Drug related problems in patients treated with oral oncolytic drugs and their association with medication adherence and drug spillage.

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Abstract

Introduction. With three cancer types in the top ten causes of death in the Netherlands, cancer is a major problem in society (Centraal Bureau voor de Statistiek, 2021). Therapy is shifting from surgical procedures, chemotherapy and/or radiation toward targeted oral therapy at home (Schott et al., 2011). This study aims primarily to identify drug related problems (DRPs) and adherence of patients treated with oral oncolytic drugs and secondarily to find out how often these drugs are wasted and what the main causes therefore are. *Method.* Thirty patients were questioned about their DRPs, adherence and medication waste during up to four interview sessions in three months. The outcomes of the interviews are analysed via an CRF. The results are analysed using descriptive statistics in IBM Statistics SPSS 23.0 and simple calculation in Excel 365 version 2205. *Results.* Patients reported mainly problems with toxicity, unconscious non-adherence, and practical subjects. The overall adherence of the patients was high. The most often mentioned lack in adherence is the intake on a different time than prescribed. The waste of medication during the research is estimated on €11,935.37, which is €2,935.76 per patient per year. The major reason for medication waste is change of medication. *Discussion.* Adherence in patients is high and can be given a boost with extra help from HCWs. Patients mainly suffer from adverse effects, which can be supported by HCWs. The wasted medication is still a problem, but there is no solution leading from this research.

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1. Introduction

The top ten causes of death in the Netherlands contains three types of cancer, which gives us a lead to the scope of the problem of cancer in society (Centraal Bureau voor de Statistiek, 2021). Historically, the conventional treatment for cancer consisted of surgical procedures, chemotherapy and/or radiation. This often included a high intensity treatment with chemotherapy via intravenous administration. In recent years, cancer therapy has been shifting towards less intravenous (IV) treatment in the hospital and more targeted oral therapy at home (Schott et al., 2011). This results in a decreased intensity of the treatment for the patient because the hospital visits decrease and the disappearance of the worries about IV lines (Liu et al., 1997).

This shift in administration of the medication also leads to a shift in responsibility for the treatment, which could affect the adherence of the patient to the treatment (Davis et al., 2021; Hullmann et al., 2015; Yeoh et al., 2015). Adherence is the extent to which the patient's behaviour matches agreed recommendations from the prescriber (Nunes, et al., 2009). Given the situation at home with patients being fully responsible for taking their medication every day, a decrease in medication adherence is lurking (Misdrahi et al., 2013). Multiple factors contribute to the risk of non-adherence, such as intake difficulties, an intake schedule that does not fit the patient's personal schedule, impaired believe in the treatment and the occurrence of adverse events (Davis et al., 2021; Hullmann et al., 2015; Mancini et al., 2013; Notenboom et al., 2014; Sawesi et al., 2014). One solution shown in literature to increase medication adherence, is shared decision making between the oncologist and the patient (National Collaborating Centre for Primary Care (UK), 2009). An honest communication between the patient and the oncologist and oncologic nurse could minimize drug-related problems and therefore improve medication adherence. As medicines do not work when they are not taken, good adherence is essential. In addition, higher medication adherence leads to higher efficacy during the therapy and better quality of life of the patient, as well as reduced drug waste (Darkow et al., 2007).

The problem of drug waste is important in general but even more so for oral oncolytic drugs, because of the soaring prices and the negative effects on the environment (Matti et al., 2020). Earlier research does not give a clear picture on the most important reasons for drug waste. Ekedahl, 2006 gives four reasons that represent over 75% of the reasons for drug waste being: (1) medicines were too old/had expired; (2) the patient had died; (3) the condition had improved; (4) there was no need to take the drug anymore (Ekedahl, 2006), while in Bekker 2018 adverse events and no/insufficient effect also play a significant role in drug waste (Bekker et al., 2018). Improvement measures could be focused on these risk factors in order to decrease drug waste and associated health care costs and environmental burden. A study on drug waste in Spain showed that in 2003 at least 129.8 million Euro was wasted on left over drugs (Coma et al., 2008). This amount only includes the drugs that the patients returned to the pharmacy. The estimation is that approximately a third of all unused drugs are returned to the pharmacy, so with that in mind the waste is

substantially higher than 130 million Euro, representing 1% of the total health care costs in Spain (Coma et al., 2008).
Speaking of the costs of wasted drugs. A patient with breast cancer costs between $18,431 and $49,827 extra than a healthy person (Allaire et al., 2016). In comparison with the 130 million Euro wasted on left-over drugs, at least 2,600 cancer patients can be treated with this money.

This study aims to identify the drug related problems (DRPs) reported by patients during their treatment with oral oncolytic drugs and the adherence of these patients during the same treatment. Secondary aims are to find out how often waste of oral oncolytic drugs occurs and which factors are associated with drug waste.

2. Method

2.1 Study design

The research started with literature research to explore the DRPs and risk factors for drug waste often mentioned. With the literature research a first list of DRPs and risk factors is set up. This list is assessed on patients and health care workers (HCWs) to see how the experiences are in practice. These results are used to refine the list based on literature, which led to a new list of DRPs and risk factors that could be used in the population study later on. This population study includes thirty patients that are interviewed one to four times.

2.2 Data source and search strategy

First, potential DRPs and factors affecting medication adherence were retrieved from literature by a search in PubMed. This search was performed between the 1st and the 19th of November 2021.

Figure 1 shows the search strategy on DRPs and factors affecting adherence in patients using oral oncolytic drugs. The search terms used were (drug related problems[Title]) AND (oncology[Title]), (drug related problems[Title]) AND (cancer[Title]) and (nonadherence[Title]) AND (cancer[Title]) AND (reasons). Inclusion criteria were presence of full text, language of the article being Dutch and/or English and the study involving humans. Exclusion criteria were: DRPs being classified, the goal of the research not being relevant and duplicates. With classified DRPs is meant that the DRPs in the outcome of the articles were not the original DRPs, but those were classified in a pre-structured manner.

Figure 2 shows the search strategy on risk factors for waste of oral oncolytic drugs. The used search terms were (medication[Title]) AND (waste[Title]), (medication[Title]) AND (wastage[Title]) and (medicines[Title]) AND (returned[Title]). The results were filtered on presence of full text, language of the article being Dutch and/or English and the study involved humans. The articles were excluded when the goal of the articles was not relevant according to the research. That is, the results of the article did not include risk factors for drug waste.

2.3 Data collection

Based on the literature research described above, a list of DRPs and risk factors of waste was composed. Both the DRPs and risk factors for drug waste mentioned in these articles were summed up, whereupon only the DRPs and risk factors that occur when the patient uses the drug were included, leading to the exclusion of factors such as prescription errors. In addition, similar DRPs and risk factors were grouped to one DRP or risk factor. The original DRPs and risk factors of all articles and their final name used in the interview list preliminary research are in appendix I.

The draft interview list was subsequently evaluated in a convenience sample of six patients and twenty-three HCWs, in order to compose the final interview list to be used in the main study.

2.4 Interviews aimed at evaluating the draft interview list

The next step is to verify the found DRPs, influences on adherence and risk factors for drug waste with oncologists, pharmacists, and patients. Therefore, twenty-three HCWs and six patients were interviewed. The group of HCWs included eight pharmacists (five outpatient and three hospital), eight oncologists (two lung, two hematologic and four medical), four oncology nurses, two general practitioners, and a pulmonologist.

These interviews were performed using the guidelines in Appendix II. These guidelines consist of some broad questions supporting the list of DRPs and risk factors composed based on the literature research. DRPs and risk factors that no one mentioned in the interviews could result in exclusion from the list and additive mentioned DRPs and risk factors could be added to the list for the interviews in the next stage of this research.

The convenience sample of patients was based on the following inclusion and exclusion criteria.

- Inclusion criteria:
  - Patient uses an oral oncolytic*
  - 2 patients > 69, min 1 man and 1 woman
  - 2 patients < 70, min 1 man and 1 woman
  - Max. 1 patient per drug
  - Min. 1 patient with variable dosing scheme
- Exclusion criteria:
  - Not treated in UMCG
  - Never treated with oral oncolytic
  - Study drugs not yet on the market

* Appendix III shows the drugs included for this research.

2.5 Preliminary interview analysis

All interviews were analysed on the DRPs, and risk factors mentioned by the participants. First the interviews were checked on DRPs, and risk factors retrieved from literature, second the additional DRPs and risk factors were added to the list for further analysis. The number of times the DRPs and risk factors were mentioned was counted. These results are shown table 2, 3 and 4. All additional DRPs and risk factors were assessed in the same way as the DRPs and risk factors from literature: if they occur when the patient uses the drug, they were included. Also, the additional DRPs and risk factors were assessed regarding overlap between them and already included DRPs and risk factors. If there was overlap the additional DRPs and risk factors could be left aside, if not, a novel item was added to the list.

As a last step of the preliminary research, based on the information from the interviews, all DRPs and risk factors were grouped and/or renamed in order to compose a list of unique and clearly defined DRPs and risk factors.

2.6 Patient study

Study design

This qualitative study was performed from March 8 until June 9 2022. For the study, a semi structured interview strategy was used. Patients were recruited from the whole population of oral oncolytic drug user of the UMCG. The goal of the study was to include at least thirty patients.

Setting

The patients were included via their oncologist and the outpatient pharmacy. The HCWs gave the first information about the study and gave the patients an information letter and informed consent form to fill in and send back to the UMCG when agreed to the terms. As soon as the letter came back to the UMCG, the patients were called by the researcher for the first interview. The interviews were performed following the instruction in appendix IV and with the help of the DRPs and risk factors in question form in appendix V. At the end of the interview, the patient and interviewer made a new appointment for the second interview. A total of up to four interviews was performed per patient.

