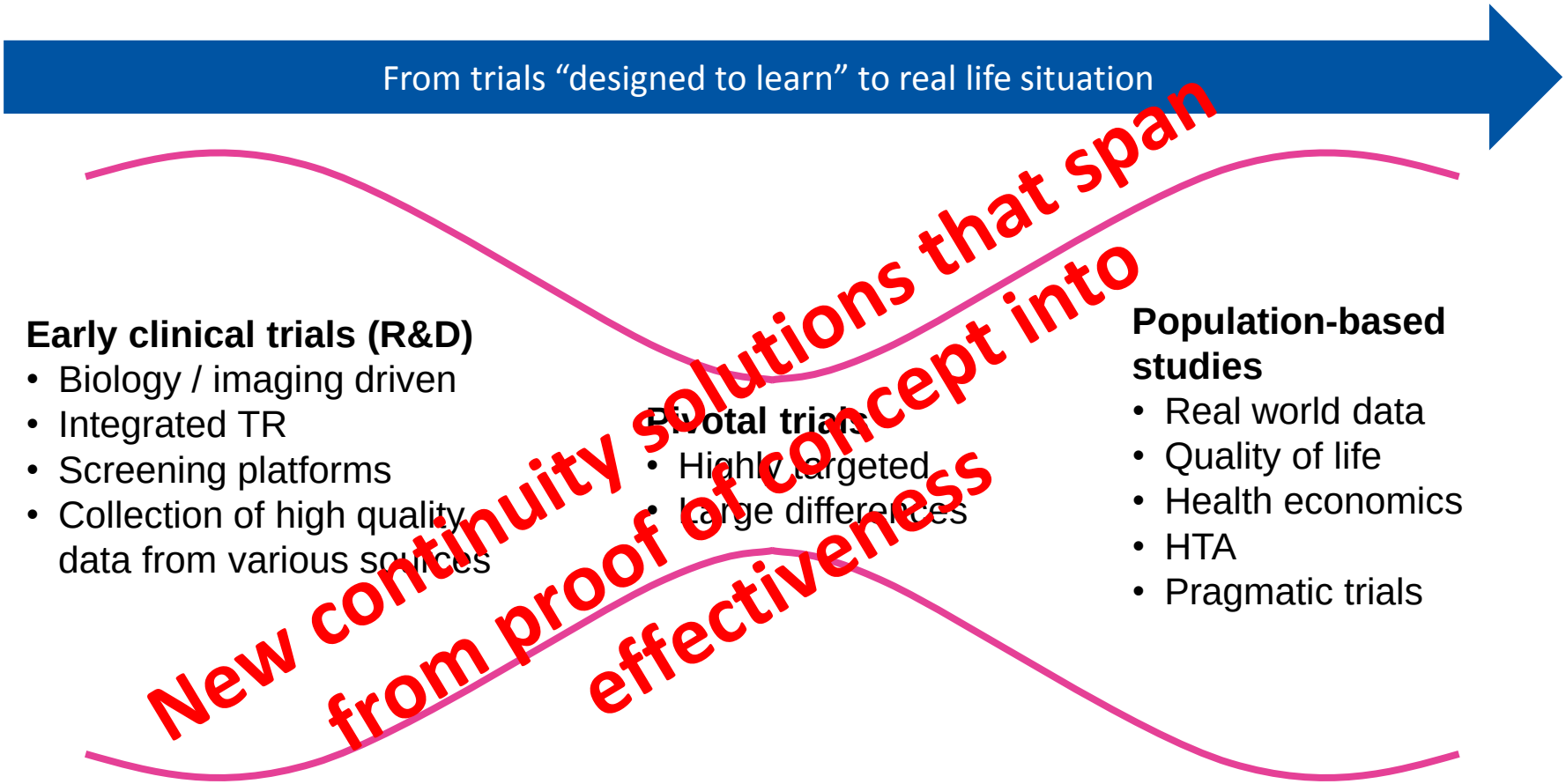
Conducting International non-commercial trials: the experience of the EORTC

Denis Lacombe, MD, MSc
EORTC, Director General
Brussels, Belgium

A world-class network	An expert HQ	Unique output
• 4,600 collaborators • 640 institutions • 37 countries • 21 groups & task-forces • 100 collaborative groups	• 191 employees • 190,000 patients in database • 24,000 patients in follow-up	• **18 new studies opened in 2015** • **48 studies open to patient entry** • 25 studies in protocol outline development • 22 studies in protocol development • 14 studies in regulatory activation • 83,551 pts on studies (2000-2015) • **Working on ≈ 190 studies**

