Aus der
Klinik und Poliklinik für
Hämatologie und Onkologie
der medizinischen Fakultät
der Ludwig-Maximilians-Universität
München

Direktor: Prof. Dr. med. Von Bergwelt

Comprehensive oncology research route: from immunology basic research to clinical real world studies and medical education in outpatient oncology

Kumulative Habilitationsschrift
zur Erlangung der Lehrbefähigung
für das Fach Hämatologie und Onkologie

Vorgelegt von

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2026

Dedicated to my family Milani and Brocard

Dedicated to my daughter Maria-Giulia Brühl

Dedicated to my patients and their families

Table of content

1 Summary of the cumulative project

This project recapitulates my research route in oncology. Structured in three pillars it reflects my evolution from basic scientist to clinician-educator:

1. **Basic Research** on hyperthermia's dual role in chemo/radiosensitization and immune activation via heat shock proteins.
2. **Clinical Translation** in outpatient-focused studies, including real-world NGS analysis, scalp cooling and the CAMPA nursing initiative.
3. **Education** with the LMU's first outpatient hemato-oncology curriculum, enhancing student engagement and fostering mentorship.

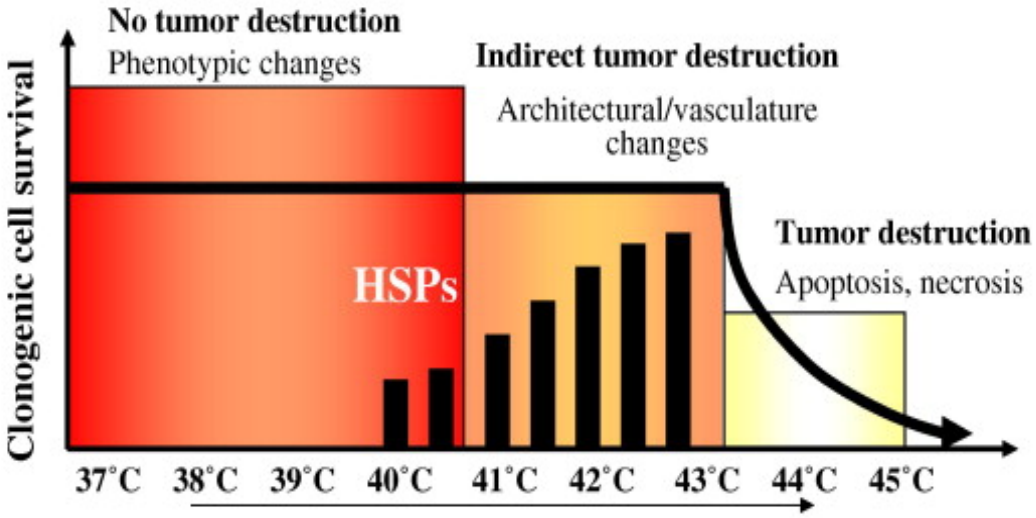
In the **first part on basic and translational research**, I summarize the pleiotropic effects that heat exposure has on tumor cells and on anticancer therapies. I describe the rationale for the application of clinical hyperthermia in the therapy of cancer based on the direct cytotoxic effect of heat and the radio-chemosensitization of tumor cells in two different cancer entities and models. Furthermore I focus on the effects of heat on the antigen presentation of tumor cells and their susceptibility to immune effector mechanisms. I describe the mechanism of antigenicity and immunogenicity mediated by the heat shock proteins, in particular HSP-70 (heat shock protein 70), in the adaptive and innate immune system in an *vitro*-model and in an experimental clinical model. The **second part is dedicated to clinical and real world research.** Here I focus on a variety of aspects of the daily practice in an outpatient setting that reflects the current health care system in Germany. Modern diagnostic methods like next generation sequencing are available and accessible to all institutions as well as cancer care devices like scalp cooling systems. I contributed to collect and analyze our experiences in the treatment of advanced cancers, on breast cancer. Furthermore, I highlight the interdisciplinary, intersectoral and multiprofessional study on nursing consultation for oral therapy for patients with gyneco-oncological cancers. **The third part summarizes the project on hemato-oncological teaching** in outpatient setting. I describe a model of online-teaching as well as tailored clerkships in the outpatient setting with mentoring program for the subspecialty in hematology and oncology. This work underscores the imperative to integrate academic rigor with ambulatory care realities, advancing precision medicine and interdisciplinary education.

2 Basic and translational research: thermal stress effects on tumor-immune interactions

2.1 Introduction

2.1.1 The rationale of clinical hyperthermia: chemo- and radiosensitization and tumor antigenicity

The primary rationale for the application of clinical hyperthermia in the therapy of cancer is based on the direct cytotoxic effect of heat and the radio-chemosensitization of tumor cells. Additional attention is given to the observation that heat and heat-shock proteins can activate the host's immune system. The expression of heat-shock genes and proteins provides an adaptive mechanism for stress tolerance, allowing cells to survive non-physiologic conditions. However, the same adaptive mechanism can ultimately favor malignant transformation by interfering with pathways that regulate cell growth and apoptosis. Cytoprotection and thermotolerance raised the concern that heat-treated tumor cells might also be resistant to attack by immune effector mechanisms. Many studies address this concern and document that heat-exposure, although transiently modulating sensitivity to cytotoxic T Lymphocytes (CTL), do not hinder cytotoxic T cell (CTL) attack. Moreover, there are promising reports of heat-related upregulation of Natural Killer (NK)-activating ligands, rendering those tumors which have lost MHC class I molecules target for NK cell attack. Heat-induced cytoprotection, therefore, does not necessarily extend protection from cytotoxic immune mechanisms. When interpreting the effects of heat, it is important to keep in mind that thermal effects on cell physiology are strongly dependent on the thermal dose, which is a function of the magnitude of change in temperature and the duration of heat exposure. The thermal dose required to induce cell death in vitro strongly varies from cell type to cell type and depends on microenvironmental factors. Therefore, to dissect the immunological behaviour of a given tumor and its micro-environment at different thermal doses, it is essential to characterize the thermosensitivity of every single tumor type and assess the proportion of cells surviving a given heat treatment.

