Multicenter clinical trials in Europe: successes and obstacles

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Medical Vice Director, EORTC HQ
Setting standards in cancer treatment

Specialist skills and capabilities include:
- Translational research
- Biomarkers
- Screening platforms
- Quality assurance
- Quality of life
- Pivotal clinical trials

Extensive experience in working with:
- Academic medical centres and other research organisations (150+)
- Pharmaceutical companies
- Regulators and other healthcare stakeholders

• A private and non-profit cancer research organisation founded in 1962
• Headquarters based in Brussels, Belgium
• Core activities are related to the design and conduct of clinical trials across a Pan-European Network
Accrual of screened patients in EORTC clinical studies in 2000 – 2013: 77071 patients

European Union

The Netherlands: 16616
France: 15389
Belgium: 8077
United Kingdom: 7230
Italy: 6709
Germany: 6599
Spain: 2946
Poland: 1126
Sweden: 894
Austria: 831
Portugal: 642
Denmark: 559
Slovak Republic: 462
Croatia: 352
Slovenia: 331
Hungary: 214
Rep. of Ireland: 200
Czech Republic: 168
Cyprus: 75
Greece: 55
Bulgaria: 49
Finland: 34
Latvia: 34
Malta: 20
Romania: 20
Luxembourg: 9
Estonia: 7

Non-European Union

Switzerland: 1639
Turkey: 631
Norway: 459
Russia: 178
Bosnia: 8
Macedonia: 6

Rest of the world: 4502
Long-term survival of cancer patients

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>1970 (%)</th>
<th>2013 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood leukemia</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>Adult leukemia</td>
<td>10</td>
<td>55</td>
</tr>
<tr>
<td>Bone cancer</td>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>0</td>
<td>95</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>40</td>
<td>90</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>30</td>
<td>65</td>
</tr>
<tr>
<td>Hodgkin’s disease</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Non-small-cell lung cancer</td>
<td>10</td>
<td>20</td>
</tr>
</tbody>
</table>
Long-term survival of cancer patients
Clinical cancer research

• Two main types of therapeutic clinical trials
  • Drug development
  • Therapeutic strategies – multidisciplinary approach
• Role of independent evaluation – the importance of investigator-driven clinical trials
EU Clinical Trial Directive (2001)

DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 4 April 2001

on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use
Facts and figures

EudraCT-registered trials

<table>
<thead>
<tr>
<th>Year</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>5028</td>
</tr>
<tr>
<td>2008</td>
<td>4627</td>
</tr>
<tr>
<td>2009</td>
<td>4619</td>
</tr>
<tr>
<td>2010</td>
<td>4400</td>
</tr>
<tr>
<td>2011</td>
<td>3766</td>
</tr>
</tbody>
</table>

Impact on EORTC activities

- Increased workload
- Prolonged timelines
- Increased cost
New clinical trial regulation proposal

“The data available support these criticisms:

• The number of applications for clinical trials fell by 25% from 2007 to 2011.

• The costs for conducting clinical trials have increased. Compared to the situation prior to the application of the Directive 2001/20/EC, the staff needs for industry sponsors to handle the clinical trial authorisation process have doubled (107%); with small companies facing an even sharper increase. For non-commercial sponsors, the increase in administrative requirements due to the Directive 2001/20/EC has led to 98% increase in administrative costs. In addition, since implementation of the Directive 2001/20/EC, insurance fees have increased by 800% for industry sponsors.

• The average delay for launching a clinical trial has increased by 90% to 152 days.”

Brussels, 17.7.2012
We need to ask the right questions

• Did the EU CTD increase protection of clinical trial patients?
  No visible added value in oncology

• Has the EU CTD established a harmonized regulatory framework?
  Definitively no

• Did CTD improve competitiveness?
  Not for academic research, and probably not for Industry

• What are the indicators of success?
  Employment in regulatory agencies and CROs
  Decrease access for patients to clinical trials
  Delays in clinical progress and innovation
Impact on EORTC activities

- Number of studies
- Staff

The future of cancer therapy
Impact on EORTC activities

Median PIS/IC length (pages)

<table>
<thead>
<tr>
<th>Period</th>
<th>Median Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995-1999</td>
<td>3</td>
</tr>
<tr>
<td>2000-2003</td>
<td>5</td>
</tr>
<tr>
<td>2004-2009</td>
<td>9</td>
</tr>
<tr>
<td>2010-2011</td>
<td>12</td>
</tr>
<tr>
<td>2012-2013</td>
<td>14</td>
</tr>
</tbody>
</table>
Impact on EORTC activities

Uncertainty is inherent in scientific research

![Bar chart showing the impact on EORTC activities from 1995-1999 to 2012-2013. The number of activities increases over time.]

