Rare Cancers:
The added value of closer cooperation

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Plan

- About EORTC
- Some specifics to be highlighted
- Examples of different models
  - Global
  - European
  - EU programs
  - Pharma industry involvement
- Perspectives
About EORTC

• Created in 1962 to improve the standard of cancer treatment in Europe through
  ▪ Independent evaluation of innovative agents.
  ▪ Test more effective therapeutic strategies (surgery, radiotherapy)

• Multinational network (300 institutions from 29 countries)

• Multidisciplinary: +/- 2,900 collaborators (clinicians, surgeons, radiotherapists, imagers, pathologists,....)

• 6,000 patients entered into EORTC trials/year
• 30 clinical trials open to patient entry
• Database of more than 180,000 patients
• Headquarters in Brussels with 180 staff members
Accrual of patients in EORTC clinical studies in 2000 - 2011: 71,905 patients

European Union:
- Austria: 810
- Belgium: 7,399
- Bulgaria: 49
- Cyprus: 73
- Czech Republic: 160
- Denmark: 529
- Estonia: 7
- Finland: 34
- France: 14,438
- Germany: 6,310
- Greece: 48
- Hungary: 210
- Italy: 6,553
- Latvia: 34
- Luxembourg: 9
- Malta: 20
- Poland: 1,082
- Portugal: 635
- Republic of Ireland: 90
- Romania: 20
- Slovak Republic: 451

European Union (Con’t):
- Slovenia: 310
- Spain: 2,867
- Sweden: 595
- The Netherlands: 15,279
- United Kingdom: 6,620

Non-EU Countries:
- Bosnia: 8
- Croatia: 352
- Macedonia: 6
- Norway: 454
- Serbia: 261
- Russia: 178
- Switzerland: 1,438
- Turkey: 631
- Ukraine: 4

Rest of the World = 3,941 patients
EORTC achievements in rare diseases

- **Soft Tissue Sarcoma**
  - Gist Trial record breaking
- **Melanoma**
  - Largest adjuvant trials in shortest time frame
- **Brain Tumors**
  - Adjuvant TMZ/XRT trial in GBM
- **Haemato-oncology**
  - Leukemia - trials / unique database
  - Lymphoma - trials / unique database
  - Children Leukemia - trials / unique database
- **Head and Neck Cancer**
  - Larynx preservation
Rare cancers require special efforts

- Adequate definition (the list is increasing with molecular classification of tumors)
- Smart but robust study methodology (tumor molecular characteristics and validated design)
- Quality Assurance for pathology review and diagnostic assays
“If you want to win your battle you have to know your battlefield”
EXAMPLES OF DIFFERENT MODELS

Intergroup Transcontinental
Intergroup European
Single group
Radiotherapy / Temozolomide adjuvant study in glioblastoma - Overall Survival


- Median OS, mo: 12.1 vs. 14.6
- 2-yr survival: 10% vs. 26%
- HR [95% C.I.]: 0.63 [0.52-0.75]
- p < 0.0001
EORTC / US / NCI-Canada Cooperation (I)

• New questions
  ▪ Other gliomas?
  ▪ Schedule of temozolomide?
  ▪ TMZ/RT?
  ▪ Adjuvant TMZ? Elderly population?
EORTC / US / NCI-Canada Cooperation (II)

Lead to a global platform of 4 large phase III trials

• A 2 arm trial addressing TMZ schedules in GBM: lead by RTOG (1300 patients)
• A 4 arm trial addressing anaplastic gliomas without 1p/19q loss addressing respective role of the concurrent and adjuvant treatment: lead by EORTC (830 patients)
• A 3 arm trials addressing role of RT and TMZ for 1p/19q co-deleted good prognosis glioma lead by NCCTG (500 patients)
• A 2 arm trial addressing role of RT and TMZ in elderly patients lead by NCIC Canada (560 patients)
What were the challenges for EORTC?