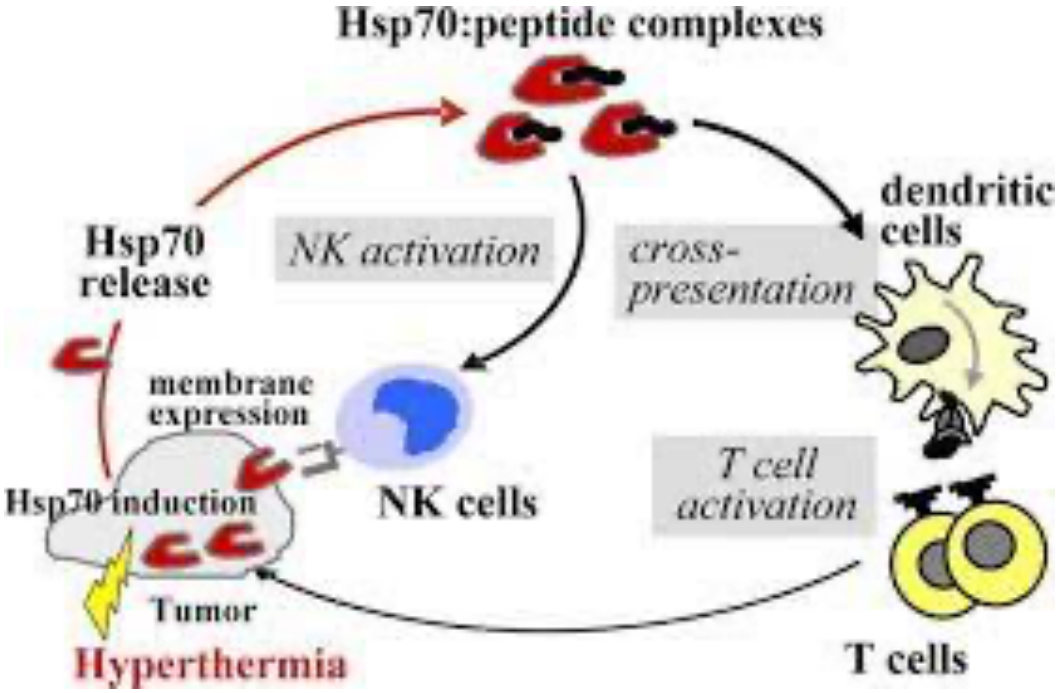


Molecular response	Cell cycle; DNA repair Apoptosis/Necrosis Induction of heat shock proteins/HSP-70 membrane expression
Clinical setting	Thermosensitisation for chemotherapy and/or radiation

2.1.2 Working hypothesis for hyperthermia: the heat shock proteins

Heat shock proteins (HSP) when released into the extracellular milieu can act simultaneously as a source of antigen due to their ability to chaperone peptides and as a maturation signal for dendritic cells, thereby inducing dendritic cells (DC) to cross-present antigens to CD8+ T-cells. HSP can also act independently from associated peptides, stimulating the innate immune system. For cross-presentation, HSP70-peptide complexes (HSP70-PC) were used from two human melanoma cell lines that differ in the expression of the tumour-associated antigen tyrosinase. Purified HSP70-PC consists of both the constitutively expressed HSC70 and the inducible HSP70. HSP70-peptide complexes purified from tyrosinase positive (HSP70-PC/tyr+) human melanoma cells, incubated with immature DCs, results in the activation of HLA-*A0201-restricted tyrosinase peptide-specific T-cells. Receptor-mediated uptake of HSP70-PC by DCs and intracellular transport are required for efficient MHC class I restricted cross-presentation of chaperoned peptides. Demonstration of HSP70-PC mediated cross-presentation of such non-mutated naturally expressed tumor antigens is of special clinical interest with regard to hyperthermia. Tumor regression and improved local control have been shown within clinical phase II/III trials integrating regional hyperthermia combined with

radiation and/or chemotherapy in multimodal treatment strategies. According to the proposed concept, local necrosis induced by hyperthermic treatment induces the release of HSPs, followed by uptake, processing and presentation of associated peptides by DCs. By acting as chaperone and a signal for DC maturation, HSP70-PC might efficiently prime circulating T-cells. Therefore, upregulating HSP70 and causing local necrosis in tumour tissue by hyperthermia offers great potential as a new approach to directly activate the immune system.



Working hypothesis for hyperthermia. *(1) Clinical hyperthermia (heat shock) upregulates HSP70 expression in tumour tissues. (2) HSP70 surface expression may occur in some tumour cells activating NK cells (3) Due to induction of local necrosis, HSP70 and HSP70-PC can be released. (4) HSP70-PC bind to APCs and induce cytokine secretion, APC activation and in parallel deliver the peptide cargo into the cross-presentation pathway for MHC class I restricted presentation and antigen specific T-cell activation.*

Milani V, *Noessner E, E, Ghose S, Kuppner M, Ahrens B, Scharner A, Gastpar R, Issels RD. Heat shock protein 70: role in antigen presentation and immune stimulation. Int J Hyperthermia 2002;18(6):563-575.*

2.2 Chemosensitization of hyperthermia in Mante Cell Lymphoma

The aim of this study was to use Mantlecell lymphoma (MCL) cell lines to investigate the potential benefit of combining clinically relevant doses of bortezomib with two different thermal doses (41.8°C/120 min and 44°C/30 min) that mimic the heterogeneity of the temperature distributions achieved within tumors during hyperthermia. Treated tumor cells were assessed for proliferation using the WST-1 assay and for apoptosis by annexin V staining, while heat shock protein (HSP) levels were determined following western blot analysis. Our results demonstrated that MCL cell lines that are sensitive to bortezomib are also thermosensitive and have low basal expression of hsp27, whereas the bortezomib-resistant MCL cell line strongly expresses hsp27 and is thermoresistant. Interestingly, pre-treatment of MCL cell lines with heat at the two different thermal doses, and the transient elevation of hsp27 and hsp70, do not impair their primary sensitivity to bortezomib. Finally, we show that the concurrent treatment of heat and bortezomib results in additive killing in MCL cell lines. In conclusion, these results suggest that the application of bortezomib, under thermal conditions, in mantle cell lymphoma cells may be beneficial and warrants further investigation.

