks time. Only 1 patient had a waiting period of less than 1 week time. 6 out of 41 (14.6%) patients assessed their waiting time as “a little problem”. 3 of these patients had to wait 2 to 3 weeks time. The other 3 patients had a waiting time of 1 to 2 weeks time.

The results of section 2.3 showed that a waiting time of 2 weeks had a higher utility than a waiting time of 1 week. However, the choice for a treatment seems not to depend on waiting time before treatment regarding the insignificant results. More details are shown in section 2.3.

Question 7 - Waiting time at the policlinic (N=41)

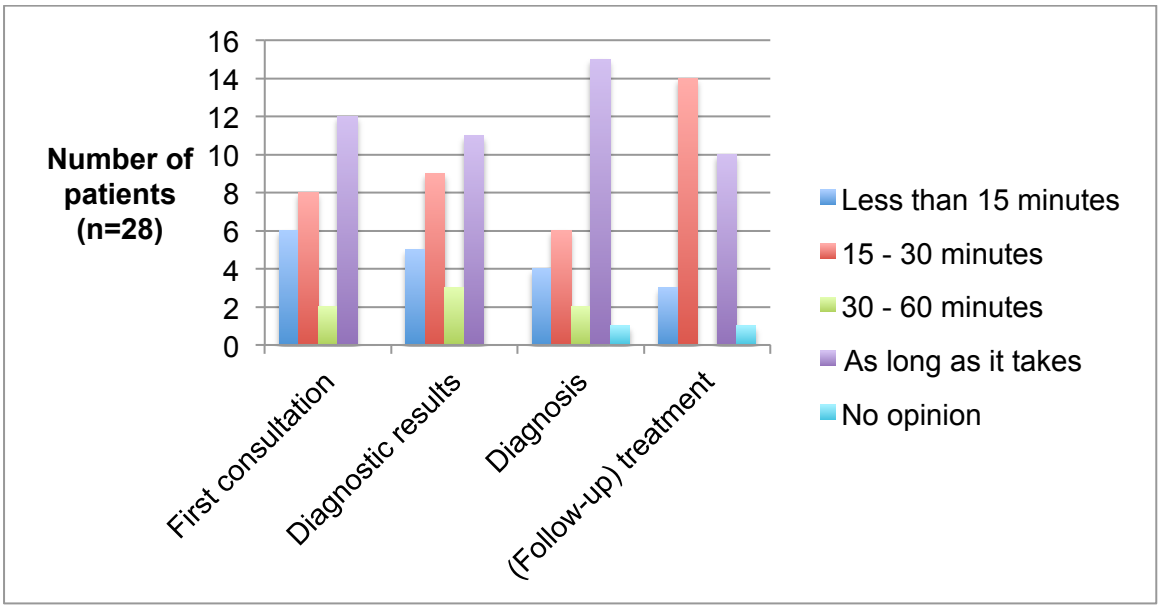
40 out of 41 patients answered this question. 9 (22%) patients indicated their physician saw them at the arranged time or earlier. 3 (7.3%) had to wait 30 to 60 minutes before they were seen. 38 (68.3%) patients were seen in less than 15 minutes or between 15 to 30 minutes.

Question 8 - Desired duration of consultations at the outpatient clinic (N=41)

We asked patients to give their opinions related to time durations of several types of consultations at the outpatient clinic. We asked them to give indications of time durations related to their first consultation, research outcomes, diagnosis and (follow-up) treatment. 6 out of 41 (15%) patients indicated they wanted to see their physician 15 to 30 minutes whatever the contents of the consultations will be. 5 out of 41 (12.5%) patients indicated they want to be seen by their physician "As long as it takes" whatever the contents of the consultations will be. Only 1 (2.4%) patient indicated he/she wants to be seen by his/her physician in 15 minutes of time, whatever the contents of the consultations will be.

Remaining patients desired diversity in durations per consultation. All results are shown in **Figure 6**. From this figure, it can be seen that majority of all patients did not prefer any specific duration of consultation. The majority of all patients had preference for a shorter duration than 30 minutes of time.

Figure 6: Desired duration of consultations with different purposes



The planned duration time for first consultation is 45 minutes time. 20 out of 41 (48.7%) patients indicate that their desired duration time for first consultation is less than 30 minutes time. Planned duration time for discussion of diagnostic results, and diagnosis are 15 minutes. A duration time of 15 to 30 minutes was preferred by 13

out of 41 (31.7%) and 11 out of 41 (26.8%) patients. The majority preferred a desired duration time of “As long as it takes”. This answer was filled out by 16 (39.0%), and 20 (48.8%) patients. Desired duration time related to (Follow-up) treatment is 15 to 30 minutes time by 20 out of 41 (48.8%) patients followed by “As long as it takes” by 15 (36.6%) patients. Planned duration time for this type of consultation is 15 minutes.

Question 9-10 - Waiting time until next consultation (N=41)

Waiting time until next consultation took for 14 (34.1%) patients less than 1 week time. For 7 (17.1%) patients it took 1 to 2 weeks time, for 8 (19.5%) patients it took 2 to 3 weeks time and for 10 (24.4%) patients it took more than three weeks time.

33 out of 41 (80.5%) patients assessed their waiting time until the next consultation as “no problem”. 3 patients judged waiting time until next consultation as a “big problem”. The 5 other patients assessed waiting time with “a small problem”. Waiting times of those last two groups of patients varied between 1 to 2 weeks up and including more than 3 weeks time.

Question 11-14 - Waiting time research trial patients (N=16)

In total, 16 patients participated in clinical trials. We asked these patients how many days were between the trial research and the test results. 3 (18.8%) trial patients answered this question with “less than 1 week”. 4 (25%) trial patients answered this question with “1 to 2 weeks”. 2 (12.5%) patients answered with 2 to 3 weeks and 5 (31.3%) patients answered this question with “more than 3 weeks”. None of the three patients treated in a chemotherapy trial had to wait more than 2 weeks. The only patient who participated in a targeted therapy trial had to wait more than 3 weeks. 1 patient answered with “not applicable”. We had missing data of 1 patient.

Besides, we asked these patients whether they experienced waiting time between the trial research and the test results as a problem. 13 out of 16 (81.3%) trial patients did not experience this waiting period as a problem. 3 patients answered this question with “a small problem”. 2 were treated with immunotherapy and 1 patient was treated with targeted therapy. 2 patients did not filled out this question.

We also asked them to what extent they experienced waiting time between the research period and the diagnosis as a problem. 13 (81.3%) patients answered this

question with “not applicable” because of diagnosis in another hospital. 2 (12.5%) patients answered with “no problem”. 1 patient answered this question with “a big problem”. These patients were all treated with immunotherapy.

In addition, we asked these patients whether they think a shorter waiting time between the study research and test results would have a positive impact on the course of patient’s disease. 1 (6.3%) patients answered with “no, completely not”, 1 (6.3%) patient answered with “a little”, and another patient (6.3%) answered this question with “yes totally”.

Question 11-14 - Waiting time last research of patients treated with standard of care (non-trial patients) (N=25)

We also asked all 25 patients who did not participate in clinical trials how many days were between the last research and the test results. 12 (48%) patients answered this question with “less than 1 week”. 8 (32%) patients answered this question with 1 to 2 weeks. 3 (12%) patients answered with “no results yet” and 2 (8%) patients indicated that their research is still on going.

We asked these patients whether they experienced waiting time between their last research and the test results as a problem as well. 17 (68%) patients experienced this period as “no problem”. 3 (12%) experienced this waiting period as a problem. These 3 patients were all treated with chemotherapy. 5 (20%) patients answered this question with “not applicable” corresponding to diagnostic tests in another hospital.

We also asked them to what extent they experienced the waiting time between the research period and the diagnosis as a problem. 17 (68%) patients answered this question with “not applicable” because of diagnosis in another hospital. The 8 other patients were diagnosed in the NKI. 4 (16%) patients answered this question with “no problem”. 3 (12%) patients answered with “a small problem”. 1 (4%) patient answered this with “a big problem”. The last patient had to wait less than 1 week.

In addition, we asked all patients who were diagnosed in the NKI if a shorter waiting period between the test results and diagnosis would have a positive impact on the course of patients’ disease. 4 (16%) patients answered with “no, completely not”. 1 (4%) patient answered with “mostly”. 3 (12%) other patients answered this question

with “yes, totally”. 2 of these patients were treated with chemo therapy. 1 with targeted therapy. The last three patients did not assess waiting time between research and diagnosis as a problem. Their total waiting times varied from 6 to 23 days.

Question 16 – Waiting time before treatment of patient treated with standard of care (N=25)

We asked patients how long they had to wait before they could start their treatement (calculated from moment of diagnosis until first treatment) 4 (25%) chemotherapy patients answered they had to wait less than 1 week. 2 (12.5%) patients answered with “1 to 2 weeks”. 10 (62.5%) answered with more than 3 weeks. We also asked patients who were treated with targeted therapy. In general, they had to wait for a shorter period. 3 (33.3%) patients indicated they had to wait 1 to 2 weeks. 1 (11.1%) patient answered with 2 to 3 weeks. 4 (44.4%) patients had to wait more than three weeks. In general, the majority of all patients who were treated with standard of care had to wait more than 3 weeks (56%).

Question 17 - Waiting time before treatment in clinical trial (N=16)

We asked all trial patients whether they experienced waiting time between research and treatment as a problem. 11 out of 16 (68.8%) trial patients did not experience that waiting period as a problem. 2 (12.5%) answered this question with “a small problem”. Only 1 patient answered this question with “a big problem”.

Question 17 - Waiting time before treatment with standard of care (N=25)

We asked all patients treated with standard of care whether they experienced waiting time between research and treatment as a problem. 14 out of 16 (56%) non-trial patients did not experience said waiting period as a problem. 6 (24%) answered this question with “a small problem”. 4 patients answered this question with “a big problem”.

Question 18-20 Waiting time before treatment in clinical trials (N=16)

11 out of 16 (68.8%) patients who participated in clinical trials confirmed that their treating physician gave an explanation about the waiting time before treatment. 2 (12.5%) patients who participated in immunotherapy trial did not confirm they were well informed about waiting time before treatment. 2 out of 16 (12.5%) patients think a shorter waiting time will totally affect the course of disease in a positive way. 10

(62.5%) patients think a shorter waiting will not result in a positive course of disease. 3 patients (18.8%) think it could have had “a bit” of impact on the course of disease.

Question 18-20 Waiting time before treatment with standard of care (N=25)

5 (20%) patients think a shorter waiting time will completely affect the course of their disease in a positive way. 10 (40%) patients think a shorter waiting will not result in a positive course of disease. 2 (8%) patients think it could have had “a bit” of impact on the course of their disease.

Comparing the results of the previous question, it seems that patients treated with standard of care are more convinced a shorter waiting time between rests results and treatment has a positive impact on the course of disease.

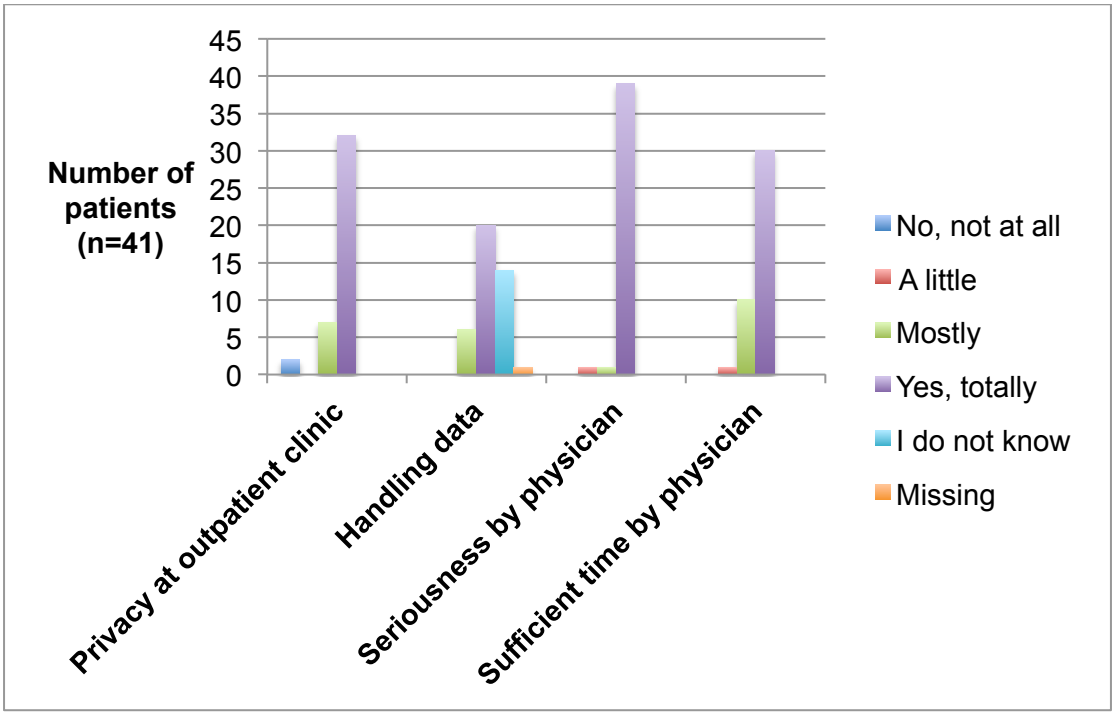
Question 22 – 25 - Privacy & Contact with treating physician (N=41)

Four questions were related to privacy at the outpatient clinic, handling data, seriousness by physician, and sufficient time by physician. The results are shown in **Figure 7.** Based on these results, most patients answered they totally agree with sufficient privacy at the policlinic, the way the NKI handles data, and seriousness and sufficient time by the treating physicians. 2 out of 41 (4.9%) patients assessed privacy at the outpatient clinic as “no, not at all”. In addition, 14 out of 41 (34.1%) patients are not quite sure whether the hospital handles data sufficiently and 6 out of 41 (14.6%) patients assessed their way of sufficiently handling data with “mostly”. Finally, 10 out of 41 (24.4%) assessed the question related to sufficient time by physician with “mostly”.

Question 26-30 - Information by, and communication with treating physician (N=41)

The question related to clear explanations by the treating physicians was assessed with “always” by 27 out of 41 (65.9%) of all patients. 11 (26.8%) patients answered this questions with “mostly”. 2 (4.9%) patients assessed this question with “sometimes”. One patient did not fill out this question.

Figure 7: Satisfaction with privacy, handling data, seriousness, and time by physician



Explanation in words about the disease, treatment, and/or test results were preferred by 17 out of 41 (41.5%) of the respondents. Explanation by means of figures-images and percentages were less popular and were filled out by 3 out of 41 (7.3%) of the respondents. Patients who indicated two answers combined explanation in words in combination with other previously mentioned methods most often. 1 patient preferred a lecture.

