# 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
Luxemburg: 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

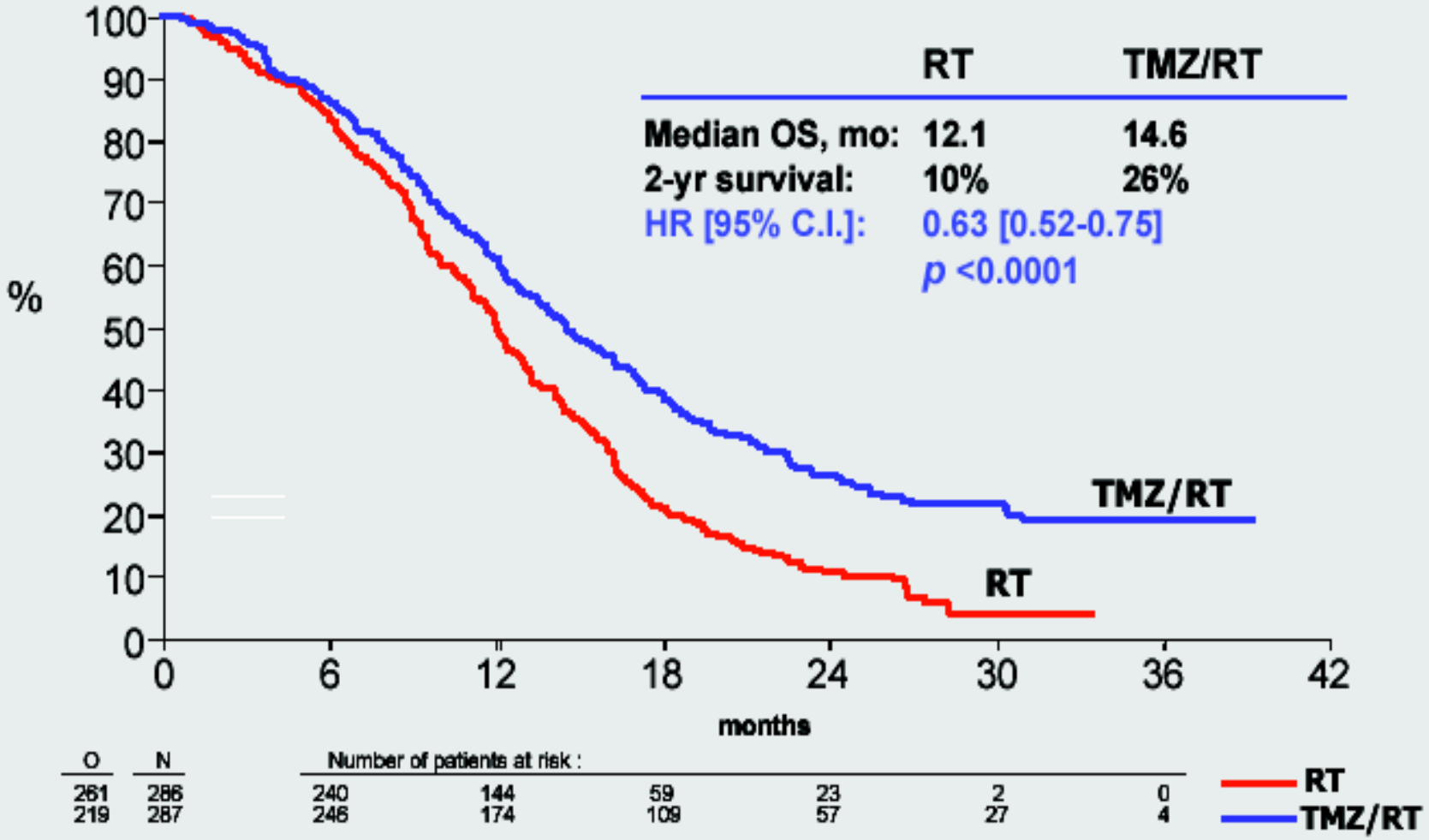
## Intergroup Transcontinental

## Intergroup European

## Single group

# Radiotherapy / Temozolomide