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 with 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!

Rate of concordance by patient sub-group

188 Second opinion requested
- 53 (28%) Total discordance
- 82 (44%) Total concordance
- 53 (28%) Partial 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

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Pathology review!
- Breast or colon carcinoma: cell lines or xenografts (n=22)
- 13023 genes sequenced, 3 millions PCR, 452 MB
- Total: 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,
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
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 Dedifferentiated Liposarcomas with JUNK overexpression
- Alk inhibitors in inflammatory myofibroblastic tumours with Alk amplification and overexpression
- 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, scientific societies-ESMO, and PAGs

• Simplify and streamline the access to compassionate use programs
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How to improve collaboration?

Perimeter:
- National
- European
- Worldwide

Structure:
- Centre Group
- Intergroup EU (EORTC)

Funding:
- National- x-fold EU FPs Partnership

Patient Advocacy Groups

Partnership with pharma industry
How to improve collaboration?

Perimeter
- National
- European
- Worldwide

Structure
- Centre
- Group

Partnership
- EU FPs
- Fold
- Perimeter
- National - x

Partnership with pharma industry

Scientific societies, research groups, industrial partners, regulatory bodies,