Besides, we asked patients if they have preference for communication with their physicians by phone, by consultation, by email, and/or through another way. 35 out of 41 (85.4%) patients preferred communication with their physician during a consultation. 1 (2.4%) patient had preference for consultation by telephone. Other 5 (12.2%) patients preferred a combination of the answers mentioned above.

In addition, 33 out of 41 (80.5%) patients answered the question “Do you have the possibility to ask your physician all your questions” with “yes, totally”. 6 (14.6%) patients answered this question with “mostly” and just 1 (2.4%) patient answered with “a little”. 1 patient did not anwer this question.

Finally, we asked patients whether they missed any information during explanation by their treating physician. 35 out of 41 (85,4%) patients did not miss any information during explanation by their treating physician. The other 6 (14.6%) patients indicated they missed information about:

- Necessarity of research
- Contents of research
- Duration of research
- Duration of treatment
- Information about metastasis

Question 31 & 32 - Cooperation between health care providers (N=41)

37 out of 41 (90.2%) indicated consultations at different departments were coordinated. 4 out of 41 (9.8%) patients indicated there is no coordination between the different departments.

Besides, 20 out of 41 (48.8%) patients thought the current way of coordinating consultations/appointments does not result in longer waiting times. 3 of these patients answered the previous question with “no”. 11 out of 41 (26.8%) patients answered this question with “I don’t know”, and 10 (24.4%) patients think the current way of coordinating consultations results in longer waiting times.

Question 33-35 - Patient participation (N=41)

31 out of 41 (75.6%) of all patients indicated they never got contradictory information. 10 (24.4%) patients indicate they have sometimes got contradictory information. No patients answered this question with “always”, or “mostly”.

In addition, we asked patients whether they got information about patient rights. 14 out of 41 (34.1%) patients indicated they got no information about patient rights. 5 out of 41 (12.2%) patients indicated they got information about patient rights but they had to ask for this information. The majority, 22 out of 41 (53.7%) patients indicated they got information about patient rights without asking.

We also asked patients whether they have had an effect on their own treatment (plan). 3 out of 41 (7.3%) patients answered this question with “never”. 4 out of 41 (9.8%) answered this question with “sometimes”. 5 out of 41 (12.2%) answered with “mostly”. Answers given by most patients were “always” and “no opinion”, which was given by 17 out of 41 (41.5%) and 11 out of 41 (26.8%) patients. 1 patient did not answer this question.

Question 36 & 37 – Aftercare (N=41)

10 out of 41 (24.4%) patients do not know whom to contact if there are any problems after consultation. 31 out of 41 (75.6%) patients know whom to contact.

30 out of 41 (73.2%) patients indicated they got enough information about disease related subjects. Points of improvement related to patient information were:

- Rules and lifestyle (n=5)
- Medication in combination with other medication (n=3)
- Coping styles (n=3)
- Where to get additional information (n=2)
- Effects and side effects of medication
- Events after treatment
- Rest and work
- Use of tools
- Events after research
- Medication in combination with food

Question 38 – 41 - Overall judgment

We asked patients whether to recommend this policlinic to family members and friends. All 41 patients unanimous would recommend this policlinic to family and friends.

Secondly, we asked patients for points of improvement. 14 out of 41 (34.1%) patients wrote the following points of improvement:

- Waiting time
    - Between preparing gemcitabine and dripping the patient
    - Before participation in clinical trials
    - Between research and test results

- More attention for factors who are not connected to the trials
- Food at the restaurant
- Provision of information (waiting time excluded)
- Information about waiting time concerning treatment
- Shorten the distance from parking place
- Personal, protected internet page with personal data about treatments and possible questions (30)
- (Re) introduction of patient card
- Communication
    - With pain clinic
    - Between health care providers
- Planning of appointments on the same day
- Desk 4 located in walking route

We asked patients which grade they would give their complete treatment trajectory, related to satisfaction in the NKI until now. The results are partly shown in **Table 12.** Quotes about patient's treatment trajectory and personal important aspects are shown in **Figure 9.**

Finally, to check whether waiting time had an impact on the grades given by patients, we calculated the correlation between these data. We registered an average total waiting time of 40.6 (n=36) days. Patients graded the NKI with an average grade of 8.7 (n=40). We found r= -0.118. This corresponds with a weak negative correlation. Besides, we calculated a p=0.498. Based on these results we conclude that the waiting time has no impact on the assessment of a patient's treatment trajectory.

Table 12: Grades (1-10)

Group	N=40	Mean	Median	Modus
Immunotherapy trial	12	8.9	9	8
Chemotherapy trial	3	9.0	9	-
Chemo therapy	15	8.5	8.8	9
Targeted therapy trial	1	9	9	9
Targeted therapy	9	8.8	9	-

2.2 Immunotherapy knowledgd statements (N=11)

Knowledge statements about PDL-1 staining tests

All 12 patients treated with immunotherapy were asked to answer 14 statements about the PDL-1 staining tests, and treatment with immunotherapy. One patient did not answer any of the 14 statements. The answers of the other 11 patients are shown in **Table 13** and **14**.

Knowledge about immunotherapy research was relatively low (correct answers = 49,4%) compared to knowledge about immunotherapy. One question that elicited substantially more “I don’t know” responses was “The test results are always right by 7 out of 11 patients (63.3% don’t know). The question with the most incorrect answers was: “The immunotherapy research gives information about the parts in the human body the cancer had formed metastasis” by 8 out of 11 (72.7%) patients.

Questions with the most correct answers were: “The physician decides on the basis of the results whether patients can be treated with immunotherapy” (90.9%), “Remaining material is saved and stored” (81.8%), and “The research says something about the heritance of lung cancer in the family of the patient (72.7%)”

All patients think the test results are always right. Patients’ answers about “The research is a test that looks at all DNA in the body of patients” and “The immunotherapy research is performed with tissue material of the lungs” were most varied.

On the question if patients could answer these questions completely, based on the information from their treating physicians, 3 out of 11 (27.3%) patients indicated “Yes, totally”. 6 out of 11 (54.5%) patients answered this question with “Mostly”. The 2 remaining patients answered with “A little”.

Table 13: Knowledge statements about immunotherapy research – PDL-1 staining test

	Correct	Incorrect	I don't know
Correct answer was "true"			
• Remaining material is saved and stored.	9	2	-
• The immunotherapy research is performed with tissue material of the lungs.	5	3	3
• The physician decides on the basis of the results of the research whether patients can be treated with immunotherapy.	10	1	-
Correct answer was "false"			
• The immunotherapy research gives information about the parts in the human body the cancer had formed metastasis.	8	2	1
• The test results are always right.	4	-	7
• The research says something about the heritance of lung cancer in the family of the patient.	1	8	2
• The research is a test that looks at all DNA in the body of patients.	3	4	4

Table 14: Knowledge statements about immunotherapy

	Correct	Incorrect	I don't know
Correct answer was "true"			
• Immunotherapy reduces the risk of metastasis	10	-	1
• There are different types of immunotherapy.	10	-	1
• Immunotherapy strengthens the immune system of patients	8	3	-
• The physician decides on the basis of the results of the research whether the patient can be treated with immunotherapy.	10	1	-
• Symptoms can be reduced through treatment with immunotherapy.	9	1	1
• Immunotherapy can be life increasing for patients.	11	-	-
Correct answer was "false"			
• Immunotherapy is used to enhance the effect of chemotherapy.	1	7	3

Knowledge statements about immunotherapy

All 11 patients treated with immunotherapy, who filled out the statements, indicated they have never heard of immunotherapy before they were diagnosed with lung cancer. The answers of the second statement section related to treatment with immunotherapy are shown in **Table 14**.

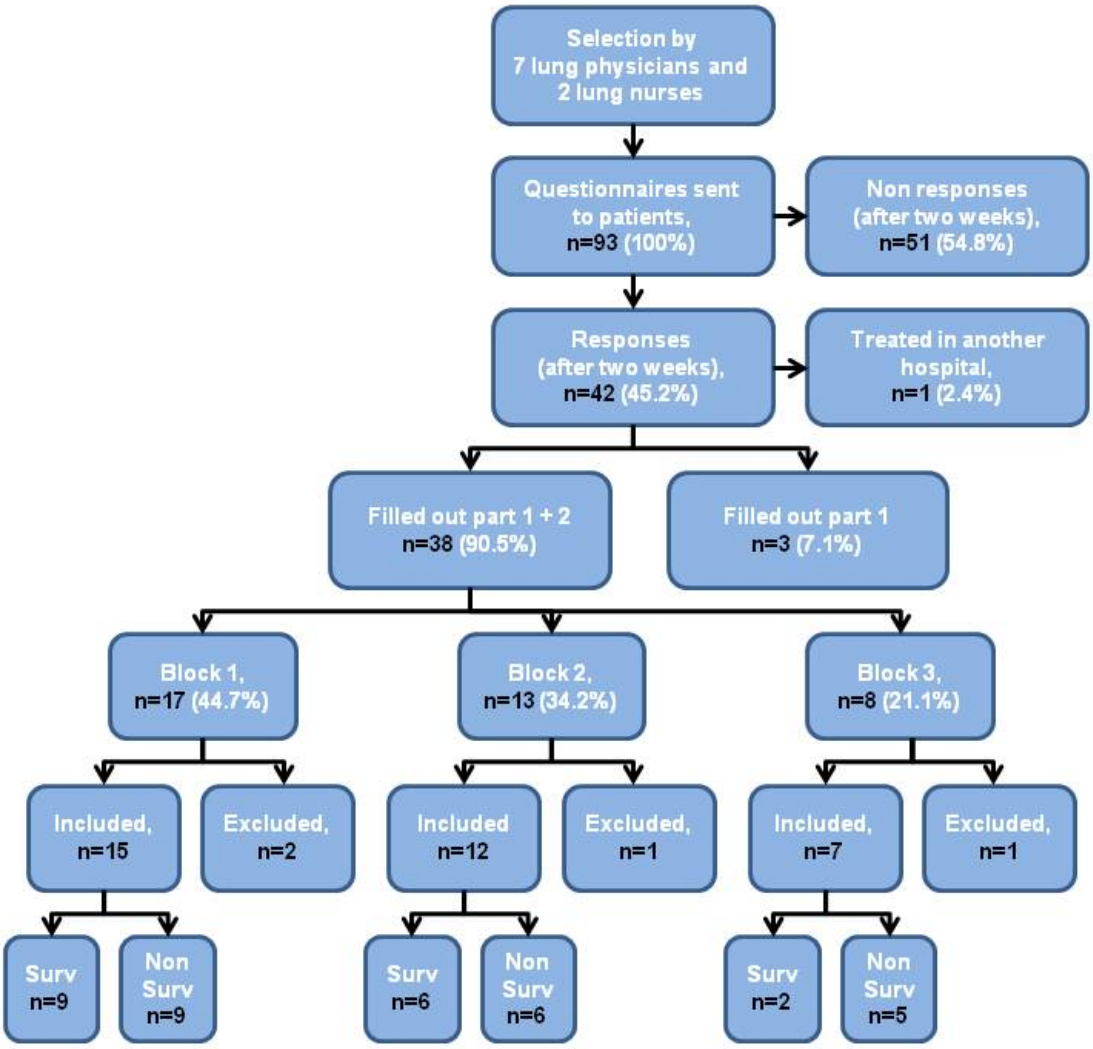
Knowledge about immunotherapy was relatively high (correct answers=84,4%) compared to knowledge about the PDL-1 staining tests. The four questions with the most correct answers were: “Immunotherapy can be life increasing for patients (100%)”. “Immunotherapy reduces the risk of metastasis” (90.9%), “There are different types of immunotherapy (90.9%), and “The physician decides on the basis of the results of the research whether the patient can be treated with immunotherapy” (90.9%). All 11 patients answered an average of 5.8 statements correctly.

3 out of 11 (27.3%) patients indicated they were completely able to fill out the answers by means of information from their treating physicians. These patients answered this question with “Yes, totally”. 5 out of 11 (45.5%) patients answered this question with “Mostly”. The 3 remaining patients answered with “A bit” or, “Totally not”.

2.3 Discrete Choice Experiment (DCE)

An overview of all patients who filled out the second part of the questionnaire is shown in **Figure 8**. This figure shows that 38 patients tried to fill out the scenarios included in the second part of the questionnaire. Finally, 17 (44.7%) patients filled out block 1. Blocks 2, and 3 were filled out by 13 (34.2%), and 8 (21.0%) patients. We excluded results of 4 patients. These patients indicated they did not understand the DCE. Finally, we analyzed the data of the 34 (89.5%) other patients.

Figure 8: Respondents in detail



From Figure 8, it can be seen that 17 out of 34 (50%) patients unanimously chosen the 12 scenarios with the highest survival (indicated as “Surv”). The other 17 (50%) patients did not consequently chose the scenarios with the highest survival (of 9 months) (indicated as “non surv”). A total number of 201 scenarios were filled out by al 17 patients. The choices of these patients were analyzed by means of explorative multiple logistic regression. The results are shown in **Table 15.**

Table 15: Patient demographics DCE

N=34	Survival N=17	Non-survival N=17
Gender		
Male	8 (47.1%)	6 (35.3%)
Female	9 (52.9%)	11 (64.7%)
Age groups (years)		
54 years and younger	5 (29.4%)	1 (5.9%)
55 – 64 years	4 (23.5%)	7 (41.2%)
65 years and older	8 (47.1%)	9 (52.9%)
Nationality		
Dutch	17 (100%)	17 (100%)
Marital status		
Married/living together	16 (94.1%)	14 (82.4%)
Widowed	1 (5.9%)	2 (11.8%)
Divorced	-	-
Single	-	-
Children		
Yes	16 (94.1%)	12 (70.6%)
No	1 (5.9%)	5 (29.4%)
Educational level		
Primary school	-	-
Secondary school	5 (29.4%)	7 (41.2%)
Secondary vocational education	1 (5.9%)	5 (29.4%)
Higher vocational education	7 (41.2%)	4 (23.5%)
University	4 (23.5%)	1 (5.9%)
Treatment method		
Clinical trial	6 (35.3%)	8 (47.1%)
Standard of care	11 (64.7%)	9 (52.9%)

The results in **Table 16** show that the most important factor in choosing for a treatment is the average survival after initial treatment. The Odds Ratio (OR) for a survival of 9 months is 2.8 times higher than the odds for a treatment with 3 months of survival (p=0.000, CI=0.95).

The second most important factor is improvement of symptoms. Compared to no improvement of symptoms is an improvement of symptoms for 2 months significantly different with an OR of 2.4 (CI =0.95). Besides, compared to no improvement of symptoms is an improvement of symptoms after two weeks significantly different with an OR of 1.6 (CI=0.95). The choice for a treatment seems not to depend on the three waiting time attributes as well as the risk of side effects. No significant differences were estimated. The attributes "Risk of side effects" and "Average survival after initial treatment" are the estimated effects logically ordered.