Milani V, *Lorenz M, Weinkauf M, Rieken M, Pastore A, Dreyling M, Issels R. Combination of hyperthermia and Bortezomib results in additive killing in mantle cell lymphoma cells. Int J Hyperthermia 2009, 25:4, 262-272*

2.3 Radiosensitization in recurrent rectal cancer

Encouraging results of phase II studies combining chemotherapy with radiotherapy have been published. In this study, I report the results of a multimodal salvage therapy including radiochemotherapy (RCT) and regional hyperthermia (RHT) in preirradiated patients with recurrent rectal cancer. All patients enrolled had received previous pelvic irradiation (median dose 50.4 Gy). The median time interval between prior radiotherapy and the onset of local recurrence was 34 months. The combined treatment consisted of reirradiation with a median dose of 39.6 Gy (30.0-45.0 Gy), delivered in fractions of 1.8 Gy/day. 5-fluorouracil was given as continuous infusion 350 mg/m(2)/day five times weekly, and RHT (BSD-2000 system) was applied twice a week within 1 h after radiotherapy. The primary endpoint was local

progression-free survival (LPFS); secondary endpoints were overall survival, symptom control, and toxicity. Results: twentyfour patients (median age 59 years) with a previously irradiated locally recurrent adenocarcinoma of the rectum were enrolled. The median LPFS was 15 months (95% confidence interval 12-18 months] with a median follow-up of 27 months (16-37 months). The overall 1-year and 3-year survival rates were 87% and 30%, respectively. Pain was the main symptom in 17 patients. Release of pain was achieved in 12/17 patients (70%). No grade 3 or 4 hematologic or skin toxicity occurred. Grade 3 gastrointestinal acute toxicity was observed in 12.5% of the patients. Paratumoral thermometry revealed a homogeneous distribution of temperatures. In conclusion, radiochemotherapy combined with RHT is an efficient salvage therapy showing high efficacy with acceptable toxicity and can be recommended as treatment option for this unfavorable group of preirradiated patients with local recurrence of rectal cancer.

***Milani V**, Pazos M, Issels RD, Buecklein V, Rahman S, Tschoep K, Schaffer P, Wilkowski R, Duehmke E, Schaffer M. Radiochemotherapy in combination with regional hyperthermia in preirradiated patients with recurrent rectal cancer. Strahlenther Onkol. 2008 ;184(3):163-8*

2.4 Heat shock and tumor antigenicity in melanoma

In the present study, I address the question whether heat shock treatment has an impact on the antigenicity of human melanoma cells and their specific recognition by cytotoxic lymphocytes. The heat shock response was induced by treating the cells with two different thermal isoeffect doses, which resulted in equivalent clonogenic survival, mimicking doses achieved during clinical hyperthermia treatment of tumors. Antigen expression and immune recognition by cytotoxic T cells was studied using the human melanoma cell lines 624.38-MEL, SK-MEL23, WM115 and WM266-4, which naturally express, process and present tyrosinase and Melan-A/melanoma antigen recognized by T cells (MART)-1-derived peptides in the context of HLA-A2 molecules. We demonstrate that during the heat shock response following the two thermal doses, heat shock protein 70 (M_r 72 kDa) (HSP70) was induced with differential kinetics; tyrosinase protein and mRNA levels dissociated with a significant increase in tyrosinase protein and a decrease in transcript levels. A similar dissociation was not observed for Melan-A/MART-1. Furthermore, tyrosinase-specific T-cell recognition did not correlate with changes in HSP70 and antigen protein levels. These results suggest that caution

has to be taken when considering protein levels as a marker for the antigenic status of a tumor. Moreover, these results document the maintenance of immunological homeostasis during recovery from heat treatment, thus challenging the view that tumor cells subjected to heat shock become resistant to CTL recognition.

Milani V, *Frankenberger B, Heinz O, Brandl A, Ruhland S, Issels RD, Noessner E. Melanoma-associated antigen tyrosinase but not Melan-A/MART-1 expression and presentation dissociate during the heat shock response. Int Immunol. 2005 Mar;17(3):257-68*

2.5 NK cell immunotherapy in colon cancer

Membrane-bound heat shock protein 70 (Hsp70) serves as a tumor-specific recognition structure for Hsp70-peptide (TKD) plus IL-2 activated NK cells. A phase I clinical trial has shown that repeated re-infusions of *ex vivo* TKD/IL-2-activated, autologous leukapheresis product is safe. This study investigated the maintenance of the cytolytic activity of NK cells against K562 cells and autologous tumor after 6 plus 3 infusions of TKD/IL-2- activated effector cells. Methods: A stable tumor cell line was generated from the resected anastomotic relapse of a patient with colon carcinoma (pT3, N2, M0, G2). Two months after surgery, the patient received the first monthly i.v. infusion of his *ex vivo* TKD/IL-2-activated peripheral blood mononuclear cells (PBMNC). After 6 infusions and a pause of 3 months, the patient received another 3 cell infusions. The phenotypic characteristics and activation status of tumor and effector cells were determined immediately before and at times after each infusion. Results: The NK cell ligands Hsp70, MICA/B, and ULBP-1,2,3 were expressed on the patient's anastomotic relapse. An increased density of activatory NK cell receptors following *ex vivo* stimulation correlated with an enhanced anti-tumoricidal activity. After 4 re-infusion cycles, the intrinsic cytolytic activity of non-stimulated PBMNC was significantly elevated and this heightened responsiveness persisted for up to 3 months after the last infusion. Another 2 re-stimulations with TKD/IL-2 restored the cytolytic activity after the therapeutic pause.
Conclusion: In a patient with colon carcinoma, repeated infusions of *ex vivo* TKD/IL-2-activated PBMNC initiate an intrinsic NK cell-mediated cytolytic activity against autologous tumor cell.

