Aims and reasons: ethical questions about palliative systemic anticancer therapy

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Chapter 1: General Introduction

Palliative systemic anticancer treatments (PST) which include chemotherapy, targeted therapy, hormonal therapy and immunotherapy, are used for patients with metastatic disease of solid tumours. The term ‘palliative’ indicates that there is no expectation of curing the disease. PST may be prescribed to prolong life and/or to improve quality of life. The possible advantages for the patient need to be weighed against the burdens of the disease and toxicity. These complex considerations make the decision to start, forego, continue, discontinue or modify palliative systemic therapy often ethically difficult for both patient and physician. The problem addressed in this study is that it often is unclear what actually good use of palliative systemic therapy is.

In the literature on palliative systemic therapy, two approaches to the question of good use of palliative systemic therapy can be found. The first approach, which was developed within studies on patient-physician communication in metastatic cancer presupposes, to put it simply, that if the patient is given good information then this will lead to good treatment. This is a procedural approach. The second approach tells us what we should not do. Randall and Downie developed a normative framework concerning when potentially life-prolonging treatment should be avoided. This is a minimal principle approach. Both approaches are ethical theories, but they are not substantial theories. The question of what is good use is not answered. So if we want to develop a more substantial ethical theory that addresses the question of what is good use of PST, we should know much more about the way in which these forms of treatment are being used, and why they are being used. To this end, I decided to take a closer look at the aims for prescribing and undergoing PST that the participants put forward in their practices and deliberations.

The fact that the literature on palliative systemic therapy was missing an explicit reflection on treatment aims, was also reflected in the study of oncology practice. During interviews with medical oncologists, it was found that they had difficulties in formulating what they considered to be the main aims of palliative systemic therapy, also when they talked about specific individual patients. The absence or lack of clarity about the aims of palliative systemic therapy in both the literature and oncology
practice is addressed in this thesis. In order to capture the details of and the interplay between the aims of palliative systemic therapy in cancer, the practice of this form of treatment needs to be studied empirically. In particular it is qualitative research which strives for in-depth understanding of practices, that enables us to find out how physicians and patients not only talk about but also deal with and think about palliative systemic therapy, how they give content to aims (even if they often find it hard to say exactly what their aims are) and how tensions are dealt with.

Three areas of practice seemed particularly relevant to this study: 1) research, where the development of new forms of therapy may introduce new aims; 2) guideline development, where - among other things - the goals of therapy are codified; and 3) clinical care, where treatment aims are given their final shape in the interaction between patients and doctors. Reflecting on these findings gives insight into the problem of the good use of palliative systemic anticancer therapy. On the basis of these considerations, the central questions of this study were:

1. What are the aims of palliative systemic anticancer therapy for patients with metastatic cancer and which role do these aims play in practice?
2. How can these aims be morally interpreted? And how do these interpretations contribute to good use of PST?

Chapter 2
In this chapter the main treatment aims of palliative chemotherapy in research trials are examined. Oncologists disagree if chemotherapy in advanced cancer is meant to improve quality of life (QoL), to prolong duration of life, or both.

Twenty-eight Randomized controlled phase III Clinical Trials (RCTs) were selected by specific search terms from PubMed and critically assessed. These RCTs were about palliative chemotherapy and included a Health-Related (HR) QoL assessment in patients with advanced colorectal cancer. We hypothesized that trials investigating second- or third-line chemotherapy would put more emphasis on weighing QoL-related outcomes than trials focusing on first-line treatment. In addition, we assumed that trials investigating ways of administration, like oral versus parenteral medication, would also concentrate more on QoL- than on PoL (prolongation of life)-related outcomes.

It turned out that the authors of the RCTs based their conclusions and recommendations on both quality of life outcomes and prolongation of life outcomes. If the QoL- and PoL-related outcomes were opposite, e.g.
the PoL in the experimental group was better than in the control group but the QoL was worse, the authors considered the PoL-outcome of overriding importance. In 13 out of 28 trials this was the case. QoL-related outcomes were of overriding importance in only 1 out of 28 cases.

We conclude that PoL-outcomes were considered most important, regardless of our hypotheses. The review presented in this chapter shows that in the context of chemotherapy in advanced colorectal cancer, ‘palliative’ refers to a life-prolonging intention, whereas within palliative care it refers to the intention to improve QoL.