Table 16: Partial results DCE (n=17)

	B	S.E.	Sig.	Exp(B)
Waiting time between referral and first consultation (2 weeks)				
• 1 week	-0.216	0.169	0.201	0.806
Waiting time between first consultation and diagnosis (3 weeks)				
• 2 weeks	0.113	0.226	0.616	1.120
• 1.5 weeks	-0.070	0.245	0.774	0.932
Waiting time between diagnosis and initial treatment (2 weeks)				
• 1 week	0.206	0.228	0.366	1.229
• No waiting time. On the day of diagnosis treatment starts	0.085	0.237	0.721	1.088
Improvement of symptoms (No improvement)				
• 2 months	0.877	0.246	0.000	2.405
• 2 weeks	0.471	0.233	0.043	1.602
Risk of side effects from initial treatment (60%)				
• 40%	0.208	0.249	0.405	1.231
• 20%	0.264	0.246	0.284	1.302
Average survival after initial treatment (3 months)				
• 9 months	1.015	0.175	0.000	2.759

Nevertheless, by means of this method it can only be concluded which levels seems more preferred than others (based on its OR in combination with the level significance described above). For that reason, relative importance is calculated in the next section.

The results in **Table 17** show the importance of each attribute. Based on these results it can be concluded that the three most important attributes are: 1) "Average survival after initial treatment" (36.8%), 2) "Improvement of symptoms" (31.8%), and 3) " Risk of side effects from initial treatment" (9.6%). The three attributes related to waiting time seem less important.

Table 17: Relative importance of attributes (n=14) (31)

Attribute	Level	Part-worth Utility	Attribute utility range	Attribute importance
Waiting time between referral and first consultation	2 weeks	0.000	0.216	(0.216/2.761) x 100% = **7.8%**
	1 week	-0.216		
Waiting time between first consultation and diagnosis	3 weeks	0.000	0.183	(0.183/2.761) x 100% = **6.6%**
	2 weeks	0.113		
	1.5 weeks	-0.070		
Waiting time between diagnosis and initial treatment	2 weeks	0.000	0.206	(0.206/2.761) x 100% = **7.5%**
	1 week	0.206		
	No waiting time	0.085		
Improvement of symptoms	No improvement	0.000	0.877	(0.877/2.761) x 100% = **31.8%**
	2 months	0.877		
	2 weeks	0.471		
Risk of side effects from initial treatment	60%	0.000	0.264	(0.264/2.761) x 100% = **9.6%**
	40%	0.208		
	20%	0.264		
Average survival after initial treatment	3 months	0.000	1.015	(1.015/2.761) x 100% = **36.8%**
	9 months	1.015		
			Total utility range: 0.261 + 0.183 + 0.206 + 0.877 + 0.264 + 1.015 = 2.761	

Figure 9: Quotes by patients

"Death is always a possibility to chose. I feel great. This will possibly change in the future. This could lead to other decisions."
- Woman, 67 years old -

"We think survival more important the the insecurity of waiting time. In this way, we reserve time for treatment."
- Woman, 74 years old -

"Most important aspect is survival".
- Woman, 73 years old -

"Survival is all I care about"
- Man, 66 years old -

"We prefer survival aboth all other aspects. We are still thankfull for my participation in the immunotherapy trial"
- Woman, 71 years old -

"I would like to thank my treating phsycian: He was in the position to arrange a consultation while he was very busy"
- Woman, 31 years old -

"They pay attention to patients. The effusion is friendly"
- Woman, 53 years old -

"I am satisfied with my treatment"
- Woman, 73 years old -

"The staff is very professional and friendly. I am very satisfied so far."
- Woman, 67 years old -

Box 3: Overview of interesting observations

1. Patients treated with standard of care are less satisfied with the time period between research and treatment. In addition, these patients think a shorter **waiting time between test results and treatment** has a positive impact on the course of disease.
2. The researches of the trial patients were more time consuming compared to the researches of patients treated with standard of care. In addition, both patient groups are comparably satisfied about the **waiting times related to their research outcomes**.
3. Planned duration time for first consultation is 45 minutes time. 20 out of 41 (48.7%) patients indicated **desired duration time for first consultation** is less than 30 minutes time.
4. 14 out of 41 (34.1%) patients are insecure whether the hospital **handles data carefully**.
5. 27 out of 41 patients always get **clear explanations** by their treating physicians. 11 (26.8%) patients mostly get clear explanations by their treating phsycian. 2 (4.9%) patients sometimes get clear information.
6. 31 out of 41 (75.6%) of patients indicated they never got **contradictory information**. 10 (24.4%) patients indicated they get contradictory information sometimes.
7. 10 out of 41 (24.4%) patients think that the **current way of coordinating consultations results in longer waiting times**.
8. 14 out of 41 (34.1%) patients indicated they got no **information about patient rights**. 5 out of 41 (12.2%) patients indicated they got information about patient rights but they had to ask for this information. The majority, 22 out of 41 (53.7%) patients indicated that they got information about patient rights without asking.
9. We also asked patients whether they have an **effect on their own treatment** (plan). 3 out of 41 (7.3%) patients indicated that they have never had an effect on their own treatment (plan). 4 out of 41 (9.8%) answered this question with “sometimes”. 5 out of 41 (12.2%) patients answered with “mostly”. Answers given by most patients were “always” and “no idea” given by 17 out of 41 (41.5%) and 11 out of 41 (26.8%) patients.
10. 33 out of 41 (80.5%) patients answered the question “Do you have the **possibility to ask your physician all your questions**” with “Yes, totally”. 6 (14.6%) patients answered this question with “Mostly” and just 1 (2.4%) patient answered with “A little”. 1 patient did not fill out this question.

2.4 Subconclusion

As explained in the introduction and method section, the study was split up into two different parts. The second part consisted of a questionnaire including a DCE and the knowledge statements about immunotherapy and the PDL-1 staining tests. In this section, these results are summarized.

Patient satisfaction & experiences

As explained in the method section, patient satisfaction and experiences among NSCLC patients treated in the NKI were analyzed in general. The first question was related to which person referred the patient to the hospital. Specialists referred most patients. This question was followed by the contactability of the NKI by phone. No patients experienced the contactability as a problem. The next question was about the assistance during a patient's first consultation. Most patients did not change their mind about their assistance during their first consultation. In addition, we asked all patients how long they had to wait before their first consultation. Most patients had to wait less than 2 weeks time before their first consultation. In general, patients were not unsatisfied with their waiting times. At following appointments, most patients were seen after the arranged time.

We also asked for patients' preferences for desired duration of consultations (with different purposes). The majority answered this question with "as long as it takes", except from duration related to consultation about "(Follow-up) treatment". In this case, majority preferred duration of 15 to 30 minutes.

Most patients had to wait less than 1 week until the next consultation. Most patients did not assess their waiting period as a problem. Besides, we asked patients how many days the trial research until moment of test results took. This part of total waiting time corresponds with the "analysis time" and "transport time". In the WTA we analyzed a "transport time" and "analysis time" of 2.7 days and 4.9 days. These time components correspond with a mean waiting time of 1 week. In practice, 3 out of 14 (21.4%) patients experienced a waiting time of less than 1 week. The other 11 (78.6%) patients experienced a waiting time of more than 1 week. Most patients did not experience this waiting period as a problem. We also asked them to what extent they experienced waiting time between the research period and the diagnosis as a problem. Most patients did not experience this waiting period as a problem.

We also asked all 25 patients who did not participate in clinical trials how many days their last research until moment of test results took. Most patients answered this question with 1 to 2 weeks. We asked these patients whether they experienced waiting time between their last research and the test results as a problem as well. Most patients did not experience this waiting period as a problem. However, we cannot compare the previous results with the trial group, it seems that the researches of the trial patients are more time consuming compared to the researches of patients treated with standard of care. In addition, it seems that both groups are comparably satisfied about the waiting times related to their research outcomes.

In addition, we asked these patients treated with standard of care to what extent they experienced waiting time between the research period and the diagnosis as a problem. Most patients did not experience this period as a problem. We asked patients treated with standard of care diagnosed in the NKI if a shorter waiting period between the test results and diagnosis would have a positive impact on the course of patients' disease. Most patients denied this statement.

We asked all patients treated with standard of care whether they experienced the waiting time between their research and treatment as problematic. However, compared to patients treated in clinical trials, patients who were treated with standard of care are less satisfied with the period between the research and treatment, based on the number of answers patients gave.

Trial patients were asked whether their treating physician explained them about waiting time before treatment. Most patients confirmed they were informed about a possible waiting period. In addition, most patients did not think a shorter waiting period resulted in a positive course of their disease. We asked the last question to all patients treated with standard care as well. Compared to the trial patients, it seems possible that patients treated with standard of care are more convinced that a shorter waiting time between test results and treatment has a positive impact on the course of disease.

All patients were asked whether they were satisfied with the way the NKI handles patient data, how seriously physicians are, if their treating physicians had enough time and whether the outpatient clinic offered enough privacy. Most patients

confirmed this question by answering this question with “Yes totally”. However, some patients do not know whether the NKI handles data carefully.

Most patients were satisfied with information, and communication with their treating physician. However, some patients wrote some points of improvement. Most patients were satisfied about the way health care providers cooperated as well. Most patients thought that the current way of coordinating consultations did not result in longer waiting times. In addition, most patients indicated they never got contradictory information. Patients were satisfied with patient participation as well. Most patients answered they never got contradictive information. However, most patients doubted whether they have had an effect on their own treatment plan.

Besides we asked all patients whether they know whom to contact (if there are problems after consultation). Most patients confirmed this question. In addition, most patients indicated they got enough information about disease related subjects. However, some points of improvement were mentioned.

Finally, we asked patients to give an overall judgement. All patients would recommend this policlinic to family and friends. This question was followed by some points of improvement. Total waiting time had no significant impact on satisfaction about patient’s treatment trajectory. In addition, trial patients marked the NKI with a higher mark than non-trial patients. After all, we summarized the ten most remarkable results in **box 3**.

Knowledge statements

In the first part of the questionnaire we included some statements about immunotherapy and the PDL-1 staining tests as well. It can be concluded that knowledge about immunotherapy research was relatively low (correct answers = 49,4%) compared to knowledge about immunotherapy (correct answers=84,4%). Most patients incorrectly answered the statement “the immunotherapy research gives information about the parts in the human body the cancer had formed metastasis”. Most patients were doubtful about the statement whether “The research says something about the heritance of lung cancer in the family of the patient”.

Discrete Choice Experiment (DCE)

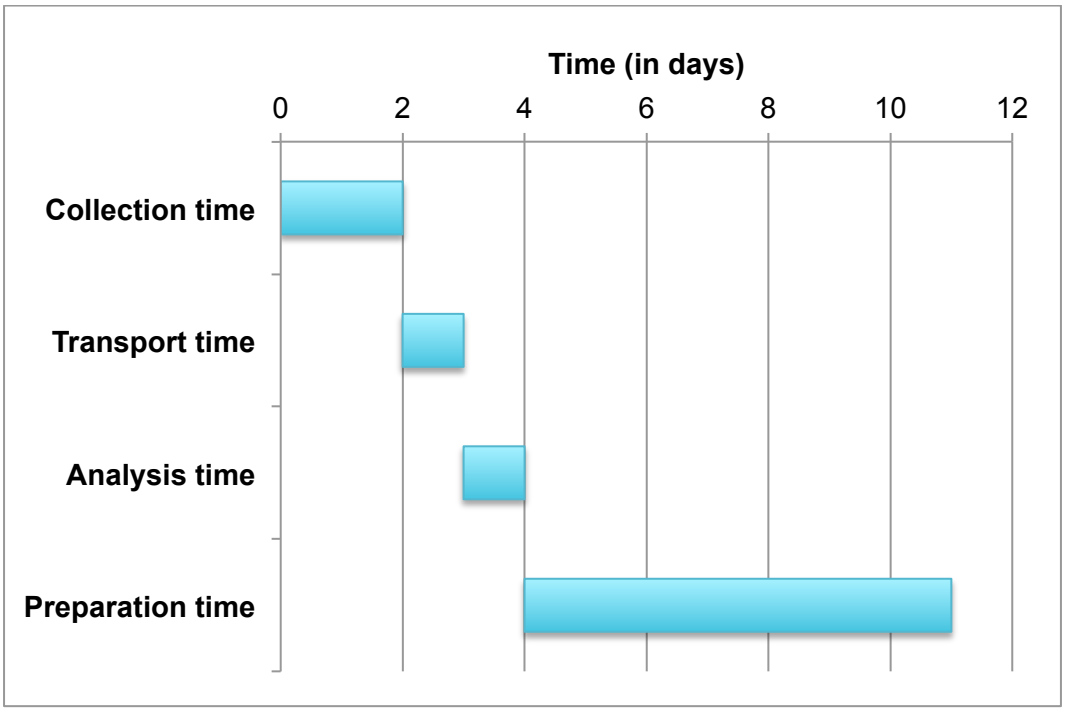
Second part was a DCE. Patients had to fill out 12 scenarios. 38 out of 41 patients filled out the second part of the questionnaire (DCE). We excluded results of 4 patients. 17 out of 34 (50%) patients unanimously chose the 12 scenarios with the highest survival. The other 17 (50%) patients did not consequently chose the scenarios with the highest survival (9 months). The choice for a treatment seems to depend on “Average survival after initial treatment’, and “Improvement of symptoms” for the second group of patients. Preference for treatment does not depend on the three waiting time attributes as the risk of side effects. The three most important attributes for the second patient group are: 1) “Average survival after initial treatment” (36.8%), 2) “Improvement of symptoms” (31.8%), and 3) ” Risk of side effects from initial treatment” (9.6%).

Conclusion

1. Waiting time analysis (WTA)

The shortest plotted waiting time was a minimum of 21 days (n=1). Based on this data it should be possible to pass the whole screening process within a period of three weeks time. However, when we plot the best results per process step it should be possible to complete the whole process in a period of 11 days. So, in the most optimistic situation, the waiting time can be sped up from 21 days until approximately factor 2 until a period of 11 days. This perfect scenario is a plotted in **Figure 10**.

Figure 10 – Perfect scenario



The shortest measured “collection time” was 2 days. 5 out of 54 patients have reached this “collection time”. For two patients, the biopsy was taken on the same day informed consent was signed. For the other patient, revision took place on the same day of informed consent. For the rest of those patients (n=3), revision took place after informed consent (n=1) and before informed consent (n=2). The shortest “transport times” (n=14 out of 48) and “analysis times” (n=4 out of 48) were (independently and) both generated in one day time.