The changing clinical research pathway



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

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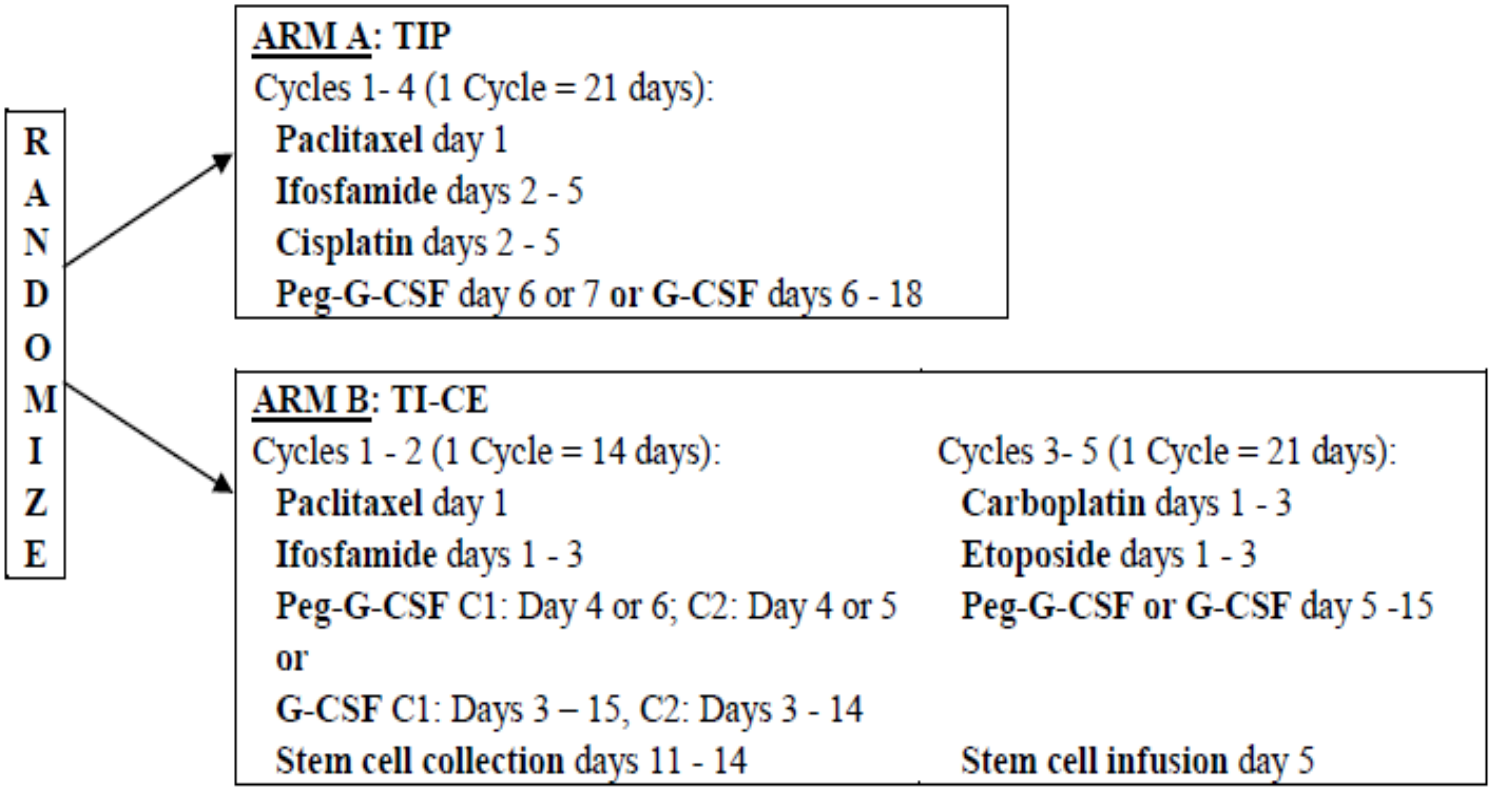
Setting the scene

- National vs International
  - Nothing compares…. (TIGER trial)
  - Nationals assume that a European expertise will come from the sum of their national expertise
  - Infrastructure/IT/CTMS/solutions: needs vs deliverables
- Academic/non commercial/IITs/Pragmatic trials/Public health trials
- Trusted body: data control and quality, publication
  - Regulatory level type of quality control?