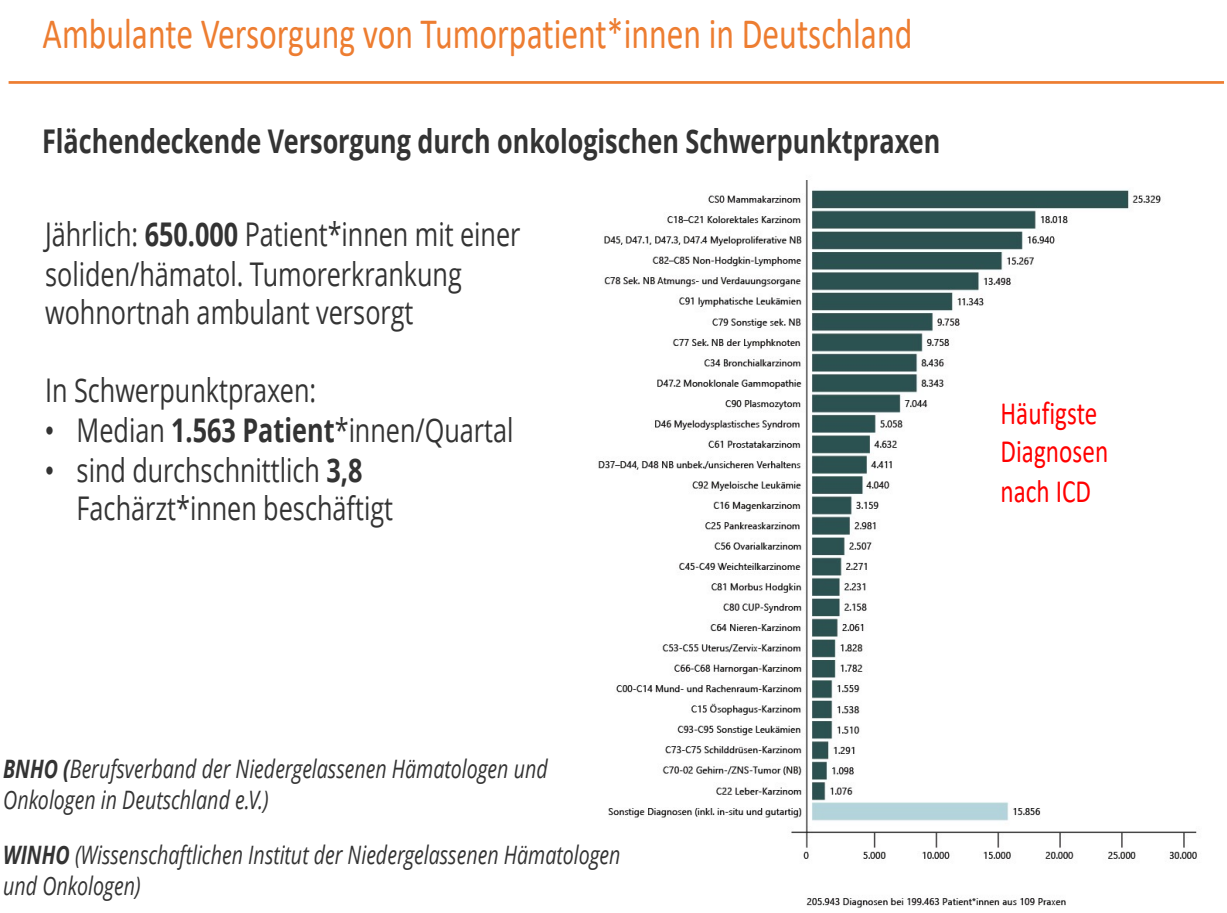
Milani V.,*Stangl S, Issels R, Gehrmann N, Wagner B, Hube K, Mayr D, Hiddemann W, Molls M. and Multhoff G. Antitumor activity of patient-derived NK cells after cell-based immunotherapy- a case report. J Transl Med. 2009 Jun 23;7(1):50.*

3 Clinical and real-world research in outpatient oncology

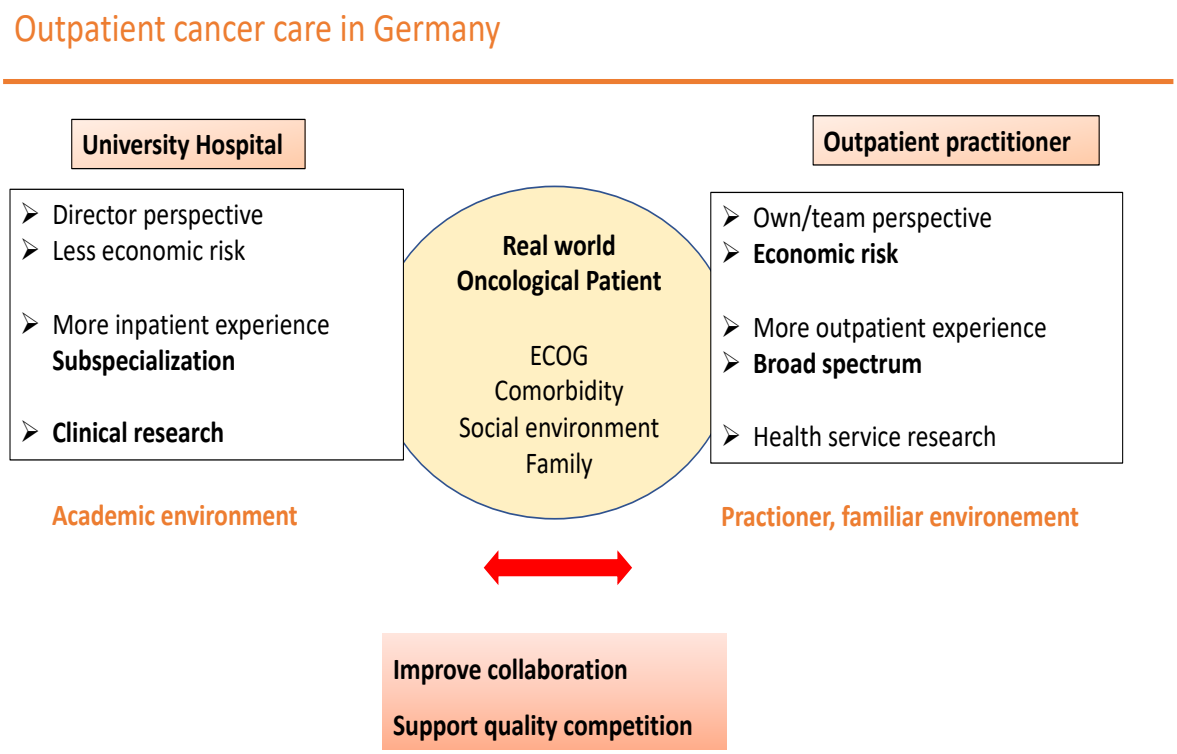
3.1 Introduction

Germany has the most expensive health care system in the European Union, due, among other things, to high costs in the inpatient sector. These costs could be greatly reduced through a stronger relocation of medicine and patient care in the outpatient sector.