Histogenex, located in Belgium, generated 11 of the 14 tissue samples in the "transport time" of 1 day. In addition, Histogenex generated all "analysis times" (n=4) of 1 day. These results show a preference for the analysis on PD-L1 expression by Histogenex. The shortest "preparation time" was 7 days generated in the M13MKD trial. Although, in general, the M14NIV trial scored the best mean "preparation times" taking a look at Table 6. Subjects of discussion are explained in the next chapter.

2. Patient satisfaction, experiences, and preferences

In general, most patients were satisfied with all items. Most remarkable outcomes related to the questionnaire are shown in **box 3**. In addition, all patients would recommend this policlinic to family and friends. This question was followed by some points of improvement. Total waiting time had no significant impact on patient satisfaction. In addition, trial patients marked the NKI with a higher mark than non-trial patients.

Survival was prioritised above all other levels by half of all patients (based on the DCE, included in the second part of the questionnaire) and above all included aspects. Other patients did not consequently choose the scenarios with the highest survival (9 months). The choice of treatment seems to depend on "Average survival after initial treatment', and "Improvement of symptoms" for the second group of patients. Preference for treatment does not depend on the three waiting time attributes as the risk of side effects. The three relatively most important attributes for the second patient group are: 1) "Average survival after initial treatment" (36.8%), 2) "Improvement of symptoms" (31.8%), and 3) " Risk of side effects from initial treatment" (9.6%).

These results gave the possibility to answer our main research question: *"What is the impact of waiting time on satisfaction, experiences, and preferences from metastatic non-small lung cancer patient's perspective?"* Based on the results of this study, we cannot conclude waiting time has a significant influence on satisfaction, experiences and preferences from NSCLC patients' perspective. However, we have discovered some differences between the trial patients and patients treated with standard of care.

Discussion & suggestions for future research

This chapter is split up into four different sections. Points of discussion related to patient satisfaction, experiences, and preferences are explained in the first three sections followed by suggestions for further research.

We conducted a retrospective, describtive exploratory study about the impact of waiting time on patient satisfaction, experiences, and preferences from stage IV NSCLC patients' perspective. The study results suggested waiting time had no significant influence on satisfaction, experiences and survival of NSCLC patients. However, we have discovered some differences between trial patients and patients treated with standard of care.

1. Waiting time analysis (WTA)

Based on the main results of the WTA, the shortest time consuming procedures were practised in the M14NGO trial. Nevertheless, the M14NGO trial had the highest mean internal procedure time of 27.6 days corresponding to 87.3% of the total waiting time. "Preparation time" was most time consuming for all four trials compared to the "collection times", "transport times", and "analysis times".
As already mentioned in the introduction, method section, and result saction, several factors could be responsible for delay. It was not possible to find these factors in detail. Nevertheless, we could exclude the external procedures (including "analysis and transport times") as most important factors that could be responsible for delay. These two steps were relatively seen as non-time consuming compared to the internal processes (including "collection and preparation times").

A second point of discussion related to the WTA is, recently implemented changes in a patient's pathway, for instance new techniques, improved planning methods, habituation to processes that must take place before patients could start with their immunotherapy treatment are possibly equitable with the current waiting times. Besides, this study was retrospective. Data of time of 5/54 patients were missing. For that reason, data was sometimes presented inexactly. In addition, all data is derived from patient information recorded in the EHR. This can result in small deviations compared to reality. In addition, calculations are based on a very small sample size as well. We analyzed all waiting times with all possible information avalaible during this period.

In addition, we did not take into account the time differences between the USA and the Netherlands because of lack of information. However, this small time differences (less than 1 day) will probably not result in big deviations in time. In some results big outliers are excluded. Therefore, the mean delays per step might not be as reliable as they are in real: the presented results will be more positive than the real values in most of the results. However, in order to prevent a real image is outlined, the outliers are included in most parts of the analysis. Besides, these outliers – which are responsible for bigger delays in waiting time – are predominantly caused by patients themselves or external processes. One can think of a patient who postponed his/her immunotherapy treatment because of a holiday period, which took 3 weeks time or tissue material which was lost at the Dutch mail-order firm.

No differences were made between access times and process times. Nevertheless, this makes no sense for the actual waiting time of all included patients: we analyzed all data out of patients' perspective. For that reason, weekend days and holidays are included in the WTA as well seen from patient's perspective: "Every day counts". However, this can lead to deviation definitions of waiting time out of patients' perspective towards a care professionals' perspective. This could lead to differences in interpretation by several parties related to waiting times.

Finally, when we compare tolerable total waiting time of 1 to 28 days set by the VIKC with our data, waiting times of 8 out of 54 (14.8%) patients meet this maximum criteria of 28 days. However, as mentioned in the introduction, this period is just a recommendation for hospitals and other health care providers. Unless, the fact that these patients are exempt from these results, we cannot accept for no reason that these patients want to be treated as exceptional.

2. Patient satisfaction and experiences

The first point of discussion related to the second part of this study: we did not carry out a correlation measurement over all scales and items. Firstly, because we included a lot of questions based on the CQI. We did not remove and did not switch any items from their original scales. Secondly, we included new questions. These questions were not all covering patient satisfaction, but experiences. For the same reason (including the small subgroups as well) we did not measure any scale scores. This could lead to unrealistic scale scores.

As already mentioned in the first paragraph of this chapter, we have discovered some differences between trial patients and patients treated with standard of care. It seems that patients who were treated with standard of care were less satisfied with the current waiting times in relation to trial patients. This can possibly be seen in the answers in general and the overall evaluation by both patient categories. However, all patients would recommend the policlinic to family and friends, patients treated with standard of care marked the policlinic worse compared to trial patients. This could be explained by the fact that trial patients were better informed about longer possible waiting times compared to patients treated with standard of care, due to, for instance, strict (prepared) information criteria for trial patients. Another reason could be the recently proven effectiveness of immunotherapy in NSCLC patients. Patients could be more hopeful, and could see this treatment method as their last resort. For that reason they could have respect for waiting time. Patients treated with standard of care could be more disappointed when they had a longer waiting period in the NKI than anticipated (i.e. compared to previous treatment methods in other hospitals) based on the previously mentioned reason. Trial patients could have accepted that they were finished with other treatment methods and or could have more respect for preparing a new treatment plan that takes more time than standard of care compared to non-trial patients. This could declare the differences in assessment and satisfaction related to waiting times. In addition, patients indicated 9 months survival with higher utitilty than all waiting time attributes and aspects. This point will be explained in more detail in the following section.

The excellent overall judgment of results (in general) could be declared by anxiousness of patients: those who could be anxious for negative reactions by their treating physicians. They could be afraid of discrimination in comparison to other patients if they filled out the questionnaire negatively. To optimize our results and to prevent the previous problem, we informed patients more than once (in the questionnaire) that their results would be treated with care and anonymity.

Fourth point: because of the fact that some patients were diagnosed with NSCLC in another hospital, they missed a part of the trajectory other patients did have endured at the NKI. This also applies for the time a patient spent in the hospital (for instance a hospital stay after surgery and the experiences of the surgery itself), and the total time the patient is under treatment at the NKI, which can affect the satisfaction,

experiences, and preferences of patients. In addition, not all of the patients who participated in the first part of the study participated in the second part as well. This point of discussion is closely related to selection of patients by the physicians. Pre-selection by the phsycians could have led to unrealistic results because of selection bias. It is unclear on the basis of which criteria the physicians asked patients to take part in the study. To prevent selection bias, physicians were strictly informed whom to include. For instance, they had to exclude patients of whom they were not quite sure about whether the specific patient met the inclusion criteria.

In addition, the questionnaires could be filled out before, after a consultation, or at home. The unknown content of a consultation, or the message a patient takes home together with a patient's mood can also have a great affect on the result the patient filled out in the questionnaire. Nevertheless, patients were asked to fill out the questionnaires themselves. However, we don't know which family members, friends were present at the moment patients filled out the questionnaires. In the questionnaire, we tried to attribute to the patient him/herself and instead of calling family members and other relatives to prevent the impact of others. In addition, patients could have forgotten some time points they filled out. This leads to our following point of discussion.

We removed question 16 from the questionnaire for patients treated with standard of care because non-trial patients indicated during the pilot they could not remember the time between moment of results and start of treatment anymore. In addition, patients did not consequently answer the questions 11 up and including question 14. For that reason, results from patients, who indicated in question 11 that they were not diagnosed at the NKI, were not included in the analysis to prevent bias of results. Possibly, they did not understand the questions well. However in our pilot version we attended to every question in detail.

3. Patient preferences

The first point of discussion related to the analysis of patient preferences is we did not reach the minimum number of required patients (n=63), which is based on the Rule of Thumb. However, we tried to improve the response rate to e-mail all non-respondents with a reminder. The majority of all included NSCLC patients considered the average survival time of 9 months as the relatively most important included aspect with the highest measured utility followed by improvement of symtoms after two months. For that reason, a complete multiple regression analysis resulted in unrealistic results (i.e. due to the imbalance of the included blocks). This has lead to the situation that we do not know anything about the importance and utility of the other included attributes and levels for this group of patients.
Several lines of thought could be the basis for this choice. Firstly, the major differences between the two average survival aspects of 3 months and 9 months relative to the small waiting times included in the DCE. Although, patients have convincingly chosen 9 months survival instead of 3 months. Secondly, only risks of side effects were shown in the DCE. Explanations about the possible side effects are only outlined in the information form. This may have weakened the utiltity of this attribute for patients. The order of the attributes could have played an important role as well. Attributes related to waiting times were displayed together. In addition, including three waiting time aspects could be hard for patients to understand or to map its personal importance. Nevertheless, all pilot patients did not indicate these attributes as hard to understand: this could be an explanation why 17 (50%) of all respondents chose the survival attribute. This attribute is displayed as the last attribute every time closest to the entry box. A last glance at this attribute may have led to preference for this attribute and its corresponding level of 9 months survival. Finally, it is possible that patients really consider average survival as the most important aspect. For that reason we did an explorative multiple regression analysis with the data of patients who did not always fill out highest survival. This leads to bias of results. We tried to include patients who seriously filled out the questionnaire by excluding patients who explained that they did not fill out the questionnaire seriously.

4. Suggestions for future research

To find out whether the results of the WTA are valid, this study must be more intensively repeated internally on a larger scale (with the main focus on the internal procedures, which are, based on the analysis more time consuming than the external procedures). If those results are positive, it is interesting to optimize the waiting times and to test the external validity of these results in other hospitals as well. It could be helpful to practice in a prospective way. In this way, the study could be prepared in detail. Besides, differences and similarities between the 5 subgroups should be studied in more detail. One must emphasize on the following questions:

1) Which processes take so long?
2) What are the underlying reasons for delay?

In addition, it can be interesting to know how patients define waiting time compared to health care providers.

Physicians, who have already indicated waiting time emerges in either radiology, results of EGFR, ALK, KRAS, ROS, and RET expression, logistical planning of consultations with a nurse practitioner and hospitalization, and the response time of the concerned firms. It would not be amiss to emphasize the points set out above, taking a closer look at the study criteria and, further taking into account the points set out in the discussion section. In addition, a cost analysis based on the waiting times and possibilities to optimize these waiting times could be very interesting. Relevant questions for this study are:

1) Which cost differences can be analyzed?
2) In which field did the highest costs occur?
3) In which fields is a possibility to save money?

Whereby the costs per platform and the transport costs must be taken into account. Possibly, profits can be made on these fields as well. Besides, it is important to look at the impact of waiting time on disease progression. Designating someone as process manager who keeps an eye on the waiting times should not be a wrong at all.

Further, interviews with patients can be enlightening (especially related to the DCE). Focus should be on shared decision making (SDM) related to survival by patients. Relevant questions are:

1) What are the reasons behind the outcome that patients consider survival as the most important attribute?
2) How do patients assess SDM today?
3) What do patients think about patient involvement and the education they receive at the NKI?
4) What are the relations between survival and QoL?
5) How important are the other five aspects compared to survival?

The first question could relate to patient demographics we did not take into account. More patients in the survival group were male. These patients were relatively younger, lived together, had children and were higher educated in comparison to non-survival patients. These points could all be reasons they chose survival, however our sample sizes were to small to measure the possible impact of these factors.

Last point of discussion: it could be interesting to measure the impact of patient demographics when the study will be performed on a larger scale.

Based on these results of this study, shorter waiting times in clinical practice will not greatly increase in more satisfaction from patients' perspective. However, health care professionals and patients can interpret this as a point of service.

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Appendix 1 – Questionnaire

Introductie

In deze studie, de studie waaraan u nu deelneemt, worden de tevredenheid en ervaringen onder longkankerpatiënten gemeten die behandeld zijn of worden behandeld met immunotherapie, chemotherapie of met de zogeheten “targeted therapy”

Wij willen graag meer inzicht krijgen in de tevredenheid en ervaringen van de patiënt over het proces rondom uw behandeling die u volgt binnen het Antoni van Leeuwenhoekziekenhuis. Op deze manier kunnen wij mogelijk verbeteringen aanbrengen in het traject voor u, medepatiënten en toekomstige patiënten.

Wanneer u een vraag niet met zekerheid kunt beantwoorden, probeert u dan een schatting te maken. En geef aan hoe het ongeveer was. Er is geen goed of fout antwoord.

Indien u vragen heeft tijdens het invullen van de vragenlijst dan kunt u contact opnemen met C. Spoolder via het volgende nummer: 06-27425031

Neemt u rustig de tijd voor het invullen. Het beantwoorden van deze vragenlijst neemt ongeveer 30 minuten in beslag.

Bij voorbaat dank voor uw tijd en moeite!

