Sarcoma Patients EuroNet

## Clinical Studies From A Patient Perspective.

Clinical studies are an essential step in the development of novel treatment methods for cancer and other diseases. They show researchers what works for the welfare of patients and what does not. In addition to safety and effectiveness they also determine whether the side effects of a new treatment are acceptable and, increasingly, what quality of life for patients is associated with a new therapy. Clinical studies are an important component of treatment concepts for rare forms of cancer because here the standard forms of therapy are often limited. Nevertheless, only up to 5 % of cancer patients actually participate in clinical studies. Recent studies show that 3 out of 5 phase III studies are not able to recruit the necessary number of patients. Many experts now criticize the high costs of studies, the long duration, the unrealistic design and lack of consideration for patient needs.

Please read an interview with Markus Wartenberg about clinical studies from the point of view of patients and patient support groups. Markus is the current President of SPAEN Sarcoma Patients EuroNet Assoc. – the international network of Sarcoma, GIST and Desmoid Patient Advocacy Groups.

***What are the most important aspects of clinical studies from the point of view of patients?***

This topic is an extremely important and complex one from the point of view of patient organizations. The first thing to realize is that people who are diagnosed with cancer and who become patients hardly ever know anything at all about clinical studies. Only a few of them will know what clinical studies are, how they are carried out, and what benefits and risks they have, and few are able to understand the terminology that is commonly used in clinical studies. When they are diagnosed, many patients do not even realize that the treatments they are undergoing are based on clinical studies which other patients before them participated in and which they may have benefitted from or not. Society as a whole and the health care system in particular make far too little effort to inform people about clinical research. As a result, it is quite common to encounter patients who think that clinical studies involve "experiments" and who thus refuse to serve as "guinea pigs". Or patients think that participating in a clinical trial is something you do as a "last resort"; they think that only when nothing else helps, maybe a trial will help them. And yet patient organizations have been educating patients about clinical studies for years and providing valuable support.

***As previously mentioned, many studies have difficulties recruiting patients, and only up to 5% of all cancer patients take part in clinical trials. What is the reason for this?***

For years, clinical studies have been developed *for* patients, but not developed *with* them. Unfortunately, the perceptions, needs, and reality of the patients rarely play a role in the design and implementation of clinical studies. Many researchers think they know what is best for patients, instead of involving patient groups in the early planning stages of a trial. There is no discussion of study endpoints that would be relevant to patients. A few simple factors are often the ones that determine whether a patient participates in a study or not.

During recruitment, numerous clinical trials lose many patients who would have been eligible for the trial. Studies have shown that clinical trials can have "leaks", like a water pipe, that can lead to one patient after another getting lost to the trial. One study showed that of 276 patients that were eligible for a trial, only 39 (14%) were included in that trial. The loss of patients was mainly due to three factors:

1. Awareness: 38 % of the patients were not referred to the study centres.
2. Design: 56 % were supposedly not eligible for the study.
3. Information: 49 % were not willing to give their written consent to the study.

***Does that correspond to your experience and do you have any practical examples?***

Absolutely! It all begins with finding out about a trial. Where should patients find information about clinical studies? On sites like www.clinicaltrials.gov or on the websites of pharmaceutical companies? That is completely unrealistic. Patients rely on their own doctors, or look for information in networks related to their disease at university centres or on websites, or they get information from other patients or from patient advocacy groups. In the case of rare cancers, the cooperation between patient groups, experts, and the pharmaceutical industry is particularly important. When it comes to communicating with the patients about the few studies that are available, it has to be done in a timely and easily understandable manner. Timely means not too early, for example, so as not to awaken great hopes that may later be disappointed as a result of delays. Another problem occurs when patients are referred to university centres: We have often experienced cases where even the doctors were not informed about the study or were not willing to get information about a study or to refer patients to the study centres because they were afraid they would lose their patient.

