Patient engagement in research on rare gynecological tumors

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Although patient engagement has become increasingly relevant, researchers find it difficult to involve patients, specifically in translational research. Particularly in rare disease research, patient engagement is crucial. First, since grant donors focus on common diseases, patients can support funding applications or may even initiate private funding for research on their disease. Second, patients can help set up collaborations to collect sufficient data.[1] Patients themselves can make their clinical data available for research or motivate their physicians to do so. Also, active patient engagement can identify relevant research questions from a patient's perspective. Different initiatives such as the European Network of Gynaecological Cancer Advocacy Groups (ENGAGE)[2] and the advisory group linked to the National Health Service of the United Kingdom (INVOLVE),[3] have been established to empower patient groups and propagate active patient involvement in research.

It can be challenging for patients to find appropriate information on their rare disease. Together with patients, researchers can establish centers of excellence as a valuable and reliable source of information. Currently, little has been reported on patient engagement in research in gynecological oncology.

OUR APPROACH TO PATIENT ENGAGEMENT

When discussing and having to explain the knowledge gaps to one of our patients, she and her family decided to initiate a fund to investigate granulosa cell tumors. A national multi-center study was started to collect clinical data, tissue, and blood samples for research. As part of this initiative, we aimed to actively involve patients in our research in various ways and in different phases of research (Table 1). We inform patients about the progress of the projects through newsletters and group meetings with the patient organization and in parallel with the donors. During these meetings, patients and their

Table 1 Opportunities for patient engagement in different phases of research

Research issue	Research phase	Method	Putative result
Identify knowledge gaps and clinical needs	Define research question	Direct contact with patients; Consultation of patient support groups	Define most urgent and most relevant research questions
Explore grant opportunities	Research funding	Collaborate with a patient organization; Mobilize 'influencers' among the patients	Apply for funding sources likely to fund your (rare disease) research
Review of study design and study procedures by patients	Design study	Collaborate with a patient organization; Test if the patient information folder is clear and if patients are willing to undergo the procedures	If patients approve study procedures and information, more patients are likely to participate
Update patients on the research progress and share novel insights	During the study	Meetings, newsletters	Help patients to better understand their disease; They can ask their physicians about novel treatment or diagnostic strategies
Receive feedback on study results	During the study	Meetings, questionnaires	Patients can drive the implementation of research findings into the clinic
Show results of research on a group level and brainstorm on future directions	Publication of results	Confer with private sponsors and patient organizations	Patients can help to prioritize the research agenda

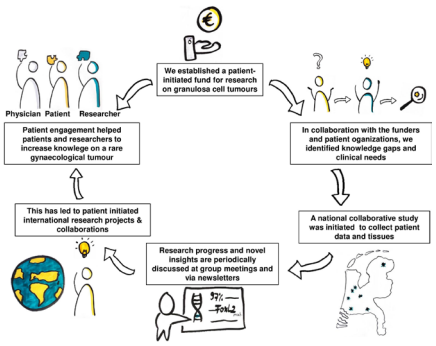

Figure 1 The concept of patient engagement in our research.

families can ask questions regarding results and new insights of the research, and the focus for future projects is discussed. In order to evaluate and improve our efforts to involve patients, we invited the members of the patient organization at one of their meetings to share their experience about involvement through a questionnaire.[4]

Patient-driven research

Active patient engagement has guided our research directions and raised novel questions. At a group meeting, members found out that they were distant relatives, which initiated a project on hereditary factors in granulosa cell tumors. We used patient international social media platforms to circulate a call for additional patients with family members also diagnosed with a granulosa cell tumor. This resulted in the identification of four affected families. Furthermore, we learned about patient concerns, for example, that having a 6-week period waiting interval between blood sampling and tumor marker results can be very stressful. Patients also appeared to be concerned about the radiation exposure resulting from repeated follow-up CT scans, even though the risks of radiation-induced cancer may be low.

