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REVIEW – CLINICAL ONCOLOGY

Research driving innovation: what are key factors for successful integration of translational science into oncology care concepts? 5th European Roundtable Meeting (ERTM) May 4th, 2018, Berlin, Germany

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Abstract

Purpose To identify key factors for successful integration of translational science into cancer care.

Results Organisation of the health care system matters to optimally bridge between public and private cancer research, cancer registries and routine care. Currently, there are deficits on various levels of connectivity. These hamper rapid and optimal transfer of innovation.

Conclusion To overcome the deficits, strategies of data sharing and infrastructures allowing fast-track implementation of translational research findings into routine care need to be developed.

Keywords Basic cancer research · Translational cancer research · Clinical cancer research · Cancer care

Introduction

The German Cancer Society (DKG) and the Union for International Cancer Control (UICC) initiated European Roundtable Meetings (ERTMs) with the goal of sharing ideas on applied strategies and best practice to identify key instruments for improving quality of cancer care. This series started in 2014. Participants from different European countries and institutions discussed health structures and transformation of the theoretical health care standards into practical approach. Further meetings described central procedures and communication networks in cancer centres including patient pathways and consideration of the patients' perspective. In the last meeting, held in 2017, a discussion was held on the needs for quality control to improve cancer (Ortmann et al. 2016a, b, 2017, 2018). The 2018 roundtable focused discussions around the interplay between basic cancer research, early phase clinical studies and large phase III trials and particularly, asking the question: How to address the challenge of translating research findings in selected patient populations to routine use for all patients? Currently, evidence-based guidelines give recommendations for routine cancer care. The evidence is ideally generated in phase III clinical studies. However, these do not necessarily reflect the routine situation and also not the representative patient population. Therefore, it is necessarily to control for acceptance of evidence-based recommendations given in guidelines and their impact on clinical outcomes. During the fifth ERTM, three major issues were identified and discussed by the participants:

1. Who or what body leads data analysis of new basic research?
2. Who or what body is responsible for the transfer and description of innovational knowledge?
3. How are outcomes fed back into basic research?

To prepare the workshop, key presentations were given on patients' expectations, a specific model to realise

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translational care in England and the role of translational centres in the health care process in Germany. These were followed by workshops and discussions that resulted in answers to the above questions.

Ralf Rambach, chair of a national network of patient support and advocacy groups, which represents 78% of all cancer patients across Germany, the Federal Association of the Haus der Krebs-Selbsthilfe, is focusing very much on the needs of the 4 million people living with cancer in Germany and the half a million that will receive a new cancer diagnosis each year.

The Association of the Haus der Krebs-Selbsthilfe sees a role for the patient voice to input into and, importantly to watchdog across multiple mechanisms with an eye on rapid uptake of innovations into routine practice, such as the assessments of oncology pharmaceuticals (Federal Joint Committee) and price negotiations (arbitration board), the certification of cancer centres, the further development of cancer guidelines and cancer registries, the updating of the social acts ("Sozialgesetzbücher") and the implementation of the national cancer plan (https://www.bundesgesundheitsministerium.de/themen/praevention/nationaler-krebsplan.html).

Major challenges to change any laws in Germany are the complexity of federalism that assigns healthcare policy to the level of federal states and the fact that the sectoral medical care system that is currently strictly divided into inpatient and outpatient care, rather than the entire patient journey. An example, says Rambach, is the assessments of the added benefit and, therefore, the reimbursement of newly approved pharmaceuticals. This frequently takes place just weeks after the approval by the EMA and is, therefore, decided often on the basis of preliminary data routine data or that from unfinished phase III trials. Dossiers are often submitted before the study ends and may lack conclusive data regarding morbidity and overall survival leading to temporary assessments and delays to a solution that satisfies all concerning parties. He would like to see a more progressive approach, rewarding companies for market approval, but with conditions attached which respond to the need for more affordable cancer treatments from a per patient perspective, expressed as six points:

1. All newly approved pharmaceuticals that enter the market with a price more than twice as high as the current standard therapy are—for a limited time frame—only allowed to be prescribed under phase III corresponding circumstances.
2. Extensive structures need to be established spanning the in- and outpatient sector that guarantee medical care for all eligible patients.
3. Data for every pharmaceutical are without exception generated following validated standard operating procedures.
4. The increased documentation effort will be payed by the health insurance companies (the system) as they will be one of the financial beneficiaries.
5. The determined data are analysed after the aforementioned time frame of the quasi phase III trial, published and used for the—retroactive—price assessment of the pharmaceutical. The price will be settled according to whether the added benefit is higher than, similar to or below the current standard therapy.
6. The pharmaceutical companies will compete with their own claims regarding the benefit of their new pharmaceutical.