Moreover, the dramatic shift of care towards ambulatory rather than inpatient setting, in particular in the field of hematology and oncology, is also due to the exponential development of new therapeutic agents that do not require hospitalization like oral targeted therapy or immunotherapy. In Germany non-academical outpatient care centers driven by oncology/hematology specialists with full reimbursement allow a nationwide, high-quality cancer care and cover about 40% of all hemato-oncological patients.



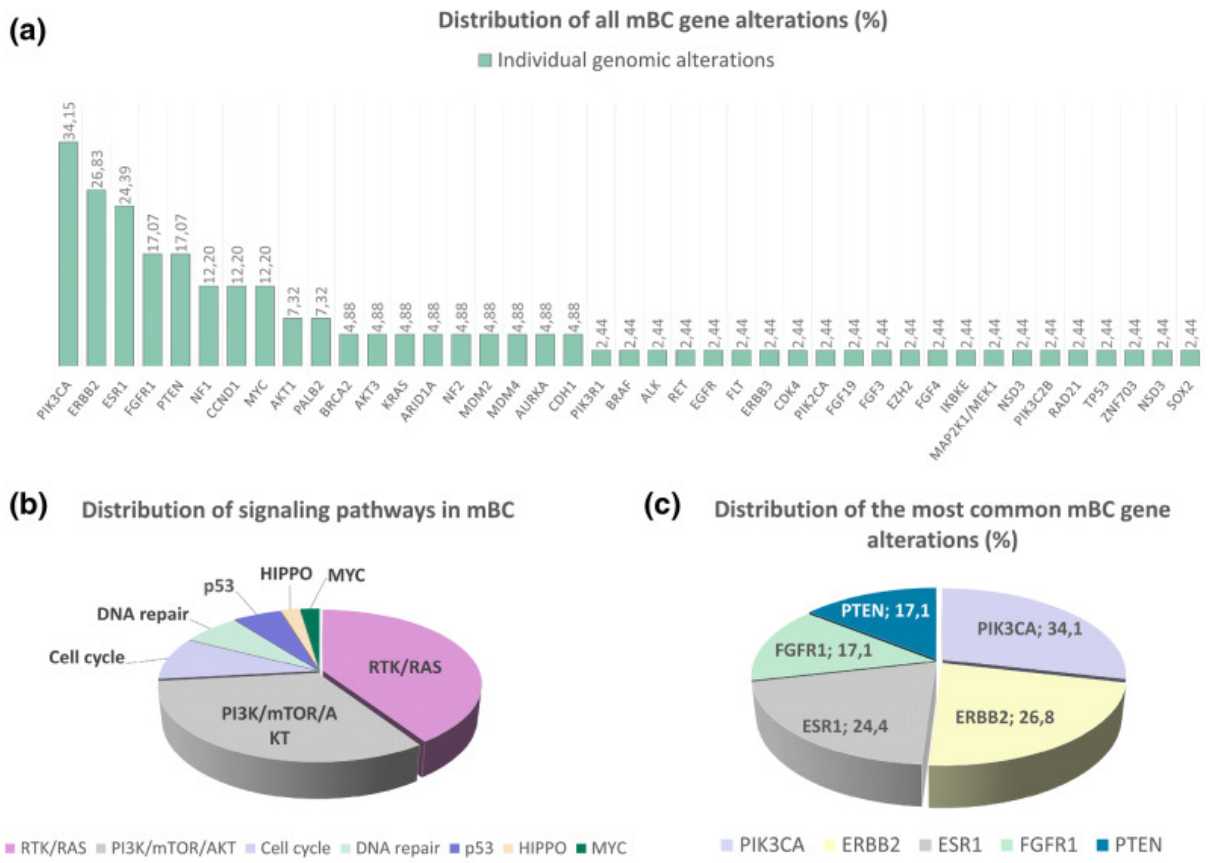
Cancer care delivery differs meaningfully between academic institutions and outpatient practices. Academic hospitals prioritize clinical research, offer highly specialized care, and operate with research funding. In contrast, outpatient providers focus on delivering accessible care to all patients—including those typically excluded from clinical trials. Strengthening collaboration and fostering quality-driven competition between these settings would enhance both clinical/real-world research and patient outcomes.



3.2 NGS in metastatic breast cancer

Next generation sequencing (NGS) together with protein expression analysis is back bone of molecularly targeted therapy in precision medicine. This study shows our experience with NGS of 324 genes in combination with protein expression in patients with advanced breast cancer (aBC). The primary purpose was to analyze the prevalence of individual genetic alterations combined with protein expression to define potential targets for an individualized therapy. Between April 2018 and September 2019, 41 patients with aBC were offered a NGS test. The test was used to detect clinically relevant genomic alterations and to support further targeted therapy decisions. Hormone receptors, ERBB2 of tumors and PD-L1 was stained by immunohistochemistry. The data was recorded up to September 2019. After prior consent 41

results were available for further analysis. The most common BC subtypes were triple-negative (n = 16), HR+/ERBB2− (n = 15), and ERBB2+ (n = 9), with one missing data of the primary tumor. 27 patients had more than one genetic alteration. The most common alterations were *PIK3CA* (n = 14) and *ERBB2* alterations (n = 11). Followed by *ESR1* (n = 10), *FGFR1* (n = 7) and *PTEN* (n = 7). 68% of the alterations were clinically relevant (tier I and II of ESCAT classification). The most common treatment recommendation was ERBB2-directed therapy (single or double blockade, trastuzumab emtansine and lapatinib) followed by alpelisib in combination with fulvestrant. Comprehensive genomic profiling combined with protein expression analysis in aBC allowed a guided personalized therapy for half of our patients.