Study Design. We could talk about this topic for hours. The central question is what new findings can be expected and how can patients really benefit from the study. There are far too many trials that simply reaffirm something already known or that attempt to confirm questionable hypotheses or that are carried out for strategic, marketing-related reasons. Very often the design of the trial -- for a variety of reasons -- is far removed from the day to day reality of the clinic or from patients' needs. Or too

much importance is placed on the opinions of statisticians or of the authorities or on concerns related to the approval process or to the question of funding. Trials often entail emotional, physical, and cognitive stress for patients, a fact which should be taken into consideration in the design of the study. Particularly clinical studies for rare cancers require innovative, methodologically different approaches which are commensurate with the rarity of these diseases. In October 2014, Rare Cancers Europe, a multi-stakeholder initiative, presented a consensus paper that contains the commonly shared ideas of doctors, researchers and patient representatives. Essentially it deals with the creation of new approaches for generating evidence about rare cancers. These include the factorization of pre-clinical data, evidence, and analyses of retrospective or anecdotal cases as well as new forms of randomized clinical studies. In practice, the information provided about studies often leaves much to be desired. Some patients are recommended for studies that have no rationale for their situation. When giving their consent, patients may feel under time pressure, or may not have properly understood what the study is about or may not even be aware of the fact that they are participating in a study. A very problematic issue that persists concerns the information material available for patients. The goal of the process of informed consent should actually be that patients give their consent after having been fully informed. Yet it is unreasonable to expect that patients can be fully informed after reading page after page of text written in specialist medical and legal jargon and featuring tables and graphs that are completely inaccessible und incomprehensible to patients. In such matters patient advocacy groups provide valuable support -- which unfortunately often remains unappreciated by those who carry out the studies.

***You mentioned emotional, physical and cognitive stress for patients.***

***What exactly do you mean by that?***

It is well known that a cancer diagnosis is a great shock for patients and their loved ones. Life changes suddenly and dramatically after a cancer diagnosis. The initial shock then gives way to enormous physical, emotional, and everyday challenges. In this respect a clinical trial represents a further, new challenge to overcome.

The **emotional aspect** plays an important role here: For most patients, clinical studies are something unknown, a new territory. The patient may feel afraid, confused, and suddenly unable to carry on and to make decisions. What's more, they often are urgently in need of a solution, and invest a great deal of hope in the trial.

The **physical aspects** pertain to questions related to the way the study is organized and how the patient's everyday life can be accommodated with regard to such matters as distance, mobility, expenses, scheduling, missing work days and undergoing additional testing and examinations. There may also be new and unfamiliar side effects and changes in quality of life to contend with.

The third aspect involves **cognitive stress**. What previous experiences with studies are there? What image does a therapy have in the market or in its use for other indications? What is the relation between risks and benefits? Another issue is the patient's worry that he or she will be assigned to the placebo arm or will receive a "non-innovative" therapy. Patients also often wish to have contact with other participants in the trial. There is also the important question: If the new medication works for me, how long will I be able to take it? These questions and many others must be taken into account in the design and implementation of clinical studies.

***Which approaches do you think could lead to better, more patient-centred studies and higher participation rates?***

As previously mentioned, the solution lies in closer cooperation, i.e. in developing studies from the perspective of the patient and in close collaboration with patient organizations. I'd like to address my appeal to two groups: On the one hand, doctors, principal investigators, researchers, and representatives of the pharmaceutical industry are called on to involve patient representatives in the early stages of a study and to make use of their knowledge. On the other hand, patient groups and patient support groups should be emboldened to demand involvement in clinical research, and to become involved in a competent way, and to educate themselves. Some initiatives have already been launched for patients to learn more and to educate themselves, such as the European Patients Academy on Therapeutic Innovations (EUPATI) or the new independent courses offered by the West German Tumour Centre in Essen, starting in 2017. We urgently need patient advocates to be involved in clinical studies, not as researchers, but as patient representatives who are well acquainted with the reality of the patients' situation.