EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

European Organisation For Research and Treatment of Cancer (EORTC)

What is the EORTC?

European Organisation for Research and Treatment of Cancer

- **Non-profit** cancer research organisation founded in 1962
- Core activities: **design and conduct of cancer clinical trials**

Multi-national
Pan-European network

Multi-disease
Brain, breast, leukemia, ovarian, sarcoma,…

Multi-disciplinary
Surgery, radiotherapy, medical oncology, translational research

Academic independence
External peer review process / approval of study protocols, clinical database control by academia, IDMC, analysis of primary endpoints, publication of primary analysis, controlled access to biological material.

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EORTC

- **International:** Conducting clinical research across Europe and rest of the World.
- **Multidisciplinary:** Spanning all aspects of cancer management, from imaging and radiology to surgery and therapeutic innovations, working with a network of over 5.500 multidisciplinary oncology experts. .
- **Multi-tumour:** Researching in all types of cancers, leaving no-one behind.
- **Independent:** Research is done with unwavering independence and accountability, making all results public.
- **Compliant with regulation** Our experts ensure our activities meet the strictest quality and reliability requirements, everywhere we are active.

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EORTC by the numbers (2017)

A world-class network	An expert HQ	Unique output
• > 5,500 collaborators • 930 institutions • 27 countries • 20 groups & task-forces • 120 collaborative groups	• 214 employees • > 198,000 patients in database • > 25,000 patients in follow-up	• **15 new studies open to patient** • **53 ongoing studies** • 25 studies in protocol outline development • 19 studies in protocol development • 9 studies in regulatory activation • **Working on ≈ 203 studies**

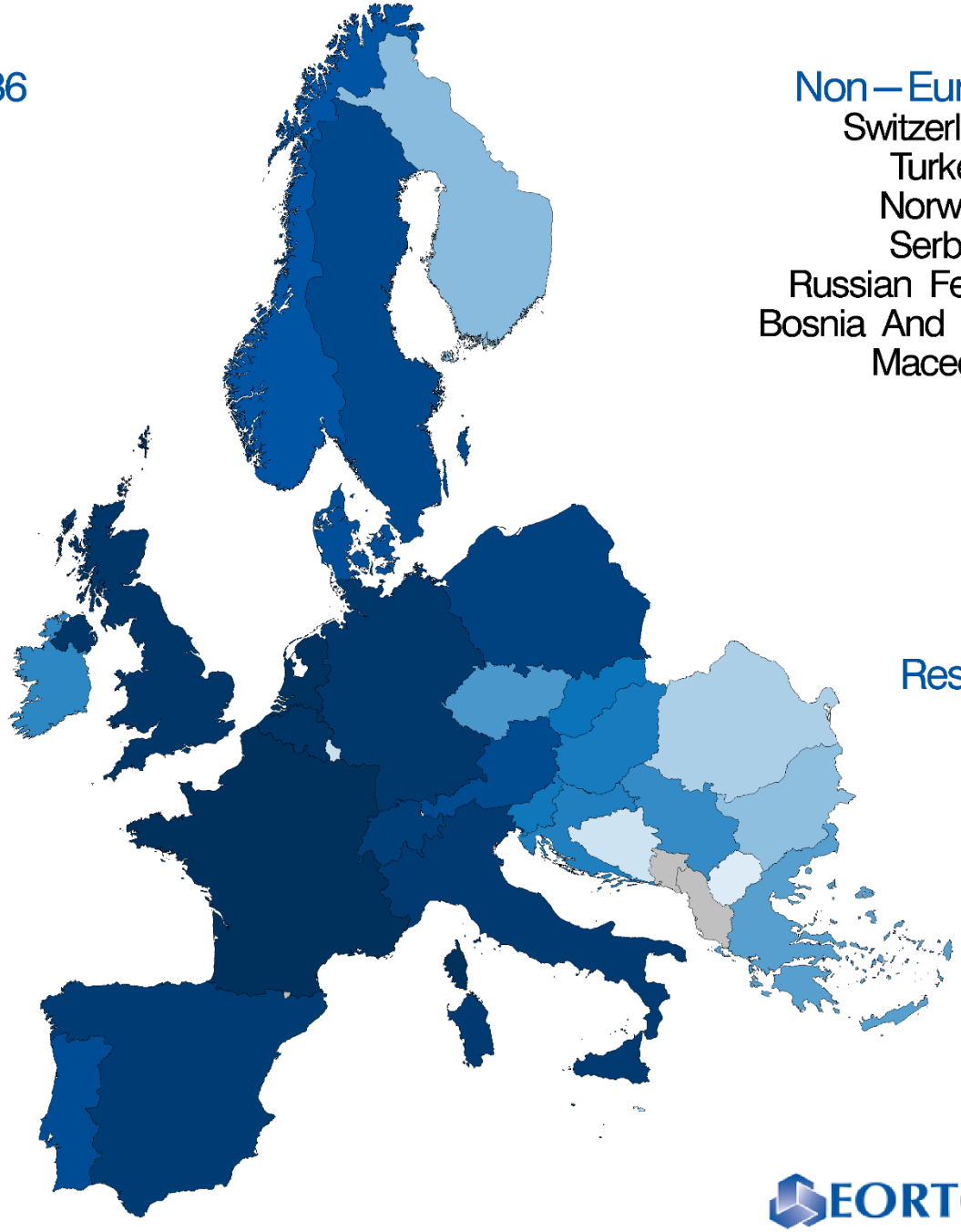
Accrual of screened patients in EORTC clinical studies from 2000 to 2017: 91771 patients

European Union: 82136

France: 18080
Netherlands: 17486
Belgium: 10030
United Kingdom: 8803
Germany: 8437
Italy: 7769
Spain: 4023
Poland: 1368
Sweden: 995
Austria: 977
Portugal: 759
Denmark: 663
Slovakia: 481
Slovenia: 472
Hungary: 393
Croatia: 374
Ireland: 304
Czech Republic: 220
Greece: 114
Cyprus: 101
Estonia: 69
Finland: 67
Bulgaria: 51
Latvia: 35
Malta: 20
Romania: 20
Lithuania: 16
Luxembourg: 9

Non–European Union: 3774

Switzerland: 2124
Turkey: 631
Norway: 497
Serbia: 287
Russian Federation: 221
Bosnia And Herzegovina: 8
Macedonia: 6



