Patient Involvement in Clinical Trials

RCE-ESMO-ESO Training Course for Rare Cancer Patient Advocates

Jan Geissler, Markus Wartenberg
LOGISTICS FOR THIS SESSION

• All questions should be addressed via the chat box only. We will also take questions and comments from the floor during the discussion time. Please use the ”raised hand system” in Zoom.

• We kindly request to put your camera on during the discussion time.

• For any technical issues, please send us an email at: rarecancerseurope@esmo.org and we will get back to you.

• The above information will also be posted in the chat box, so everyone is aware.
Agenda of today

- What is a clinical trial?
- What input can patient advocates provide into clinical trial design and conduct?
- (Why should +) How can patient advocates be more involved in clinical trials?
- Discussion

Jan Geissler
WECAN, EUPATI, Patvocates

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SPAEN Sarcoma Patients EuroNet
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Disclosures Jan Geissler

- Contributions to IMI-funded EU consortium projects HARMONY and EUPATI by EFPIA companies

- Support for Community Advisory Boards (CABs) provided by Amgen, Alexion, Celgene, Incyte, Janssen, Jazz, Novartis, Pfizer, Servier and Takeda

- Advisory roles and consultancy on patient engagement to Amgen, Alnylam, Bristol-Myers Squibb, Bayer, Biomarin, Janssen, Novartis, Pfizer, Roche, Servier, Takeda, UCB
What is a clinical trial, and how can patient advocates provide input?

Jan Geissler
Workgroup of European Cancer Patient Advocacy Networks (WECAN)
European Patients’ Academy (EUPATI)
Patvocates
What is a clinical trial?

- A clinical trial is a clinical study in which (human) participants are assigned according to a pre-defined therapeutic strategy or plan (protocol) to receive a health-related intervention, such as a medicine, in order to investigate its effects on health outcomes, usually compared to another (or sometimes no) treatment.

- Clinical trials are used to evaluate clinical practices that do not fall within the current practices, or to evaluate a new medicine (investigational medicinal product).

- Clinical trials are used to generate data on the safety and efficacy of the intervention.

- Clinical trials are conducted only after a regulatory authority approval and ethics committee review.

Source: EUPATI.eu
In medicines development, of 8,000 molecule candidates, only 5 ever get into human clinical trials, and only 1 makes it to market.

It takes over 12 years before a new medicine can be made available to patients and reimbursement starts.

Only about 2% of substances evaluated in early research make it to the market as new medicines.

Source: EUPATI.eu
Phases of medicines research & development

- Computer-based modelling
- "In vitro" (in the petri dish) and animal testing
- "In vivo" (in humans)
- Regulatory phase
- Market access, reimbursement and surveillance

Source: EUPATI.eu
In different phases of clinical trials, dosing, safety and efficacy are tested in an increasing number of patients.

Phase I trials:
First-in-human, dose, toxicity, therapeutic effect
In different phases of clinical trials, dosing, safety and efficacy are tested in an increasing number of patients.

**Phase I trials:**
- First-in-human, dose, toxicity, therapeutic effect

**Phase II trials:**
- Therapeutic effect, optimal dose, toxicity

Source: EUPATI.eu
In different phases of clinical trials, dosing, safety and efficacy are tested in an increasing number of patients.

**Phase I trials:**
First-in-human, dose, toxicity, therapeutic effect

**Phase II trials:**
Therapeutic effect, optimal dose, toxicity

**Phase III trials:**
Large multicentre comparative studies on safety and efficacy of the new medicine compared to standard medicine. Goal: market authorization.

Source: EUPATI.eu
If results of Phase III study show an acceptable benefit-risk ratio, a Marketing Authorisation Application (MAA) is submitted to the Regulatory Authority (e.g. EMA) containing all non-clinical, clinical, and manufacturing) known to date. The review process usually takes 12-18 months.

Then, many countries require an assessment of value, clinical effectiveness or cost effectiveness to decide on reimbursement (often called Health Technology Assessment).
After regulatory approval decision, late-phase trials optimize therapy and collect more (safety) data.
(Why should +) How can patient advocates be more involved in clinical trials?