adjuvant study in glioblastoma - Overall Survival

New Engl. J Med, March 2005



# 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

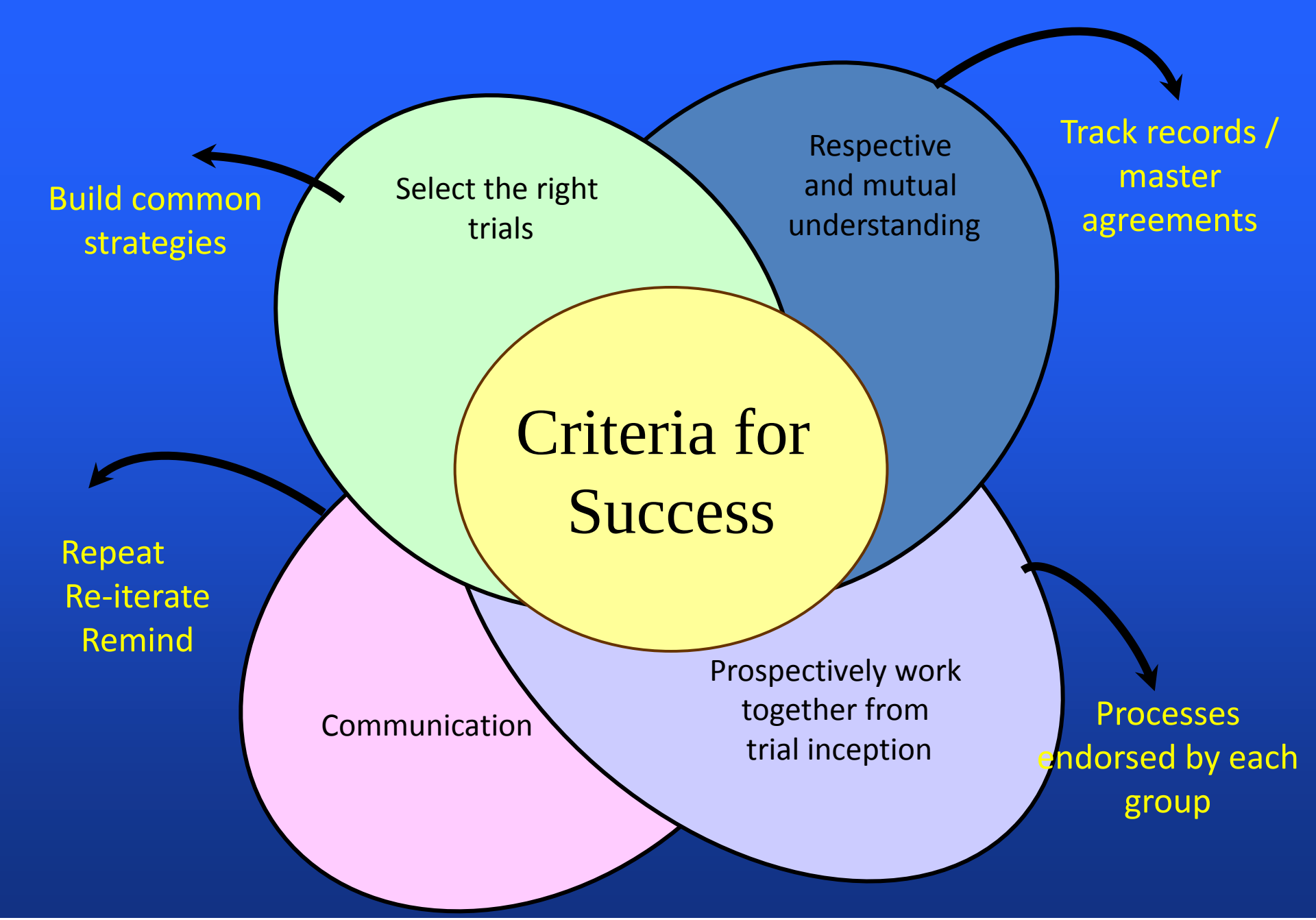
**Costs**

- 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