Rest of the world: 5861

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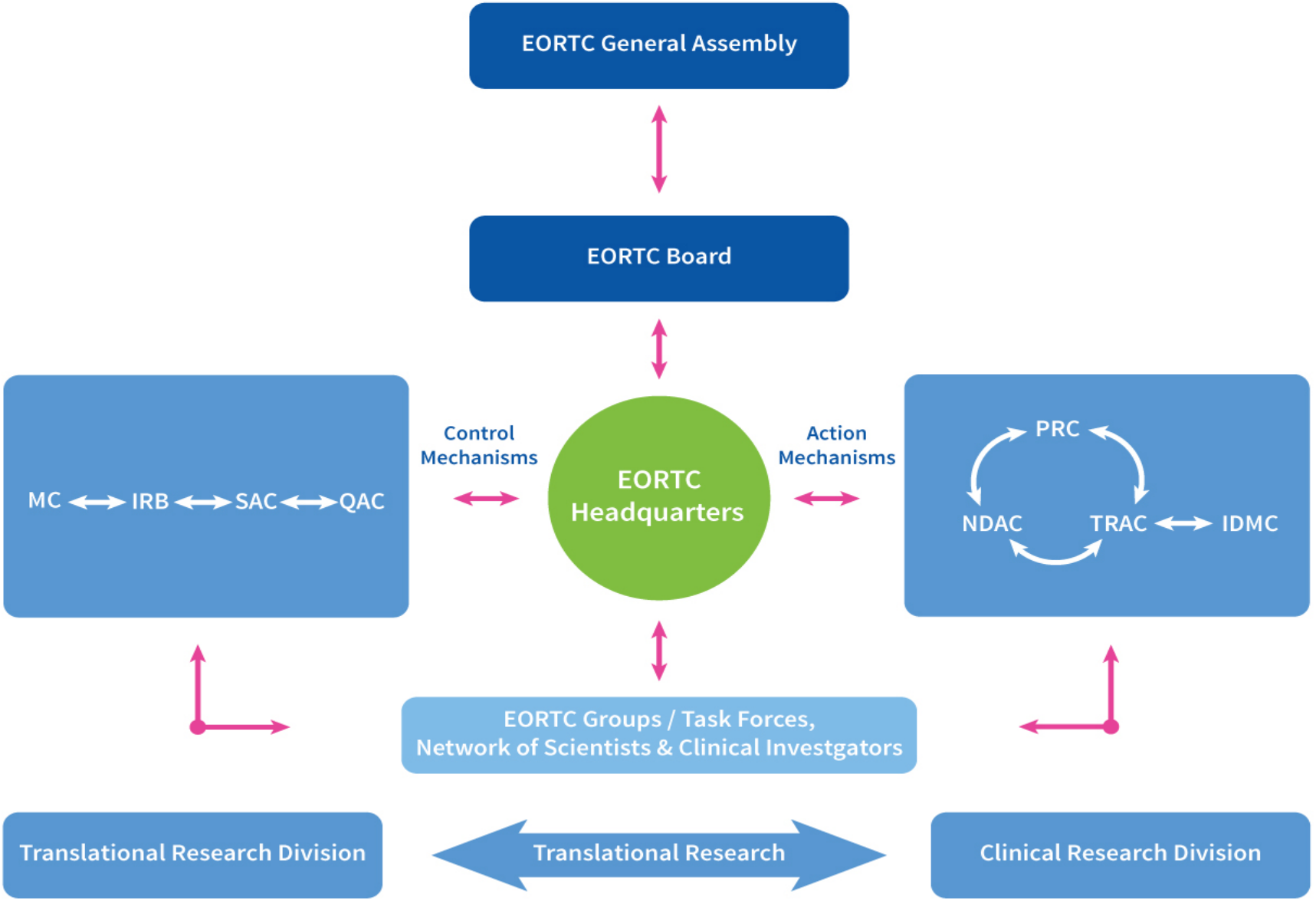
Governance



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EORTC Clinical Research Division

- Tumor specific groups
  - Brain Tumor
  - Breast Cancer
  - Lung Cancer
  - Leukemia
  - Lymphoma
  - Endocrine Tumors
  - Melanoma
  - Soft Tissue and Bone Sarcoma
  - Gastro-Intestinal Tract Cancer
  - Genito-Urinary Cancers
  - Gynecological Cancer
  - Head and Neck Cancer
- Other clinical groups
  - Infectious Diseases
  - Quality of Life
  - Radiation Oncology
- Task Forces
  - Elderly
  - Cutaneous Lymphoma

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EORTC Translational Research Division

- Pharmacology and Molecular Mechanisms
- Pathobiology
- Imaging

Activities

- Clinical trial
- Infrastructure building: genomic testing, surgery and radiotherapy initiatives, late follow-up (survivorship)
- Development of QOL questionnaires
- Guidance, criteria. For example:
  - RECIST (Response Criteria in Solid Tumors)
  - RTQA
- Participation in the development of the oncology community
- Collaboration with regulators, payers, oncology academia, patients …
- Education, teaching
  - Many courses, Early Career Investigator program

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Environment is evolving *faster* than ever before

- Precision oncology and immunotherapy are here to stay and more is on the way
- New clinical research models and trial designs are emerging
- New clinical research infrastructures are needed as the forms and the methods of clinical research are evolving
- Clinical research landscape is changing
  - Complex and multidisciplinary datasets/data integration
  - Regulatory challenges are moving targets: upcoming regulations
  - Traditional partners have different expectations (industry..)
  - New partners have new demands (HTA…)

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The 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