Responding to questioning on the medicines focus, Rambach explained that his network is excited about working with a national industry umbrella organisation and the German Cancer Research Centre to establish a new think tank to take a full healthcare perspective and identify new areas for research. Nicolas Philippou highlighted the need for structured capacity building of national patient organisation representatives to be skilled participants in these new platforms.

Chris Harrison introduced the key concepts of the 2015-2010 Public Health England national cancer strategy to transform care delivered to all those affected by cancer and achieve world class outcomes. As an example, Greater Manchester is one of the three vanguard areas that shares learning with a further 16 cancer alliances across England based on a model of:

- Managing and directing additional transformation funding (£200 m over 2 years).
- Aligning with new service models—e.g. radiotherapy networks.

Within Manchester, there is a unique partnership between The Christie, the University of Manchester and Cancer Research UK providing a single campus and the excellence necessary for a unified strategy and setting of priorities for cancer. The coordinated leadership and budgets create a patient-facing model bringing basic research, translational research and clinical research into a clinical-academic campus which manages 14,000 newly diagnosed patients and 45,000 patients in total a year and serves a population of 3.5 Million in the Greater Manchester region. The main clinical-academic hub is connected to a devolved network of 15 hospital and community locations at which Christie staff provide specialist cancer treatments.

Giving an example of lung cancer, Harrison explained that the region served by MCRC has a high proportion (47%) of lung cancer patients diagnosed at stage IV, the second highest rate in England.

Working in close collaboration with 14 general practitioner practices the trial encouraged people to have a

low-dose computed tomography of the lungs by making these services convenient and accessible to people identified as being at high risk of lung cancer. Amazingly, 1 in 33 people screened were shown to have lung cancer, luckily, the majority (80%) at stage I or II. This successful early detection methodology is now being rolled out across all 19 alliances in England, said Harrison. In addition, our researchers are working cross discipline in a number of projects alongside private sector partners to bring research fields together for the benefit of revealing the wealth of insights that the trial data (including blood and biopsies and low dose CT scans) may bring.

The MCRC is focused on aligning research with busy clinics, fostering a mindset that everyone participates and that all data are useful. Cancer Science Teams are creating the "soil" for growing discoveries that will change cancer care.

There was a challenge from the audience about the role of industry, giving the example of France, where law prohibits university research through industry funds. Harrison explained that cancer research at The Christie has about two-thirds commercial versus public funding. Giving the example of the advanced cellular therapy centre which includes partnerships with industry, but also highlighting that the pacemaker for introduction into clinical practice is NICE—the National Institute for Health and Cancer Excellence—and following this guidance is mandatory.

Harrison went on to emphasise that the excellence at MCRC is shared with the extended referral network across the region. This currently has 15 locations in total with the MCRC oncologists regularly holding consults, chemotherapy services and multidisciplinary team engagement with ten referral clinics, community-based chemotherapy provision and provision of radiotherapy services via a network of linear accelerators at three sites including the MCRC main site (a fourth site is planned). Comprehensive cancer care, including end of life care, is therefore managed as a network at centre and regional level, explained Harrison. Harnessing the data for all in the network including patient-reported quality of life data and export of data to the cancer registry and the first steps, with the exciting potential of mining of these data with support of artificial intelligence (AI) approaches on the horizon. The next step is to harness these initiatives to publish real-time real-world outcome data on patients treated in Manchester.

Johannes Bruns presented from the perspective of harnessing personalised medicine in routine care. There is much promise for the future, but currently, this is not driving spend in the health system. In fact, a robustly built firewall is in place between the publically funded health care system and the development science space, which has multiple and largely private sector funders. In Germany, 1 billion Euro per day is spent in public health care. Spending in the private sector is less transparent, but there is no mechanism for the two segments to talk with one another, there are no processes to manage operational flow or collaboration between the two.