D. Hempel, F. Ebner, Garg A, Trepotec Z, Both A, Stein W, Gaumann A, Güttler L, Janni W, Degregorio A, Hempel L, ***V. Milani.*** *Real world data analysis of next generation sequencing and protein expression in metastatic breast cancer patients. Sci Rep 2020 Jun 26; 10 (1):1045*

3.3 Scalp cooling for Chemotherapy-Induced Alopecia

The aim of this survey was to assess the efficacy and the feasibility of scalp cooling (SC) in an outpatient hematological and oncological center in a real-world setting. We prospectively monitored cancer patients from August 2017 to October 2019 receiving oncological treatments with SC, using the sensor-controlled system "DigniCap." Effectiveness was defined by a self-estimated hair loss < Grad 2 (<50%) according to the Common terminology Criteria for adverse events V4.0 or not requiring a wig. Withdrawal from SC on patient's demand was considered as failure. Tolerability and safety were also evaluated. Results: Ninety-four patients with chemotherapy for their primary (52%) or metastatic (48%) disease had a total of 634 SC sessions. SC was well accepted with increasing experience of the nurses (withdrawal for any reason 29/94). Among the female population (N = 85) 54% received a (neo-)adjuvant chemotherapy. Forty-eight percentages received a taxane-based therapy, 35% anthracycline-based, 17% platin compounds, and others. The overall success rate in the female sample was 72%. In the male group (N = 9), the majority had a metastatic disease (6/9) and received a taxane-based therapy (5/9). The rate of withdrawal by discomfort and pain was high, and the success rate was 44%. Conclusion: Our study confirms the satisfaction of patients with SC to prevent chemotherapy-induced alopecia. SC increases acceptance of the recommendation and administration of chemotherapy and decreases the degree of distress of patients and their treating physicians. Reimbursement remains a major issue in the outpatient setting.

Ergebnisse : Frauen N=85

Tumorentität	N	Alter	Abbruch	Perücke	Erfolg
Primäres BC	**38**	**54**	**12**	**10**	**68%**
Met BC	**19**	**54**	**3**	**3**	**84%**
Prim. Ovar-CA	4	60	1	3	0%
Met. Ovar-CA	5	60	2	0	67%
Gyn (Endo, Vulva)	6	70	0	1	83%
Bronchial-Ca	4	76	0	0	100%
Sarkom	3	75	3	1	*0%*
GI	2	57	1	1	*50%*
GU	1	67	0	0	*100%*
Lymphome	3	75	2	3	*0%*
TOTAL	**85**		**24**	**22**	***72%***

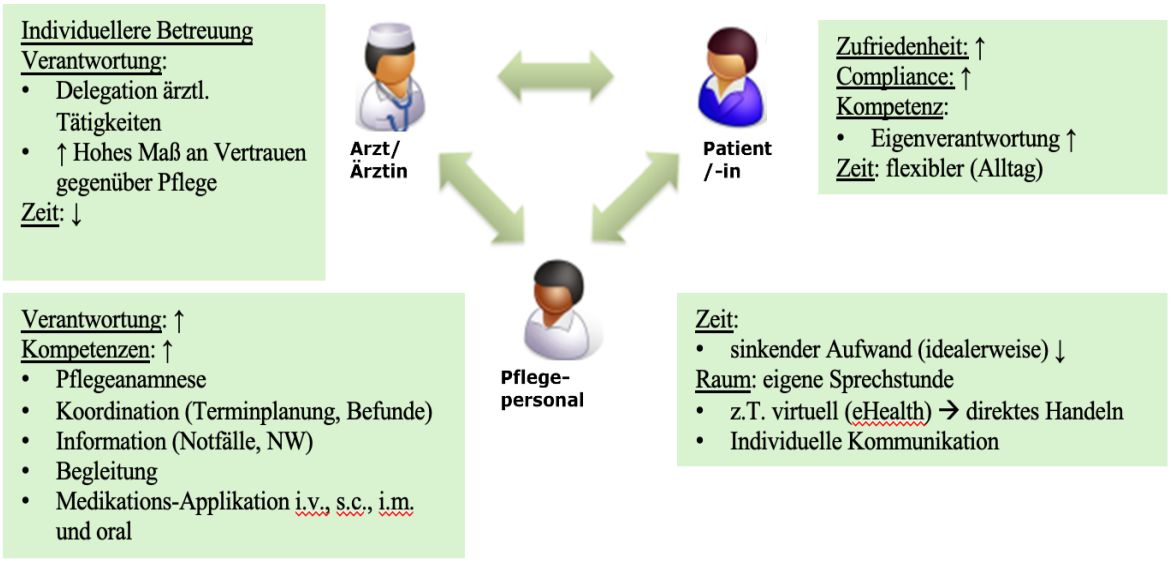
Keim et al; Oncol Res Treat 2022;45(7-8):395-399

Keim S, Hempel L, Ebner F, Retzer-Lidl M, Wohlmuth K, Hempel D, ***Milani V****. Scalp Cooling for Prevention of Chemotherapy-Induced Alopecia for Women and Men with Various Cancer Entities: A Two-Year Survey of an Outpatient Cancer Center in Germany. Oncol Res Treat. 2022;45(7-8):395-399. doi: 10.1159/000523759. Epub 2022 Feb 25. PMID: 35220298.*

3.4 Nursing consultation for oral tumor therapy (CAMPA initiative)

The increase of oral tumor therapies (OTT) poses new challenges in patient care. Within CAMPA (Care improvement for advanced or metastatic breast and ovarian cancer patients treated with PARP-inhibitors), additional nursing support for patients treated with PARP-inhibitors was developed. Methods: Additional nursing support (1 year) was evaluated in breast and gynecooncological cancer patients at an academic and a non-academic outreach center. From 02/22 to 02/24, quality of life, contacts, adherence, documentation of drug intake, hospitalization, and adverse events were evaluated, using CANKADO-ePRO and validated questionnaires reviewed by the Ethics Committee of Medical Faculty, LMU Munich. Satisfaction with care was recorded from 03/23 to 02/24. Supporting materials and interprofessional checklists were explored. Results: The collective (n = 50) included 41 patients with ovarian, 4 with fallopian tube and 5 with breast cancer. Adherence measured by continuous documentation of medication intake was high among patients (78.0%). Quality of life improved from 68.6% to 81.4%, strongly correlating with decreasing numbers of side effects ($p = 0.003$) (Spearman $|\rho| = 0.93$). Satisfaction with care was very high (4.97 out of 5 points). 94.6% agreed that nursing consultation was essential for therapy safety compared to the doctor's consultation alone ($p < 0.05$). The reduction in time and care effort was significant ($p < 0.05$), having its maximum within the first three months. In conclusion, standardized nursing consultation was highly appreciated with an important contribution to adherence and improvement in quality of life. Delegation of therapy management to nurses reduces time effort and increases their responsibility, improving interprofessional care at academic and non-academic institutions.