Burock et al. Eur.J.Cancer (2013), http://dx.doi.org/10.1016/j.ejca,2013.05.016

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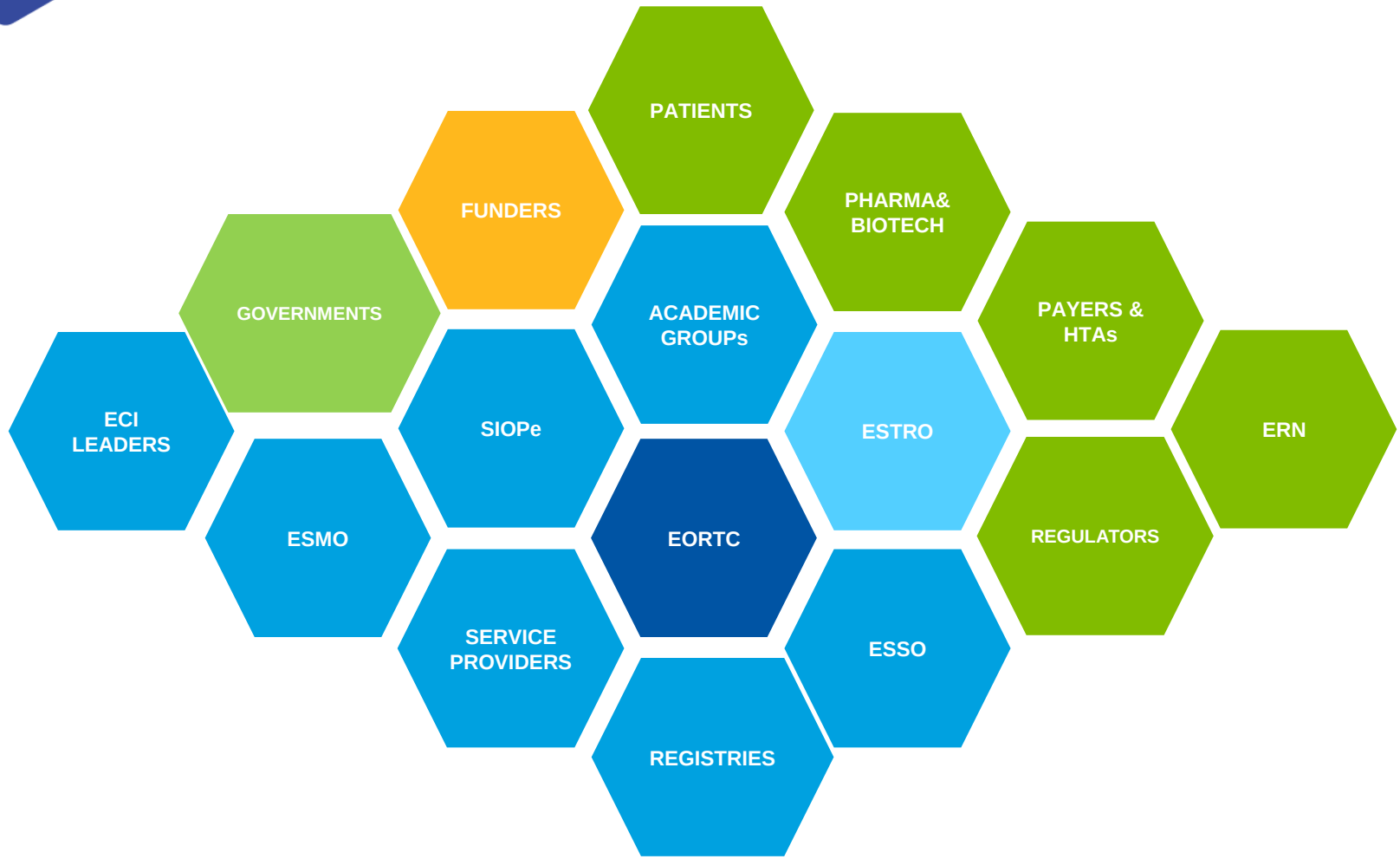
Partnerships made possible



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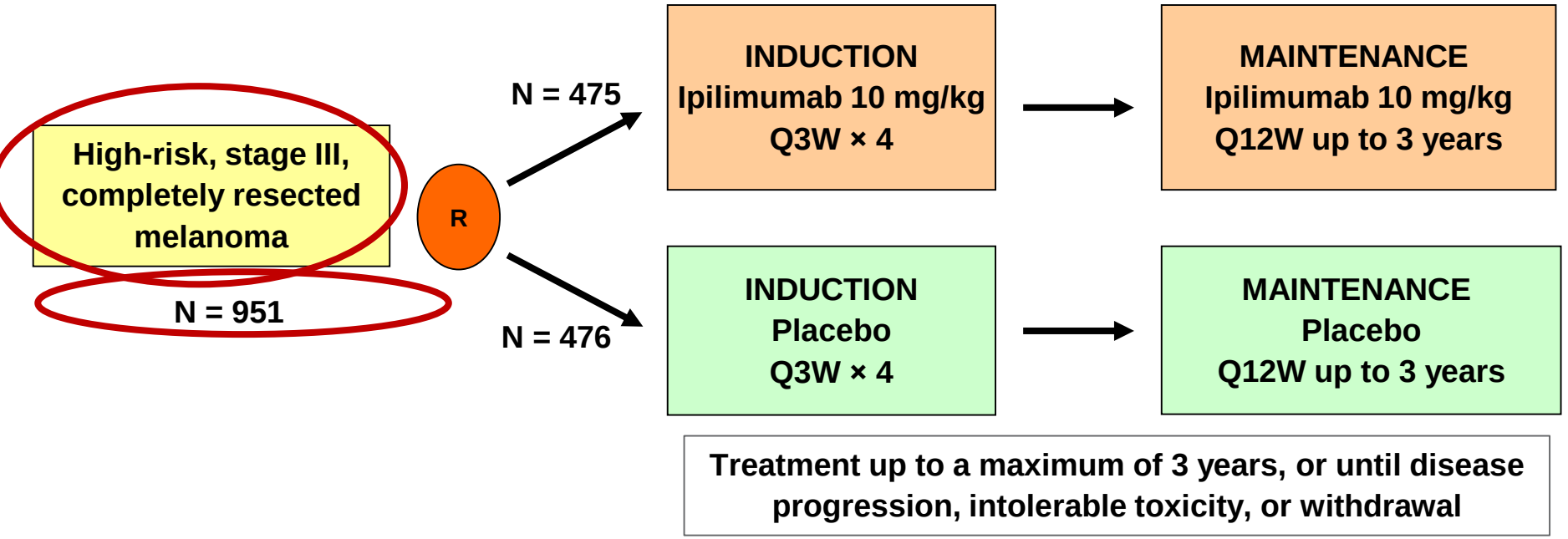
Main roles and functions

To ensure appropriate up-to-date methodology use in every study or research conducted under the EORTC flag

Adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): a randomised, double-blind, phase 3 trial.

Eggermont et al, Lancet Oncol. 2015



1° end-point:

Recurrence Free Survival, assessed by IRC

- Designed to detect HR=0.75 with 90% power, corresponding to an increase from 58.3% to 66% in 1-year and from 35.4% to 45.9% in 3-year recurrence-free survival

Adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): a randomised, double-blind, phase 3 trial.

SURVIVAL ANALYSIS

- Definition & computation of endpoint: right censoring, interval censoring? Competing risks?
- Survival curves: estimation of %survival at time t; median time to survival; Precision & CI.
- Comparison between treatment arms: log-rank test, stratified or not? Cox PH model, stratified or adjusted? What if PH assumption not met?
- Impact of missing data , deviations to study protocol? Bias? Sensitivity analyses?