• The first transatlantic trial to be set up (2006) after the implementation of the European directive (2004)

• The first transatlantic “clinico-genomic” trial

• The first transatlantic trial to be set up in cooperation with a pharmaceutical partner

• The first transatlantic trial with a prospective QART programme.
Strategic challenges for intergroup trials

Feasibility
- Clinical questions
- Reference treatments
- Biological material
- Patient access

Administration
- Working procedures
- Regulatory environment
- QA/ QC
- Contracts/agreements

Costs
- Direct
- Indirect

Flexibility for interpretation and implementation of trial processes
How to address these challenges?

- Frequent working meetings/TC: NCI/NCI-C / EORTC
- Develop master documents (protocol, contracts etc.)
- Common data elements
- Harmonize terminology
- Streamline methodological approaches
- Mutual benefits of peer review processes
- Common procedures for cooperation with industry
- Common approaches to regulatory bodies
Criteria for Success

- Select the right trials
- Respective and mutual understanding
- Prospectively work together from trial inception
- Processes endorsed by each group
- Track records / master agreements
- Build common strategies
- Repeat
- Re-iterate
- Remind

Build common strategies

Select the right trials

Respective and mutual understanding

Prospectively work together from trial inception

Processes endorsed by each group

Track records / master agreements
How does it function?

According to the principles of shared intergroup policies

- EORTC HQ holds a central FWA (OHRP approved assurance)
- EORTC HQ has set up an IRB under the FWA
  - Ensures EORTC procedures do follow 45 CFR part 46 requirements /HHS regulations
  - Ensures a yearly review of transatlantic trials
- EORTC has cooperation on Phase III trials with
  - RTOG: 2 brain and 1 pancreas cancer studies
  - NCCTG: 1 brain cancer study
  - SWOG: 1 closed GU study
  - GOG: 1 study in Gynecological sarcoma (IRCI)
  - CALGB: 1 leukemia trial
IRCI: International Rare Cancer Initiative

Member organizations

- UK National Cancer Research Network
- Cancer Research UK
- US National Cancer Institute
- European Organization for Research and Treatment of Cancer
The work leading to this result has received funding from the EC’s 7th Framework Programme under grant agreement no 278742
Objectives

- To address major academic questions arising in a selected groups of soft tissue and bone sarcomas, in localized and metastatic phase.

- Create a reliable, efficient, multinational network of clinical researchers.

- Enable cooperation and collaborations between the network and with patient advocacy groups

- Involvement of reference centers representing national sarcoma groups as well as national reference institutions in countries without a formal sarcoma group.
ENGOT: European Network of Gynaecological Oncological Trial Groups

A phase III Trial of postoperative chemotherapy or no further treatment for patients with stage I-II medium or high risk endometrial cancer

Lead by Scandinavian groups

EORTC Joining

Unique approach: EORTC infrastructure for rare tumors to be used remotely by the lead group
EORTC 90101 (CREATE Trial)

Trial Design (Simon’s Design)

6 Parallel cohorts in different diseases
Main question: efficacy in marker positive patients.
Approx no. patients screened: 365 (if marker positive patients are 60%)

Marker Screening (ALK/MET)

Response Assessment

2-week turnaround

First stopping rule
(if marker is not sufficiently prevalent in the cohort to continue)
If <2 / 20 pts are marker + == Close cohort

Second stopping rule
(intermediate assessment of responses in marker + group per cohort)
Treat 12 marker + pts, if >= 2 respond
Treat 23 additional pts.

Final assessment
(‘total cohort’ assessment)
if out of 35 >= 6 respond == Successful
Target indications

- Anaplastic large cell lymphoma
  - (ALCL; ALK alterations)
- Inflammatory myofibroblastic tumor
  - (IMFT; ALK alterations)
- Papillary renal cell carcinoma type 1
  - (PRCC; MET alterations)
- Alveolar soft part sarcoma
  - (ASPS; MET alterations)
- Clear cell sarcoma
  - (CCSA; MET alterations)
- Alveolar rhabdomyosarcoma
  - (ARMS; MET and ALK alterations)
Cancer clinical trials in the 21st century

New Model of Collaboration

- Public Funding
- Patients Organizations
- Charities
- Industry
- Policy Makers
- Academia
THANK YOU FOR YOUR ATTENTION