Algemeen

Geslacht	O Man	O Vrouw
Geboortedatum	____ - ____ - _____	
Nationaliteit	O Nederlands(e)	
	O Anders, namelijk _____	
Burgerlijke staat	O Gehuwd/samenwonend	O Gescheiden
	O Weduwe/weduwnaar	O Alleenstaand
Kinderen	O Ja, ik heb ___ kinderen	O Nee
Hoogste opleiding	O Lagere school	
	O Middelbare school	
	O MBO (Middelbaar Beroeps Onderwijs)	
	O HBO (Hoger Beroeps Onderwijs)	
	O Universiteit	
	O Anders, namelijk _____	

Verwijzing

1. Wie heeft u doorverwezen naar het Antoni van Leeuwenhoek ziekenhuis?

O Dit was op mijn eigen verzoek
O Mijn huisarts
O Een specialist uit een ander ziekenhuis
O Op aanraden van een patiënt die onder behandeling staat/ heeft gestaan in het AVL
O Anders, namelijk: _____

Bereikbaarheid

2. Is het een probleem om de polikliniek overdag telefonisch te bereiken?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal
O Niet van toepassing

Uw eerste afspraak

3. Welke persoon is of welke personen zijn met u meegegaan tijdens uw eerste consult (afspraak) in het ziekenhuis?

O Niemand
O Mijn partner
O Een of meerdere van mijn kinderen
O Andere familieleden of een vriend/vriendin
O Iemand anders, namelijk: _____

4. Welke persoon is of personen had u achteraf liever meegenomen naar uw eerste consult in het ziekenhuis?

O Niemand
O Dezelfde persoon/personen
O Iemand anders, namelijk: _____

5. Hoe lang heeft u moeten wachten voordat u bij de polikliniek terecht kon?

O Minder dan 1 week
O 1 tot en met 2 weken
O 2 tot en met 3 weken
O Meer dan 3 weken

6. In hoeverre heeft u de wachttijd tot aan uw eerste consult (afspraak) als een probleem ervaren?

O Een groot probleem
O Een klein probleem
O Geen probleem

Wachttijd op de polikliniek

7. Hoe lang moet u in het algemeen wachten na de afgesproken tijd?

O Ik word meestal geholpen op of voor de afgesproken tijd
O Minder dan 15 minuten
O Tussen 15 tot en met 30 minuten
O Tussen 30 tot en met 60 minuten
O Meer dan 60 minuten

Tijdsduur van afspraken op de polikliniek

8. Wilt u voor de onderstaande afspraken op de polikliniek aangeven hoe lang een afspraak op de polikliniek volgens u mag duren?

Eerste afspraak (consult):

O Minder dan 15 minuten
O Tussen 15 tot en met 30 minuten
O Tussen 30 tot en met 60 minuten
O Zolang als nodig
O Geen mening

Uitslag van een onderzoek:

O Minder dan 15 minuten
O Tussen 15 tot en met 30 minuten
O Tussen 30 tot en met 60 minuten
O Zolang als nodig
O Geen mening

Diagnose:

O Minder dan 15 minuten
O Tussen 15 tot en met 30 minuten
O Tussen 30 tot en met 60 minuten
O Zolang als nodig
O Geen mening

Uitleg over (vervolg)behandeling:

O Minder dan 15 minuten
O Tussen 15 tot en met 30 minuten
O Tussen 30 tot en met 60 minuten
O Zolang als nodig
O Geen mening

9. Hoe lang moet u in het algemeen wachten op een vervolgafspraak met uw behandelend arts?

O Minder dan 1 week
O 1 tot en met 2 weken
O 2 tot en met 3 weken
O Meer dan 3 weken

10. In hoeverre heeft u de wachttijd tussen de vervolgafspraken na uw eerste afspraak als een probleem ervaren?

O Een groot probleem
O Een klein probleem
O Geen probleem

Wachttijd immunotherapie onderzoek

Nu gaan wij u een paar vragen stellen over de wachttijd omtrent het zogenoemde 'immunotherapie onderzoek'. Dit onderzoek is uitgevoerd om u te laten meedoen aan de immunotherapie studie.

11. Hoeveel dagen zaten er tussen het immunotherapie onderzoek en de uitslagen van het onderzoek?

O Minder dan 1 week
O 1 tot en met 2 weken
O 2 tot en met 3 weken
O Meer dan 3 weken

12. In hoeverre heeft u de wachttijd tussen het immunotherapie onderzoek en de uitslagen van het immunotherapie onderzoek als een probleem ervaren?

O Een groot probleem
O Een klein probleem
O Geen probleem

13. In hoeverre heeft u de wachttijd tussen de onderzoeken en de diagnose longkanker als een probleem ervaren?

O Niet van toepassing, de diagnose longkanker is in een ander ziekenhuis of elders gesteld
O Een groot probleem
O Een klein probleem
O Geen probleem

14. Denk u dat een kortere wachttijd tot de testuitslagen van het immunotherapie onderzoek een positieve invloed zou hebben op het verloop van uw ziekte?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

Stellingen over uw immunotherapie onderzoek

U leest nu een aantal stellingen over het immunotherapie onderzoek en de bijbehorende uitslagen. Dit onderzoek is uitgevoerd om u te laten meedoen aan de immunotherapie studie.

15A. Wilt u aankuisen of de volgende stellingen naar uw mening juist of onjuist zijn?

		Juist	Onjuist	Weet ik niet
1.	Het onderzoek geeft informatie over de plekken in het lichaam waar de patient is uitgezaaid	O	O	O
2.	Rest-materiaal (materiaal dat is overgebleven na het onderzoek), wordt bewaard en opgeslagen	O	O	O
3.	Het onderzoek wordt uitgevoerd met tumorweefsel van de longen	O	O	O
4.	De uitslag van het onderzoek is altijd juist	O	O	O
5.	Het onderzoek zegt iets over de erfelijkheid van longkanker in de familie van de patient	O	O	O
6.	Het onderzoek is een test die al het DNA in het lichaam van de patient bekijkt	O	O	O
7.	De arts bepaalt aan de hand van de uitslag van het immunotherapie onderzoek of u behandeld kunt worden met immunotherapie.	O	O	O

15B. Kon u vraag 15A beantwoorden door middel van de informatie die u van uw behandelend arts heeft gekregen?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

Wachttijd behandeling

17. In hoeverre heeft u de wachttijd tussen het immunotherapie onderzoek en de behandeling met immunotherapie als een probleem ervaren?

O Een groot probleem
O Een klein probleem
O Geen probleem

18. Heeft uw arts u uitgelegd waarom u moest wachten op uw immunotherapie behandeling?

O Ja
O Ja, maar ik heb hier naar moeten vragen
O Nee

19. Heeft uw arts u op de hoogte gehouden over de wachttijd voor de immunotherapie behandeling?

O Ja
O Nee

20. Denkt u dat een kortere wachttijd tussen uitslag van het immunotherapie onderzoek en de behandeling een positieve invloed zou hebben op het verloop van uw ziekte?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

Stellingen over immunotherapie

21A. Wist u voorafgaand aan de diagnose longkanker van het bestaan van immunotherapie?

O Ja O Nee

U leest nu een aantal stellingen over immunotherapie.

21B. Wilt u aankuisen of de volgende stellingen naar uw mening juist of onjuist zijn?

		Juist	Onjuist	Weet ik niet
1.	Immunotherapie verkleint de kans op uitzaaiingen	O	O	O
2.	Immunotherapie wordt gebruikt om de werking van chemotherapie te versterken	O	O	O
3.	Er bestaan verschillende soorten immunotherapie	O	O	O
4.	Immunotherapie versterkt het afweerssysteem van de patiënt	O	O	O
5.	De arts bepaalt aan de hand van de uitslag van het immunotherapie onderzoek of u behandeld kunt worden met immunotherapie.	O	O	O
6.	Door middel van immunotherapie kunnen klachten worden verminderd	O	O	O
7.	Immunotherapie kan de levensduur van een patiënt verlengen	O	O	O

21C. Kon u vraag 21B beantwoorden door middel van de informatie die u van uw behandelend arts heeft gekregen?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

Privacy

22. Biedt de polikliniek voldoende privacy?
(bijvoorbeeld aan de balie, bij het omkleden, bij gesprekken, vertrouwelijk omgaan met gegevens)?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

23. Wordt er zorgvuldig met uw gegevens omgegaan?

O Weet ik niet
O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

Contact met uw behandelend arts

24. Neemt uw behandelend arts u serieus?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

25. Heeft uw behandelend arts genoeg tijd voor u?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

Informatie en communicatie door uw behandelend arts

26. Legt uw behandelend arts u informatie op een begrijpelijke manier uit?
(Bijvoorbeeld omtrent bijwerkingen of gevolgen van onderzoeken of de behandeling)

O Nooit
O Soms
O Meestal
O Altijd

27. Uitleg over uw ziekte, behandeling of uitslag zijn het makkelijkst voor u om te begrijpen als het is uitgelegd in:
(Meerdere antwoorden mogelijk)

O Woorden
O Percentages
O Figuur/ afbeelding
O Tabel
O Anders, namelijk: _____

28. Welke communicatiemethode met uw behandelend arts heeft uw voorkeur?

O Telefonisch
O Consult (afspraak)
O Email
O Anders, namelijk: _____

29. Krijgt u de mogelijkheid om uw behandelend arts al uw vragen te stellen?

O Nee, helemaal niet
O Een beetje
O Grotendeels
O Ja, helemaal

30. Heeft u informatie gemist in de uitleg van uw arts?
(Meerdere antwoorden zijn mogelijk)

O Nee, ik heb geen informatie gemist in de uitleg
O Ja, over wat de ziekte precies inhoudt
O Ja, over waarom het onderzoek nodig is
O Ja, over wat het onderzoek inhoudt
O Ja, over waarom behandeling nodig is
O Ja, over wat de behandeling inhoudt
O Ja, informatie over de tijdsduur van het onderzoek
O Ja, informatie over de tijdsduur van de behandeling
O Ja, informatie over de wachttijd tot de uitslag van het onderzoek
O Ja, anders namelijk_____

Samenwerking tussen zorgverleners

31. Worden afspraken op verschillende afdelingen volgens u op elkaar afgestemd?

O Ja
O Nee

32. Zorgen de op elkaar afgestemde afspraken voor een langere wachttijd?
(Bekeken over het gehele behandeltraject)

O Ja
O Nee
O Weet ik niet

33. Heeft u het idee dat u tegenstrijdige informatie heeft gehad?

O Nooit
O Soms
O Meestal
O Altijd

Inspraak patiënt

34. Krijgt u informatie over uw rechten als patiënt?
(Bijvoorbeeld een second opinion of inzage van uw patiëntendossier)

O Ja
O Ja, maar ik heb naar deze informatie moeten vragen
O Nee

35. Heeft u inspraak over uw behandeling/behandelplan?

O Nooit
O Soms
O Meestal
O Altijd
O Weet ik niet

Nazorg

36. Zijn er onderwerpen waarover u naar uw idee onvoldoende informatie krijgt?
(Meerdere antwoorden mogelijk)

O Niet van toepassing
O Werking en bijwerkingen van medicatie
O Medicijngebruik in combinatie met andere medicijnen
O Gebeurtenissen na het onderzoek
O Gebeurtenissen na de behandeling
O Regels voor leefstijl
O Rust en werken
O Het gebruik van hulpmiddelen
O Omgaan met de ziekte of aandoening
O Waar ik aanvullende informatie kan vinden (patiëntenvereniging, website)
O Anders, namelijk: _____

37. Weet u met wie u contact kunt opnemen als zich na het bezoek aan de polikliniek problemen voordoen (aanspreekpunt) **?**

O Ja O Nee

Totaaloordeel

38. Zou u deze polikliniek bij uw vrienden en familie aanbevelen?

O Beslist niet
O Waarschijnlijk niet
O Waarschijnlijk wel
O Beslist wel

39. Wat zou u graag verbeterd zien?

_____

_____

_____

40. Met welk cijfer zou u uw gehele behandelingstraject in het NKI in zijn totaal beoordelen?

_____ (0 = heel erg slecht, 10 = uitstekend)

Wilt u controleren of u alle vragen heeft ingevuld?

Appendix 2 – Discrete Choice Experiment (block 1)

Patiënten voorkeuren

Naast onze interesse in uw ervaringen omtrent de behandeling die u in het Antoni van Leeuwenhoek ziekenhuis (AVL) ondergaat, zijn wij ook geïnteresseerd in uw voorkeuren voor de behandeling van longkanker. We willen u vragen om een aantal keuzes te maken tussen verschillende behandelingen.

Om u te helpen met het maken van een keuze en om u wat uitgebreidere informatie te geven, kunt u de extra informatie op **pagina 11** doorlezen. Nu volgt eerst een voorbeeld. De vragen starten op **pagina 3**.

Als u vragen heeft over dit onderdeel van de vragenlijst kunt u contact opnemen met C. Spoolder via het volgende nummer: 06-27425031

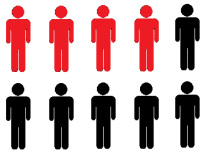
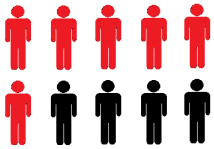
Voorbeeldscenario (Gelieve niet invullen)

Hieronder ziet u een voorbeeld. U wordt gevraagd om te kiezen tussen **behandeling A** waarbij

- De wachttijd tussen de verwijzing en het eerste consult in het AVL 1 week is,
- De wachttijd tussen het eerste consult in het AVL en de diagnose 1.5 weken is,
- De wachttijd tussen de diagnose en behandeling 1 week is,
- Na 2 weken na het starten met de behandeling vermindering van klachten optreedt,
- De kans op bijwerkingen 4/10 patiënten treft
- De gemiddelde overlevingsduur na het starten van de behandeling 3 maanden is

of behandeling B waarbij

- De wachttijd tussen de verwijzing en het eerste consult in het AVL 2 weken is,
- De wachttijd tussen het eerste consult in het AVL en de diagnose 3 weken is, de wachttijd tussen de diagnose en behandeling 2 weken is,
- Na 2 maanden na het starten met de behandeling vermindering van klachten optreedt,
- De kans op bijwerkingen 6/10 patiënten treft
- De gemiddelde overlevingsduur na het starten van behandeling 9 maanden is.

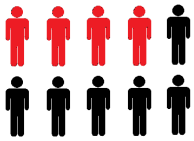
	Behandeling A	**Behandeling B**
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	1 week	2 weken
Wachttijd tussen eerste consult in het AVL en diagnose	1.5 weken	3 weken
Wachttijd tussen diagnose en behandeling	1 week	2 weken
Hoe spoedig uw klachten verbeteren	Na 2 weken	Na 2 maanden
Kans op bijwerkingen door behandeling	40% (4 op de 10 patiënten) 	60% (6 op de 10 patiënten) 
Gemiddelde overlevingsduur na het starten van de behandeling	3 maanden	9 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*	**X**	

U kunt een kruisje zetten in het lege blokje onder de behandeling van uw voorkeur. In het bovenstaande voorbeeld heeft de patiënt gekozen voor behandeling A.

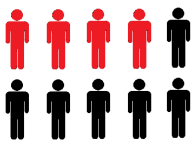
Vragen (Scenario's)

Stelt u zich voor dat dit uw eerste bezoek is aan het Antoni van Leeuwenhoek ziekenhuis. U bent in het Antoni van Leeuwenhoek ziekenhuis voor een passende behandeling. Bij elk van de volgende **12 scenario's**, willen wij u vragen om te kiezen tussen twee soorten behandelingen (A of B). U kiest voor de behandeling die uw voorkeur heeft.