100

Ipilimumab Placebo

Ipilimumab	234	475	276	205	67	5
Placebo	294	476	260	193	62	4

Figure 2: Kaplan-Meier curves of recurrence-free survival, as assessed by IRC

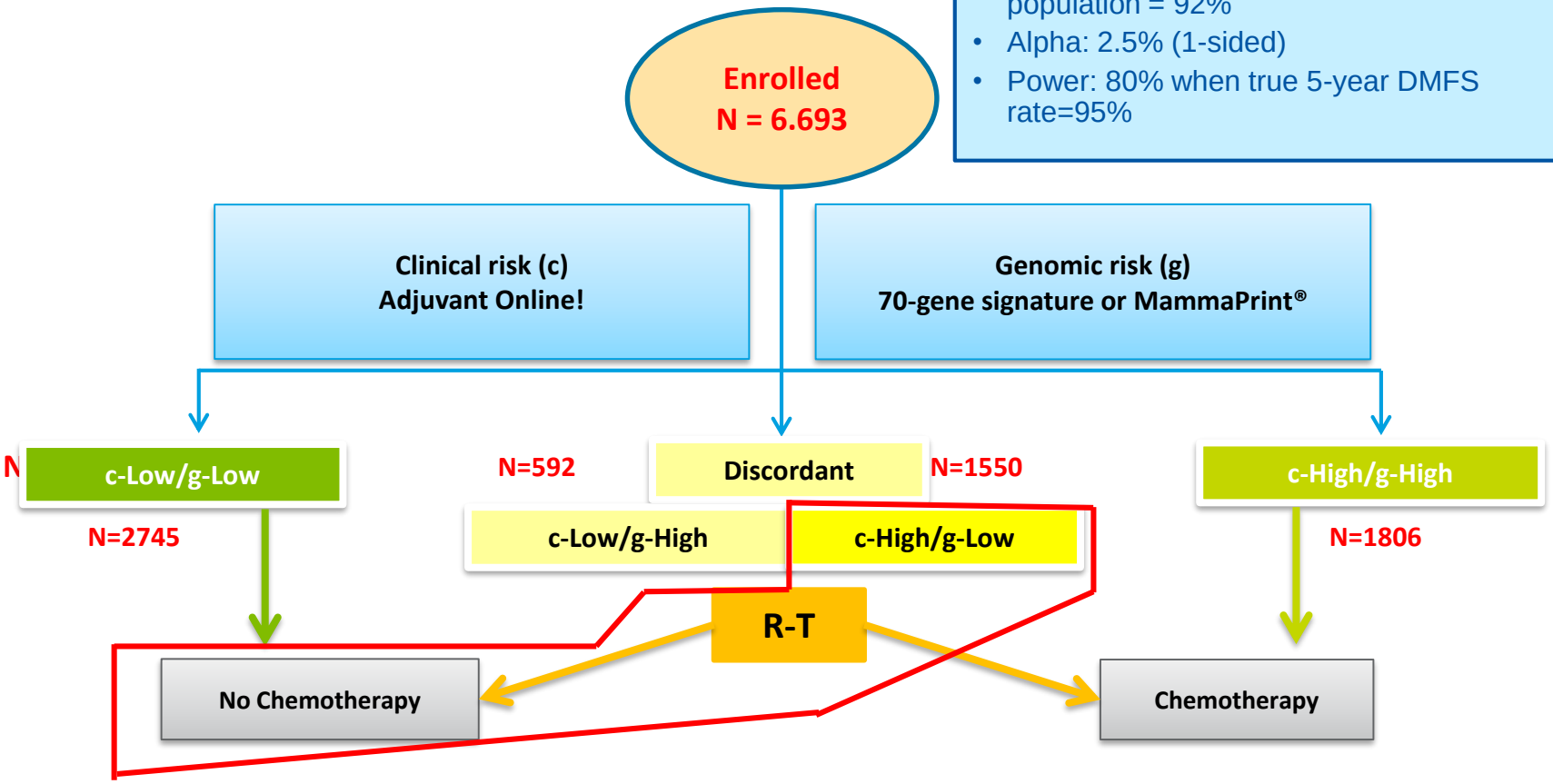
Interpretation Adjuvant ipilimumab significantly improved recurrence-free survival for patients with completely resected high-risk stage III melanoma. The adverse event profile was consistent with that observed in advanced melanoma, but at higher incidences in particular for endocrinopathies. The risk–benefit ratio of adjuvant ipilimumab at this dose and schedule requires additional assessment based on distant metastasis-free survival and overall survival endpoints to define its definitive value.

70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer, Mindact study

Cardoso et al, NEJM 2016

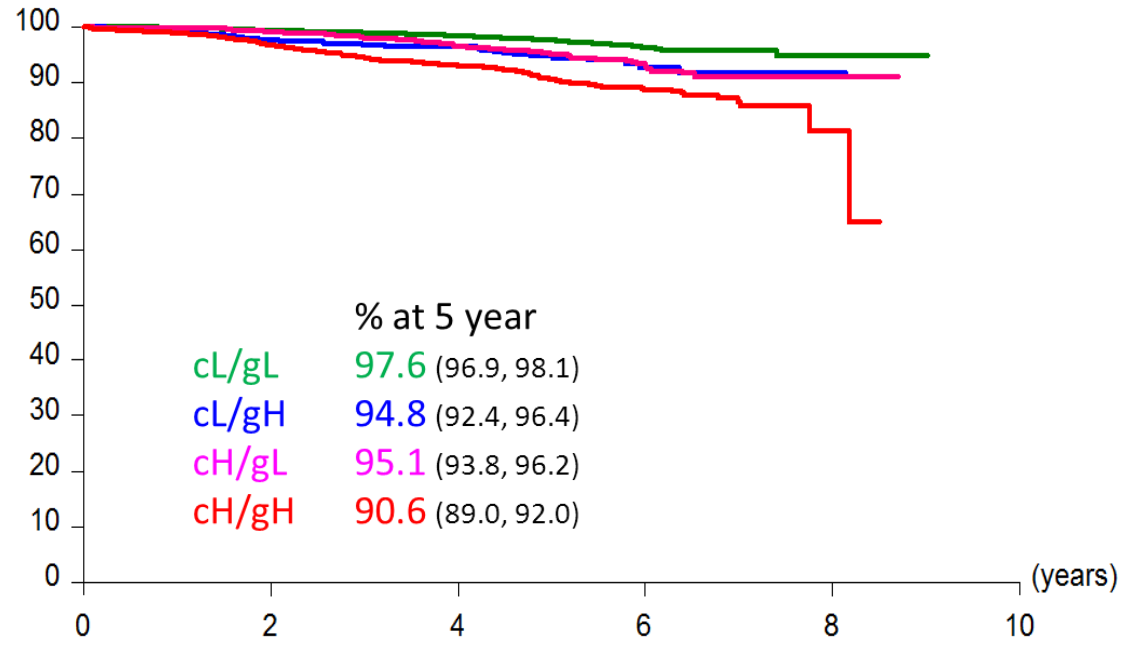
End-point

- Distant Metastasis Free Survival at 5 years
- Null hypothesis: 5-year DMFS rate in PT population = 92%
- Alpha: 2.5% (1-sided)
- Power: 80% when true 5-year DMFS rate=95%



70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer, Mindact study Cardoso et al, NEJM 2016