Neue Arbeitsaufteilung im OTT-Modell



Hirschberg L, Henze F, Paradies K, Winkler S, Schinköthe T, Haidinger R, Kates R, Hempel D, Mahner S, Kost B, Koenig A, Lippach K, Trillsch F, Theurich S, Harbeck N, ***Milani V, Wuerstlein R****. Evaluation of therapy support through a standardized nursing consultation for patients undergoing oral tumor therapy in gynecological oncology within the prospective CAMPA initiative. Eur J Oncol Nurs. 2025 Feb;74:102770. doi: 10.1016/j.ejon.2024.102770. Epub 2024 Dec 21. PMID: 39799641.*

4 Medical teaching in outpatient setting

4.1 Introduction

A stronger integration and promotion of the outpatient sector has already been stipulated in the "Masterplan 2020" and the new Medical Licensing Regulations (NKLM), planned from 2025. Several problems in teaching arise for physicians working in the outpatient sector. Long journeys for lecturers or students as well as high-cost pressure and time stress in the daily routine make it difficult to hold courses. As a consequence, students gain significantly more insights into inpatient care during their studies. The inpatient cases are often more critically ill and thus not representative of common case presentation. Furthermore, medical education in the ambulatory care setting and interaction with health professionals provides a valuable learning experience that contributes to the understanding of interprofessional practice. Thus, the evaluation of intersectoral teaching systems is important to support the development of medical teaching from university hospitals and teaching hospitals to teaching practices in oncology.

4.2 LMU-pilot project: online and bedside teaching in outpatient care

The purpose of this study was to describe the experience of online and practical medical teaching in the outpatient hemato-oncological primary care setting and to analyze challenges and chances for students and teachers in specialized outpatient institutions. The study involving medical students of the Ludwig-Maximilians-University (LMU) in their 6th-7th semester evaluates content and didactic methodology of online teaching seminars, bed-side clerkships and mentoring regarding one selected oncological center. The data was collected via questionnaires using Likert-scaled items.

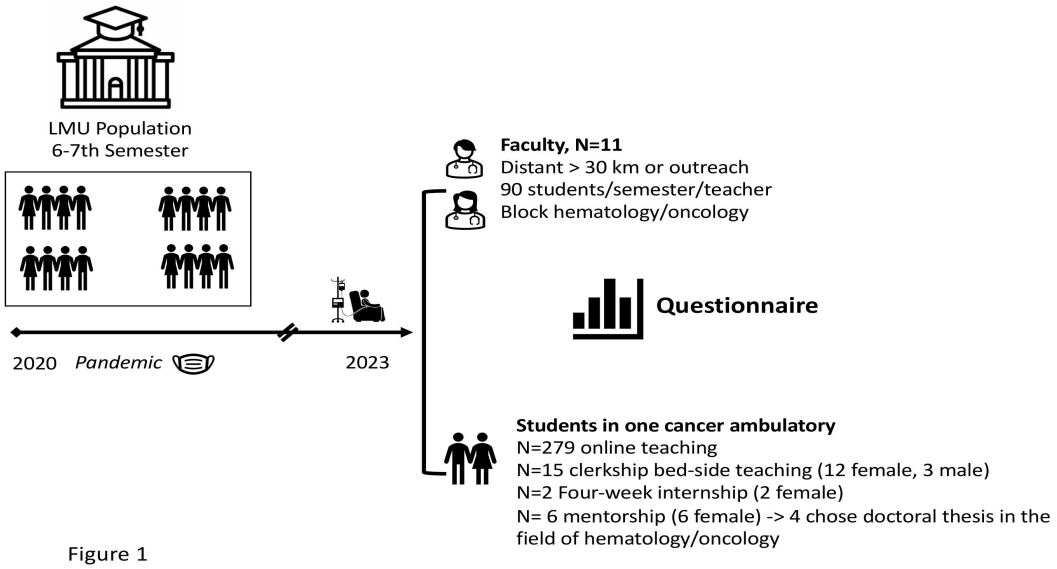


Figure 1

Our results show that in our outpatient cancer center a total of 279 students attended the online lessons (2020-2023). 102 evaluations were collected, and all aspects of teaching of the online seminars and clerkship were rated very well (mean score of 1.2 on the item "overall evaluation" with a small range of 1.0-1.3, n = 102). Criticism was mainly leveled at technical issues (n = 16). The evaluations (n = 10) of the students attending a one-day bed side teaching revealed high interest in learning the practice in the outpatient setting. 90% stated an improvement in understanding of outpatient practice as well as intersectoral processes due to the one-day bedside teaching and favored an integration of this new teaching format into the regular medical curriculum. Two students applied for a four-week internship and six chose a mentorship in hematology-oncology, resulting in four medical thesis projects in this field. We can conclude that increased participation of outpatient centers in medical education improved knowledge on outpatient medicine and interprofessional care and generated interest in the field of oncology. Outpatient cancer specialists should be more involved in the curriculum of medical students.

