Brussels 10 2 2012

Consensus Recommendations on Improving the Methodology of Clinical Research on Rare Cancers

Organizational and regulatory aspects of clinical studies in rare cancers

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EORTC

Conticanet

Topics

- Networks
- Diagnosis
- Banking- Tumor samples
- Trial incentives
- Datasharing
- Collaborations
- Interactions withe regulatory bodies

Networks and PAGs

- Health care Networks
  - with quality control programs

involving

- Reference centers, within quality control programs. They improve health care and they improve accrual in trials as well as clinical quality within clinical trials.

- Patient information about expert centers and clinical trials.

Pathology review !

Brussels 10 2 2012

Rate of concordance by patient sub-group

188
Second opinion requested

- **53 (28%) Total discordance**
- **53 (28%) Partial concordance**
- **82 (44%) Total concordance**

178
Second opinion not requested

- **17 (10%) Total discordance**
- **44 (25%) Partial concordance**
- **117 (65%) Total concordance**

For 56 % the diagnosis is not totally correct

For 35 % the diagnosis is not totally correct

Sciencexpress Research Article

The Consensus Coding Sequences of Human Breast and Colorectal Cancers

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- Breast or colon carcinoma: cell lines oru xenografts (n=22)
- 13023 genes sequenced, 3 millions PCR, 452 MB
- otal : n=90 mutated genes per cell lines
- Identification of n=189 significant genes
- Mean: n=11 (total genome n=14 à 20)
- Transcription, adhesion, invasion
- CANdidates CANcer (CAN) genes
  - « Expected »: p53, KRAS, APC, MRE11…
  - Oncogenes for other tissues : MLL3, EPHB6..
  - Unexpected: PKHD1, tubuline tyr ligase TTLL3
- CAN genes C. du sein ≠ C. colorectal

Tumor banking and registries

- Tumor banks
- Facilitating the donation of tumor tissues across countries
  - Less specific informed consent
  - useful for advancing science
  - Economic value (competition with Far east)
- Linked with prospective clinical data bases and registries
- Within collaborative networks focusing on health care
  - properly funded for quality of care reasons,

Menu

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- Survey
- Export
- Patient
- Audit
- Online Help

Welcome to conticabase

The CONTICANET database and tumour bank

This database contains anonymised information describing the tumour, treatment and follow-up as well as tumour sample availability and molecular biology analyses for mesenchymal tumours except GIST and bone tumours.

The tool can be used as a local center database thanks to its **rules for access to patient data and material**. It will be maintained and updated centrally. Please follow this **this link** to fill the account application form

The query tool allows users to ask questions about the overall content of the database in order to evaluate the feasibility of specific collaborative studies.

We hope this database will become an important tool for increasing our knowledge on these rare tumours and for developing joint research programmes.

Website requirements

This website has been designed for both **Firefox 3** (advised) and **Internet Explorer 7** (or older versions). Please note that some features may not work correctly with other web browsers.

Content overview

conticabase currently contains the following data from **26** out of the **43** registered centres :

- **4804** Patients
- **4826** Tumours
- **5699** Samples (**5493** Paraffins and **2600** Frozens)

Clinical trials

- Enrich the informations collected from Rare cancer trials need to be richer in information in order to maximize their efficiency, e.g. a long follow up for each patient.

- Observational clinical studies on selected patient subgroups
  - natural history and clinical characteristics
  - tailored to answer specific open questions
  - value of retrospective and observational research
  - research resource allocation decisions.

Incentives for clinical trials

- Incentives for orphan drugs devpt for pharma companies
- Drug supply by pharma to academics before any approval?
- Screen rare tumors in Phase 1 setting
  - based on molecular screening
  - screen new drugs also in rare cancers
- A need framework study protocols on specific rare cancers liable to be sequentially exploited for different drugs ?

Sharing information from trials

- Share the results of the trials including industry sponsored trials in..
- Large multisources databases, Metabases, Registries
  - Funding issues
- Collaboration between pharma companies
  - Comparing drugs in tumors with unmet needs
  - Combining drugs

Collaborations

- In rare cancers, national, international, even global collaborations should be pursued to make investigator-driven studies possible.
- Clinical Trial Directive is currently under revision. It is recommended that it is improved in some crucial aspects.
- Sponsorship of international trials for investigator-driven studies
  - difficult to comply with regulations which differ from country to country,

A World Sarcoma Network is needed

Conticanet AUSTRALASIAN SARCOMA STUDY GROUP GSF GETO EORTC European Organisation for Research and Treatment of Cancer SARC Sarcoma Alliance for Research through Collaboration Collaborating for a Cure. GISG German Interdisciplinary Sarcoma Group EuroBoNeT

The World Sarcoma Network (2009)