A Randomized phase III trial comparing conventional-dose chemotherapy with high dose chemotherapy as first salvage treatment in relapsed or refractory germ cell tumors

Schema



Treatment is to continue until disease progression, unacceptable toxicity, or completion of all protocol treatment, whichever comes first.

A Global Collaboration

Participating Countries

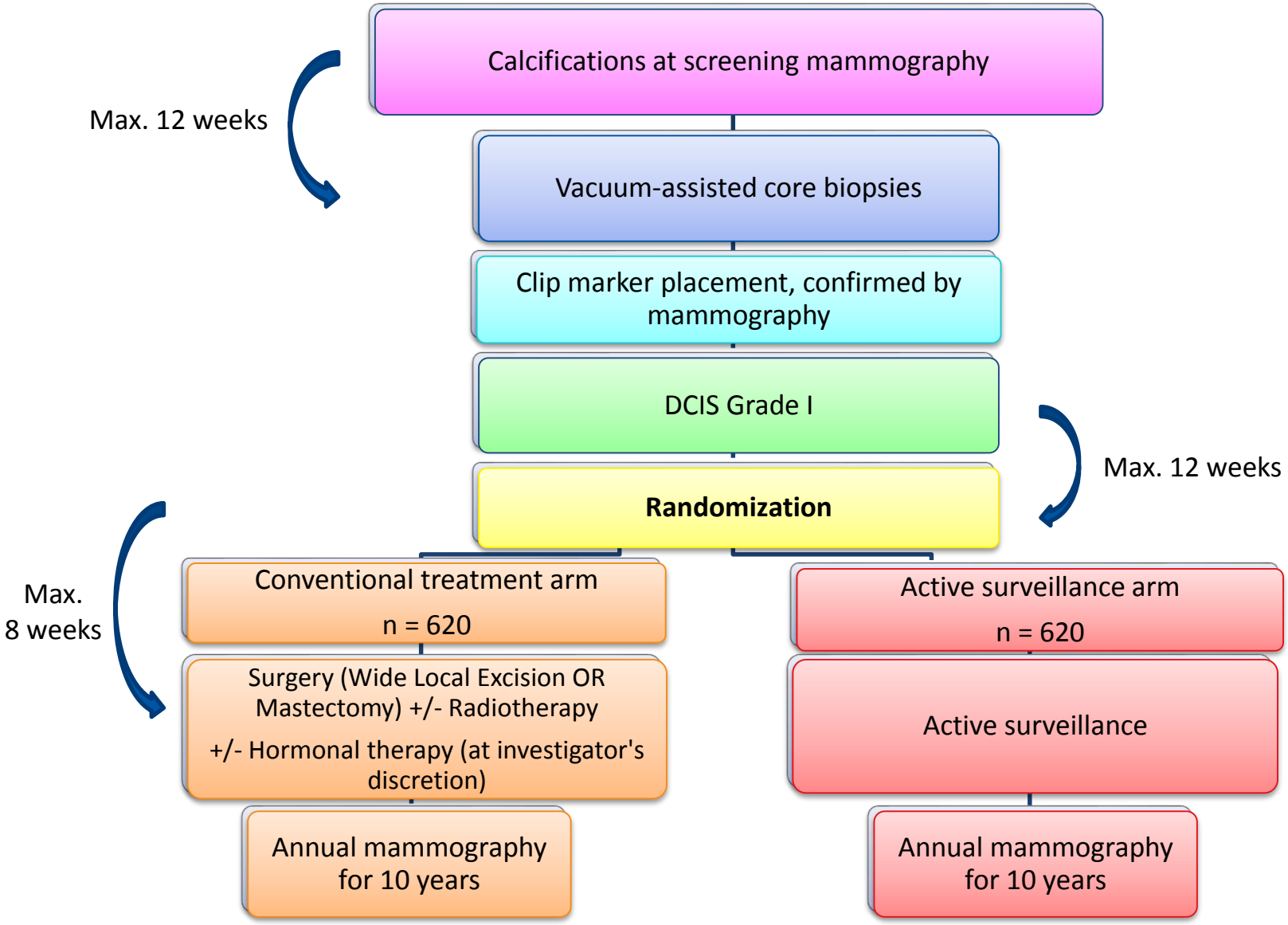
- North America
  - USA and Canada (via US cooperative groups)
- Europe via **EORTC**:
  - United Kingdom (ICR)
  - Italy
  - France (Unicancer)
  - Germany (KKS)
  - Belgium
  - Denmark
  - Netherlands
  - Switzerland
  - Spain
  - Ireland (ICORG)
- Australia, and New Zealand likely to join via ANZUP