Realising this future requires intelligent data, team work across disciplines and inclusion of all stakeholders patients, insurers, development partners, commercial entities, cancer centres and clinicians. Patient sovereignty must be at the core of this system, which both generates evidence for routine care and hypotheses for further research as well as providing the patient with current tailored information, access to relevant clinical research opportunities, analyses and other services. We envisage a system with the patients in charge of how their data are shared explained Bruns. Within the data box, the data can be shared and added to different datasets. The patient decides who to hand over the key to his data to. In cases such as research data, the institution leading the study will also be asked for approval. For example, says Bruns trustworthy institutions can send a query to the databox, e.g. to look for possible study participants. If the patient has consented, they will be informed about new study offers or research projects and can share their data with requesting research group.

The German Cancer Society, with others, has developed a white paper proposing operationalisation of a translational mechanism between the two segments explained Bruns (https://www.krebsgesellschaft.de/deutsche-krebsgesellschaft.html). This envisages a managed grey zone between the two segments, aiming to translate new findings into routine care. This gateway will have agreed treatment protocols and data collection, decision milestones and be restricted to specific research centres or, for example, the comprehensive cancer centres and their referral networks. This targeted generation of routine data can then be provided to the GBA for approval of broader uptake.

This mechanism is already being tested in Cologne, with a population of 18 million people and approximately 10% of Germany's lung cancer patients. The Cologne led lung cancer network has a cohort of 20,000 patients that now have access to new therapies. The network has 2 years funding to reach defined milestones and report data for decision point on continuation. This is an exciting opportunity to harness innovations and drive change in the standard of care rapidly. There are historical barriers in old established systems with fixed processes. In addition, insurers are airing financing concerns, but they must be the funders of this mechanism in the future.

Summary of workshops and key take away messages

Organisation matters to optimally bridge between cancer registries, basic research and clinical research and care. Guidelines processes should be managed by professional

bodies and not be influenced by the issue of cost-effectiveness. However, they are time-consuming and lack the ability to respond well to rapidly changing fields. Marketing authorisation should be managed by a separate body. Currently, thresholds of acceptability are often not pre-set and can seem arbitrary; in addition, the clinical perspective is often not accepted due to perceived conflict of interest. These too are time-consuming and fast-track mechanisms at times raise concerns. Declaration of interests is critical and a "guidelines watch" could be a good way of ensuring transparency internationally. These deficits require attention. Key needs for optimal transfer of innovation are:

1. A foundation of data sharing and openness

To learn more rapidly from what is being done, research and funding of research need to be shaped such that questions from multiple audiences can be answered. This requires some basic precursors such as transparency of data, built on a foundation of maximised completeness and quality of data. Critical here is that all stakeholders need to be part of the definition of innovation and be motivated to accept the principles of evidence-based medicine and verification of process and outcomes by population-based datasets (Figs. 1, 2).

2. New infrastructure to fast-track translational research findings into routine care

A critical body or agency with combined financing from government as well as insurers is envisaged that builds a mechanism to harness data from cancer registries, basic research data and routine clinical practice (Table 1).