Chapter 3

In order to find out which value judgements and treatment aims are incorporated into oncology guidelines, recent, preferably evidence-based, clinical practice guidelines, were studied. It is inevitable that there are value judgements in the practical recommendations contained in guidelines with regard to palliative chemotherapy. A value judgement is defined as a statement about the value of a patient outcome. Setting treatment aims may form an important part of these value judgements. This chapter describes:

1. the value judgements that influence the process of developing guidelines for palliative chemotherapy, and
2. whether these value judgements were made explicit in the final guideline report.

The development process of six Dutch oncology guidelines in which palliative chemotherapy plays a substantial role was studied. We observed 14 guideline development groups (GDGs) meetings, conducted 20 semi-structured interviews with individual GDG members (including the chairs), and analysed the minutes of GDG meetings and subsequent versions of the guidelines.

We identified the following value judgments in the process of guideline development:

1. consensus on what valuable minimum patient outcomes should be,
2. the preference for tailored treatment in situations where there is no evidence of treatment effect,
3. preference for ‘doing something’ even when there is sufficient evidence that treatment is ineffective, and
4. the patient outcome of ‘prolonging life’ was considered important.
These value judgements were not reflected in the final guideline reports although they had influenced the recommendations. The third and fourth of these value judgements are very relevant to patients with incurable metastatic cancer when making decisions on whether to have chemotherapy and if so, what kind. The user of a guideline should know the reasons that treatment X is recommended. For example physicians have difficulties not giving treatment and assume that patients want to do something more than just ‘watchful waiting’. Also the idea that physicians assume patients attach much value to a few months gain in survival, might have influenced the recommendation for treatment X. The conclusion of this chapter is that value judgements including setting certain treatment aims, should be made explicit in guidelines, so that clinicians can transparently discuss treatment options with individual patients.

Chapter 4

Cost considerations are a specific element within treatment decisions that might influence the formulation of treatment aims. The high costs of new disease-modifying, but non-curative, treatments in advanced cancer are increasingly regarded as problematic. This chapter describes oncologists’ beliefs about their ethical obligations concerning cost considerations regarding these types of treatments.

Thirty-six physicians involved in oncology care were interviewed, 17 of whom had participated in working groups on national oncology guidelines. Questions about cost issues were part of a larger interview about ‘ethical aspects of palliative chemotherapy’. The questions concerned the beliefs and actions of the physician in relation to expensive new disease-modifying treatments for advanced cancer.

In considering costs of expensive treatments we distinguished three levels in the analysis of the interview data: individual patient care, hospital policies, and national guideline development. Generally speaking, physicians were reluctant to consider costs in individual patient care believing that this compromised their ethical obligations towards the patient. They did consider cost relevant at the level of hospital policies regarding coverage for drugs. The examples respondents gave were mainly about agreements between physicians, e.g. the local policy concerning medical grounds for certain treatments. Regarding the role of cost considerations in national practice guideline development, opinions were divided. Sometimes respondents believed it was necessary to weigh costs and sometimes they believed costs should explicitly be excluded.
These distinctions about costs between different levels of decision-making were understood to be morally relevant as physicians separated their role as direct care provider from that of taking part in decisions about coverage. Nevertheless, cost considerations will always be problematic for physicians because of the fundamental tension between the physician’s obligation to act in the best interest of the individual patient, and the inevitability of shared resources in modern health care. The chapter shows that cost effectiveness in the consultation room does not fit the beliefs and actions of physicians and therefore it does not influence the setting of treatment aims. Sometimes it does, however, at the levels of hospital policies and national guideline development.

Chapter 5

This chapter presents a multiple longitudinal case study about clinical care in which the process that leads to initiating, modifying, and stopping palliative systemic therapy is analyzed. This study shows that in clinical practice the treatment course does not often correspond with clear decision-making and clear treatment aims but is frequently more erratic. Our purpose was to analyse these processes in the form of trajectories and to analyze what sets a trajectory apart from a decision.

Thirteen patients with metastatic colorectal and pancreatic cancer for whom palliative chemotherapy was a treatment option, were studied with observations and disease permitting, were interviewed three times. Thirty treating professionals were also interviewed.

We analysed three characteristics of the treatment course that contributed to the erratic nature of this course: 1) the treatment (with or without chemotherapy) contained many options; 2) these options were not stable entities to be decided upon, but changed their identity over the course of treatment, and 3) contrary to the closure a decision implies (option X means no option Y, Z, etc), the treatment course was a continuous process in which options instead remained open.