Distant Metastasis Free Survival



O	N	Number of patients at risk :				corrected risk
77	2745	2628	2331	735	33	cL/gL
32	592	550	484	136	2	cL/gH
82	1550	1457	1317	311	9	cH/gL
171	1806	1689	1462	395	11	cH/gH

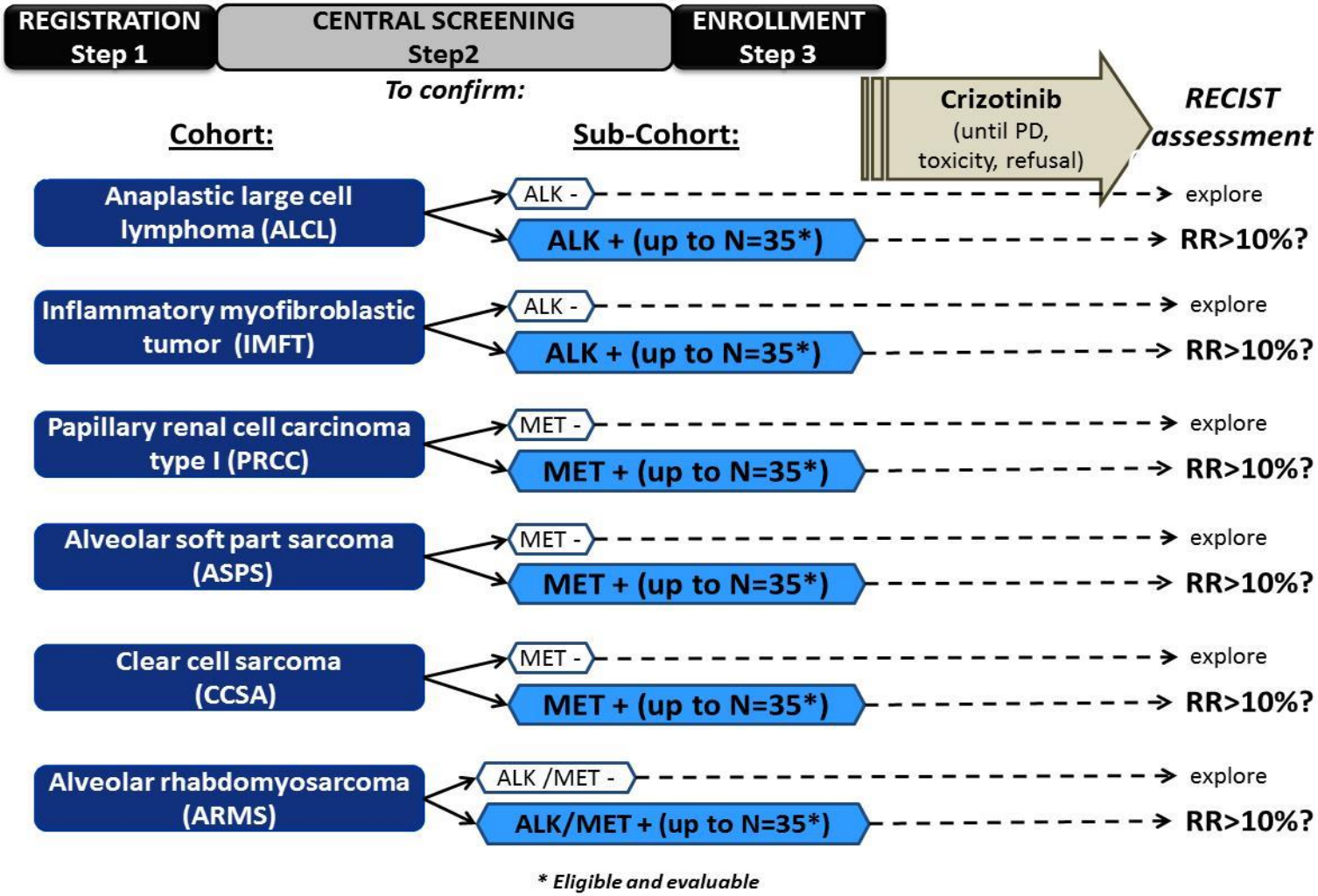
CONCLUSIONS

Among women with early-stage breast cancer who were at **high clinical risk and low genomic risk for recurrence**, the receipt of no chemotherapy on the basis of the 70-gene signature led to a 5-year rate of survival without distant metastasis that was 1.5 percentage points lower than the rate with chemotherapy.

Given these findings, approximately 46% of women with breast cancer who are at high clinical risk might not require chemotherapy.

Cross-tumoral phase 2 clinical trial exploring Crizotinib in patients with advanced tumors induced by causal alterations of ALK and/or MET

Study coordinator: P. Schöffski



1° End-point

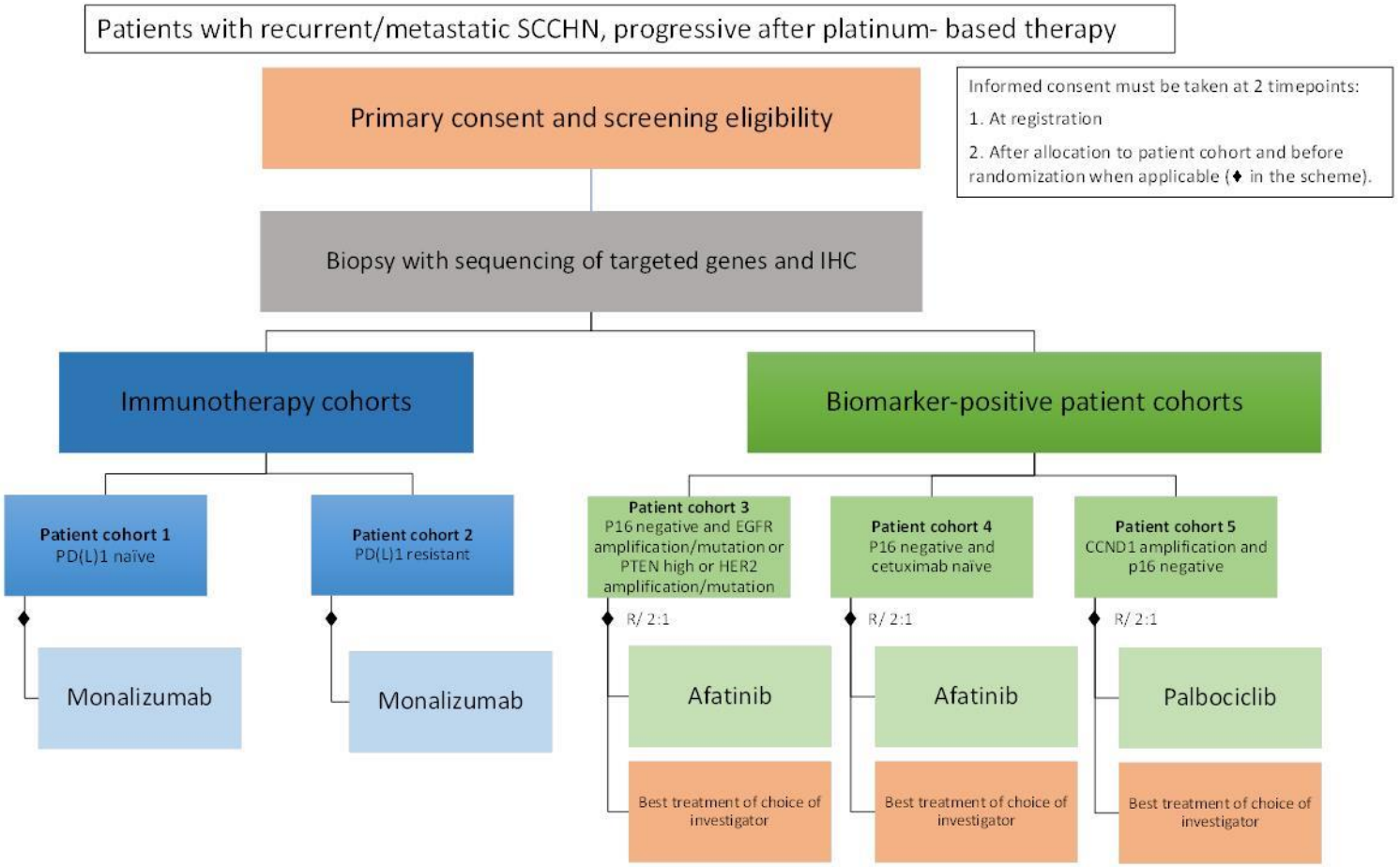
Response Rate (RECIST v1.1)