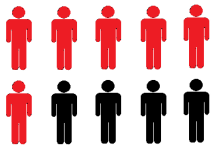
Scenario 1:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult in het AVL	1 week	2 weken
Wachttijd tussen eerste consult in het AVL en diagnose	2 weken	3 weken
Wachttijd tussen diagnose en behandeling	1 week	2 weken
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 weken	Na 2 maanden
Kans op bijwerkingen behandeling	≤ 20 % (bij 2 op de 10 patiënten of minder) 	40% (4 op de 10 patiënten) 
Gemiddelde overlevingsduur na het starten van de behandeling	3 maanden	9 maanden
Welke behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

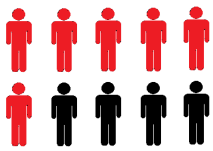
Scenario 2:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult in het AVL	1 week	2 weken
Wachttijd tussen eerste consult in het AVL en diagnose	2 weken	3 weken
Wachttijd tussen diagnose en behandeling	Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling	1 week
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 maanden	Geen verbetering. De klachten zullen niet verminderen of hetzelfde blijven als gevolg van de behandeling.
Kans op bijwerkingen behandeling	≤ 20 % (bij 2 op de 10 patiënten of minder) 	40% (4 op de 10 patiënten) 
Gemiddelde overlevingsduur na het starten van de behandeling	9 maanden	3 maanden
Welke behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

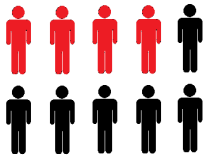
Scenario 3:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	1 week	2 weken
Wachttijd tussen eerste consult in het AVL en diagnose	1.5 weken	2 weken
Wachttijd tussen diagnose en behandeling	2 weken	Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 weken	Na 2 maanden
Kans op bijwerkingen door behandeling	60% (6 op de 10 patiënten) 	≤ 20 % (bij 2 op de 10 patiënten of minder) 
Gemiddelde overlevingsduur na het starten van de behandeling	9 maanden	3 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

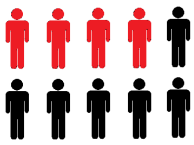
Scenario 4:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	2 weken	1 week
Wachttijd tussen eerste consult in het AVL en diagnose	1.5 weken	2 weken
Wachttijd tussen diagnose en behandeling	2 weken	Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 weken	Na 2 maanden
Kans op bijwerkingen door behandeling	60% (6 op de 10 patiënten) 	≤ 20 % (bij 2 op de 10 patiënten of minder) 
Gemiddelde overlevingsduur na het starten van de behandeling	9 maanden	3 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

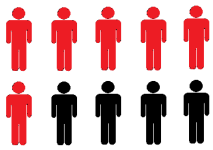
Scenario 5:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	1 week	2 weken
Wachttijd tussen eerste consult in het AVL en diagnose	1.5 weken	2 weken
Wachttijd tussen diagnose en behandeling	Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling	1 week
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 maanden	Geen verbetering. De klachten zullen niet verminderen of hetzelfde blijven als gevolg van de behandeling.
Kans op bijwerkingen door behandeling	40% (4 op de 10 patiënten) 	60% (6 op de 10 patiënten) 
Gemiddelde overlevingsduur na het starten van de behandeling	3 maanden	9 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

Scenario 6:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	2 weken	1 week
Wachttijd tussen eerste consult in het AVL en diagnose	2 weken	3 weken
Wachttijd tussen diagnose en behandeling	1 week	2 weken
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 weken	Na 2 maanden
Kans op bijwerkingen door behandeling	≤ 20 % (bij 2 op de 10 patiënten of minder) 	40% (4 op de 10 patiënten) 
Gemiddelde overlevingsduur na het starten van de behandeling	3 maanden	9 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

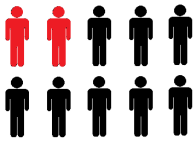
Scenario 7:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	2 weken	1 week
Wachttijd tussen eerste consult in het AVL en diagnose	3 weken	1.5 weken
Wachttijd tussen diagnose en behandeling	Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling	1 week
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 weken	Na 2 maanden
Kans op bijwerkingen door behandeling	60% (6 op de 10 patiënten) 	≤ 20 % (bij 2 op de 10 patiënten of minder) 
Gemiddelde overlevingsduur na het starten van de behandeling	3 maanden	9 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

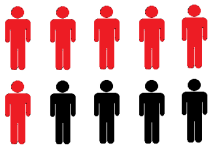
Scenario 8:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	1 week	2 weken
Wachttijd tussen eerste consult in het AVL en diagnose	3 weken	1.5 weken
Wachttijd tussen diagnose en behandeling	Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling.	1 week
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Geen verbetering. De klachten zullen niet verminderen of hetzelfde blijven als gevolg van de behandeling.	Na 2 weken
Kans op bijwerkingen door behandeling	≤ 20 % (bij 2 op de 10 patiënten of minder) 	40% (4 op de 10 patiënten) 
Gemiddelde overlevingsduur na het starten van de behandeling	9 maanden	3 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

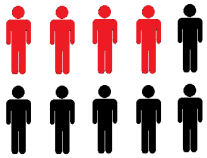
Scenario 9:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	2 weken	1 week
Wachttijd tussen eerste consult in het AVL en diagnose	1.5 weken	2 weken
Wachttijd tussen diagnose en behandeling	2 weken	Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Geen verbetering. De klachten zullen niet verminderen of hetzelfde blijven als gevolg van de behandeling.	Na 2 weken
Kans op bijwerkingen door behandeling	≤ 20 % (bij 2 op de 10 patiënten of minder) 	40% (4 op de 10 patiënten) 
Gemiddelde overlevingsduur na het starten van de behandeling	9 maanden	3 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

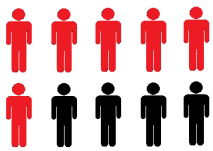
Scenario 10:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	2 weken	1 week
Wachttijd tussen eerste consult in het AVL en diagnose	3 weken	1.5 weken
Wachttijd tussen diagnose en behandeling	1 week	2 weken
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 maanden	Geen verbetering. De klachten zullen niet verminderen of hetzelfde blijven als gevolg van de behandeling.
Kans op bijwerkingen door behandeling	60% (6 op de 10 patiënten) 	≤ 20 % (bij 2 op de 10 patiënten of minder) 
Gemiddelde overlevingsduur na het starten van de behandeling	9 maanden	3 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

Scenario 11:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	1 week	2 weken
Wachttijd tussen eerste consult in het AVL en diagnose	1.5 weken	2 weken
Wachttijd tussen diagnose en behandeling	Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling	1 week
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Na 2 maanden	Geen verbetering. De klachten zullen niet verminderen of hetzelfde blijven als gevolg van de behandeling.
Kans op bijwerkingen door behandeling	40% (4 op de 10 patiënten) 	60% (6 op de 10 patiënten) 
Gemiddelde overlevingsduur na het starten van de behandeling	3 maanden	9 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

Scenario 12:

	Behandeling A	Behandeling B
Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL	1 week	2 weken
Wachttijd tussen eerste consult in het AVL en diagnose	2 weken	3 weken
Wachttijd tussen diagnose en behandeling	1 week	2 weken
Hoe spoedig uw klachten verbeteren na het starten van de behandeling	Geen verbetering. De klachten zullen niet verminderen of hetzelfde blijven als gevolg van de behandeling.	Na 2 weken
Kans op bijwerkingen door behandeling	60% (6 op de 10 patiënten) 	≤ 20 % (bij 2 op de 10 patiënten of minder) 
Gemiddelde overlevingsduur na het starten van de behandeling	3 maanden	9 maanden
Welk behandeling heeft uw voorkeur? *(Een antwoord aankruisen)*		

Toelichting- en contactformulier

Hieronder is er ruimte voor toelichting

_____

_____

_____

_____

_____

_____

_____

Hartelijk dank voor uw deelname.

Wilt u nogmaals controleren of u alle vragen heeft ingevuld.

Wilt u de vragenlijst na het invullen inleveren bij de balie op de polikliniek.

Door het invullen van deze vragenlijst geeft u aan dat u akkoord gaat met het gebruik van uw gegevens voor de doeleinden van dit onderzoek. Uw gegevens zullen niet verstrekt worden aan derden.

Voor verdere vragen kunt u contact opnemen met:

C. Spoolder	(Onderzoekster)	c.spoolder@nki.nl	06-27425031
P. Baas	(Longarts)	p.baas@nki.nl	
V. Retèl	(Postdoc)	v.retel@nki.nl	

Informatie scenario's

Stelt u zich voor dat dit uw eerste bezoek is aan het Antoni van Leeuwenhoek ziekenhuis. U bent in het Antoni van Leeuwenhoek ziekenhuis voor een passende behandeling van uw ziekte.

De behandeling zal verschillen op basis van 6 verschillende factoren:

1. Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL
2. Wachttijd tussen eerste consult in het AVL en diagnose
3. Wachttijd tussen diagnose en behandeling
4. Hoe spoedig uw klachten verbeteren na het starten van de behandeling
5. Kans op bijwerkingen door behandeling
6. Gemiddelde overlevingsduur na het starten van de behandeling

Onderstaand kunt u **extra informatie** vinden over de 6 verschillende factoren:

1. **Wachttijd tussen verwijzing en eerste consult (afspraak) in het AVL**

De tijdsperiode tussen het verwijzen van de patiënt door een zorgverlener buiten het AVL (bijv. de huisarts) tot het moment dat u uw eerste afspraak heeft in het ziekenhuis (AVL)

- *1 week*
- *2 weken*

2. **Wachttijd tussen eerste consult in het AVL en diagnose**

De tijdsperiode tussen het plaatsvinden van de eerste afspraak in het ziekenhuis (AVL) tot het moment dat u uw diagnose heeft ontvangen

- *1.5 weken (anderhalve week)*
- *2 weken*
- *3 weken*

3. **Wachttijd tussen diagnose en behandeling**

De tijdsperiode tussen het moment dat u uw diagnose heeft ontvangen tot het moment dat uw behandeling wordt gestart

- *Geen wachttijd. Op de dag van diagnose wordt gestart met de behandeling*
- *1 week*
- *2 weken*

4. **Hoe spoedig uw klachten verbeteren na het starten van de behandeling**

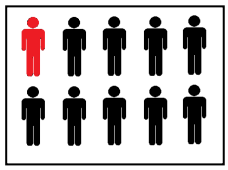
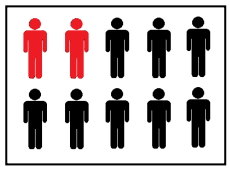
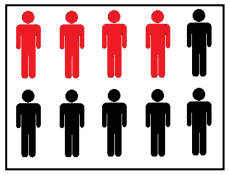
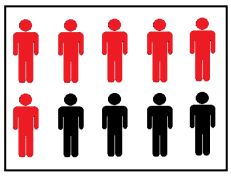
   De periode tussen het starten van de behandeling tot dat de klachten en symptomen van uw ziekte minder worden
   - *2 weken*
   - *2 maanden*
   - *Geen verbetering. De klachten zullen niet verminderen of hetzelfde blijven als gevolg van de behandeling.*

Wat betreft klachten/symptomen kunt u bijvoorbeeld denken aan: hoesten, benauwdheid, vermoeidheid, piepende ademhaling, heesheid en opgeven van bloed etc.

5. **Kans op bijwerkingen door behandeling**

   - *≤ 20 %*
     (bij 2/10 mensen of minder dan 2/10 mensen zorgt de behandeling voor bijwerkingen)
   - *40%*
     (bij 4/10 mensen zorgt de behandeling
     voor bijwerkingen)
   - *60%*
     (bij 6/10 mensen zorgt de behandeling voor bijwerkingen)

    = 1 patiënt met bijwerkingen


of




Wat betreft bijwerkingen kunt u bijvoorbeeld denken aan: koorts, diarree, misselijkheid, verminderde eetlust, braken, concentratieproblemen etc.

6. **Gemiddelde overlevingsduur na het starten van de behandeling**
   - *3 maanden*
     (de gemiddelde overlevingsduur van patiënten die starten met deze behandeling is 3 maanden)
   - *9 maanden*
     (de gemiddelde overlevingsduur van patiënten die starten met deze behandeling is 9 maanden)