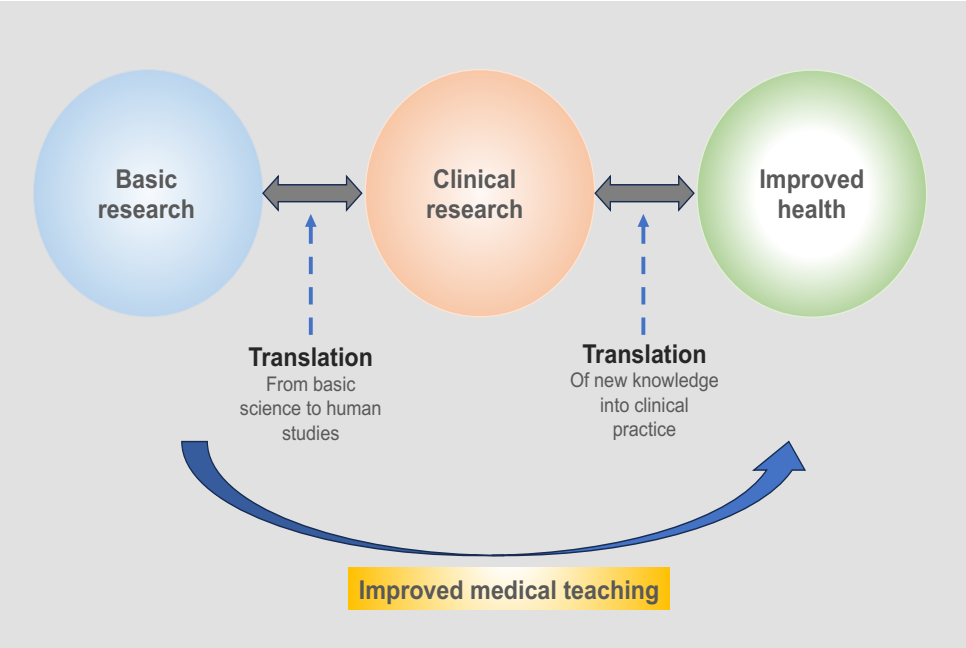
Outcome of mentoring	Evaluation of mentoring
LMU-mentees of the program LMU-Mentoring (6 th- 7th semester)	6 (6 female, 0 male)
One-day clerkship	5
Four- week clerkship	2
Doctoral thesis in hematology/oncology at LMU	4
Pursue/completion	2 (pathology, genetic)
Initiation	2 (Gyn-oncology, Leukemia)
Cancer-related area of research	
Basic research	2
Clinical research	2
Chose a cancer-related discipline for future	
Attended scientific meetings	4
Publication (congress, journal)	>2

*Forster M, Winkler S, Fischer MR, Hempel D, **Milani V**. Hemato-oncological outpatient care in medical education: a German pilot-project. J Cancer Res Clin Oncol. 2025 May 20;151(5):172. doi: 10.1007/s00432-025-06198-7. PMID: 40394330; PMCID: PMC12092479.*

5 Conclusion and future directions

The evolving landscape of oncology demands fluency across bench-to-bedside and inpatient-to-outpatient continuums. This thesis lays a foundation for such integration, advocating science that serves not only academic inquiry but also the daily realities of patients and practitioners. The modern oncologist must navigate an increasingly complex landscape—from molecular mechanisms to health system economics—to deliver equitable, evidence-based care. This habilitation thesis exemplifies the advantage of a clinician-scientist fluent in all research areas:

- Basic Science Literacy: enables critical appraisal of emerging therapies.
- Translational Agility: accelerates bench-to-bedside implementation.
- Real-World Pragmatism: ensures innovations are feasible beyond academic centers.



Such versatility transforms patient care and policy. Crucially, it also redefines mentorship.

Future Directions and final vision

1. **Mentorship Programs**
    - Establish an LMU Oncology Translational Fellowships, pairing fellows with basic scientists, outpatient clinicians, and policymakers
2. **Educational Reform**
    - Implement a mandatory outpatient intersectoral oncology clerkship
    - Develop virtual reality modules to simulate intersectoral care transitions, enhancing preparedness for ambulatory practice.

The oncologist of the future will be equally skilled in research, in patient care and healthcare systems. This thesis explores how interdisciplinary training can prepare such leaders, proving that deep interdisciplinary roots yield the broadest impact. Integrating these approaches, we can mentor a generation to not only advance science but also expand access and its benefits.

6 List of publications as first or last Author

1. Forster M, Winkler S, Fischer MR, Hempel D, **Milani V.**
   Hemato-oncological outpatient care in medical education: a German pilot-project.
   J Cancer Res Clin Oncol. 2025 May 20;151(5):172. doi: 10.1007/s00432-025-06198-7. Journal impact factor 2,7

2. Hempel D, Ebner F, Garg A, Trepotec Z, Both A, Stein W, Gaumann A, Güttler L, Janni W, Degregorio A, Hempel L, **Milani V.**
   Real world data analysis of next generation sequencing and protein expression in metastatic breast cancer patients. Sci Rep 2020 Jun 26; 10 (1):10459 Journal impact factor 3.998

3. Hirschberg L, Henze F, Paradies K, Winkler S, Schinköthe T, Haidinger R, Kates R, Hempel D, Mahner S, Kost B, Koenig A, Lippach K, Trillsch F, Theurich S, Harbeck N, **Milani V** *Wuerstlein R*. Evaluation of therapy support through a standardized nursing consultation for patients undergoing oral tumor therapy in gynecological oncology within the prospective CAMPA initiative.
   Eur J Oncol Nurs. 2025 Feb;74:102770. * equally contributed. Journal impact factor 1,6

4. Keim S, Hempel L, Ebner F, Retzer-Lidl M, Wohlmuth K, Hempel D, **Milani V.**
   Scalp Cooling for Prevention of Chemotherapy-Induced Alopecia for Women and Men with Various Cancer Entities: A Two-Year Survey of an Outpatient Cancer Center in Germany.
   Oncol Res Treat 2022;45(7-8):395-399. Journal impact factor 2,7

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8 Acknowledgement

I am deeply grateful to Prof. Rolf Issels for his loyalty and mentorship over the past two decades. My sincere thanks go to Prof. von Bergwelt, Prof. Lars Lindner, and especially Prof. Nadia Harbeck for their valuable support and guidance throughout this work. Finally, I want to thank Prof. Rachel Würstlein for her friendship and support, both professionally and personally.

Zürich, 08. Februar 2026

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