Study population

For the main interviews, the following inclusion criteria were used to include patients.

- Use of one or more oral oncolytic drugs*
- Age 18 years and older
- Life expectancy of at least six months
- Speaking Dutch
- Independent able to give informed consent

* Appendix III shows the drugs included for this research.

Besides the inclusion criteria, all patients are treated in the UMCG for the diagnosis cancer.

Primary and secondary outcome measures

The primary outcome measures were the DRPs patients mentioned during the interviews and adherence of the patients to the prescribed treatment. This focused on four aspects: (1) intake on different time; (2) intake of different dose; (3) forgot an intake and (4) consciously skipping an intake. The secondary outcome measures are to find out what the major causes of drug waste of oral oncolytic drugs are.

Data collection

The data was collected via telephone interviews. All interviews were recorded and after the interview, the researcher listened to the recording to verify the results. The researcher filled in the case report form shown in Appendix IV. The information on the form was thereafter digitalized using REDCap 10.0.23.

Data analysis

IBM SPSS Statistics 23.0 was used to analyse the data. The data was analysed using descriptive statistics. On top of that, simple calculations were made about absolute and relative counts of the results regarding DRPs, adherence and risk factors for waste using Excel 365 version 2205. The goal of these tests was to calculate the mean number of DRPs there were in the study population. To show what types of DRPs were most important in the population, the various categories of DRPs are used instead of all specific defined DRPs. This gives a better view on the most common problems.

3. Results

3.1 Literature research

The search terms searching for DRPs and adherence problems resulted in thirty-three articles (figure 1). After all articles were evaluated on the criteria shown in figure 1, seventeen articles were left over to use to abstract DRPs from. The second part of the literature research was focused on the risk factors for drug waste. The search terms searching for risk factors for drug waste led to forty-eight results (figure 2). After all, forty-eight articles were evaluated on the criteria shown in figure 2, 10 articles were left to abstract risk factors for drug waste from.

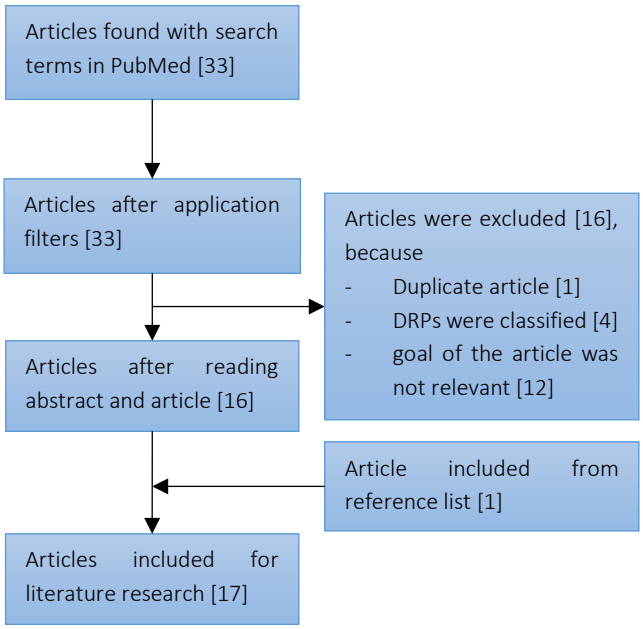

Figure 1. Search strategy on DRPs and influence on adherence in patients using oral oncolytic drugs

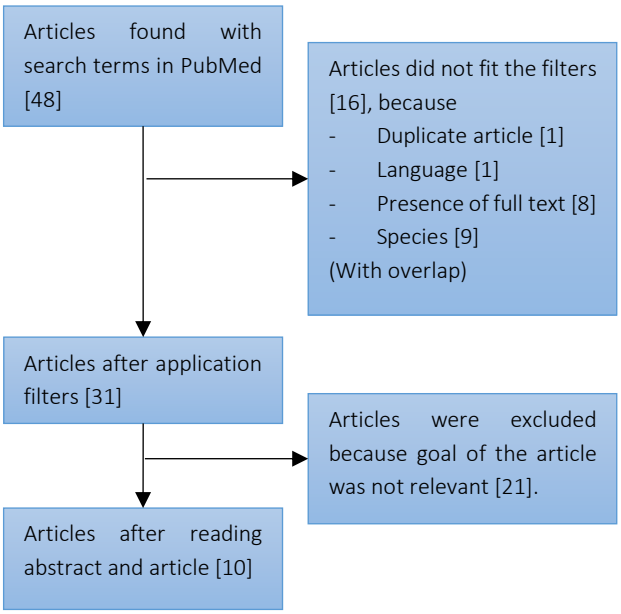

Figure 2. Search strategy on risk factors for drug waste in patients using oral oncolytic drugs

3.2 DRPs and risk factors extracted from literature

The analysis of the articles on DRPs, adherence problems and risk factors resulted in table 1 and 2.

Table 1. DRPs extracted from literature with its references.

TOXICITY	
Adverse effects	(Adisa et al., 2008; Davis et al., 2021; Degu & Kebede, 2021; Hullmann et al., 2015; Iskandarsyah et al., 2014; Kucuk et al., 2020; Notenboom et al., 2014; Sawesi et al., 2014; Shinn et al., 2019; Spencer et al., 2020; Vucur et al., 2021; Yap et al., 2014; Yeoh et al., 2015; Yismaw et al., 2020; Zhang et al., 2021; Zhao et al., 2021)
INFORMATION PROVISION	
Information too complex	(Iskandarsyah et al., 2014; Notenboom et al., 2014; Yap et al., 2014; Yismaw et al., 2020)
Information too extensive	(Notenboom et al., 2014; Shinn et al., 2019)
Information about adverse effects disturbing	(Notenboom et al., 2014; Yap et al., 2014)
Information incomplete	(Zhang et al., 2021)

KNOWLEDGE	
Complex intake schedule	(Sawesi et al., 2014; Spencer et al., 2020)
Misunderstanding about change in therapy	(Yeoh et al., 2015)
MEDICATION ADHERENCE	
Unconscious adherence problems	
Moment of intake complicated	(Hullmann et al., 2015; Zhang et al., 2021)
Ran out of medicine	(Yismaw et al., 2020)
Forgot an intake	(Davis et al., 2021; Hullmann et al., 2015; Shinn et al., 2019; Spencer et al., 2020; Yismaw et al., 2020; Zhang et al., 2021)
Lifestyle interference	(Davis et al., 2021; Hullmann et al., 2015; Sawesi et al., 2014; Spencer et al., 2020)
Exhausted of intake	(Iskandarsyah et al., 2014)
Conscious adherence problems	
No trust in effectiveness	(Davis et al., 2021; Hullmann et al., 2015; Iskandarsyah et al., 2014)
Insecure about indication	(Yeoh et al., 2015)
Does not think intake is necessary	(Hullmann et al., 2015)
No believe in treatment	(Iskandarsyah et al., 2014)
Refuses intake	(Hullmann et al., 2015; Vucur et al., 2021)
Stops intake when symptoms are gone	(Adisa et al., 2008; Davis et al., 2021; Sawesi et al., 2014)
Afraind of adverse effects	(Davis et al., 2021; Notenboom et al., 2014; Shinn et al., 2019)
PRACTICAL PROBLEMS	
Text too small	(Notenboom et al., 2014)
Opening package too difficult	(Notenboom et al., 2014)
Intake too difficult	(Hullmann et al., 2015)
Unpleasant taste	(Hullmann et al., 2015)
Dose change too difficult	(Yismaw et al., 2020)
Swallow problems	(Hullmann et al., 2015; Yismaw et al., 2020)
Pills too large	(Hullmann et al., 2015)

Table 2. Risk factors for drug waste extracted from literature with its references.

Costs	(Bekker et al., 2018)
Treatment was stopped	(Bekker et al., 2018; Coma et al., 2008; Ekedahl, 2006; Khandelwal et al., 2012; Langley et al., 2005; Law et al., 2015; Mackridge & Marriott, 2007; Ueki et al., 2022; West et al., 2014, 2016)
Healing/clinical picture improved	(West et al., 2014, 2016)
Change of medication	(Bekker et al., 2018; Coma et al., 2008; Ekedahl, 2006; Khandelwal et al., 2012; Langley et al., 2005; Mackridge & Marriott, 2007; Ueki et al., 2022; West et al., 2014, 2016)
Adverse effects	(Bekker et al., 2018; Coma et al., 2008; Ekedahl, 2006; Khandelwal et al., 2012; Langley et al., 2005; Law et al., 2015; Mackridge & Marriott, 2007; Ueki et al., 2022)
No/less effectiveness	(Bekker et al., 2018; Coma et al., 2008; Ekedahl, 2006; Khandelwal et al., 2012; Law et al., 2015)
Received too much	(West et al., 2014, 2016)
Medication non-adherence	(Ekedahl, 2006)
Patient was deceased	(Bekker et al., 2018; Coma et al., 2008; Ekedahl, 2006; Khandelwal et al., 2012; Langley et al., 2005; Mackridge & Marriott, 2007; West et al., 2014, 2016)
Medication expired	(Bekker et al., 2018; Coma et al., 2008; Ekedahl, 2006; Langley et al., 2005; Law et al., 2015; Mackridge & Marriott, 2007; West et al., 2014, 2016)
Delivered wrong medication	(Langley et al., 2005; Mackridge & Marriott, 2007)

3.3 Overview DRPs and risk factors identified from interviews

The number of HCWs and patients who mentioned the DRPs is shown in the table 3. The most frequently mentioned DRP by both HCWs and patients was adverse effects. Besides adverse effects, information being too extensive, information about adverse effects being disturbing and information being contradictory were mentioned by the patients, as well as nonadherence and lifestyle interference. HCWs mentioned most DRPs identified in literature. The DRPs that none of the HCWs mentioned were being insecure about the indication and misunderstanding about the use during absence of symptoms. Those two were also not mentioned by the patients. Overall, the most frequently mentioned DRPs are adverse effects [27], forget an intake [17], complex intake schedule [13] and pills being too big [11].

