Towards a patient-driven approach to adverse events of targeted agents in oncology

Christine Bettine Boers

The research presented in this dissertation was performed at the Department of Medical Oncology of Leiden University Medical Center, Leiden, The Netherlands, and the Waterland Hospital, Purmerend, The Netherlands.

The research described in this thesis was funded by Amgen, Bayer, EUSA Pharma, GlaxoSmithKline, Novartis, Pfizer, Roche, and the Impaqtt Foundation.
Financial Support for the publication of this dissertation was provided by the Leiden University Medical Center, and support of Gildeprint.

Cover design	Monica Schokkenbroek
Layout	Christine B. Boers-Doets
Printed by	Gildeprint
ISBN	978-94-93117-00-6

Summary

Context

Targeted anticancer therapies are used in treating many types of cancer in both adults and children. In addition to an increase in the number of targeted anticancer therapies, there are also broader indications, resulting in a growing number of patients with cancer eligible for these treatments. The duration of the treatments that are mainly in the outpatient setting can vary from months to years. Targeted therapies are used as monotherapy, and also used as a combination with cytotoxic chemotherapy and/or radiation therapy.

Research and practice also show that adverse events due to these treatments can cause the therapy to be temporarily interrupted, a dose reduction applied, or treatment to be discontinued prematurely, despite its effective anticancer effect. The adverse event profile of targeted therapies is multidimensional with varying degrees of impact on quality of life. Many adverse events are mainly symptomatic. As a result, these can only be perceived and measured by the patient, while the treatment team is responsible for an adequate recording of the adverse events. When treatment is provided, the resulting interventions do not always fit seamlessly with the needs of the patient. This discongruity indicates a need for an integrated patient-driven approach to adverse events.

Aims

The central question of this dissertation is whether available methods and instruments can serve as a basis for the realization of an integrated patient-driven approach to targeted therapy-associated adverse events.

Findings

Our research identified three notable findings:

1. Current adverse event measurement instruments may be of limited value for the assessment, reporting, grading, and evaluation of targeted therapy-associated skin and mucosal reactions. Overall, the incorporation of the patient's voice is limited.
2. There is currently limited scientific adverse event knowledge available to build evidence-based treatment guidelines.
3. The generated scientific adverse event knowledge that has become available is not imbedded broadly in clinical and research practice.

Conclusions

The recognition and assessment of the adverse events by means of patient-reported outcomes and the treatment of adverse events are generally accepted pillars in the care of patients with cancer.

In order to obtain meaningful outcomes, the application of well-defined adverse event terminology in combination with the development of appropriate adverse event assessment, reporting, grading, and evaluation scales are needed to obtain a detailed picture of the patient status. In addition, this may contribute to an effective use of financial resources since intensive, time-consuming and long-term adverse event treatments are avoided as much as possible.

In order to achieve a systematic approach to these adverse events it is important that all stakeholders are involved in the treatment so that the targeted anticancer therapy can be continued in order to achieve best results. Stakeholders include the patient, their support system, medical specialists, nurses, data managers, skincare therapists, oncological foot care providers, pharmacists, laboratory technicians, pharmaceutical companies, insurers, government and approval authorities.

Implications for research and daily practice

Targeted therapy-associated adverse events should be approached in an integrated, interdisciplinary team model of care and in a systematic fashion. The co-care model proposed in this thesis offers a framework for this approach in which the three findings in this thesis can be embedded:

1. The development of a combined three-part patient-reported assessment and grading instrument that maps the symptoms and signs of an adverse event and their impact on health related quality of life.
2. The generation of evidence-based targeted therapy-associated adverse event treatment guideline.
3. Establishing training programs for healthcare providers especially for those involved in clinical trials and those who work on a daily basis with patients on targeted therapies is indicated.

This thesis was intended to provide an early view into a patient-driven approach to targeted anticancer therapy-associated adverse events conceptual co-care model which is expected to have future impact on improving the patients' quality of life, improving the outcome of the targeted anticancer therapy, and to lower the costs of adverse event treatment.

About the author

Curriculum Vitae

Christine Boers-Doets was born April 19th 1968 in Rheinberg, Germany. She currently lives with her husband Edwin and her three children Esmée, Danique, and Loran, in Wormer, The Netherlands.

After finishing secondary school at the Realschule in Rheinkamp, Germany, she moved to the Netherlands to complete class 4 & 5 of the HAVO in Venray. After finishing secondary school, she studied nursing at the HBO-V in Eindhoven and completed this education in 1992 in Alkmaar, The Netherlands. She received her bachelor degree in 1988 and her nursing degree in 1992. Besides being full-time employed as a nurse at the St Lucas Hospital in Amsterdam, The Netherlands, she finished her master degree in Health Sciences from 1993 to 1997 at the University of Utrecht. From 1997 till 2012 Christine has worked as clinical nurse specialist and research coordinator at the Waterland Hospital in Purmerend, The Netherlands.

In 2012 she founded the Impaqtt Foundation to be able to complete her research program with special attention to finalizing the COMTT and the BeCet trial on the one hand and raising awareness and funding for more next generation patient-driven studies and patient support projects on the other hand. In 2013 she founded her own company *Cancer*Med. She is an active member of MASCC, the Multinational Association of Supportive Care in Cancer. With her research, teaching, and mentoring she supports pharmaceutical companies, policymakers, universities, hospitals, homecare organizations, footcare specialists, and patient advocacies on how to help patients conquer cancer. Targeted anticancer therapies, inclusive endocrine therapies and immuno-oncology, have her upmost attention.

Besides being fulltime employed, Christine started her PhD journey in 2006 at the Radboud University Nijmegen, The Netherlands. In 2008, the Leiden University Medical Center (LUMC), The Netherlands became involved. In 2010, she moved her PhD project entirely to the LUMC, where she completed her PhD in 2019.