Due to successful patient engagement, in particular through the patient organization,[5] more than 100 patients were enrolled in our national study within 2 years. This represents five times the annual incidence (17–20 cases) of granulosa cell tumors in our country. We experienced that patients understandably have a great sense of urgency. These patients do not want research on their disease to be a low priority and find it hard to accept that clinical breakthroughs for rare tumours take a long time. Patients appreciate being informed on all the steps in the research process, both the successes and failures, to understand the time it takes to answer research questions. To further support research, three fundraising initiatives have been undertaken by patients with the aim of setting up a sustainable funding source for granulosa cell tumor research. Frequent contact between researchers and the patient organizations also helped patients to better understand and manage their disease. Our research group provided the patients with evidence-based information on granulosa cell tumors and updated them on the latest developments in the field.

Evaluation of patient engagement

Sixteen patients responded anonymously through our questionnaire (online supplementary table 1). The majority felt they could always approach the research team. The interaction with the research group was adequate and helped to better understand their disease. Most patients would have liked to be involved even more, particularly in the implementation phase of the research and helping to translate findings to current practice. They varied in the role they would like to play, from being informed or giving their opinion or advice, to being a full partner or initiator. In general, patients felt more empowered and reassured.

SUMMARY

The interactions with donors and the collaborations with patient groups have guided our research, led to novel patient-initiated research projects, and facilitated patient recruitment and data collection (Figure 1). The evaluation of active patient engagement in our study showed that patients felt strengthened by our research and the interaction with the research team helped them to better understand their disease.

Challenges in patient engagement

The implementation of patient engagement seems to be hampered by concerns about time and costs. In our experience, patient engagement speeds up decisions and progress in research with moderate time investment. We attended meetings organized by the patient organization, answered questions from the patient group via e-mail, and sent newsletters regularly. Also, it may be difficult to translate research findings into lay terms. However, this helps to communicate results to a broader audience and to implement research findings into practice and policy. Finally, it proved to be a challenge to find a balance between our role as researcher and as (treating) physician, especially when patients asked clinical questions on their specific situation at group meetings. Both patients and researchers have to acknowledge these separate roles in different settings.

Support in rare disease research

Receiving direct private financial support can be crucial to initiate research on a rare disease. Apart from our patient's fund, another example of a private initiative is the Granulosa Cell Tumour Research Foundation which has raised more than $300 000 for research since 2004.[6] This fund started an online community of granulosa cell tumor patients and after the founder passed away, her husband returned to university to study oncology and started working in the laboratory at the age of 60, dedicating the rest of his life to study his wife's disease.

It can be frustrating to patients with a rare disease that knowledge on their disease is lacking, so they start investigating their own disease. A third-year medical student cultured his own tumor cells, recognizing his rare disease was unlikely to be investigated by anyone else.[7] To date, most scientific focus and financial resources are on common cancers. It is often assumed that advances made in these tumors would directly or indirectly benefit all cancer patients. However, rare tumors can have distinct features, such as a specific *FOXL2* mutation in ~97% of the tumors.[8] Therefore it is essential that as many different disease pathways and potential targets for treatment are studied, to advance drug discovery for all cancers.

Actions following patient engagement

We reviewed the concerns of our patients. First, improvements in the laboratory procedures reduced the waiting time for test results from 6 weeks to 3 weeks. We are also exploring other imaging modalities without radiation, such as MRI, that could potentially replace repeated CT scanning in the future and reduce radiation exposure.

Tools to increase patient engagement in research

Tools and platforms are now available to guide patient engagement. In collaboration with the European Network of Gynaecological Oncological Trial groups (ESGO–ENGOT), ENGAGe started to involve and train patients for active

involvement in various stages of clinical trials. Another successful example is the Angiosarcoma Project, which enables patients to share their clinical information and allow for the acquisition of tumor tissue samples for research by giving online consent.[1] Patients were empowered to actively help stimulate research progress by overcoming barriers in data and tissue collection.

Despite great initiatives, patient engagement is still not common practice. Cooperation between investigators and patients can be mutually beneficial, particularly in studies on rare diseases. Education on how to effectively engage patients is needed. Here we aim to provide tools for patient engagement and to motivate physicians and researchers to actively engage patients in their research.

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