Table 3. Count of DRPs during first interview sessions by both HCWs and patients.

DRPs	Mentioned by number of HCWs*	Mentioned by number of patients	Total times mentioned
Adverse effects	22	5	27
Information too complex	8	0	8
Information too extensive	6	1	7
Information about adverse effects disturbing	2	1	3
Information contradictory	4	1	5
Complex intake schedule	13	0	13
Misunderstanding about therapy change	3	0	3
Difficult administration time	9	0	9
Ran out of medicine	3	0	3
Forgot to take	13	4	17
Lifestyle interference	6	3	9
Tired of intake	2	0	2
Insecure about indication	0	0	0
Does not think it's necessary	3	0	3
No believe in the treatment	3	0	3
Refuses	4	0	4
Misunderstanding use during absence symptoms	0	0	0
Fear of adverse effects	4	0	4
Text too small	4	0	4
Opening package difficult	7	0	7
Intake too difficult	4	0	4
Unpleasant taste	6	0	6
Dose adjustment too complicated	2	0	2
Swallowing problems	8	0	8
Too big pills	11	0	11

*HCWs = health care workers

The HCWs and patients were also asked if there were other DRPs that were not mentioned during the interview. In table 4, the additional DRPs are summed up. There were no patients that added extra DRPs, but the HCWs did mention extra DRPs. Most frequently the necessity of taking too many tablets at one moment was mentioned. Besides that, the influence on a person's lifestyle and the availability only via the outpatient pharmacy were mentioned.

Table 4. Additional mentioned DRPs by both HCWs and patients that were not extracted from literature.

DRPs	Mentioned by number of HCWs*	Mentioned by number of patients	Total times mentioned
Unpleasant smell	1	0	1
Do not touch drugs	1	0	1
Do not touch other people	1	0	1
Clean toilet after use	1	0	1
Drugs cannot be in touch with other drugs	1	0	1
Too many tablets	8	0	8
Too small tablets	1	0	1
Influences lifestyle	2	0	2
Only available via outpatient pharmacy	3	0	3
Difficult communication with pharmacy	1	0	1

*HCWs = health care workers

All risk factors of drug waste found in literature were mentioned in one or more interviews. The most frequently mentioned risk factor of drug waste by both HCWs and patients was change of medication [24].

Table 5. Count of risk factors for drug waste during first interview sessions by both HCWs and patients

Risk factors for waste	Mentioned by number of HCWs*	Mentioned by number of patients	Total times mentioned
Costs	2	0	2
Discontinue treatment	16	0	16
Improvement illness/cure	1	0	1
Change of medication	21	3	24
Adverse effects	17	0	17
No/unwanted effects	12	0	12
Too much delivered	9	0	9
Medication non-adherence	11	2	13
(acute) passing away	18	1	19
Short shelf life	1	0	1
Received the wrong medicine	3	0	3

*HCWs = health care workers

3.4 Finalisation of list of DRPs and risk factors for waste for further interviews

The information provided during the interviews and literature research led to the final list of DRPs and risk factors for drug waste, in respectively table 6 and 7.

Table 6. Adjusted list of DRPs based on the list extracted from literature and the first session of interviews.

TOXICITY
Adverse effects
INFORMATION PROVISION
Information too complex
Information too extensive
Information about adverse effects disturbing
Information incomplete
Information contradictory
KNOWLEDGE
Complex intake schedule

PRACTICAL PROBLEMS
Text too small
Opening package too difficult
Intake too difficult
Pills too large
Pills too small
Problems with number of pills
Unpleasant taste
Unpleasant smell
Swallow problems

MEDICATION ADHERENCE	Dose change too difficult
Unconscious adherence problems	Hindered by cleaning the toilet after use
Moment of intake complicated	
Ran out of medicine	
Forgot an intake	
Lifestyle interference	
Exhausted of intake	
Conscious adherence problems	
No trust in effectiveness	
Stops intake when symptoms are gone	
Afraid of adverse effects	

Table 7. Adjusted list of risk factors for drug waste based on the list extracted from literature and the first session of interviews.

Treatment was stopped
Adverse effects
End of treatment
Change of medication
Received too much
Medication expired
Delivered wrong medication
Dose changes

3.5 Results patient study

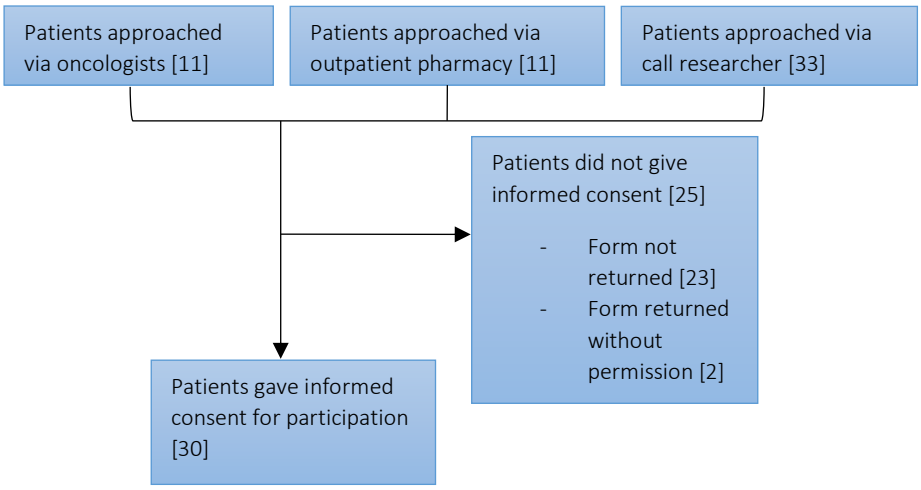

Figure 3. Flowchart of the inclusion of the patients via the different routes used to approach patients.

Figure 3 shows the inclusion pathway of the patients approached for this research. Of all thirty patients included in the study, the characteristics are shown in table 8.

Table 8. Baseline characteristics included data

Patient characteristics	Group size (%)
Total participants	30
Total interviews	53
Sex	
Male	16 (53.3)
Female	14 (46.7)
Age (years)	44 - 82
18-65	14 (46.7)
65>	16 (53.3)
Subdepartment	
Lung oncology	2 (6.7)
Medical oncology	17 (56.7)
Haematology	11 (36.7)
Oral oncolytic drug used	
Tyrosine kinase inhibitors (TKI)*	20 (66.7)
Adjuvant endocrine therapy (AET)*	2 (6.7)
Pyrimidine antagonist (PA)*	4 (13.3)
Others*	4 (13.3)

*TKI's used by participants: axitinib, cabozantinib, crizotinib, dabrafenib+trametinib, ibrutinib, imatinib, osimertinib, palbociclib, pazopanib and ruxolitinib. AET's used by participants: enzalutamide. PAs used by participants: capecitabine. Other medicine used by participants: anagrelide, hydroxycarbamide and venetoclax.

Figure 4 shows the categories of DRPs and how often they are mentioned during the four interviews as a percentage of the patients completed the interview. Interview 1 was completed by thirty participants, interview 2 by eleven participants, interview 3 by nine participants and interview 4 by three participants. The specific DRPs that belong to the groups are shown in table 6.

The most often mentioned DRP category is toxicity, which contains all types of adverse effects. Information provision is often mentioned in the first interview, and practical problems are respectively most often mentioned during the fourth interview. DRPs belonging to conscious non-adherence are not mentioned during one of the sessions. Beside these predefined problems, some patients mentioned other problems that were not questioned being: confrontation difficulties by taking the medication [2], finding it hard to have no physical contact [1] and finding it hard to differentiate between the pills [1].

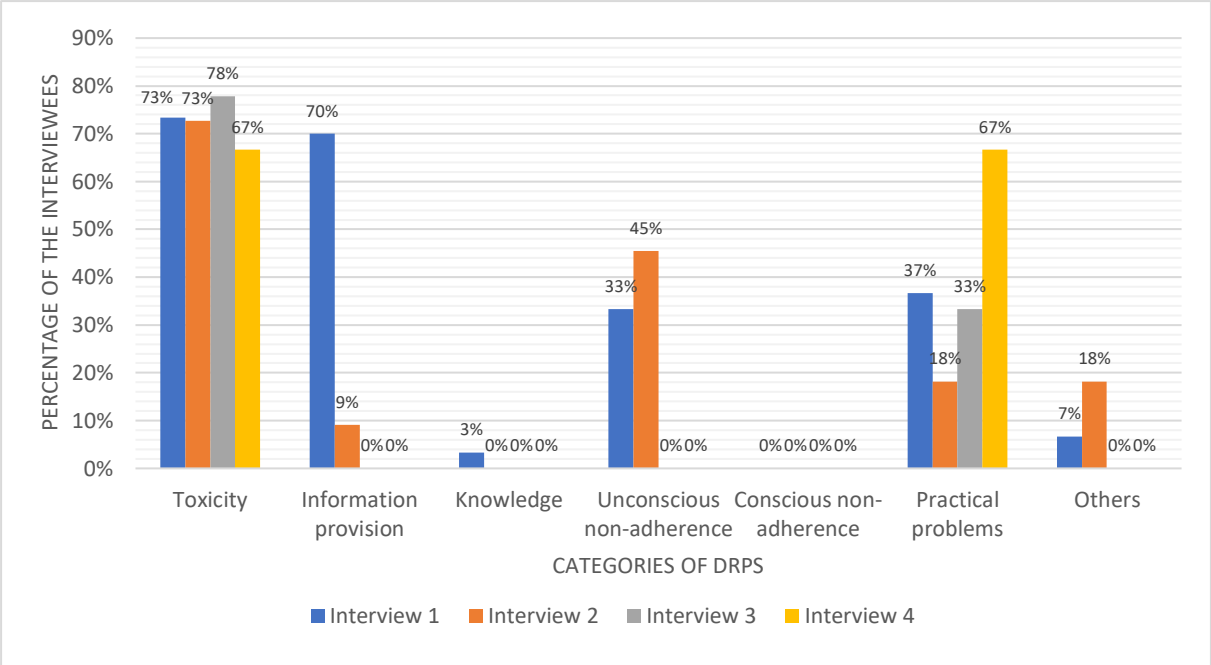

Figure 4. Percentage of patients that mentioned one or more types of the DRP types during the first, second, third and fourth interview.