Design:

Simon 2-stage

A pilot study of personalized treatment in patients with recurrent/metastatic squamous cell carcinoma of the head and neck

Study Coordinator: J.P. Machiels



1° objective: to assess the efficacy of molecular targeted drugs or immunotherapy in patients with non-curable recurrent/metastatic SCCHN harboring pre-defined biomarkers

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EORTC HQ Staff 2016

CONFERENCES AND COURSES

- **30th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, Dublin, Ireland, 13-18 November 2018**
  - Chairs: Charlie Swanton, Antoni Ribas, James Gulley
- **IBCD 2018: Innovation and Biomarkers in Cancer Drug Development, (Joint meeting of EORTC, AACR, EMA, NCI), 29-30 November 2018, Brussels, Belgium**
  - Chairs: Roberto Salgado, Denis Lacombe
- **ECCO-EORTC-AACR-ESMO "Methods in Clinical Cancer Research", Zeist, The Netherlands, June 2019**
- **EORTC Quality of Life in Cancer Clinical Trials Conference, 16-17 may 2019**
- **EORTC Courses at EORTC HQ:**
  - **Patient Course, 3 March 2018,**
  - **Statistics for non Statisticians Course, 12-15 June 2018,**
  - **One day at EORTC, September 2018,**
  - **IDMC course, Date TBA**
- **EORTC Survivorship Summit, March 2020, Brussels**