Markus Wartenberg
SPAEN Sarcoma Patients EuroNet (www.sarcoma-patients.eu)
Deutsche Sarkom-Stiftung / German Sarcoma Foundation (www.sarkome.de)
NCT Essen-Cologne (CCCE, WTZ Patient Advisory Board)
Declaration of Interests

2019 - 2021:
- No direct or personal payments from researching industry
- No consultancy or financial research relationships

Sustaining Partnerships, grants, project-sponsorships or honoraria only directly to the organisations:
- SPAEN Sarcoma Patients EuroNet e.V. (since 2009)
- German Sarcoma Foundation (since Jan. 1st, 2020)
**Prevention and screening mostly irrelevant**

**Late or incorrect diagnosis**

**Lack of information and patient groups**

**Widespread, small populations of patients**

**Shortage of local medical expertise**

**Incomplete registries and tissue banks**

**Methodological barriers (in traditionally-designed clinical trials)**

**Not enough clinical trials for rare cancers**

**Regulatory barriers**

**Reimbursement challenges for treatments**

**Inequitable access to therapies and care**

**Stigma**

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**Rare cancer (five year relative) survival is worse at 48.5% than common cancer at 63.4%.**


With kind approval from Kathy Oliver, IBTA
K. Oliver: Some of the Challenges of Rare Cancers…

Prevention and screening mostly irrelevant
Late or incorrect diagnosis
Lack of information and patient groups
Widespread, small populations of patients
Shortage of local medical expertise
Incomplete registries and tissue banks
Methodological barriers (in traditionally-designed clinical trials)
Not enough clinical trials for rare cancers
Regulatory barriers
Reimbursement challenges for treatments
Inequitable access to therapies and care
Stigma

Several of these challenges have directly or indirectly to do with deficits in cancer research!

With kind approval from Kathy Oliver, IBTA
Engagement of Patient Groups in Clinical Research...

In Germany today: Only rarely in Oncology...

Clinical studies: Basic knowledge (information transfer)
Publication of current or planned trials
Making studies more understandable to patients
Supporting the recruitment e.g. in rare "subtypes" or reg. spec. mutations
Patient Groups & Clinical Trials
Cooperation with information / education “Informed Consent”
Quality of Life Aspects
Publication/ dissemination of study results
Research- Involvement???
In a very early stage in Germany...
Why “Patient Involvement in Clinical Research”?
And why should patient advocates be interested in?

The meaning of medicine & health care
>>> support to / benefits for people!
Patients (relatives) must be the focus – they are the real "customers“

- Everyone can be a patient / relative tomorrow (including doctors, researchers, politicians!)
- Patients = are a cross section through our society
- Patients are citizens, voters, taxpayers, contributors!!! They/We have rights to be involved, to be listened to!

Patients bear the ultimate risk in clinical trials:
The "risk for their lives" – through e.g.

- new drugs in clinical trials
- wrong research questions
- inappropriate study designs
- missing / insufficient information
- delays in research & development
- lack of access to therapies due to cost…
- etc.

Patients know best – what it means to have a disease, to live with a special condition!

- Patients are the real experts!
- The views of doctors and patients can differ
- Rare Cancers: Patients often know more than their doctors
- Patient Groups have access to the very first source of information – to the patients / relatives
- New field: Personalised medicine / precision oncology…
Increasing criticism of the “old” study system…

- Focus on the patient: often ignored / neglected
- Results of Clinical Trials: often far away from real life and real needs
- Over 1 million studies published worldwide: Some experts complain: 85% are useless, waste of money
- A lot of resources are spent into: Doing things right – instead of – doing the right things
- Challenges with Clinical Trials in Rare Cancers: By definition - clinical evidence - is more difficult to build in rare than in frequent cancers…
- Difficult: Gaps between FDA/EMA approvals and HTA
- Often research is driven by company objectives, financial interests, academic reputation/careers/publications, research funds, utilization of study units, etc.

Why Most Clinical Research Is Not Useful

John P. A. Ioannidis 1, 2

1 Biostatistics and Computational Biology, Memorial Sloan Kettering Cancer Center, New York, New York, USA
2 Department of Epidemiology and Biostatistics, Weill Cornell Medical College, New York, New York, USA

Why most published research findings are false: Ioannidis JP, Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece

‘Clinical Trials System is Broken,’ FDA Drug Chief Says

Annals of Oncology

Rare Cancers Europe (RCE) methodological recommendations for clinical studies in rare cancers: a European consensus position paper
Trying to describe a vision…

Clinical Research is not an end in itself! Ultimately, it
◼ should benefit patients and the society,
◼ must lead to more effective > better (more affordable) therapies >
◼ thus to increased knowledge and benefits/values.

“Patient Involvement in Clinical Research” is the permanent dialogue with the patient and her/his relatives (i.e. the real customer). It is a partnership process between patients (s. t. expert-patients) and researchers / medical professionals >>> to bring questions, insights, experiences, wishes, preferences, real life information of/from patients early on in the R & D Process. This is done on a peer to peer level and with the common goal – to conduct research faster, more efficient, more target-/patient-oriented – closer to real life and of higher quality!
Early Patient Involvement in Clinical Research... 