Figure 5 shows the overall adherence of all patients reported during all interviews. Overall, most patients strictly follow the prescribed therapy. The most exceptions were made in the timing of the medication. Little to no exceptions were made by the patients on dosing and skipping/forgetting a dose as a whole.

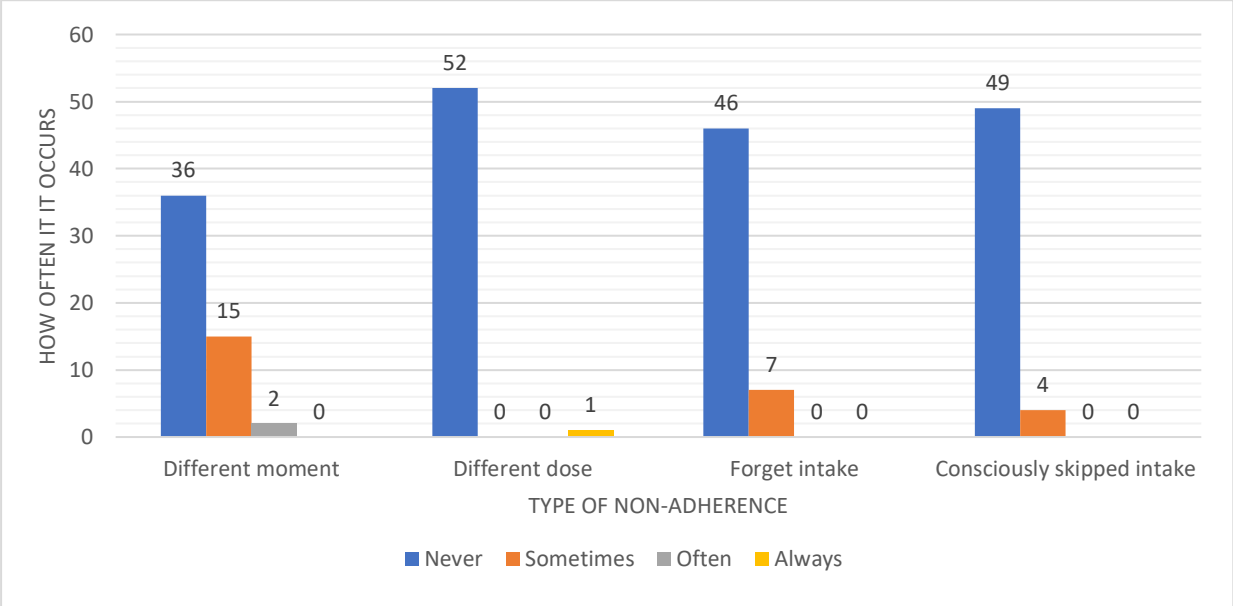

Figure 5. Adherence of patients reported during all the different interviews.

Table 9. Overview of the number of left-over drugs and the reasons they were wasted of both oral oncolytic drugs and others.

	Total pills left over (oral oncolytic drug)	Unopened boxes left over (oral oncolytic drug)	Times mentioned as reason
Treatment was stopped	98 (70)	4 (4)	2
because of adverse effects	40 (40)	1 (1)	1
because treatment ended	58 (30)	3 (3)	2
Change of medication	266 (66)	4 (2)	4
Received too much	40 (12)	0 (0)	2
Medication expired	15 (15)	0 (0)	1
Delivered wrong medication	0 (0)	0 (0)	0
Dose changes	4 (4)	0 (1)	1
Other: wrong storage	3 (3)	0 (0)	1
Other: treatment not necessary anymore	28 (0)	1 (1)	1
TOTAL	**374 (118)**	**8 (5)**	**13**

A total of 118 pills of oral oncolytic drugs were wasted in between the first month before the interview and the day of the last interview. The ratio of oral oncolytic drugs left over versus the other medication left over is 1:2.2. An average of 7.63 pills of all types of medication per month and 3.93 oral oncolytic pills per participant were wasted in the duration of the research. The total costs for the wasted oral oncolytic drugs during the time of the interviews is estimated on €11,935.73. A total of five unopened boxes with oral oncolytic drugs were wasted during the research in thirty participants.

The research was about the 53 interviews considering each four weeks of medication waste, so a total of 53*4*7 = 1484 days is monitored.

$$\frac{11{,}935.73}{1484} * 365 = 2935.67\ euro\ per\ patient\ per\ year$$

Table 10. Calculation on the estimated amount of money wasted on oral oncolytic drugs during the interviews (Ministerie van Volksgezondheid, 2022)

Wasted drug	Dosage (mg)	Number of pills wasted	Price per pill	Total price
Osimertinib	80	30	€ 205.01	€ 6,150.30
Imatinib	400	52	€ 38.21	€ 1,986.92
	100	15	€ 9.80	€ 147.00
Capecitabine	900	4	€ 3.04	€ 12.16
Cabozantinib	40	14	€ 212.35	€ 2,972.90
Trametinib	2	3	€ 222.15	€ 666.45
TOTAL				**€ 11,935.73**

4. Discussion

The main DRPs for patients using oral oncolytic drugs are toxicity, followed by unconscious non-adherence and practical problems with drug intake. The most often mentioned DRP, adverse effects, is a topic that already has the attention of doctors (Odijk et al., 2018). Even though it still is the most often mentioned DRP. The second DRP involved unconscious adherence problems. The major problem in this aspect is to implement the drug intake into the daily life of the patient. The final issue is practical problems. The most important practical problem is the difficult intake (Hullmann et al., 2015; Yismaw et al., 2020).

Given the fact that a total of 53 interviews were taken for this research and each interview the participants were asked about the drugs they had left over and could not use again, the total amount of drugs wasted in the period of the research does not seem much. But with the high prevalence of the disease, the total costs for wasted medication are rising. The most important reason for drug waste is the change of medication.

Most often mentioned DRPs in the articles selected during the literature research were toxicity, problems with information provision, unconscious non-adherence, and conscious non-adherence. Toxicity and unconscious adherence problems are also highly represented in the interview results, but problems with information provision and conscious adherence problems are not. The absence of conscious adherence problems could be because patients with a cancer diagnosis are more likely to believe their diagnosis and trust the treatment the doctor offers them then in the general population of patients. Information provision was primarily mentioned in the first interview session, possibly because the patient took problems of a longer period of time to tell during the first interview, while during the second, third and fourth interview they only look back on the previous four weeks. Not all patients had contact with HCWs in the previous four weeks and in this brief period of time the chance of problems with information provision are lower than in the whole period before the research started.

Risk factors for drug waste that were highly represented in the literature research were adverse effects, treatment ended, medication changed, and medication expired. The major represented reasons for drug waste in the research were that the treatment was stopped because it ended, the patient received too much medication and that the patient had to change medication. Two of the three reasons also came forward in the literature research, while receiving too much was not that much represented in the literature research. The other way around adverse effects and expired medication were topics in the literature research, which didn't come forward in the patient study. Because patients only get their oral oncolytic drugs for a brief period of up to three months, the chances of getting expired are therefore limited to the minimum. Adverse effects did actually often occur in the patients, but it was only once the reason to have medication left over, because the adverse effects led to a change in medication in this specific participant.

The strength of the research lies mainly in its design. Performing the interviews via telephone makes it easily accessible for most patients, which leads to the possibility to include a wide variety of patients based on age, diagnosis, and severity of the disease. Another positive effect of the telephone consultation is that the patient is in its own safe environment and can take the time they need to answer the questions. The patient has everything at hand to answer questions about the medication they use, so they can look it up if they don't know it for sure.

This research was limited by the number of patients that completed all four interview sessions, being only three participants. The longer the follow-up, the more changes patients could possibly experience, which can have influence on the DRPs and waste of medication. The goal was to complete 120 interviews with 30 patients, but this research included 30 patients finishing only 53 interviews.

Another limitation was that the distribution of patients over the diverse types of cancer was not equal, where most of the patients were treated in the medical oncology or haematology department and only 2 patients suffer from lung cancer. The severity of the several types of cancer can differ much, so therefore this could have influence on the type and amount of DRPs mentioned by the participants.

A major part of the participants was treated with a TKI at the time of the interviews, so therefore little information was obtained on DRPs during use of PAs and AETs.

The key difference between the total of problems during the first session and the other three is potentially caused by the fact that all thirty participants had their first interview, while only 11 participants also had a second, 9 a third and 3 a fourth. This could not only have an influence on the amount of DRPs mentioned in total, but also the type of DRPs mentioned by these participants. The influence on the DRPs could be both ways, depending on the participants included in the follow up sessions.