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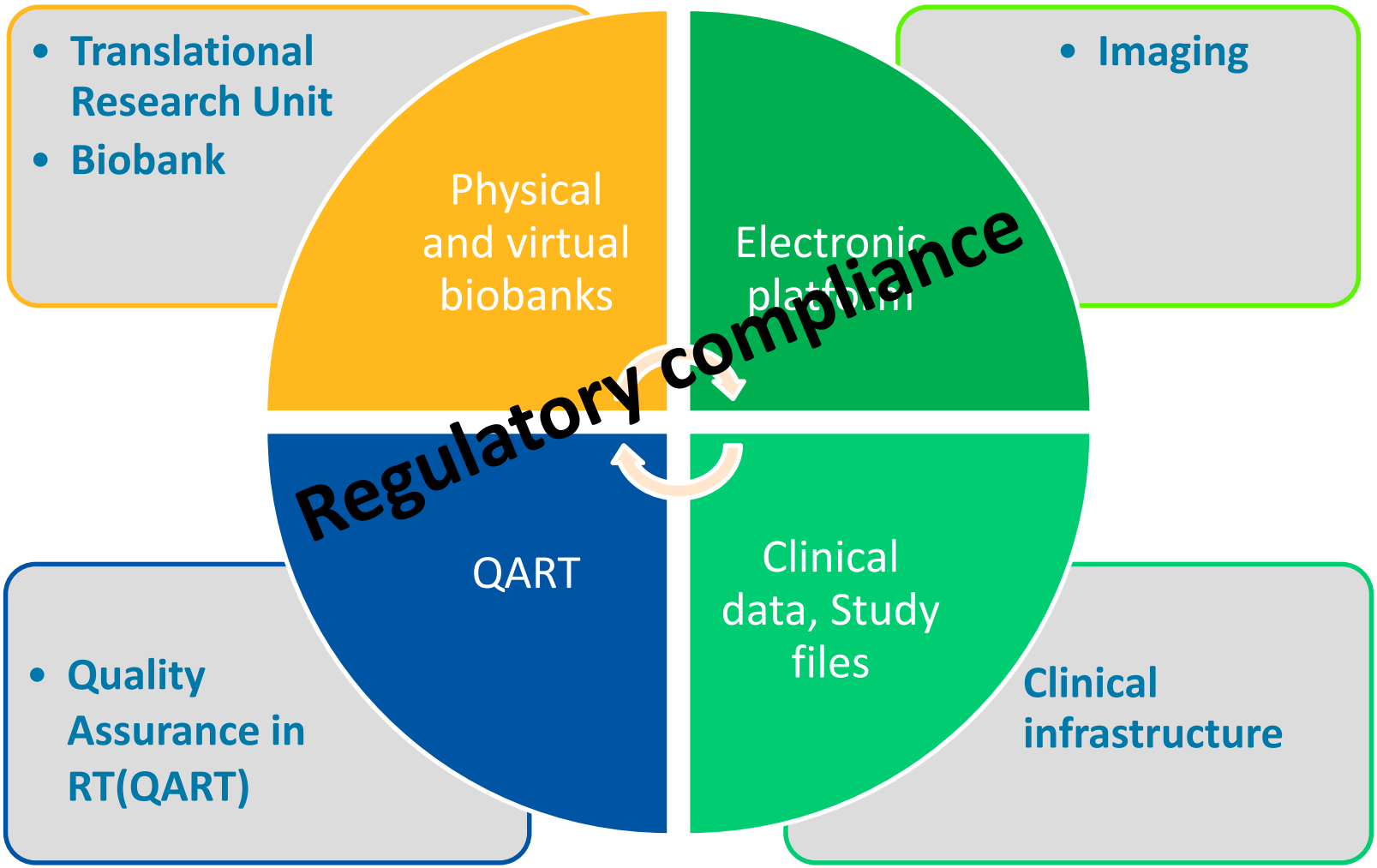
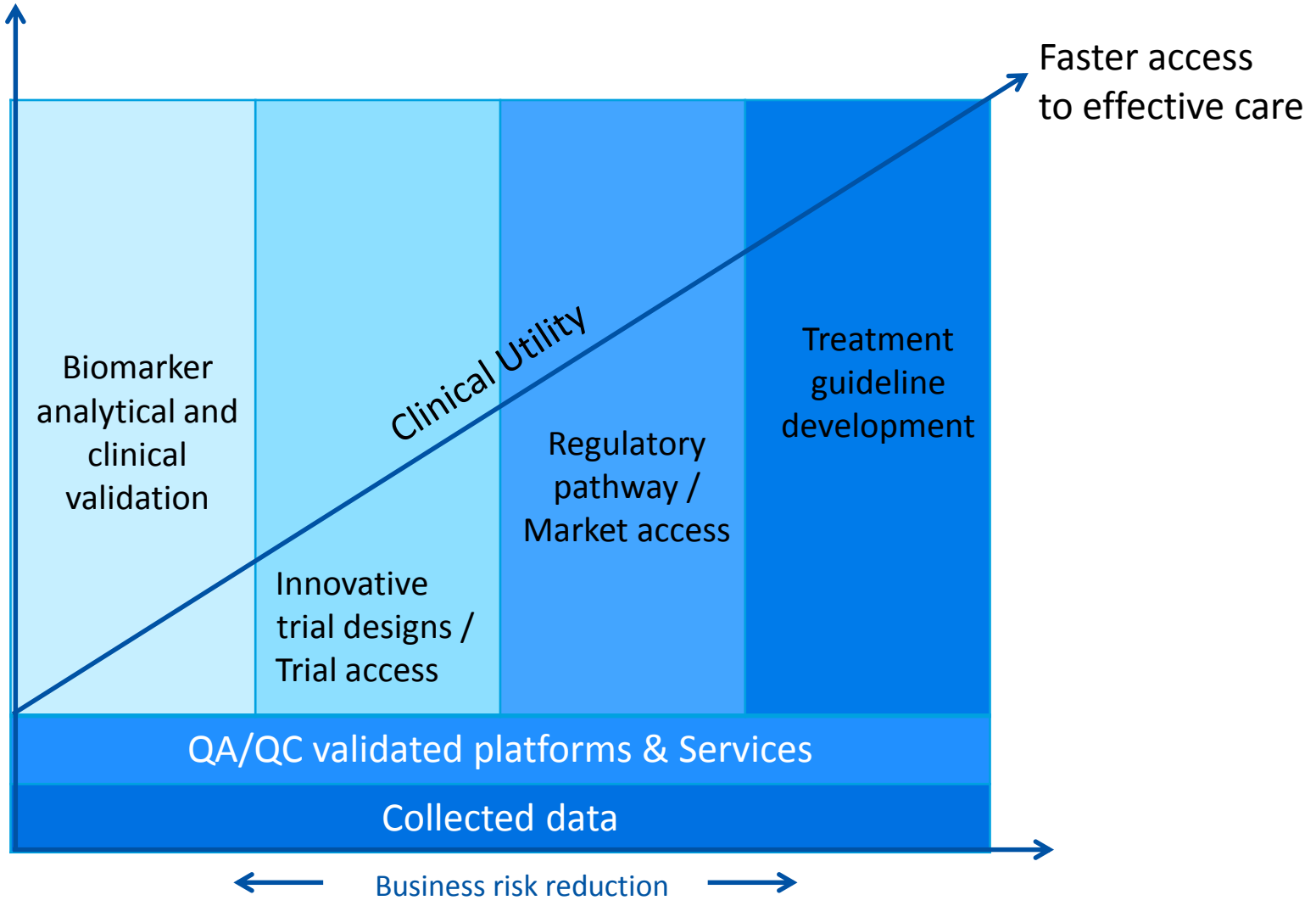
Back-up slides

EORTC Infrastructure to support new generation clinical trials



Towards a data driven Healthcare



Re-engineering the processes but also the methods towards patient centred research

- Robustness of data sets / methodological evidence
- Better anticipation of therapeutic strategies in real life
- Addressing access to clinical research
  - Patient to protocols
- Addressing access in health care
  - Optimal use of treatments
- Relevance of patient centred end-points
- Approaches to robustness of patient centred end-points

TRANSFORMING ASSETS AND STRENGTHS

SPECTA (Screening Cancer Patients for Efficient Clinical Trial Access)

SPECTA is an agile and adaptable infrastructure to reach patients outside of clinical trials. It includes

- A protocol for longitudinal collection of cancer patient data and human biological material without immediate interventional intent
- An informed consent form allowing future unspecified use of the collected data and human biological material, provided that all undefined testing eventually obtains ethical committee approval (without repeat consent)
- The logistics: a biobanking and testing infrastructure, to be activated according to the needs of the attached clinical trials or research projects