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

# 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

# Eurosarc Kick off meeting

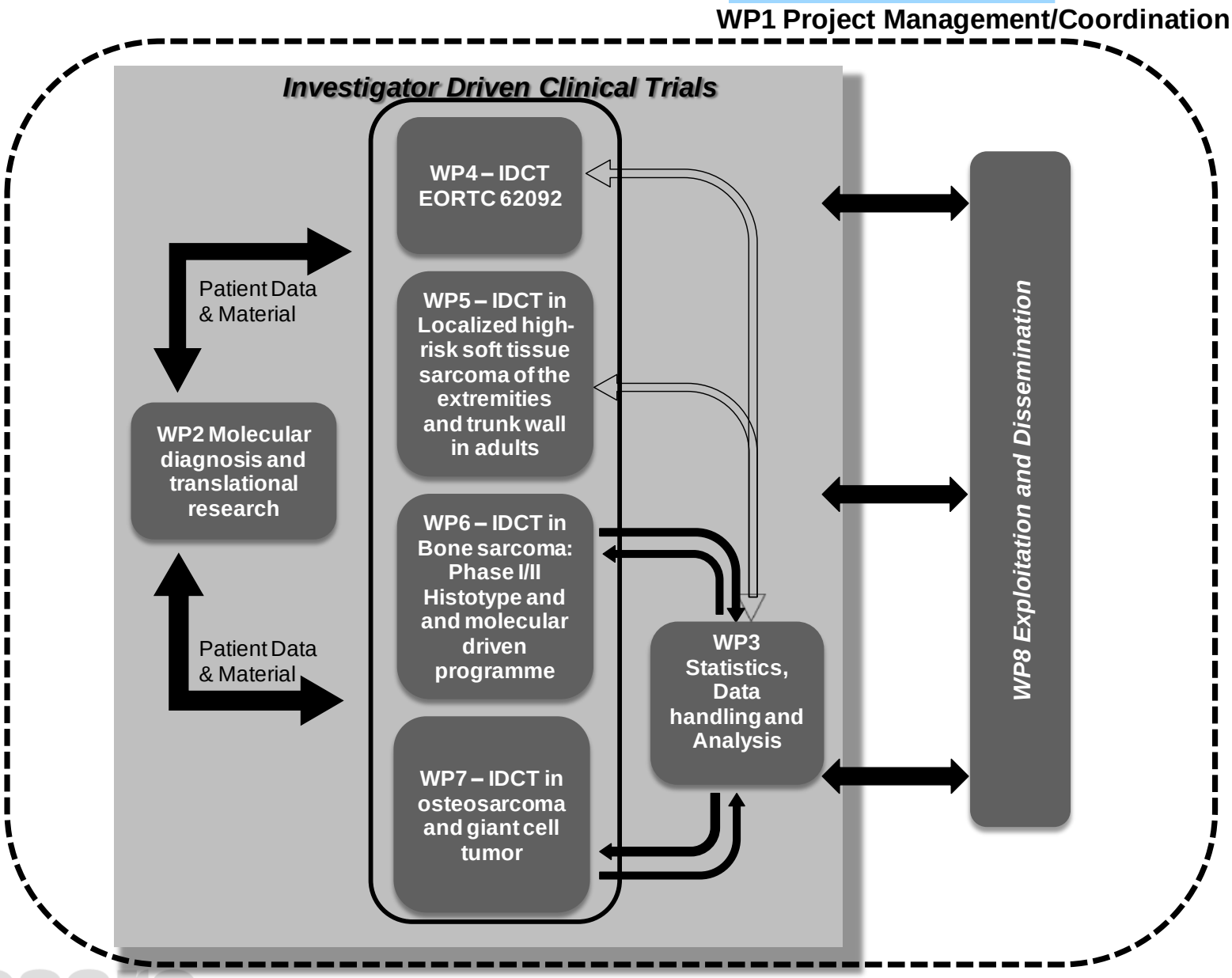
# Project Presentation

Eurosarc

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.