- 1995-1999: 3 activities
- 2000-2003: 5 activities
- 2004-2009: 9 activities
- 2010-2011: 12 activities
- 2012-2013: 14 activities

EORTC

The future of cancer therapy
Really?
In financial terms, really.

<table>
<thead>
<tr>
<th>Country</th>
<th>Compound Annual Growth Rate of Biomedical R&amp;D Expenditures (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>-2.6</td>
</tr>
<tr>
<td>United States</td>
<td>-1.9</td>
</tr>
<tr>
<td>Europe</td>
<td>-0.4</td>
</tr>
<tr>
<td>Taiwan</td>
<td>5.2</td>
</tr>
<tr>
<td>Japan</td>
<td>5.7</td>
</tr>
<tr>
<td>India</td>
<td>6.7</td>
</tr>
<tr>
<td>Australia</td>
<td>6.9</td>
</tr>
<tr>
<td>Singapore</td>
<td>10.0</td>
</tr>
<tr>
<td>South Korea</td>
<td>11.4</td>
</tr>
<tr>
<td>China</td>
<td>32.8</td>
</tr>
</tbody>
</table>

In financial terms, really.
Changing clinical research environment

- Disease fragmentation
- Unaffordable drug development and treatments
- Pay for performance is around the corner
- Academics may be slower to realize the consequences
  - The need for new sources of funding is evident
  - The need for collaboration, tissue and data sharing less so
- The number of cancer survivors is increasing and their problems are not being tackled
Changing clinical research pathway
Changing clinical research pathway

From trials “designed to learn” to real life situation

Early clinical trials (R&D)
- Biology / imaging driven
- Integrated TR
- Screening platforms
- Collection of high quality data from various sources

Pivotal trials
- Highly targeted
- Large differences

Population-based studies
- Real world data
- Quality of life
- Health economics
- HTA
- Pragmatic trials
Roadmap for change: SPECTA

Molecular Screening Platform

1st line trial

2nd line trial

3rd line trial

Standard treatment (no open trial)

First line

Second line

Third line

Academia investment

Industry cooperation

EORTC: The future of cancer therapy
Roadmap for change: dialogue

EORTC SPECTAprogram

Screen and Treat

SPECTAplatforms
- SPECTAcolor
- SPECTAbrain
- SPECTAmel

SPECTApath
- PathoBiology
- Biobanking
- Scientific/operational support

SPECTAforum
- Industry
- EMA (FDA)
- Patient representative

SPECTAreg
- Competent bodies
- Regulatory affairs research
Roadmap for change: tissue sharing

- Biosample resources associated with trials are important
- Changing research and regulatory environment
- Strict implementation of policies is mandatory

EORTC acts as the coordinator of the chain of custody
## Roadmap for change: technical excellence

<table>
<thead>
<tr>
<th>Year</th>
<th>Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>VISTA/ORTA</td>
</tr>
<tr>
<td>2001</td>
<td>eForms / eQueries</td>
</tr>
<tr>
<td>2002</td>
<td>RA database</td>
</tr>
<tr>
<td>2003</td>
<td>Web-based eCRF</td>
</tr>
<tr>
<td>2005</td>
<td>Virtual tumor bank</td>
</tr>
<tr>
<td>2009</td>
<td>Imaging / RTQA platforms</td>
</tr>
<tr>
<td>2011</td>
<td>Integrated CTMS/CDMS</td>
</tr>
<tr>
<td>2014</td>
<td>Cloud-based CDISC/ODM CDMS</td>
</tr>
</tbody>
</table>
Roadmap for change: diversification

<table>
<thead>
<tr>
<th>EORTC HQ fellows 1991-2013</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical doctors</td>
<td>78</td>
</tr>
<tr>
<td>Medical doctors / statisticians</td>
<td>3</td>
</tr>
<tr>
<td>Statisticians</td>
<td>32</td>
</tr>
<tr>
<td>Lawyers</td>
<td>2</td>
</tr>
<tr>
<td>Health economists</td>
<td>9</td>
</tr>
<tr>
<td>Computer scientist</td>
<td>1</td>
</tr>
<tr>
<td>Communication experts</td>
<td>2</td>
</tr>
<tr>
<td>Biomedical scientists</td>
<td>13</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>140</strong></td>
</tr>
</tbody>
</table>
Roadmap for change: collaboration

Pharmaceutical industry
- Drug and assay development
- Drug supply
- Marketing

CRO
- Regulatory affairs
- Site management
- Site training
- On site monitoring
- Drug supply process
- Management of biological samples

Study conduct
- Site selection

ARO
- Scientific concept
- Protocol development
- Trial design
- Data management
- IDMC
- Statistical analysis
- Reporting
- Publication

As mortality decreases, what about morbidity?

Roadmap for change: survivorship

SAVE THE DATE

1st EORTC Cancer Survivorship Summit

30 - 31 January 2014
Square Meeting Centre
Brussels, Belgium
Roadmap for change: partnership
Thank you