How can patients be involved in protocol development?

Denis Lacombe, MD

Director, EORTC HQ

Brussels, Belgium

This presentation has to be interpreted with the fact that it is given by a professional and therefore can only represent one sided point of view

Clinical research is complex..

- It is multidisciplinary and the various actors do not necessarily have the global understanding and have varying interests and needs
- Patient representatives may be seen just as an additional stakeholder
- Important to balance the respective role of each in an ever growing complexity of the field

Patients and public

	Individual ethics	Collective ethics
Clinical question	Patient own interest	Benefit to a larger community/public health
Protocol design	Accepting risks i.e. being randomized to a placebo	Not taking risks for solving questions which could benefit future patients
Trial conduct	Personal involvement in making a certain trial happening i.e. contributing to the optimisation of the PIS/IC	On going follow up such as PRO, addressing patient compliance
Recruitment	Providing information on specific trials	General training on clinical research

Defining the clinical questions

What is the relevance of the protocol?

- Is it the right question to address?
- Is it a patient oriented question?
  - Treatment optimisation
  - Treatment de-escalation
  - QoL , symptoms control..
- Is it a drug development question?
  - Is it compatible with a patient oriented question
- Is it a trial purely designed to learn?
  - Document biology, mechanism of action…
- Is it a changing practice trial?

Protocol design

Insights into the methodology

- Relevant end-points: PFS, OS, QoL, RR, rate of events at a certain time point..
  - Hard end-point at the light of QoL
- Meaningful difference
  - Probably disease specific
- Management of toxicities
  - Early trials
- Reference arms: observation, placebo, cross over, registered control or pragmatic control, several control arms
- Frequency of treatments, visits and follow up: protocol burden

Trial conduct

Protocol operations

- Development of study specific tools such as PIS/IC, trial leaflets or questionnaires and their cultural and language customization
- Addressing patient compliance to protocol
- Improving patient adherence to treatment
- Ensuring adequate reporting of side effects /PRO

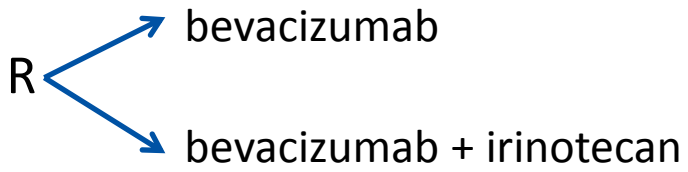
Trial recruitment

Patient access

- For potential trial subjects
  - Supporting the understanding of a clinical trial
  - Placing a given protocol in the context of the overall disease management
  - Explaining the risks and benefits
- For general patient population and public
  - Explaining the need of clinical research
  - Providing information on patient rights and benefits
  - Placing clinical research and medical practice in perspective

Things may not necessarily be clear cut…
The example of Bevacizumab in glioblastoma

- Bevacizumab development in advanced glioblastoma:



PFS6: 42.6% vs 50.3%
mOS: 9.2 vs 8.7 mths

"conclusion: bevacizumab, alone or in combination with irinotecan, was well tolerated and active in recurrent glioblastoma"

Friedman HS et al. J Clin Oncol.2009;27(28):4733-40.doi:101200/JCO.2008.19.8721

- And few studies single arm, single agent or in combination
- Difficulties for conclusion
  - No prospective randomized study with no bevacizumab arm
  - Issues with imaging interpretation
- Rejection by EMA

Remaining questions for bevacizumab in glioblastoma

- Optimal timing for use of bevacizumab is unknown
- Is there a subgroup that may derive a specific benefit?
- Is there any interest for combination with CT?
- Impact on QoL and neuro-cognitive functions

- Need to address these questions in prospective trials has been slown down due to compassionate program use in part supported by patient groups
- New trials are now on going but with some years of delay

Additional contributions

- Simplify and harmonize regulatory frameworks
- Facilitate tissue research
- Streamline data exchange
- Support new forms of research
- Stimulate dialogue with ethical review boards and competent authorities