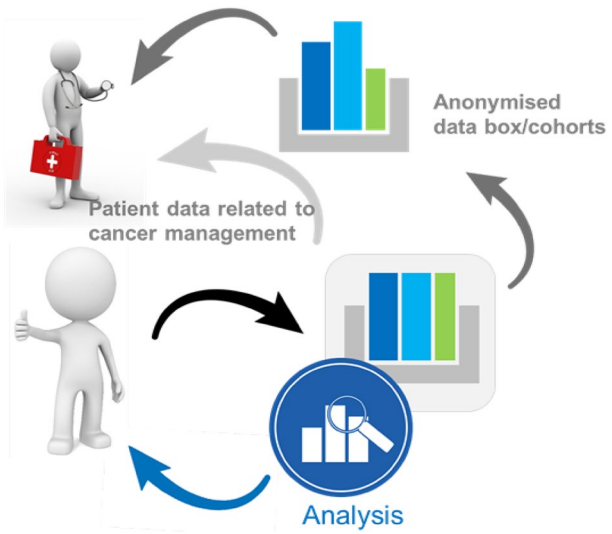

Fig. 1 Model for data flow and management

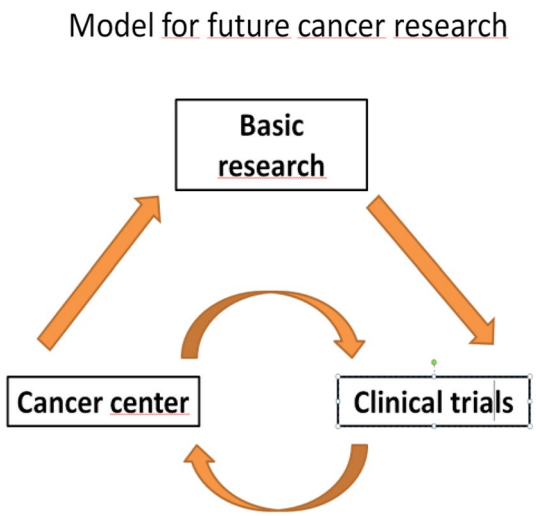

Fig. 2 Model for future cancer research

Main Tasks would be:

- Follow and interpret the change (often varying across the country).
- Define vital issues (bones of discontent), clinical dilemma's.
- Develop scenarios with implications for capacity development.

Key features are:

- Representation from all stakeholder groups.
- Independence.
- Connectivity at national, regional and local levels.
- Integrated approach, with structured and fair decision-making.
- Public cancer research funding to support financing phase IV post-approval clinical studies.
- A focus on outcomes data to compliment that of clinical trials.

Conclusion

In many national settings, despite many changes and much progress there are gaps in services and deficits in communication that are barriers to optimal connectivity between cancer registries, basic research, clinical research and cancer care. Strategies of data sharing and infrastructures need to be developed allowing fast-track implementation of translational research finding into routine care. An integrated approach is necessary to reflect data gained in routine care to basic, translational and clinical cancer research (Fig. 2).

Table 1 Physician and patient needs for fast track translational research finding into routine care

Physician-centred analysis	Patient-centred functions
Availability of cross-sectoral data	All-time availability of the data (comfort, e.g. app)
Scientific utilisation	Improved information and self-determination
Longitudinal data	Quality improvement through transparency
Rate indications, populations	Better supply of research opportunities
Quality assurance	Contribution to larger, coordinated study cohorts

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Compliance with ethical standards

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References

https://www.sciencedirect.com/journal/european-journal-of-cancer/special-issue/10CBVRJ1DGD

Ortmann O, Helbig U, Torode J (2016a) Improving cancer care in Europe: which institutional health structures might be beneficial and why? 1. European Roundtable Meeting (ERTM), 16th May 2014, Berlin, Germany. J Cancer Res Clin Oncol. 142(1):1–4. https://doi.org/10.1007/s00432-014-1906-x **(Epub 2015 Feb 3)**

Ortmann O, Torode J, Helbig U (2016b) Improving structural development in oncology: transformation of theoretical health care standards and knowledge into a practical approach—2nd European Roundtable Meeting (ERTM), May 8, 2015, Berlin. Germany. J Cancer Res Clin Oncol 142(4):807–811. https://doi.org/10.1007/s00432-015-2052-9 **(Epub 2015 Oct 19)**

Ortmann O, Helbig U, Rösler W (2017) Current developments in cancer care: including the patients' perspective—3rd European Roundtable Meeting (ERTM) June 17, 2016, Berlin, Germany. J Cancer Res Clin Oncol 143(4):673–676. https://doi.org/10.1007/s00432-016-2320-3 **(Epub 2016 Dec 17)**

Ortmann O, Helbig U, Torode J, Schreck S, Karjalainen S, Bettio M, Ringborg U, Klinkhammer-Schalke M, Bray F (2018) Quality control and improvement of cancer care—what is needed? 4th European Roundtable Meeting (ERTM) May 5th, 2017, Berlin. Germany. J Cancer Res Clin Oncol 144:1097–1102