WP1 Project Management/Coordination
Investigator Driven Clinical Trials
WP4 – IDCT EORTC 62092
WP5 – IDCT in Localized high-risk soft tissue sarcoma of the extremities and trunk wall in adults
WP6 – IDCT in Bone sarcoma: Phase I/II Histotype and and molecular driven programme
WP7 – IDCT in osteosarcoma and giant cell tumor
Patient Data & Material
Patient Data & Material
WP2 Molecular diagnosis and translational research
WP3 Statistics, Data handling and Analysis
WP8 Exploitation and Dissemination

# 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**

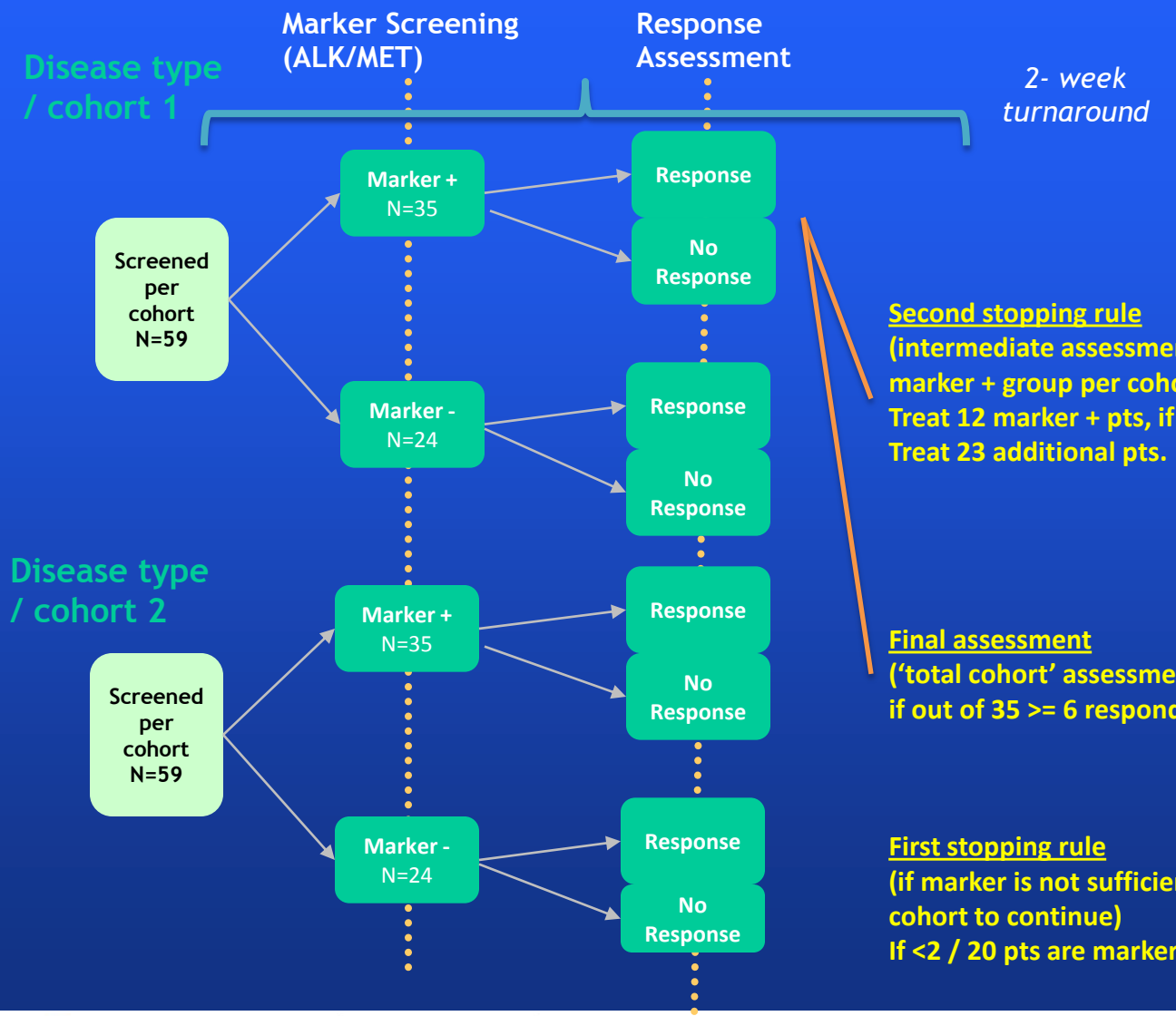
**Lead by Scandinavian groups**

**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%)

**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**

**First stopping rule**

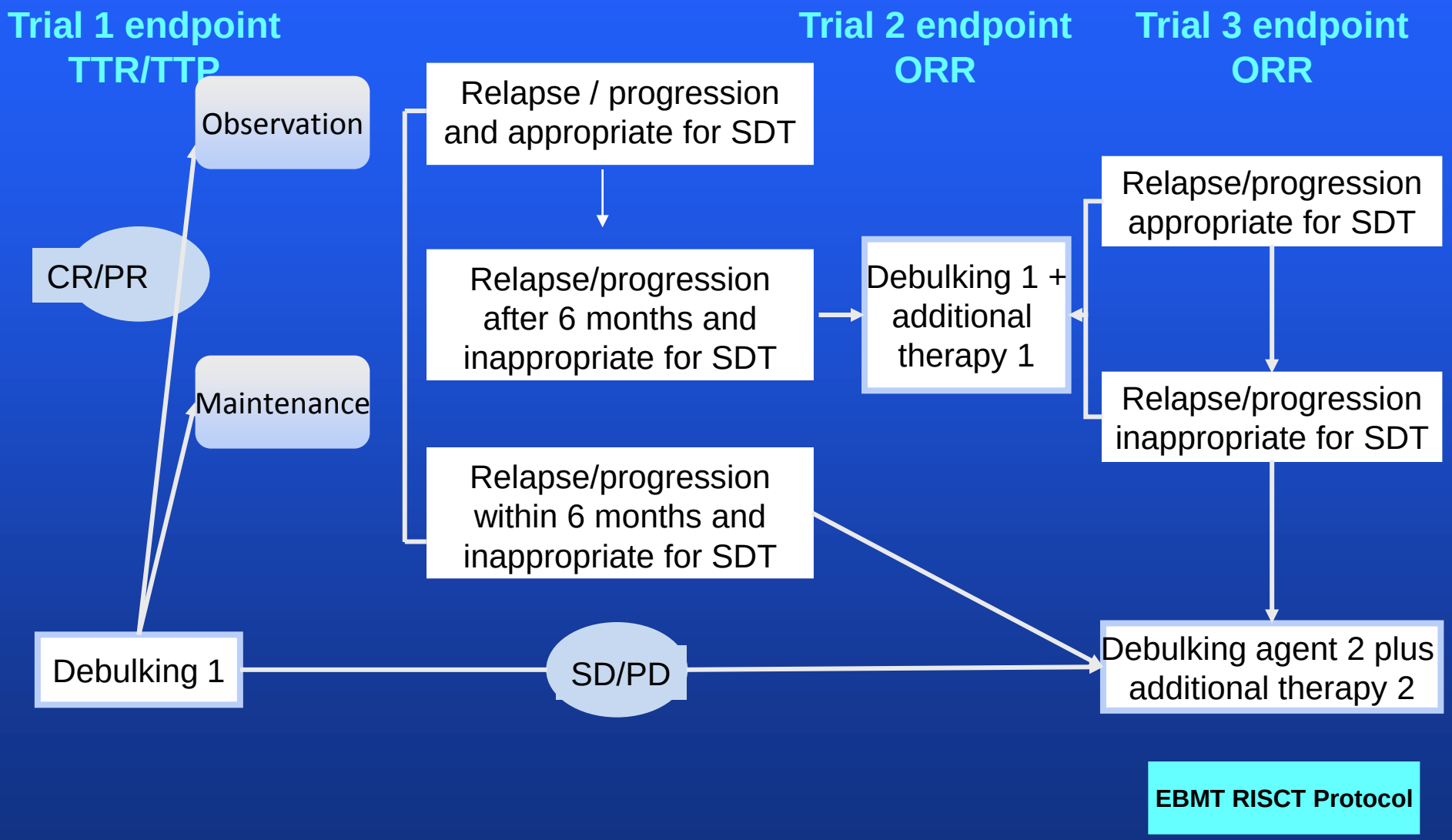
**(if marker is not sufficiently prevalent in the cohort to continue)**