Because of these treatment course characteristics, we wanted to see how it works out to think and speak in another ‘exemplary situation’ (in other words: use a different vocabulary) than decision making. Therefore in the discussion section we introduced the term trajectory: what are the consequences of speaking about the treatment of metastatic cancer in terms of ‘trajectory making’? The chapter concludes that communication models should be adapted. A treatment course is characterised by many and changeable options that often do not result in closure. Just as
for good decision-making, criteria for prudent practice for good trajectory making are suggested. It is important to be flexible regarding the use of guidelines in clinical practice, so that all possibilities in the process of trying out, evaluating and adapting can be fully explored. At the same time vigilance about the overall direction of the process is warranted.

Chapter 6

In this chapter we analyse situations in which treatment aims do not seem to serve any clear purpose at all, because of the probable ineffectiveness of the treatment. Even though at first sight it does not seem advisable, physicians do sometimes prescribe ‘probably ineffective palliative systemic therapy’ (PIPST). In the casuistry discussed in this chapter, it even appeared to be a form of good care. The central question in this chapter is ‘Can giving PIPST be justified in specific situations, and if so, how can this be done?’

Three major objections can be distinguished in the casuistry. First, if patients received complete and honest information, then they would decline further treatment. Second, according to their professional standards, doctors may only prescribe treatment that has proven to be effective, therefore not treatment that will probably be ineffective. Third, treatment should do as little harm as possible. However, these three objections do not always prove to be as strong as they appear: sometimes well-informed patients still wish to have treatment, there is always a small probability of benefit, and the harm it does may be tolerated by the patient. This still does not mean that the doctor now has a positive argument with which to justify the prescription of PIPST. Is there a justification for PIPST, and if there is, what form would it take?

In practice it seems that there are reasons other than effectiveness that make patients want to undergo PIPST. For example, they want to ‘have tried everything’. Could this also be an argument for doctors to prescribe PIPST, namely that the treatment is ‘suited’ to the patient’s life? In order to examine suitability, we introduce the concept of ‘narrative coherence’. The physician may justify prescribing PIPST if this fits into a coherent life story. Of course this does not mean that the objections a doctor has to prescribing PIPST disappear; there will always be tensions if at the end of life the patient’s wishes do not correspond with professional considerations of the doctor.
Chapter 7: General Discussion

The aim of this dissertation was to gain insight into what good use of palliative systemic anticancer therapy is. In order to do so the aims of palliative systemic therapy (PST) were studied; the way they are shaped in research, guideline development and clinical practice and how those who are involved with PST deal with these aims. These empirical findings on the aims of PST are used to develop a more substantial ethical theory about the good use of PST. This general discussion answers the two main research questions and makes some methodological reflections.

The first research question was: what are the aims of palliative systemic anticancer therapy for patients with metastatic cancer and which role do these aims play in practice? This question is answered by distinguishing three categories of aims:

1. General aims. These aims are usually cast in a quantifiable form. Examples are life prolongation-related outcomes such as OS and TTP, but also quality of life improvement and symptom reduction.

2. Personal aims. These aims are related to what individual patients consider important and/or are changeable.

3. Reasons. Reasons are specific motives given by the patient for strongly wanting a therapy, even if it has virtually no chance of reaching a specific general or personal aim.

The second research question was: how can these aims be morally interpreted? And how do these interpretations contribute to good use of PST? In order to do that the value of each category of aims for specific practices has to be established. The guiding idea is that within a practice, PST is used in a good way if it can be expected to contribute to an aim that is relevant to that practice. To a certain extent these three categories of aims were found in all practices studied (research, guideline and the clinical).

The conclusion is that ‘good use’ of palliative systemic therapy differs between practices. The value of each category of aims for specific practices has to be established. The guiding idea is that within a practice, PST is used in a good way when it may be expected to contribute to an aim that is relevant to that practice. Good use of PST in research practice is related to clear general aims. Good use of PST within clinical practice translates those general aims into patient-dependent and changeable personal aims. This translation requires continuous adjustments. Guidelines are meant to help with the translation of general aims into personal aims.
Summary

Current guidelines do this inappropriately because they are implicit about the aims and value judgements they involve. In some situations, ‘reasons’ (motives unrelated to aims) may lead to good use of PST in clinical practice. However, ‘reasons’ must be invoked very carefully as they may form a basis for possibly toxic treatments.

This general discussion chapter presents a checklist that might help the clinician and with that his/her patient to clarify treatment aims and reasons and look for the ‘fitting’ good use of palliative systemic therapy. The checklist includes the following questions:

1. For what aim am I prescribing this treatment?
2. Am I shaping the treatment in a flexible way?
3. Do I realize that the treatment will affect ways of dying?

In the methodological reflections of this chapter some insight into what occurred behind the scenes during the phases of data collection and analysis of this empirical ethical research project is given. Furthermore recommendations for new research are made.