A limitation related to the amount of left-over medication is that earlier research showed that patients passing away also play an important part in the amount of left-over medication (Bekker et al., 2018; Coma et al., 2008; Ekedahl, 2006; Khandelwal et al., 2012; Langley et al., 2005; Mackridge & Marriott, 2007; West et al., 2014, 2016). This aspect is not included in this research, so this could have a decreasing effect on the amount of wasted medication.

For further research it would be interesting to expand the number of included patients to see what happens with the DRPs these patients experience. With expanding the patient group, the distribution of cancer types and drugs used could be distributed more equal. It would be interesting to do subgroup-analysis with these larger groups to find out what type of patients suffer from what type of DRPs, to give the oncologists the possibility to tackle these problems more structurally.

At this moment, an important aspect on drug waste is giving the patients a limited amount of drug. Sometimes this results in the delivery of extra pills to the patient before they come to the UMCG again. For further research it is interesting to research what the costs are for delivering the medication to the patients

instead of giving them enough drugs until the next appointment. It would be interesting to find out where the break-even point of this system lies. A cost-benefit analysis could be made for further research.
Also, more structured research could be done to the waste of meds by tracking the medication dispensing and placing that next to the patient's usage.

Doctors and oncologic nurses could conclude from this research that they can possibly have more attention for adverse effects of the oncologic drug and give more information about how the patients can tackle the problems, with or without medication. Instead of giving comedication to help against adverse effects, the doctor can also give a prescription, so the patient has the lead over the treatment, and he/she has something up their sleeve in case they need it. Also, collaboration with dieticians to treat adverse effects on the gastro-intestinal tract could be helpful for these patients.
The doctor or nurse could also partly prevent adverse effects to tell the patients what they can do when specific adverse effects occur, which therefore could also decrease the complaints about the adverse effects. It would be helpful if the doctor, oncologic nurse, pharmacist and/or home care would help with the planning of these medicines, to make an intake schedule as accessible as possible for the patient, to increase the chances for the patient to succeed in the daily intake. Also, reminders as an alarm of application that reminds the patient and the intakes coupled to daily habits such as brushing teeth and meals is proven to help patients with reminding to the intake (Kini & Ho, 2018).
If the drugs allow it, practical problems with the intake could be resolved by taking the medication with yogurt or custard. Not only can it make the intake easier, but it can also reduce the troubles with smell and taste of the pills.
With the results about the medication waste and the implications for further research, there is no need to change the protocol on medication dispensing at this moment. It is important to know what the cost-benefit calculations of different dispensing scenario's (including at-home delivery) are, before taking any action. The load for the patient during its period of disease does not need to increase before having any further information about different scenario's.

To conclude, the adherence of patients using oral oncolytic drugs is high and with some extra help, this could even be optimised. Looking at the DRPs, there is also a role for HCWs, because patients mainly suffer from adverse effects. A secondary conclusion is that drug waste still is a slight problem, but that this research doesn't produce a solution for that.

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6. Appendix

6.1 DRPs and risk factors for drug waste extracted from literature

Article included	DRP in article	Category in interview
Adisa et al 2008	Feels well	Stop when symptoms are gone
	Drug side effects	Adverse effects
	Others	Others
Davis et al 2021	Side effects	Adverse effects
	Do not think I need this medication anymore	Stop when symptoms are gone; does not think it's necessary
	Do not think this medication is working for me	No trust in effectiveness
	Have concerns about possible side effects	Afraid of adverse effects
	Have concerns about long term effects from this medicine	Afraid of adverse effects
	Did not have the medicine because the pharmacy was out	Ran out of medication
	Have trouble managing all the medicines I take	Intake schedule complex
	Would have taken the medicine but simply missed it	Forgot an intake
	Missed it because of a busy schedule	Lifestyle interference and forgot an intake
	Problems forgetting things in my daily life	Lifestyle interference and forgot an intake
Degu et al 2021	Adverse drug reaction	Adverse effects
Hullmann et al 2015	Just forget	Forgot an intake
	Am not home	Moment of intake complicated
	Hard to swallow pills	Swallow problems and pills too large
	Hate the taste	Unpleasant taste
	Do not like side effects	Adverse effects
	Interferes with activity	Lifestyle interference
	Do not think it necessary	No trust in effectiveness;
	Ran out/did not fill	Ran out of medication
	Others	Others
Iskandarsyah et al 2013	Lack of awareness and knowledge	Information too extensive
	Treatment beliefs	No trust in effectiveness
	Emotional burden	Exhausted of intake; refuses
	Severe side effects	Adverse effects
	Unmet information needs	Information incomplete
Kucuk et al 2020	Adverse drug event occurring	Adverse effects
	Unclear problem/complaint	Others
Sawesi et al 2014	Side effects	Adverse effects
	Lifestyle interference	Lifestyle interference
	Number of prescriptions	Complex intake schedule
	Disease stage	Stop when symptoms are gone
Shinn et al 2018	Adverse effects	Adverse effects
	Worries about adverse effects	Afraid of adverse effects
	Cognitive dysfunction	Information too complex
	Forget intake	Forgot an intake
Spencer et al 2019	Forget intake	Forgot an intake
	Do not refill prescription	Ran out of medication
	Adverse effects	Adverse effects
	Trouble remembering	Forgot an intake

	Hard to follow prescription Lifestyle interference	Complex intake schedule; intake too complex Lifestyle interference
Ting et al 2015	Adverse drug events	Adverse effects
Vucur et al 2021	Adverse drug reaction Contraindication due to comorbidity	Adverse effects Information contradictory
Wuensch et al 2015	Adverse drug reaction	Adverse effects
Yap et al 2014	Lack of knowledge in medication management Lack of knowledge in side effects management	Information too complex Information about side effects disturbing
Yismaw et al 2020	Adverse effects Does not understand instructions Patient forgets to take Drug product not available Cannot swallow/administer drug	Adverse effects Information too complex; misunderstanding about change in therapy; dose adjustment difficult Forgot an intake Ran out of medicine Swallow problems; intake too difficult; pills too large
Zhang et al 2021	Necessary information not provided Patient uses/takes less drug than prescribed or does not take the drug at all Patient takes food that interacts Inappropriate timing or dosing intervals	Information incomplete; text too small Forgot an intake Intake schedule complex Moment of intake complicated
Zhao et al 2021	Adverse reactions	Adverse effects

Article included	**Risk factor in article**	**Category in interview**
Bekker et al 2018	Condition had resolved	Treatment was stopped
	Passed expiry date	Medication expired
	Treatment changed	Change of medication
	Adverse events	Had to stop the treatment, because of adverse effects
	No/insufficient effect	No/less effectiveness
	Patient was deceased	Patient was deceased
	Lower costs for larger package	Costs
Coma et al 2008	Out of date	Medication expired
	Change treatment	Change of medication
	Adverse drug reaction	Had to stop the treatment, because of adverse effects
	Do not need anymore/cured	Had to stop the treatment because treatment was ended
	Not effective	No/less effectiveness
	Patient's death	Patient was deceased
Ekedahl et al 2006	Expiry date passed/medicines too old	Medication expired
	Change in care and/or drug handling	Change of medication
	New treatment	Change of medication
	No need anymore/condition improved	Had to stop the treatment because treatment was ended
	Adverse drug reaction	Had to stop the treatment, because of adverse effects
	Inefficient	Had to stop the treatment because treatment was ended
	Subtotal-therapy changes	Change of medication
	Lack of effect and/or deterioration	No/less effectiveness
	Non-compliance	Medication non-adherence
	Death of the patient	Patient was deceased

Khandelwal et al 2011	Switched medication	Change of medication
	Side effects	Had to stop the treatment, because of adverse effects
	Therapy ineffective	No/less effectiveness
	Deceased	Patient was deceased
Langley et al 2005	Adverse drug reaction	Had to stop the treatment, because of adverse effects
	Medication changed or stopped by doctor	Change of medication Had to stop the treatment because treatment was ended
	Medication error (on order/prescription/supply)	Delivered wrong medication
	Out of date	Medication expired
	Patient died	Patient was deceased
Mackridge et al 2007	Adverse drug reaction	Had to stop the treatment, because of adverse effects
	Clear-out of older or expired medicines	Medication expired
	Change in prescription	Change of medication
	Supplied in error	Delivered wrong medication
	Patient death	Patient was deceased
Law et al 2015	Physician asked to stop it	Had to stop the treatment because treatment was ended
	Experienced side effects	Had to stop the treatment, because of adverse effects
	Condition resolved/symptoms improved	Had to stop the treatment because treatment was ended
	Medication expired	Medication expired
Ueki et al 2021	Change or discontinuation of medication after preparation	Change of medication
	Expired medications	Medication expired
	Discontinuation due to adverse reactions such as allergic reactions	Had to stop the treatment, because of adverse effects
West et al 2016	Medication changed	Change of medication
	Condition got better	Treatment was stopped
	Medication expired	Medication expired
	There was extra stock	Received too much
	Stopped by patient	Had to stop the treatment because treatment was ended
	Condition got better	Healing/clinical picture improved
	Patient passed away	Patient was deceased
West et al 2014	Medication changed or discontinued by doctor	Change of medication
	Excessive stock	Received too much
	Medication changed	Change of medication
	Passed expiry date	Medication expired
	Condition improved/resolved	Had to stop the treatment because treatment was ended
	Condition resolved	Healing/clinical picture improved
	Patient's death	Patient was deceased

6.2 Appendix II: guidelines preliminary research

Questions interview HCW

(use list DRPs and risk factors as guideline)

1. What problems experiences the patient from your perspective during the use of oral oncolytic drugs?
2. During the use of oral oncolytic drugs some boxes of medicines can be left over. Why do you think that is?