Appendix 3 – Screening failures of immunotherapy trials

Figure 4A: Distribution of included patients per trial

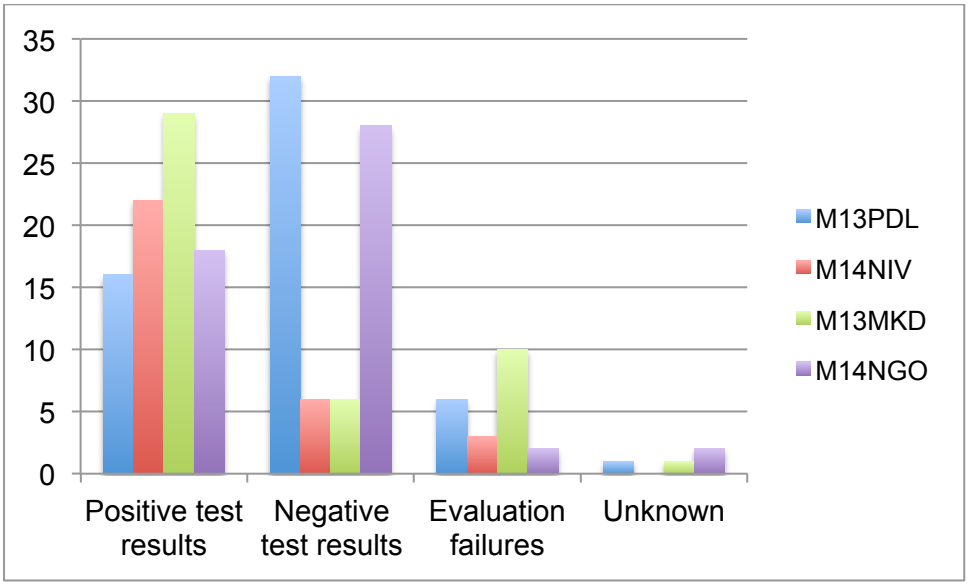


Figure 4B: Distribution of included patients per trial in percentages

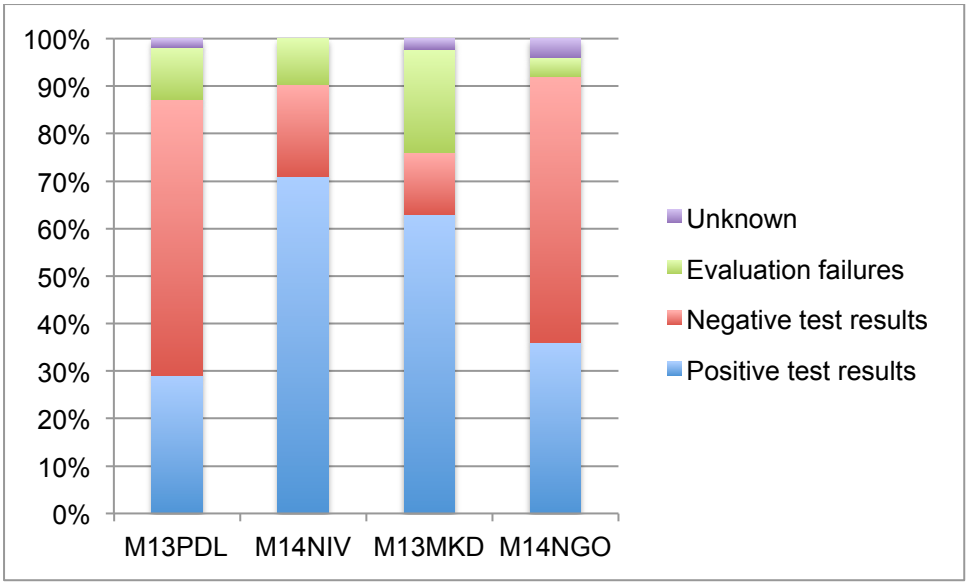


Figure 4C: Distribution of screening failures per trial

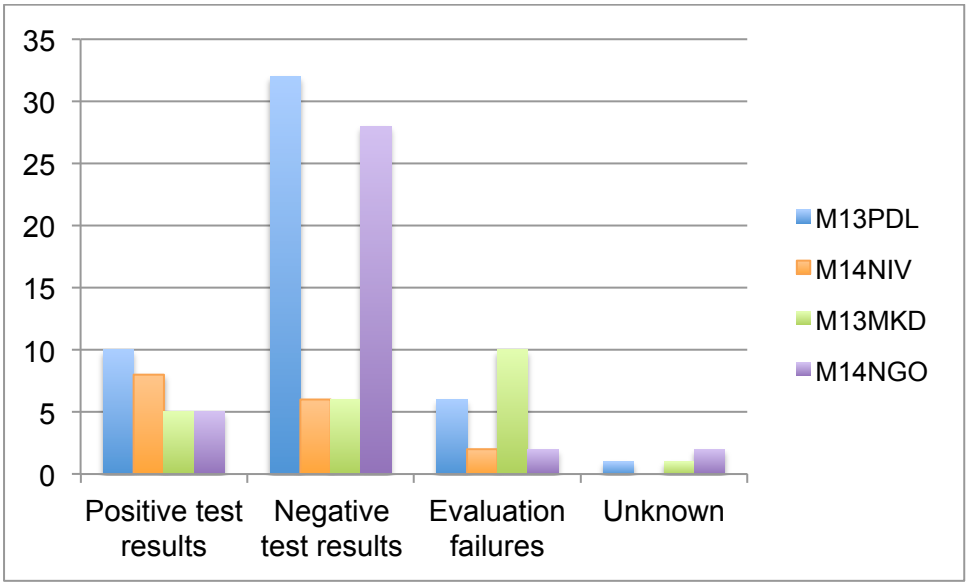
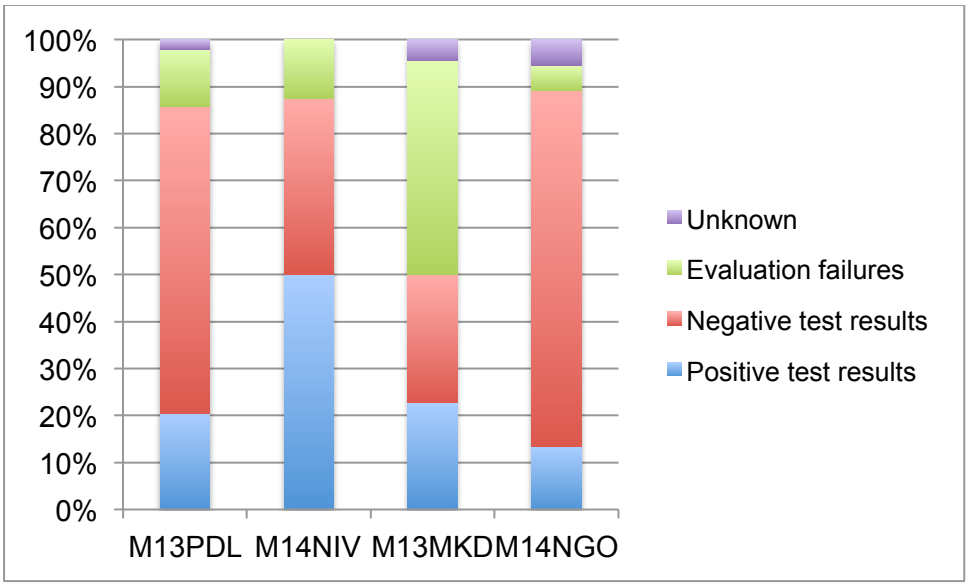


Figure 4D: Distribution of screening failures per trial in percentages



Appendix 4 – Overview of patients' answers (per subgroup)

Question	Answer	Immuno therapy trial (IMT) (n=12)	Chemo therapy Trial (CTT) (n=3)	Chemo therapy (CT) (n=16)	Targeted therapy trial (TTT) (n=1)	Targeted therapy (TT) (n=9)	Trials (n=16)	Non-trials (n=25)	Total (n=41)
Referral									
1. Who referred you to the AVL?	Own request	5 (41.7%)	1 (33.3%)	6 (37.5%)		3 (33.3%)	6 (37.5%)	9 (36%)	15 (36.6%)
	General practitioner			1 (6.3%)				1 (4%)	1 (2.4%)
	Physician	4 (33.3%)	1 (33.3%)	7 (43.8%)	1 (100%)	3 (33.3%)	6 (37.5%)	10 (40%)	16 (39.0%)
	Patient	1 (8.3%)					1 (6.3%)		1 (2.4%)
	Other: Partner			1 (6.3%)				3 (12%)	3 (7.3%)
	Other: Son					1 (11.1%)			
	Other: Health insurance company					1 (11.1%)			
	Combi: Own request + daughter	1 (8.3%)					2 (12.5%)		2 (4.9%)
	Combi: Own request + specialist		1 (33.3%)						
	Missing	1 (8.3%)		1 (6.3%)		1 (11.1%)	1 (6.3%)	2 (8%)	3 (7.3%)
Contactability									
*2. Is it a problem to get in touch with someone at the policlinic by phone?	No, completely not	6 (50%)	2 (66.6%)	11 (68.8%)	1 (100%)	5 (55.6%)	9 (56.3%)	16 (64%)	25 (61.0%)
	A little	5 (41.7%)		4 (25%)		4 (44.4%)	5 (31.3%)	8 (32%)	13 (31.7%)
	Mostly	1 (8.3%)	1 (33.3%)				2 (12.5%)		2(4.8%)
	Yes, totally								
	Not applicable			1 (6.3%)				1 (4%)	1 (2.4%)
First consultation									
3. Which person(s) assisted you during your first visit at the AVL?	Nobody		1 (33.3%)				1 (6.3%)		1 (2.4%)
	Partner	6 (50%)	1 (33.3%)	10 (62.5%)	1 (100%)	4 (44.4%)	8 (50%)	14 (56%)	22 (53.7%)
	One/more child(ren)	2 (16.7%)		1 (6.3%)		1 (11.1%)	2 (12.5%)	2 (8%)	4 (9.8%)
	Family/friends			1 (6.3%)		1 (11.1%)		2 (8%)	2 (4.9%)
	Combi: Partner + Family/friends	1 (8.3%)					5 (31.3%)	7 (28%)	12 (29.3%)
	Combi: Partner+ Child	3 (25%)	1 (33.3%)	4 (25%)		3 (33.3%)			

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
4.	Who preferably assisted you during your first visit at the AVL, in retrospect?	Nobody		1 (33.3%)	1 (6.3%)		2 (22.2%)	1 (6.3%)	3 (12%)	4 (9.8%)
		Same person	11 (91.7%)	2 (66.6%)	14 (87.5%)	1 (100%)	6 (66.7%)	14 (87.5%)	20 (80%)	34 (92.9%)
		Missing	1 (8.3%)		1 (6.3%)		1 (11.1%)	1 (6.3%)	2 (8%)	3 (7.3%)
5.	How long did you wait before you could visit the policlinic?	Less than 1 week	5 (41.7%)	1 (33.3%)	5 (31.3%)	1 (100%)	3 (33.3%)	7 (43.8%)	8 (32%)	15 (36.6%)
		1-2 weeks	4 (33.3%)	1 (33.3%)	8 (50%)		6 (66.7%)	5 (31.3%)	14 (56%)	19 (46.3%)
		2-3 weeks	3 (25%)	1 (33.3%)	2 (12.5%)			4 (25%)	2 (8%)	6 (14.6%)
		More than 3 weeks			1 (6.3%)				1 (4%)	1 (2.4%)
6.	To what extent you have experienced waiting time until your first consultation (appointment) as a problem?	No problem	9 (75%)	2 (66.6%)	10 (62.5%)	1 (100%)	8 (88.9%)	12 (75%)	18 (72%)	30 (73.2%)
		Small problem	2 (16.7%)	1 (33.3%)	2 (12.5%)		1 (11.1%)	3 (18.8%)	3 (12%)	6 (14.6%)
		Big problem			4 (25%)				4 (16%)	4 (9.8%)
		Missing	1 (8.3%)					1 (6.3%)		1 (2.4%)
Waiting time at the outpatient clinic										
*7.	How long do you have to wait before you are seen by your physician (most of the time)?	Arranged time/earlier	3 (25%)	1 (33.3%)	2 (12.5%)		3 (33.3%)	4 (25%)	5 (20%)	9 (22.0%)
		Less than 15 min	3 (25%)		8 (50%)	1 (100%)	4 (44.4%)	4 (25%)	12 (48%)	16 (39.0%)
		15-30 min	4 (33.3%)	2 (66.6%)	4 (25%)		2 (22.2%)	6 (37.5%)	6 (24%)	12 (29.3%)
		30-60 min	1 (8.3%)		2 (12.5%)			1 (6.3%)	2 (8%)	3 (7.3%)
		More than 60 min								
		Missing	1 (8.3%)					1 (6.3%)		1 (2.4%)

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
Desired duration at the policlinic										
8 A	First consultation	Less than 15 min	2 (16.7%)	1 (33.3%)	2 (12.5%)		1 (11.1%)	3 (18.8%)	3 (12%)	6 (14.6%)
		15-30 min	4 (33.3%)		7 (43.8%)	1 (100%)	2 (22.2%)	5 (31.3%)	9 (36%)	14 (34.1%)
		30-60 min			1 (6.3%)		2 (22.2%)		3 (12%)	3 (7.3%)
		As long as it takes	5 (41.7%)	2 (66.6%)	6 (37.5%)		4 (44.4%)	7 (43.8%)	10 (40%)	17 (41.5%)
		Missing	1 (8.3%)					1 (6.3%)		1 (2.4%)
8 B	Diagnostic results	Less than 15 min	1 (8.3%)		2 (12.5%)	1 (100%)	3 (33.3%)	2 (12.5%)	5 (20%)	7 (17.1%)
		15-30min	5 (41.7%)		6 (37.5%)		2 (22.2%)	5 (31.3%)	8 (32%)	13 (31.7%)
		30-60min	1 (8.3%)	1 (33.3%)	1 (6.3%)		1 (11.1%)	2 (12.5%)	2 (8%)	4 (9.8%)
		As long as it takes	4 (33.3%)	2 (66.6%)	7 (43.8%)		3 (33.3%)	6 (37.5%)	10 (40%)	16 (39.0%)
		No opinion								
		Missing	1 (8.3%)					1 (6.3%)		1 (2.4%)
8 C	Diagnosis	Less than 15 min		1 (33.3%)	1 (6.3%)	1 (100%)	2 (22.2%)	2 (12.5%)	3 (12%)	5 (12.2%)
		15-30 min	4 (33.3%)		5 (31.3%)		2 (22.2%)	4 (25%)	7 (28%)	11 (26.8%)
		30-60 min	1 (8.3%)		1 (6.3%)		1 (11.1%)	1 (6.3%)	2 (8%)	3 (7.3%)
		As long as it takes	5 (41.7%)	2 (66.6%)	9 (56.3%)		4 (44.4%)	7 (43.8%)	13 (52%)	20 (48.8%)
		No opinion	1 (8.3%)					1 (6.3%)		1 (2.4%)
		Missing	1 (8.3%)					1 (6.3%)		1 (2.4%)
8 D	(Follow-up) treatment	Less than 15 min			3 (18.8%)		1 (11.1%)		4 (16%)	4 (9.8%)
		15-30min	7 (58.3%)	1 (33.3%)	7 (43.8%)		5 (55.6%)	8 (50%)	12 (48%)	20 (48.8%)
		30-60min								
		As long as it takes	4 (33.3%)	2 (66.6%)	6 (37.5%)		3 (33.3%)	6 (37.5%)	9 (36%)	15 (36.6%)
		No opinion				1 (100%)		1 (6.3%)		1 (2.4%)
		Missing	1 (8.3%)					1 (6.3%)		1 (2.4%)
9	How long do you have to wait for a follow-up appointment with your treating physician?	Less than 1 week	5 (41.7%)	1 (33.3%)	6 (37.5%)		2 (22.2%)	6 (37.5%)	8 (32%)	14 (34.1%)
		1-2 weeks	1 (8.3%)		3 (18.8%)		3 (33.3%)	1 (6.3%)	6 (24%)	7 (17.1%)
		2-3 weeks	3 (25%)	2 (66.6%)	3 (18.8%)			5 (31.3%)	3 (12%)	8 (19.5%)
		More than 3 weeks	3 (25%)		2 (12.5%)	1 (100%)	4 (44.4%)	4 (25%)	6 (24%)	10 (24.4%)
		Missing			2 (12.5%)				2 (8%)	2 (4.9%)

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
10	To what way you have experienced waiting time between follow-up appointments after you first appointment as a problem?	No problem	10 (83.3%)	3 (100%)	13 (81.3%)		7 (77.8%)	13 (81.3%)	20 (80%)	33 (80.5%)
		Small problem	2 (16.7%)			1 (100%)	2 (22.2%)	3 (18.8%)	2 (8%)	5 (12.2%)
		Big problem			3 (18.8%)				3 (12%)	3 (7.3%)
Waiting time research										
11	How many days were between the study research/last research and the test results?	Less than 1 week	2 (16.7%)	1 (33.3%)	3 (18.8%)		2 (22.2%)	3 (18.8%)	12 (48%)	15 (36.6%)
		1-2 weeks	3 (25%)	1 (33.3%)	3 (18.8%)		5 (55.6%)	4 (25%)	8 (32%)	12 (29.3%)
		2-3 weeks	2 (16.7%)					2 (12.5%)		2 (4.9%)
		More than 3 weeks	4 (33.3%)			1 (100%)		5 (31.3%)		5 (12.2%)
		Not applicable		1 (33.3%)				1 (6.3%)		1 (2.4%)
		No result			1 (6.3%)		2 (22.2%)		3 (12%)	3 (7.3%)
		Research is ongoing			2 (12.5%)				2 (8%)	2 (4.9%)
		Missing	1 (8.3%)					1 (6.3%)		1 (2.4%)
12	To what extent did you experience waiting time between the study research/last research and the test results of the research as a problem?	No problem	9 (75%)	2 (66.6%)	11 (68.8%)		6 (66.7%)	11 (68.8%)	17 (68%)	28 (68.3%)
		Small problem	2 (16.7%)					2 (12.5%)		2 (4.9%)
		Big problem			3 (18.8%)	1 (100%)		1 (6.3%)	3 (12%)	4 (9.8%)
		Not applicable			2 (12.5%)		3 (33.3%)		5 (20%)	5 (12.2%)
		Missing	1 (8.3%)	1 (33.3%)				2 (12.5%)		2 (4.9%)