Studies pipeline

- nilotinib in PVNS with t(1,2) M-CSF-col6A3 fusion gene
- mTOR inhibitors in PEComas, and in tumours of the TSC complex
- Aplidin in Dedifferenciated Liposarcomas with JUNK overexpression
- Alk inhibitors in inflammatory myofibroblastic tumours with Alk amplification and over expression
- IGF1R inhibitors in GIST with IGF1R over-expression and amplification
- MDM2 inhibitors (nutlin3a) in WDLPS with MDM2 amplification
- MET inhibitors in sarcomas with translocation involving fusion genes encoding for abnormal transcription factors (ASPS, CCS)
- VEGFR2 inhibitors in ASPS

Regulatory aspects

- Major bottlenecks to investigator-driven wide collaborations in the Regulatory fields
- A need for regular consultations between regulatory bodies, pharma, academia, scientifc societies-ESMO, and PAGs
- Simplify and streamline the access to compassionate use programs

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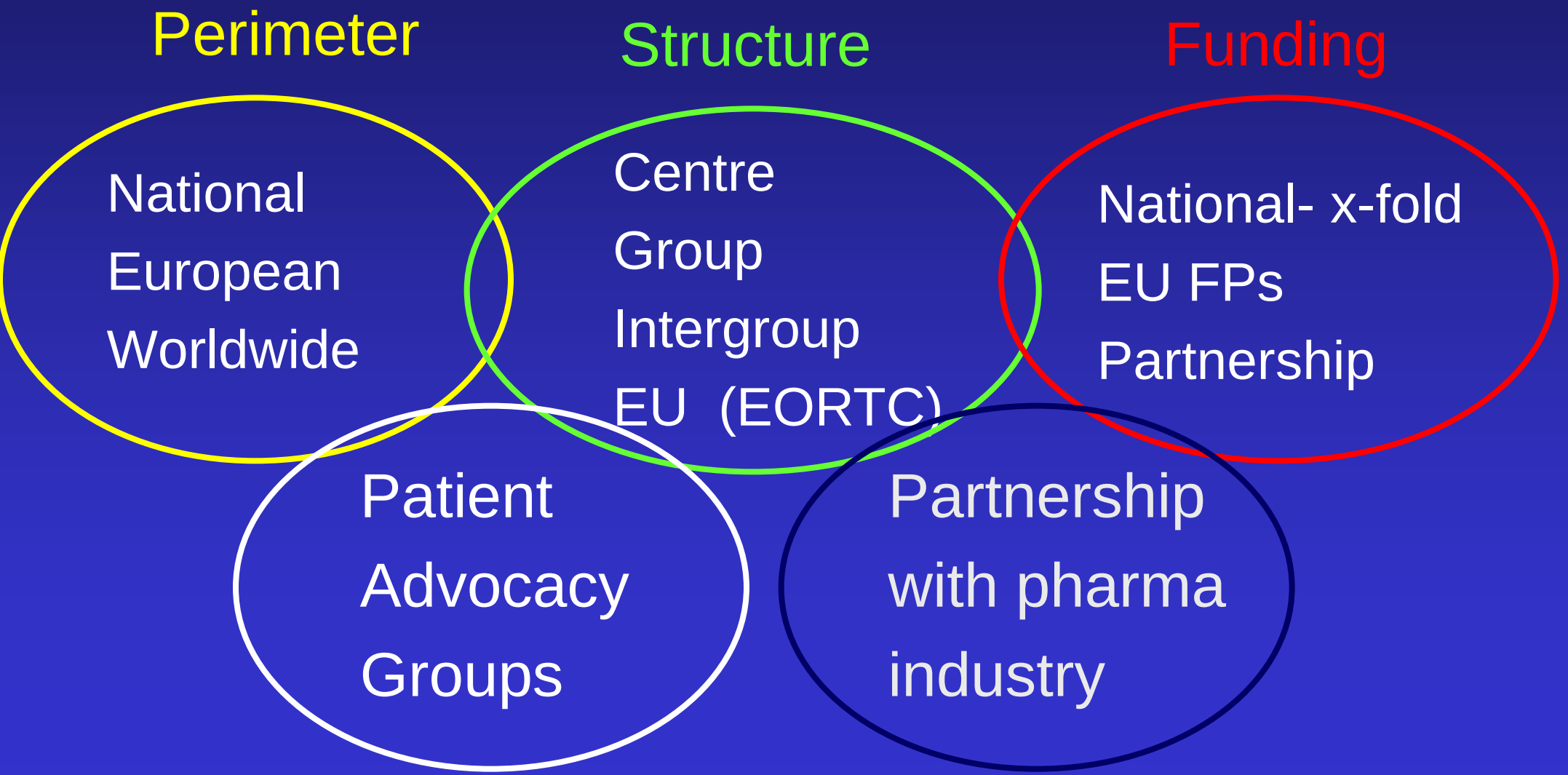
How to improve collaboration ?



How to improve collaboration ?