Questions interview patients

(use list DRPs and risk factors as guideline)

1. How do you experience the treatment with oral oncolytic drugs?
2. What problems do you experience?
    a. In case there are no problems: do you think other patients experience problems? What kind of problems could that be?
3. Is it always possible to take your drugs properly?
    a. How do you manage to take it properly? Do you use tools?
    b. Do you ever (intentionally or unintentionally) skip a dose?
4. Do you think your drugs are effective? Do you have faith in your treatment?
5. Do you ever have medicines left over?
    a. What is the reason you have them left over?
    b. What do you do with these medicines?
    c. What medicines were left over?
6. Did we forget to ask something about the problems of the medicine use? Of the waste of medicines?

LIJST VAN DRPS

TOXICITEIT

- Bijwerkingen

VOORLICHTING

- Informatie te ingewikkeld
- Informatie te uitgebreid
- Informatie over bijwerkingen verontrustend
- Informatie tegenstrijdig

KENNIS

- Complex innameschema
- Misverstand over verandering therapie

THERAPIETROUW

- Onbewuste therapietrouw problemen
  - Toedientijd is lastig
  - Geneesmiddel was op
  - Vergeten
  - Leefstijl interferentie
  - Inname vermoeidheid
- Bewuste therapietrouw problemen
  - Vertrouwen in werking
  - Onzekerheid over indicatie
  - Denkt dat het niet nodig is
  - Geloof in behandeling
  - Weigert
  - Misverstand dat geneesmiddel niet nodig is bij afwezigheid van symptomen
  - Angst voor bijwerkingen

PRAKTISCHE PROBLEMEN

- Tekst te klein
- Openen verpakking te moeilijk
- Inname te ingewikkeld
- Onprettige smaak
- Dosis aanpassen te ingewikkeld
- Slikproblemen
- Te grote pillen

<u>LIJST VAN RISICOFACTOREN VOOR VERSPILLING</u>

- Kosten (grote verpakking goedkoper)
- (Plotseling) staken behandeling
- Verbetering ziekte/genezen
- Verandering medicatie
- Bijwerkingen
- Geen/niet gewenst effect
- Krijgt te veel mee
- Therapie ontrouw
- Overlijden
- Te kort houdbaar
- Foutief geneesmiddel meegekregen

6.3 Appendix III: List of drugs participants had to use for inclusion (ATC codes)

Tyrosine kinase inhibitors			
alectinib	L01ED03	lenvatinib	L01EX08
brigatinib	L01ED04	pazopanib	L01EX03
ceritinib	L01ED02	sunitinib	L01EX01
crizotinib	L01ED01	afatinib	L01EB03
entrectinib	L01EX14	dacomitinib	L01EB07
lorlatinib	L01ED05	erlotinib	L01EB02
bosutinib	L01EA04	gefitinib	L01EB01
dasatinib	L01EA02	lapatinib	L01EH01
imatinib	L01EA01	neratinib	L01EH02
nilotinib	L01EA03	osimertinib	L01EB04
ponatinib	L01EA05	vandetanib	L01EX04
dabrafenib	L01EC02	abemaciclib	L01EF03
encorafenib	L01EC03	palbociclib	L01EF01
regorafenib	L01EX05	ribociclib	L01EF02
sorafenib	L01EX02	idelalisib	L01EM01
vemurafenib	L01EC01	fedratinib	L01EJ02
acalabrutinib	L01EL02	ruxolitinib	L01EJ01
ibrutinib	L01EL01	everolimus	L01EG02
cabozantinib	L01EX07		

Adjuvant endocrine therapy	
tamoxifen	L02BA01
anastrozole	L02BG03
exemestaan	L02BG06
letrozole	L02BG04
abiraterone	L02BX03
apalutamide	L02BB05
bicalutamide	L02BB03
cyproterone	G03HA01
enzalitamide	L02BB04
nilutamide	L02BB02

Pyrimidine antagonist	
capecitabine	L01BC06
trifluridine/tipiracil	L01BC59

6.4 Appendix IV Instructions interview main research

Instructions interview I

Allereerst bedankt dat u tijd wilde vrijmaken voor ons onderzoek. Ik ben erg blij dat u deel wilt nemen aan dit onderzoek.
{Voorstellen}
Ik studeer Medische Farmaceutische Wetenschappen en hiervoor doe ik een onderzoek aan het UMCG. Ik onderzoek de problemen die mensen kunnen ondervinden bij het gebruik van medicijnen voor de behandeling van kanker. Ook kijk ik daarbij of het wel eens gebeurt dat mensen deze medicijnen overhouden. Hiervoor zouden wij u graag 4 keer willen interviewen met telkens ongeveer een maand ertussen. Vandaag is het eerste interview. Dit interview zal ongeveer 30/45 minuten in beslag nemen. De volgende interviews zullen wat korter zijn, ongeveer 15 à 20 minuten, omdat niet alles opnieuw aan bod komt. De resultaten van de interviews worden gebruikt om beter in kaart te brengen hoe de patiënten hun behandeling ervaren en waar hierbij winst te behalen valt. De interviewgegevens worden anoniem verwerkt, dat wil zeggen dat uw persoonlijke gegevens niet gebruikt of genoemd zullen worden. Verder zal wat u vertelt tijdens dit interview vertrouwelijk behandeld worden en niet gedeeld worden met anderen, dus ook niet met uw arts en verpleegkundigen. U bent volledig vrij in wat u zegt tijdens deze interviews. Als u tijdens een van de interviews besluit dat u niet meer verder wilt gaan, dan mag u dat te allen tijde aangeven. Wij zullen dan stoppen met het interview en het vervolg van het onderzoek. Daarnaast zou ik graag dit gesprek willen opnemen zodat ik het gesprek nog eens rustig kan terugluisteren. Vindt u dit goed? Om dit ook vast te leggen op de recorder vraag ik zo nogmaals, als de recorder loopt, of u toestemming geeft dat dit gesprek wordt opgenomen.

Algemene vragen over patiënt en behandelingen/ziektes

1. Wat is uw hoogst genoten opleiding?
2. Woont u met iemand samen?
3. Klopt het dat u op dit moment **insert oraal oncolyticum** gebruikt?
    a. Welke dosis gebruikt u van dit middel?
    b. Hoe vaak gebruikt u dit middel?

Geneesmiddel gerelateerde problemen

4. Ervaart u problemen bij het gebruiken van de **insert oraal oncolyticum**?
    a. Welke problemen zijn dat?
    Doorvragen op problemen die de patiënt benoemd. Categorisch doorvragen en bij bevestigende antwoorden verder inzoomen, bijv. heeft u ook problemen bij het innemen van de medicatie? Zo ja, wat voor problemen? Te grote pillen, slikproblemen, vieze smaak etc.
    Antwoordmogelijkheden p.8

Therapietrouw

5. Hoe gaat het met het innemen van de medicijnen?
    a. Kunt u vertellen hoe bij u het gebruik van uw medicijnen op een alledaagse dag gaat? Hoe neemt u uw medicijnen in? Op welke momenten? *Doorvragen over inname ritueel*
    b. Neemt u de medicijnen wel eens op een ander moment? Zo ja, hoe vaak?
    c. Neemt u wel eens een andere dosis van de medicijnen? Zo ja, hoe vaak?
    d. Vergeet u wel eens medicijnen in te nemen? Zo ja, hoe vaak?
    e. Neemt u de medicijnen wel eens bewust niet in? Zo ja, hoe vaak?

Antwoord suggesties: nooit – soms – geregeld – vaak – altijd OF x keer per week (testen in pilot)

Verspilling

6. Heeft u afgelopen maand medicijnen overgehouden van een behandeling?

Antwoord suggesties: nooit – soms – geregeld – vaak – altijd OF x keer per week (testen in pilot)

   a. Was dit van ****naam oraal oncolyticum?

Indien sprake van overgebleven medicatie:

   b. Hoeveel verpakkingen heeft u overgehouden?
      i. Kunt u zich herinneren hoeveel tabletten/capsules?
   c. Kunt u zich herinneren of er verpakkingen niet aangebroken waren, zo ja hoeveel?
   d. Wat heeft u met deze overgebleven medicijnen gedaan? *Huisvuil, apotheek, anders …*

Risicofactoren voor verspilling (alleen als patiënt bij verspilling aangeeft medicijnen over te houden)

7. Wat is de reden dat u medicijnen heeft overgehouden?
   a. Arts te veel voorgeschreven; apotheek te veel meegegeven; eerder gestopt dan gepland; niet alles ingenomen; gestopt ivm bijwerkingen; anders, ……

   Doorvragen in de richting van verschillende risicofactoren. Eerst globaal, bij bevestigend antwoord verder inzoomen. Antwoordmogelijkheden p.9

Toelichtingsvragen

We hebben het nu uitgebreid gehad over de mogelijke problemen die u ervaart en hoe u de medicijnen inneemt. Daarnaast wil ik u nog wat vragen stellen over de gang van zaken om de behandeling heen, zoals het bepalen van de behandeling en het meegeven van medicijnen. Allereerst…

8. Naar wie gaat u toe voor vragen over uw ziekte en de behandeling? *Oncoloog, oncologisch vpk, apotheker, huisarts, anders…*
9. Denkt u dat de behandeling effect heeft? *Niet/een beetje/behoorlijk/absoluut*
10. Gebruikt u een hulpmiddel dat u eraan herinnert uw medicijnen te nemen? *Ja/nee*
    a. Wat voor hulpmiddel? *Pillendoos, wekker, app, afstreeplijst, baxterrol, etc.*
11. Krijgt u andere hulp bij uw medicijnen? *Ja/nee*
    a. Door wie? *Thuiszorg, buurvrouw, partner, ouders, kinderen*
    b. Wat doet diegene?