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
13	To what extent did you experience the time between the research period and the diagnosis as a problem?	No problem	2 (16.7%)		3 (18.8%)		1 (11.1%)	2 (12.5%)	4 (16%)	6 (14.6%)
		Small problem			1 (6.3%)		2 (22.2%)		3 (12%)	3 (7.3%)
		Big problem	1 (8.3%)		1 (6.3%)			1 (6.3%)	1 (4%)	2 (4.9%)
		Not applicable	9 (75%)	3 (100%)	11 (68.8%)	1 (100%)	6 (66.7%)	13 (81.3%)	17 (68%)	30 (73.2%)
		Missing								
14	Do you think a shorter waiting time between the tests results and the diagnosis/research would have a positive impact on the course of your disease?	No, completely not	1 (8.3%)		2 (12.5%)		2 (22.2%)	1 (6.3%)	4 (16%)	5 (12.2%)
		A little	1 (8.3%)					1 (6.3%)		1 (2.4%)
		Mostly			1 (6.3%)				1 (4%)	1 (2.4%)
		Yes, totally	1 (8.3%)		2 (12.5%)		1 (11.1%)	1 (6.3%)	3 (12%)	4 (9.8%)
		Not applicable	9 (75%)	3 (100%)	11 (68.8%)	1 (100%)	6 (66.7%)	13 (81.3%)	17 (68%)	30 (73.2%)
		Missing								
Knowledge Statements PDL-1 staining test										
15 B	Could you answer question 15A (statements) by means of the information you physician gave to you?	No, completely not								
		A little	2 (16.7%)							
		Mostly	6 (50%)							
		Yes, totally	3 (25%)							
		Missing	1 (8.3%)							

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
Waiting time before treatment										
16	How long did you have to wait before you could start your treatment?	Less than 1 week			4 (25%)				4 (16%)	
		1-2 weeks			2 (12.5%)		3 (33.3%)		5 (20%)	
		2-3 weeks					1 (11.1%)		1 (4%)	
		More than 3 weeks			10 (62.5%)		4 (44.4%)		14 (56%)	
		Missing					1 (11.1%)		1 (4%)	
17	To what extent did you experience time between research and treatment as a problem?	No problem	9 (75%)	2 (66.6%)	10 (62.5%)		4 (44.4%)	11 (68.8%)	14 (56%)	25 (61.0%)
		Small problem	2 (16.7%)		3 (18.8%)		3 (33.3%)	2 (12.5%)	6 (24%)	8 (19.5%)
		Big problem			3 (18.8%)	1 (100%)	1 (11.1%)	1 (6.3%)	4 (16%)	5 (12.2%)
		Missing	1 (8.3%)	1 (33.3%)			1 (11.1%)	2 (12.5%)	1 (4%)	3 (7.3%)
18	Do you think a shorter waiting time between test results and treatment has a positive effect on the course of your disease?	No, completely not	9 (75%)	1 (33.3%)	6 (37.5%)		4 (44.4%)	10 (62.5%)	10 (40%)	20 (48.8%)
		A little	1 (8.3%)	1 (33.3%)	5 (31.3%)	1 (100%)	2 (22.2%)	3 (18.8%)	7 (28%)	10 (24.4%)
		Mostly			1 (6.3%)		1 (11.1%)		2 (8%)	2 (4.9%)
		Yes, totally	2 (16.7%)		4 (25%)		1 (11.1%)	2 (12.5%)	5 (20%)	7 (17.1%)
		Missing		1 (33.3%)			1 (11.1%)	1 (6.3%)	1 (4%)	2 (4.9%)
19	Did your treating physician explain you why you had to wait before you could start with your treatment?	No	2 (16.7%)					2 (12.5%)		
		Yes	8 (66.6%)	2 (66.6%)		1 (100%)		11 (68.8%)		
		Yes, but I had to ask for this information								
		Missing	2 (16.7%)	1 (33.3%)				3 (18.8%)		

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
20	Did your treating physician keep in touch with you about your current waiting time?	No	4 (33.3%)					4 (25%)		
		Yes	6 (50%)	2 (66.6%)		1 (100%)		9 (56.3%)		
		Missing	2 (16.7%)	1 (33.3%)				3 (18.8%)		
Knowlegde statements immunotherapy										
21 A	Did you know about immunotherapy before your diagnosis?	No	11 (91.7%)							
		Yes								
		Missing	1 (8.3%)							
21 C	Could you answer question 21B (statements) by means of the information you physician gave to you?	No, completely not								
		A little	2 (16.7%)							
		Mostly	5 (41.7%)							
		Yes, totally	3 (25%)							
		Missing	2 (16.7%)							
Privacy										
*22	Does the outpatient clinic provide for enough privacy?	No, completely not		1 (33.3%)	1 (6.3%)			1 (6.3%)	1 (4%)	2 (4.9%)
		A little								
		Mostly	1 (8.3%)		3 (18.8%)		3 (33.3%)	1 (6.3%)	6 (24%)	7 (17.1%)
		Yes, totally	11 (91.7%)	2 (66.6%)	12 (75%)	1 (100%)	6 (66.7%)	14 (87.5%)	18 (72%)	32 (78.0%)
		Missing								
23	Does the AVL handle your data carefully?	No, completely not								
		A little								
		Mostly	1 (8.3%)		3 (18.8%)	1 (100%)	1 (11.1%)	2 (12.5%)	4 (16%)	6 (14.6%)
		Yes, totally	5 (41.7%)	2 (66.6%)	8 (50%)		5 (55.6%)	7 (43.8%)	13 (52%)	20 (48.8%)
		No opinion	6 (50%)	1 (33.3%)	4 (25%)		3 (33.3%)	7 (43.8%)	7 (28%)	14 (34.1%)
		Missing			1 (6.3%)				1 (6.3%)	1 (2.4%)

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
Contact with your treating physician										
*24	Does your treating physician take your seriously?	No, completely not								
		A little	1 (8.3%)					1 (6.3%)		1 (2.4%)
		Mostly				1 (100%)		1 (6.3%)		1 (2.4%)
		Yes, totally	11 (91.7%)	3 (100%)	16 (100%)		9 (100%)	14 (87.5%)	25 (100%)	39 (95.1%)
*25	Has your treating physician enough time for you?	No, completely not								
		A little	1 (8.3%)					1 (6.3%)		1 (2.4%)
		Mostly	2 (16.7%)	2 (66.6%)	4 (25%)	1 (100%)	2 (22.2%)	4 (25%)	6 (24%)	10 (24.4%)
		Yes, totally	9 (75%)	2 (66.6%)	12 (75%)		7 (77.8%)	11 (68.8%)	19 (76%)	30 (73.2%)
Information and communication by your treating physician										
*26	Does your physician explain things clear?	Never								
		Sometimes	2 (16.7%)					2 (12.5%)		2 (4.9%)
		Mostly	3 (25%)	1 (33.3%)	5 (31.3%)	1 (100%)	1 (11.1%)	5 (31.3%)	6 (24%)	11 (26.8%)
		Always	7 (58.3%)	2 (66.6%)	10 (62.5%)		8 (88.9%)	9 (56.3%)	18 (72%)	27 (65.9%)
		Missing			1 (6.3%)				1 (6.3%)	1 (2.4%)
*27	Explanation about your disease, treatment, and/or test results is easier for you to understand when it is explained in	Words	3 (25%)	1 (33.3%)	8 (50%)		5 (55.6%)	4 (25%)	13 (52%)	17 (41.5%)
		Percentages					1 (11.1%)		1 (4%)	1 (2.4%)
		Figure/image			2 (12.5%)				2 (8%)	2 (4.9%)
		Table								
		Other: words + lecture					1 (11.1%)		1 (4%)	1 (2.4%)
		Combi: words + percentages	1 (8.3%)			1 (100%)		12 (75%)	8 (32%)	20 (48.8%)
		Combi: percentages + figure/image		1 (33.3%)						
		Combi: words + percentages + figure/image		1 (33.3%)						
		Combi: words + table + percentages + figure/image			2 (12.5%)					
		Combi: words + figure/image	6 (50%)		4 (25%)		2 (22.2%)			
		Combi: words + percentages + table	1 (8.3%)							
		Combi: words + table	1 (8.3%)							

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
28	Which communication method with your treating physician do you prefer?	Telephone					1 (11.1%)		1 (4%)	1 (2.4%)
		Consultation	11 (91.7%)	3 (100%)	12 (75%)	1 (100%)	8 (88.9%)	15 (93.8%)	20 (80%)	35 (85.4%)
		Email								
		Combi: consult + Email			1 (6.3%)			1 (6.3%)	4 (16%)	5 (12.2%)
		Combi: telephone + consult + Email			1 (6.3%)					
		Combi: telephone + consult	1 (8.3%)		2 (12.5%)					
*29	Are you in the position to ask your treating physician all of your questions?	No, completely not								
		A little	1 (8.3%)					1 (6.3%)		1 (2.4%)
		Mostly		1 (33.3%)	3 (18.8%)	1 (100%)	1 (11.1%)	2 (12.5%)	4 (16%)	6 (14.6%)
		Yes, totally	11 (91.7%)	2 (66.6%)	13 (81.3%)		7 (77.8%)	13 (81.3%)	20 (80%)	33 (80.5%)
		Missing					1 (11.1%)		1 (4%)	1 (2.4%)
30	Did you miss any information during explaination by you threating physician?	No, anwered by 35/41 (85,4%) patients				Yes, answered by 6/41 (14.6%) patients about: • Why research is necessary • Contents of research • Duration of research • Duration of treatment • Information about metastasis				
Cooperation between health care professionals										
*31	Are consultations at different apartments coordinated?	No	1 (8.3%)		2 (12.5%)		1 (11.1%)	1 (6.3%)	3 (12%)	4 (9.8%)
		Yes	11 (91.7%)	3 (100%)	14 (87.5%)	1 (100%)	8 (88.9%)	15 (93.8%)	22 (88%)	37 (90.2%)
		Missing								
32	Does the current way of coordination consultations/appointments result in longer waiting times?	No	4 (33.3%)	2 (66.6%)	7 (43.8%)	1 (100%)	6 (66.7%)	7 (43.8%)	13 (52%)	20 (48.8%)
		Yes	5 (41.7%)		4 (25%)		1 (11.1%)	5 (31.3%)	5 (20%)	10 (24.4%)
		No opinon	3 (25%)	1 (33.3%)	5 (31.3%)		2 (22.2%)	4 (25%)	7 (28%)	11 (26.8%)

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
Patient participation										
*33	Do or did you ever have or had the idea you get or got contradictive info?	Never	8 (66.6%)	3 (100%)	12 (75%)		8 (88.9%)	11 (68.8%)	20 (80%)	31 (75.6%)
		Sometimes	4 (33.3%)		4 (25%)	1 (100%)	1 (11.1%)	5 (31.3%)	5 (20%)	10 (24.4%)
		Mostly								
		Always								
*34	Did you get information about patient rights?	No	3 (25%)		7 (43.8%)	1 (100%)	3 (33.3%)	4 (25%)	10 (40%)	14 (34.1%)
		Yes, but I had to ask for it	2 (16.7%)		2 (12.5%)		1 (11.1%)	2 (12.5%)	3 (12%)	5 (12.2%)
		Yes	7 (58.3%)	3 (100%)	7 (43.8%)		5 (55.6%)	10 (62.5%)	12 (48%)	22 (53.7%)
*35	Do you have an effect on your own treatment (plan)?	Never	2 (16.7%)		1 (6.3%)			2 (12.5%)	1 (4%)	3 (7.3%)
		Sometimes	3 (25%)			1 (100%)		4 (25%)		4 (9.8%)
		Mostly		1 (33.3%)	2 (12.5%)		2 (22.2%)	1 (6.3%)	4 (16%)	5 (12.2%)
		Always	4 (33.3%)	1 (33.3%)	7 (43.8%)		5 (55.6%)	5 (31.3%)	12 (48%)	17 (41.5%)
		No opinon	3 (25%)	1 (33.3%)	5 (31.3%)		2 (22.2%)	4 (25%)	7 (28%)	11 (26.8%)
		Missing			1 (6.3%)				1 (4%)	1 (2.4%)
Aftercare										
*36	Are there subjects you do not get sufficient information about?	Yes, answered by 30/41 (73.2%) patients					No, answered by 11/41 (26.8%) patients about: • Rules and lifestyle (n=5) • Medication in combination with other medication (n=3) • Coping styles (n=3) • Where to get additional information (n=2) • Effects and side effects of medication • Events after treatment • Rest and work • Use of tools • Events after research • Medication in combination with food		

			IMT	CTT	CT	TTT	TT	Trials	Non-trials	Total
*37	Do you know whom to contact if there are any problems after consultation?	No	1 (8.3%)	1 (33.3%)	4 (25%)		4 (44.4%)	2 (12.5%)	8 (32%)	10 (24.4%)
		Yes	11 (91.7%)	2 (66.6%)	12 (75%)	1 (100%)	5 (55.6%)	14 (87.5%)	17 (68%)	31 (75.6%)
Overall judgement										
*38	Would you recommend this policlinic to family and friends?	Absolutely not								
		Probably not								
		Probably yes								
		Absolutely yes	12 (100%)	3 (100%)	16 (100%)	1 (100%)	9 (100%)	16 (100%)	25 (100%)	41 (100%)
40	Which grade would you give your complete treatment trajectory in the AVL until now?	5			1 (6.3%)				1 (4%)	1 (2.4%)
		6								
		7								
		8	5 (41.7%)	1 (33.3%)	5 (31.3%)	1 (100%)	3 (33.3%)	7 (43.8%)	8 (32%)	15 (36.6%)
		9	4 (33.3%)	1 (33.3%)	8 (50%)		4 (44.4%)	5 (31.3%)	12 (48%)	17 (41.5%)
		10	3 (25%)	1 (33.3%)	1 (6.3%)		2 (22.2%)	4 (25%)	3 (12%)	7 (17.1%)
		Missing			1 (6.3%)				1 (4%)	1 (2.4%)