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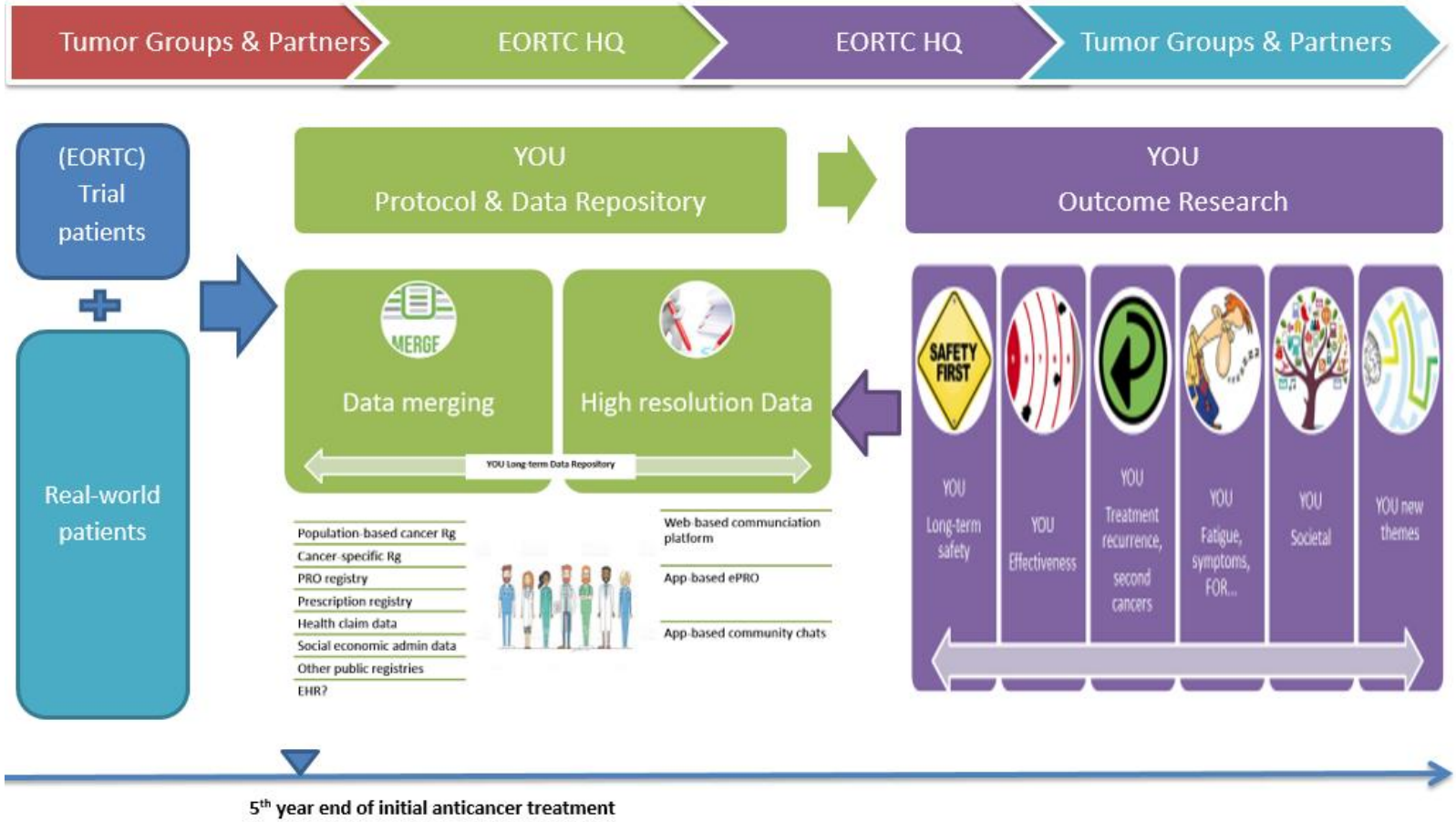
E^2-RADIATE

- Offer in Europe an integrated platform that can efficiently collect information on radiation treatment and techniques, linked to clinical information, detailed diagnostic and treatment planning images
- Build on the existing QART programs of the EORTC
  - Harmonized registration of patients: common std data elements
  - Link clinical database with DICOM format image
  - Adaptive platform accommodating new techniques
  - Partnership and data sharing
- Focus on 2 projects (5Y):
  - Particle therapy: registry with objective to normal tissue sparing as compared to photons and probability to lower complications
  - Oligometastatic patients: identification of patients and patterns of care

The YOU protocol and research platform



The EORTC Early Clinical Investigator Leadership Program

- **33** promising ECIs selected by EORTC groups
- November 2017-March 2019
- **Objective:** raise the next generation of EORTC leaders with full competence to navigate in an evolving environment beyond the sciences, what they need to know to be driving clinical research program 2020-2030 beyond science and medicine

The ECI program is built around six unique dimensions

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EORTC leadership

People leadership

Field work projects

- Building trust
- Connecting medical & cross-functional networks
- Coaching
- Strengths and passions
- Managing energy
- Inspirational Leadership & role modeling

- Communication: Summary vs. synthesis
- Being present as a Medical Affairs Leader
- Negotiation theory
- Effective interactions
- Communicating for impact

We need to work differently..

- Eliminate waste / Improve efficiency
- From siloed tumor based projects to transversal approaches
- Technology based clinical research and bioinformatics

Infrastructure projects

- HBM related infrastructure: SPECTA
- Surgery related infrastructure: SURCARE
- Radiotherapy related infrastructure (E^2-RADIatE)
- Long term outcome/survivorship infrastructure: YOU

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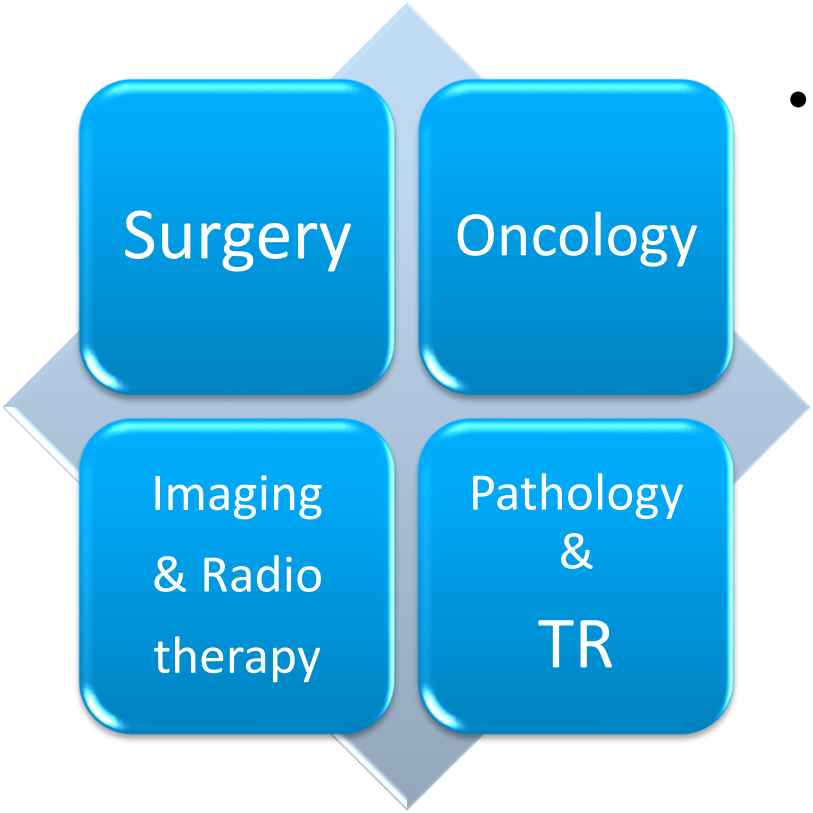
SurCare: An integrated quality assurance program for Prospective Surgical Clinical Research

Updates



- Methodology of Integrated QA
  - Credentialing
    - Assessment of surgical / hospital expertise
  - Standardization
    - Standard surgical protocol
    - Guideline development
    - Definition of quality indicators
  - Central review
    - Use intraoperative pictures for QC
    - Review of surgical complications
    - Review of pathology

Investing in the next generation of clinical investigators

- EORTC fellowships
- ECCO-AACR-EORTC-ESMO Methods in Clinical Cancer Research Workshop
- Early Career Investigator (ECI) Leadership programme

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Education, training and QOL