Hartelijk dank voor uw tijd en openheid over de vragen. Wij zouden u graag over vier weken weer bellen. Heeft u voorkeur voor een moment? Over vier weken is het …. *Afspraak maken over wanneer weer bellen*

Instructions interview II and III

Dank u wel dat u opnieuw tijd heeft kunnen vrijmaken voor dit interview. Het interview zal opnieuw worden opgenomen, als u hier geen bezwaar tegen heeft. Dit interview zal wat korter zijn dan het eerste interview, omdat we vandaag alleen in zullen gaan op de aspecten die veranderd zijn ten opzichte van de vorige keer dat wij elkaar spraken. Zijn er dingen die u vooraf graag wilt melden? Zo niet, dan gaan we van start.

Algemene vragen over patiënt en behandelingen/ziektes

De vorige keer dat wij elkaar spraken werd u behandeld met **geneesmiddelen invullen**

1. Zijn er veranderingen in de medicijnen die u gebruikt sinds de vorige keer dat wij elkaar spraken? *Ja/nee*
   a. Huidig middel + dosis uitvragen

Geneesmiddel gerelateerde problemen

Vorige keer gaf u aan last te hebben van **DRPs vorig interview invullen**

2. Ervaart u nog steeds dezelfde problemen?
    a. Zijn er problemen opgelost?
    b. Zijn er problemen bijgekomen?

    Doorvragen op problemen die de patiënt benoemd. Categorisch doorvragen en bij bevestigende antwoorden verder inzoomen, bijv. heeft u ook problemen bij het innemen van de medicatie? Zo ja, wat voor problemen? Te grote pillen, slikproblemen, vieze smaak etc. Antwoordmogelijkheden p.8

Therapietrouw

3. Is de inname van uw medicijnen veranderd ten opzichte van een maand geleden?
    Terugkoppelen op vergeten/andere dosis/ander moment t.o.v. vorig interview?
    Bijv. vorige keer gaf u aan dat u ong. 2x per week uw medicatie te vergeten, hoe gaat dat nu?

Verspilling

Vorige keer gaf u aan ongeveer x hoeveelheid medicijnen over te hebben na een behandeling.

4. Hoe is dat over de afgelopen maand gegaan?
Antwoord suggesties: nooit – soms – geregeld – vaak – altijd OF x keer per week (testen in pilot)

    a. Was dit van ****naam oraal oncolyticum?

    Indien sprake van overgebleven medicatie:

    b. Hoeveel verpakkingen heeft u overgehouden?
        i. Kunt u zich herinneren hoeveel tabletten/capsules?
    c. Kunt u zich herinneren of er verpakkingen niet aangebroken waren, zo ja hoeveel?
    d. Wat heeft u met deze overgebleven medicijnen gedaan? *Huisvuil, apotheek, anders …*

Risicofactoren voor verspilling (alleen als patiënt aangeeft medicatie over te houden)

5. Wat is de reden dat u medicijnen heeft overgehouden?

    a. Arts te veel voorgeschreven; apotheek te veel meegegeven; eerder gestopt dan gepland; niet alles ingenomen; gestopt door bijwerkingen; anders, ……

    Doorvragen in de richting van verschillende risicofactoren. Eerst globaal, bij bevestigend antwoord verder inzoomen. Antwoordmogelijkheden p.9

Toelichtingsvragen

6. Is uw inspraak in de behandeling veranderd? *Zo ja, …*
    a. In hoeverre had u inspraak in de huidige behandeling? *Niet/een beetje/grotendeels/volledig*

7. Is er volgens u wat veranderd in de effectiviteit van de behandeling? *Zo ja, …*
    a. In welke mate denkt u dat de behandeling effect heeft? *Niet/een beetje/behoorlijk/absoluut*
8. Zijn de hulpmiddelen die u gebruikt voor uw medicijnen veranderd? *Zo ja, …*
    a. Wat gebruikt u nu als hulpmiddel? *Pillendoos, wekker, app, afstreeplijst, bexterrol*
9. Is er wat veranderd in de hulp die u krijgt bij uw medicijnen? *Zo ja, …*

a. Wat is hierin veranderd? *Meer of minder hulp/andere persoon die helpt/andere taken*

Hartelijk dank weer voor uw tijd en openheid over de vragen. Wij zouden u graag over vier weken weer bellen. Heeft u voorkeur voor een moment? Over vier weken is het …. *Afspraak maken over wanneer weer bellen*

Instructions interview IV

We zijn alweer aangekomen bij het laatste interview met betrekking tot dit onderzoek. Heel erg bedankt dat u elke keer tijd hiervoor heeft willen vrijmaken. Het interview zal opnieuw worden opgenomen, als u hier nog steeds geen bezwaar tegen heeft. Zijn er dingen die u vooraf graag wilt melden? Zo niet, dan gaan we van start.

Algemene vragen over patiënt en behandelingen/ziektes

De vorige keer dat wij elkaar spraken werd u behandeld met **geneesmiddelen invullen**

1. Zijn er veranderingen in de medicijnen die u gebruikt sinds de vorige keer dat wij elkaar spraken? *Ja/nee*
    a. *Huidig middel + dosis uitvragen*

Geneesmiddel gerelateerde problemen

Vorige keer gaf u aan last te hebben van **DRPs vorig interview invullen**

2. Ervaart u nog steeds dezelfde problemen?
    a. Zijn er problemen opgelost?
    b. Zijn er problemen bijgekomen?

    Doorvragen op problemen die de patiënt benoemd. Categorisch doorvragen en bij bevestigende antwoorden verder inzoomen, bijv. heeft u ook problemen bij het innemen van de medicatie? Zo ja, wat voor problemen? Te grote pillen, slikproblemen, vieze smaak etc. Antwoordmogelijkheden p.8

Therapietrouw

3. Is de inname van uw medicijnen veranderd ten opzichte van een maand geleden?

Terugkoppelen op vergeten/andere dosis/ander moment t.o.v. vorig interview?
Bijv. vorige keer gaf u aan dat u ong. 2x per week uw medicatie te vergeten, hoe gaat dat nu?

Verspilling

Vorige keer gaf u aan ongeveer x hoeveelheid medicijnen over te hebben na een behandeling.

4. Hoe is dat over de afgelopen maand gegaan? Hield u opnieuw medicijnen over?
Antwoord suggesties: nooit – soms – geregeld – vaak – altijd OF x keer per week (testen in pilot)

a. Was dit van ****naam oraal oncolyticum?

Indien sprake van overgebleven medicatie:

b. Hoeveel verpakkingen heeft u overgehouden?
    i. Kunt u zich herinneren hoeveel tabletten/capsules?

c. Kunt u zich herinneren of er verpakkingen niet aangebroken waren, zo ja hoeveel?
d. Wat heeft u met deze overgebleven medicijnen gedaan? *Huisvuil, apotheek, anders …*

Risicofactoren voor verspilling

5. Wat is de reden dat u medicijnen heeft overgehouden?

    a. Arts te veel voorgeschreven; apotheek te veel meegegeven; eerder gestopt dan gepland; niet alles ingenomen; gestopt door bijwerkingen; anders, ……

    Doorvragen in de richting van verschillende risicofactoren. Eerst globaal, bij bevestigend antwoord verder inzoomen. Antwoordmogelijkheden p.9

Toelichtingsvragen

6. Is uw inspraak in de behandeling veranderd? *Zo ja, …*
    a. In hoeverre had u inspraak in de huidige behandeling? *Niet/een beetje/grotendeels/volledig*
7. Is er volgens u wat veranderd in de effectiviteit van de behandeling? *Zo ja, …*
    a. In welke mate denkt u dat de behandeling effect heeft? *Niet/een beetje/behoorlijk/absoluut*
8. Zijn de hulpmiddelen die u gebruikt voor uw medicijnen veranderd? *Zo ja, …*
    a. Wat gebruikt u nu als hulpmiddel? *Pillendoos, wekker, app, afstreeplijst, bexterrol*
9. Is er wat veranderd in de hulp die u krijgt bij uw medicijnen? *Zo ja, …*
    a. Wat is hierin veranderd? *Meer of minder hulp/andere persoon die helpt/andere taken*

Vriendelijk bedanken voor alle interviews en de inkijk bij de patiënt.

6.5 Appendix V List of how to question the DRPs and risk factors

Geneesmiddelgerelateerde problemen

TOXICITEIT – heeft u bijwerkingen ervaren bij het middel? Zo ja, welke? Wat gedaan om deze te verminderen?

- Bijwerkingen

VOORLICHTING – wat vond u van de informatie die u kreeg over uw medicijnen? Afhankelijk van het antwoord:

- Wat vond u van de complexiteit van de informatie?
- Wat vond u van de omvang van de informatie? *Uitgebreid genoeg? Te uitgebreid?*
- Was informatie over bijwerkingen verontrustend?
- Was informatie tegenstrijdig?

KENNIS – begreep u alles rondom de inname van uw medicijnen? Begreep u alles rondom gewijzigde medicijnen?

- Is het innameschema complex?