In the future: 
Doing research with or through patients – instead of doing research only for patients or about them...

• Research = better - faster – more efficient and more meaningful = closer to real life / to real needs
• studies = part of cancer treatment and part of the patient experience
• better recruitment
• change of scientific culture
• more public confidence in research

Patients are only participants in clinical trials (subjects of research)

Collaboration e.g. with patient groups to share/to disseminate information and knowledge

Patient Experts are early and actively involved in studies and research projects

Patients & Experts/Researchers are Research Partners

Partnership

Engagement

Participation

Involvement
Patient involvement in clinical development in practice

- **Research Priorities**
  - High expertise in disease area required
  - Setting research priorities: gap analysis, early horizon scanning, matching unmet needs with research, defining patient-relevant added value and outcomes
  - Protocol synopsis: design, target population
  - Protocol design: relevant endpoints, PRO, in-/exclusion criteria, diagnostic procedures, patient-reported outcomes/QoL measures, benefit/risk balance, ethical issues, mobility issues/logistics, data protection, adherence measures
  - Trial Steering Committee: protocol follow up, improving access, adherence
  - Information to participants: protocol amendments, new safety information
  - Investigator meetings: trial design, recruitment challenges, opportunities, can trigger amendments
  - Data & Safety Monitoring Committee: benefit/risk, drop-out issues, amendments

- **Trial Design and Planning**
  - Trial Design and Planning: research priorities, trial design, protocol amendments, new safety information, investigator meetings, data & safety monitoring committee
  - Regulatory Affairs: MAA evaluation, EPAR summaries, package leaflets, updated safety communications, lay summary of results

- **Trial Conduct and Operations**
  - Patient Information: content, visual design, readability, language, dissemination
  - Ethics Review: content, visual design, readability, language
  - Informed Consent: content, visual design, readability, language
  - Study Reporting: summary of interim results, dissemination to patient community
  - Post-Study Communication: contribution to publications, dissemination of research results to patient community/professionals

- **Market Authorization and Post-approval**
  - Assessment of value: patient-relevant outcomes, patient priorities

- **Fundraising for Research**
  - High expertise in disease area required
  - Medium expertise in disease area required
  - Contractual issues, travel expenses, support for family members, mobility

Patient involvement in trial protocol design in practice

Increase patient relevance, patient value, and patient-relevant outcomes with input on
- Patient priorities in risk/benefit
- Patient-relevant endpoints
- Choice of QoL/PRO instruments
- Inclusion/exclusion criteria (“real-world”)
- Mobility / logistics
- Drug administration
- Diagnostics (frequency, necessity)
- Ethical aspects (e.g. cross-over)

Setting research priorities

Protocol synopsis

Protocol design
- relevant endpoints,
- PRO
- in-/exclusion criteria
- diagnostic procedures
- patient-reported outcomes measures
- benefit/risk balance
- ethical issues,
- mobility issues/logistics,
- data protection
- adherence measures

High expertise in disease area required

Research Priorities

Trial Design and Planning

Medium expertise in disease area required

Practical Considerations

Patient Information

Informed Consent

Ethics Review

Study Reporting

Post-Study Communication

Health Technology Assessment

Market Authorization and Post-approval

Regulatory Affairs

Fundraising for research

Increased patient relevance, patient value, and patient-relevant outcomes with input on
- Patient priorities in risk/benefit
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Some aspects for “rare cancer patient organisations”…

“Patient Involvement in Clinical Research”…means…

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
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<tbody>
<tr>
<td>Enormous opportunities for change</td>
<td>To understand how research works and which language is spoken = Basic Research Training!</td>
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<td>Close peer to peer cooperation with experts, researching companies</td>
<td>To prepare your organisation to be part of the research process…</td>
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<tr>
<td>and other stakeholders</td>
<td></td>
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<tr>
<td>General changing mindset, that this topic is a core success factor</td>
<td>To understand that countries are differently developed on this topic. E.g. UK has a history in cancer for more than 20 years…</td>
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<tr>
<td>for research and not just a nice PR idea</td>
<td>(maybe) to unite with other patient organizations to make general progress on the topic…</td>
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Discussion & questions

- In your country: Do you see a changing mindset of medical experts/researchers to involve patients/patient advocates in clinical trials / in clinical research?
- What are the main challenges you experienced as patient advocates in engaging in the design and conduct of clinical trials?
- What are the specific challenges of rare cancers when engaging in clinical trials?
- If you engaged in clinical trials design or conduct, where was your engagement as a patient advocate in clinical trials most effective?
- Do you feel well prepared, well trained to take part in such project?

Use Zoom “Q&A” and/or “Raise Hand”