**If <2 / 20 pts are marker + == Close cohort**

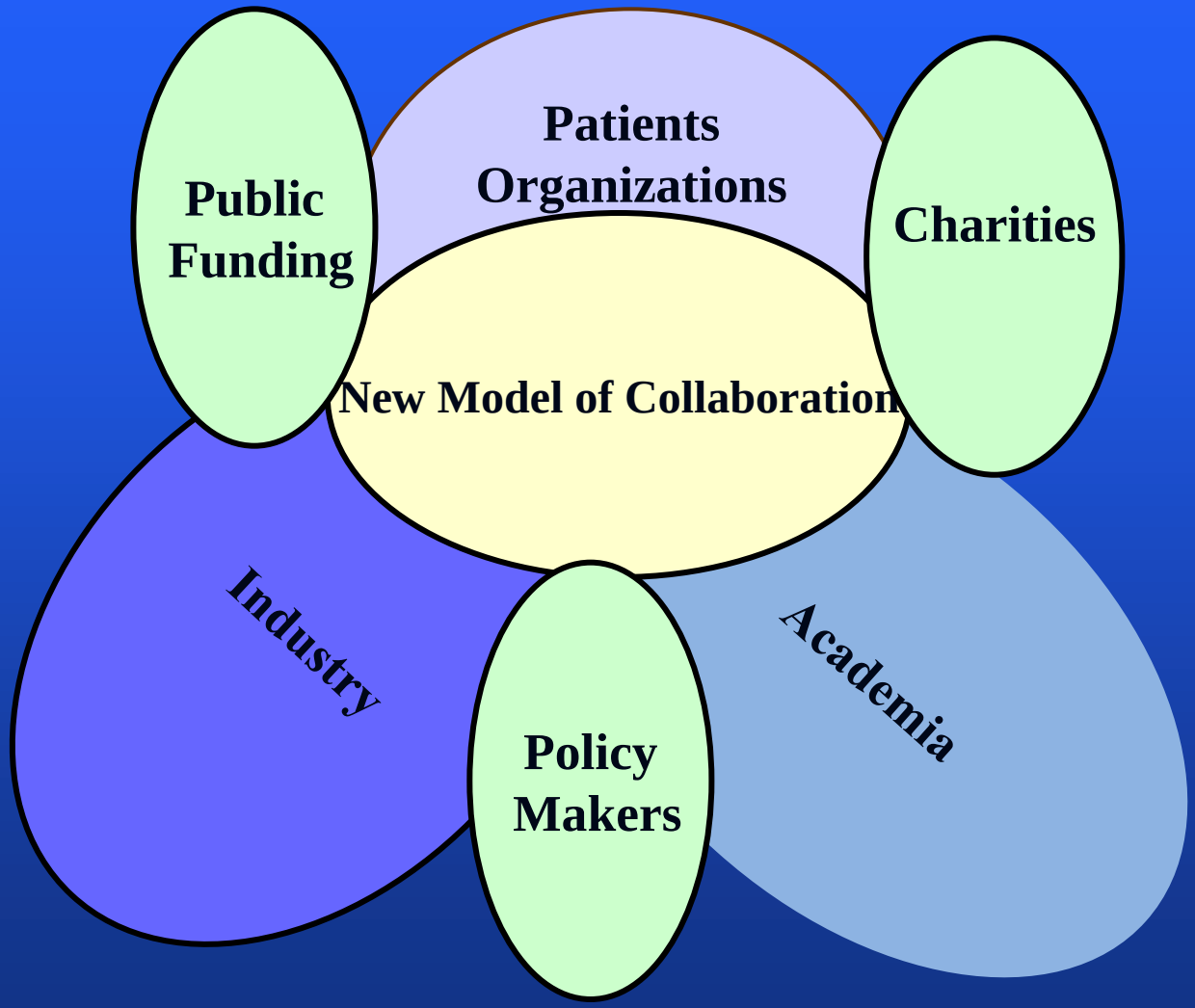
# EORTC 90101 (CREATE)
## Target indications

- 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)

# EORTC CLTF platform



# Cancer clinical trials in the 21th century



# THANK YOU FOR YOUR ATTENTION