THERAPIETROUW

- Onbewuste therapietrouw problemen – u gaf aan wel eens uw medicijn te vergeten; komt dat bijvoorbeeld dat het moment van inname niet past bij uw dagelijkse activiteiten; of omdat u al zoveel pillen slikt (innamevermoeidheid)?
  - Is de toedientijd lastig ?
  - Heb u medicatie wel eens moeten overslaan, omdat het geneesmiddel op was (of u onvoldoende had meegekregen van de apotheek)?
  - Bent u wel eens een inname vergeten?
  - Vindt u het lastig om de medicijnen in uw leven in te passen?
  - Is er sprake van inname vermoeidheid bij u? *Heeft u wel eens totaal geen zin meer om de medicatie elke dag opnieuw op de juiste momenten in te nemen?*
- Bewuste therapietrouw problemen – u gaf aan bewust wel eens medicijnen niet te nemen. Hoe komt dat? En dan verder inzoomen; evt specifiek vragen naar twijfel aan werkzaamheid en/of bijwerkingen als oorzaak.
  - Heeft u vertrouwen in de werking van het medicijn?
    - Denkt u dat u kunt stoppen als de klachten voorbij zijn?
  - Bent u bang voor bijwerkingen?

PRAKTISCHE PROBLEMEN – u heeft aangegeven problemen bij het innemen van medicatie te ervaren. Hadden die met de verpakking te maken (tekst te klein; openen verpakking moeilijk)? Of lag het aan de pillen zelf (smaak, grootte, slikproblemen, geur, te veel pillen). Etc.

- Heeft u er last van dat de tekst te klein is?
- Vindt u het openen van de verpakking moeilijk?
- Vindt u de inname van de medicijnen lastig? *Zo ja, …*
  - Heeft u last van te grote pillen?
  - Of juist te klein?
  - Vindt u de smaak onprettig?
  - Heeft u last van onprettige geur?
  - Heeft u last van slikproblemen?
  - Heeft u moeite met de hoeveelheid pillen die u moet innemen?
- Is het aanpassen van de dosis te ingewikkeld?

Alleen bij geneesmiddelen waarbij speciale maatregelen gelden in verband met omgevingsbesmetting

- Vindt u het lastig dat u het toilet moet schoonmaken na gebruik?

Risicofactoren voor verspilling

- U heeft aangegeven dat u medicijnen hebt overgehouden die teruggebracht moesten worden naar de apotheek. Hoe kwam dat?
  - Te veel meegekregen
  - Moest stoppen met de behandeling

        - Omdat ik bijwerkingen had
        - Omdat ik klaar was met de behandeling
    - Moest een lagere dosis gaan gebruiken
    - Ben overgegaan op ander medicijn
    - De medicijnen bleken over de vervaldatum te zijn
    - Verkeerd geneesmiddel was afgeleverd

6.6 Appendix VI Forms used during the main interviews to analyse

Case report form I

RUG/UMCG	**GEBRUIK ORALE ONCOLYTICA (GOOL)**	**202100768**	**ONDERZOEKER:**_____
DEELNEMER #			Interview 1
(1) PATIËNT EIGENSCHAPPEN		DATUM __/__/____	
Geslacht		Orale oncolyticum	
Leeftijd	Type kanker	Comorbiditeiten	
Hoogst genoten opleiding		Dosis	
Sociale context		Comedicatie	
o Geen opleiding	o VMBO-g/t, havo-, vwo-onderbouw	o HAVO, VWO	o Anders, namelijk _____
o Basisonderwijs	o MBO2 en 3	o HBO-, WO-bachelor	_____
o VMBO-b/k, MBO1	o MBO4	o HBO-, WO-master, doctor	_____
o Woont met partner	o Woont met ouders	o Meermaals per week sociaal contact	o Anders, namelijk _____
o Woont met partner en kinderen	o Woont met vrienden	o Wekelijks sociaal contact	_____
o Woont alleen	o Dagelijks sociaal contact	o Maandelijks sociaal contact	_____

(2) GENEESMIDDELGERELATEERDE PROBLEMEN		
[ ] Bijwerkingen	( ) Inname vergeten	( ) Pillen te groot
[ ] Informatie te complex	( ) Leefstijl interferentie	( ) Pillen te klein
[ ] Informatie te uitgebreid	( ) Inname vermoeidheid	( ) Smaak onprettig
[ ] Informatie incompleet	[ ] Bewuste therapietrouw problemen	( ) Geur onprettig
[ ] Informatie over bijwerkingen verontrustend	( ) Gebrek aan vertrouwen in medicijn	( ) Slikproblemen
[ ] Informatie tegenstrijdig	{ } Denkt te kunnen stoppen na verdwijnen klachten	( ) Moeite met hoeveelheid pillen
[ ] Innameschema complex	( ) Angst voor bijwerkingen	[ ] Aanpassen dosis ingewikkeld
[ ] Onbewuste therapietrouw problemen	[ ] Tekst te klein	[ ] Toilet schoonmaken na gebruik
( ) Toedientijd lastig	[ ] Openen verpakking moeilijk	[ ] Anders, namelijk _____
( ) Geneesmiddel was op	[ ] Inname medicijnen lastig	_____

(3) THERAPIETROUW					
Ander moment inname	nooit	soms	geregeld	vaak	altijd
Andere dosis inname	nooit	soms	geregeld	vaak	altijd
Dosis vergeten in te nemen	nooit	soms	geregeld	vaak	altijd
Dosis bewust niet innemen	nooit	soms	geregeld	vaak	altijd

(4) VERSPILLING					
Medicatie over 1 maand	nooit	soms	geregeld	vaak	altijd
Hoeveel verpakkingen over	1	2	3	4	5
Hoeveel tabletten/capsules	1	2	3	4	5
Onaangebroken verpakkingen	1	2	3	4	5
Overgebleven medicatie…	[ ] Apotheek	[ ] Anders, namelijk_____			
	[ ] Huisvuil	_____			

(5) RISICOFACTOREN VOOR VERSPILLING	
[ ] Te veel meegekregen	[ ] Dosis verandering
[ ] Behandeling gestaakt, omdat	[ ] Verandering medicatie
( ) Bijwerkingen	[ ] Medicatie over vervaldatum
( ) Behandeling afgelopen	[ ] Verkeerd geneesmiddel geleverd
[ ] Anders, namelijk _____	

(6) TOELICHTINGSVRAGEN					
1. Wie is uw vraagbaak?	[ ] Oncoloog	[ ] Oncologisch verpleegkundige	[ ] Apotheker	[ ] Huisarts	
	[ ] Anders, namelijk _____				
3. Denkt u dat de behandeling effect heeft?		Nee	Een beetje	Behoorlijk	Absoluut
4. Gebruikt u een hulpmiddel voor die u herrinert aan de medicatie?		Ja/nee	namelijk_____		
4a. Krijgt u andere hulp bij uw medicijnen?	Ja/nee	Wie?_____	Wat?_____		

Extra aantekeningen/toelichting op de achterkant

Case report form II, III and IV

RUG/UMCG	**GEBRUIK ORALE ONCOLYTICA (GOOL)**	**202100768**	**ONDERZOEKER:_____**
DEELNEMER #			Interview 2 en 3
(1) PATIËNT EIGENSCHAPPEN		DATUM __/__/____	
Orale oncolyticum		Comedicatie	
Dosis			

(2) GENEESMIDDELGERELATEERDE PROBLEMEN		
[ ] Bijwerkingen	( ) Inname vergeten	( ) Pillen te groot
[ ] Informatie te complex	( ) Leefstijl interferentie	( ) Pillen te klein
[ ] Informatie te uitgebreid	( ) Inname vermoeidheid	( ) Smaak onprettig
[ ] Informatie incompleet	[ ] Bewuste therapietrouw problemen	( ) Geur onprettig
[ ] Informatie over bijwerkingen verontrustend	( ) Gebrek aan vertrouwen in medicijn	( ) Slikproblemen
[ ] Informatie tegenstrijdig	{ } Denkt te kunnen stoppen na verdwijnen klachten	( ) Moeite met hoeveelheid pillen
[ ] Innameschema complex	( ) Angst voor bijwerkingen	[ ] Aanpassen dosis ingewikkeld
[ ] Onbewuste therapietrouw problemen	[ ] Tekst te klein	[ ] Toilet schoonmaken na gebruik
( ) Toedientijd lastig	[ ] Openen verpakking moeilijk	[ ] Anders, namelijk _____
( ) Geneesmiddel was op	[ ] Inname medicijnen lastig	_____

(3) THERAPIETROUW					
Ander moment inname	nooit	soms	geregeld	vaak	altijd
Andere dosis inname	nooit	soms	geregeld	vaak	altijd
Dosis vergeten in te nemen	nooit	soms	geregeld	vaak	altijd
Dosis bewust niet innemen	nooit	soms	geregeld	vaak	altijd

(4) VERSPILLING					
Medicatie over 1 maand	nooit	soms	geregeld	vaak	altijd
Hoeveel verpakkingen over	1	2	3	4	5
Hoeveel tabletten/capsules	1	2	3	4	5
Onaangebroken verpakkingen	1	2	3	4	5
Overgebleven medicatie…	[ ] Apotheek	[ ] Anders, namelijk_____			
	[ ] Huisvuil	_____			

(5) RISICOFACTOREN VOOR VERSPILLING	
[ ] Te veel meegekregen	[ ] Dosis verandering
[ ] Behandeling gestaakt, omdat	[ ] Verandering medicatie
( ) Bijwerkingen	[ ] Medicatie over vervaldatum
( ) Behandeling afgelopen	[ ] Verkeerd geneesmiddel geleverd
[ ] Anders, namelijk _____	

(6) TOELICHTINGSVRAGEN					
3. Is de effectiviteit veranderd?	Ja/nee, hoeveel effectief?	Nee	Een beetje	Behoorlijk	Absoluut
4. Gebruikt u een ander hulpmiddel van voorheen?		Ja/nee	namelijk_____		
4a. Krijgt u andere hulp met uw medicijnen?	Ja/nee	Wie?_____		Wat?_____	

Extra aantekeningen/toelichting hieronder of op de achterkant