Getting started…

Feasibility: exportability of the concept

- Control arm
- Acceptability: i.e. LORD trial
- Operational feasibility ex Surtime
- Access to facilities/std of care: i.e. failure follow up imaging initiative in lung cancer or conflict of end-point in H&N when follow up needed is imaging and std practice is endoscopy

The LORD trial design



Patient eligibility

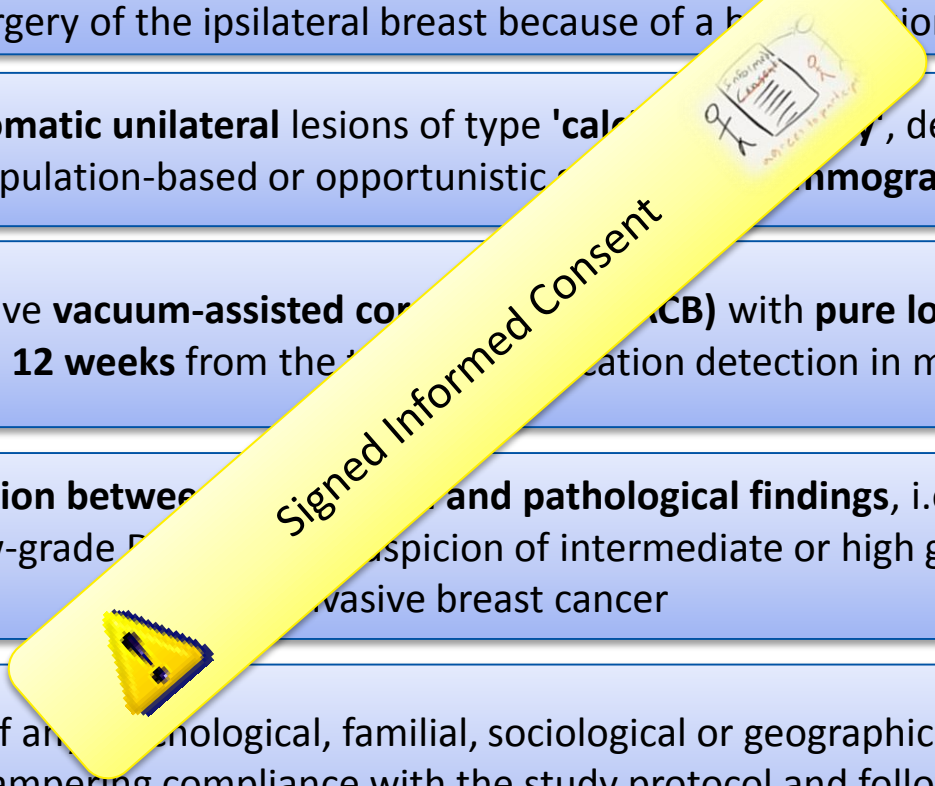
Women ≥ 45 years of age
Any menopausal state
No personal or family history of BRCA 1/2 m tion
Prior surgery of the ipsilateral breast because of a b ion allowed

Asymptomatic unilateral lesions of type **'calc y'**, detected by population-based or opportunistic **mmography**

Representative **vacuum-assisted co CB)** with **pure low-grade DCIS** taken **within 12 weeks** from the ation detection in mammography

Good correlation betwee and pathological findings, i.e. both findings confirm low-grade D spicion of intermediate or high grade DCIS or vasive breast cancer

Absence of an hological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule



Regulatory and legal

- National applications/sponsorship:
  - VHP
- Ethics:
  - Varying operations
  - Varying requirements
  - Insurance requirements

Operational aspects

- Drug supplies:
    - IMP related costs to be compensated
    - Coordination of delivery
    - Labels in multiple languages
- PIS/ICs
    - Local/national aspects
    - Validation of translations
- Biobanking
    - Over estimation of the capacities of virtual biobanking
- Data sharing capacities and processes
- Auditable set of SOPs per international standards

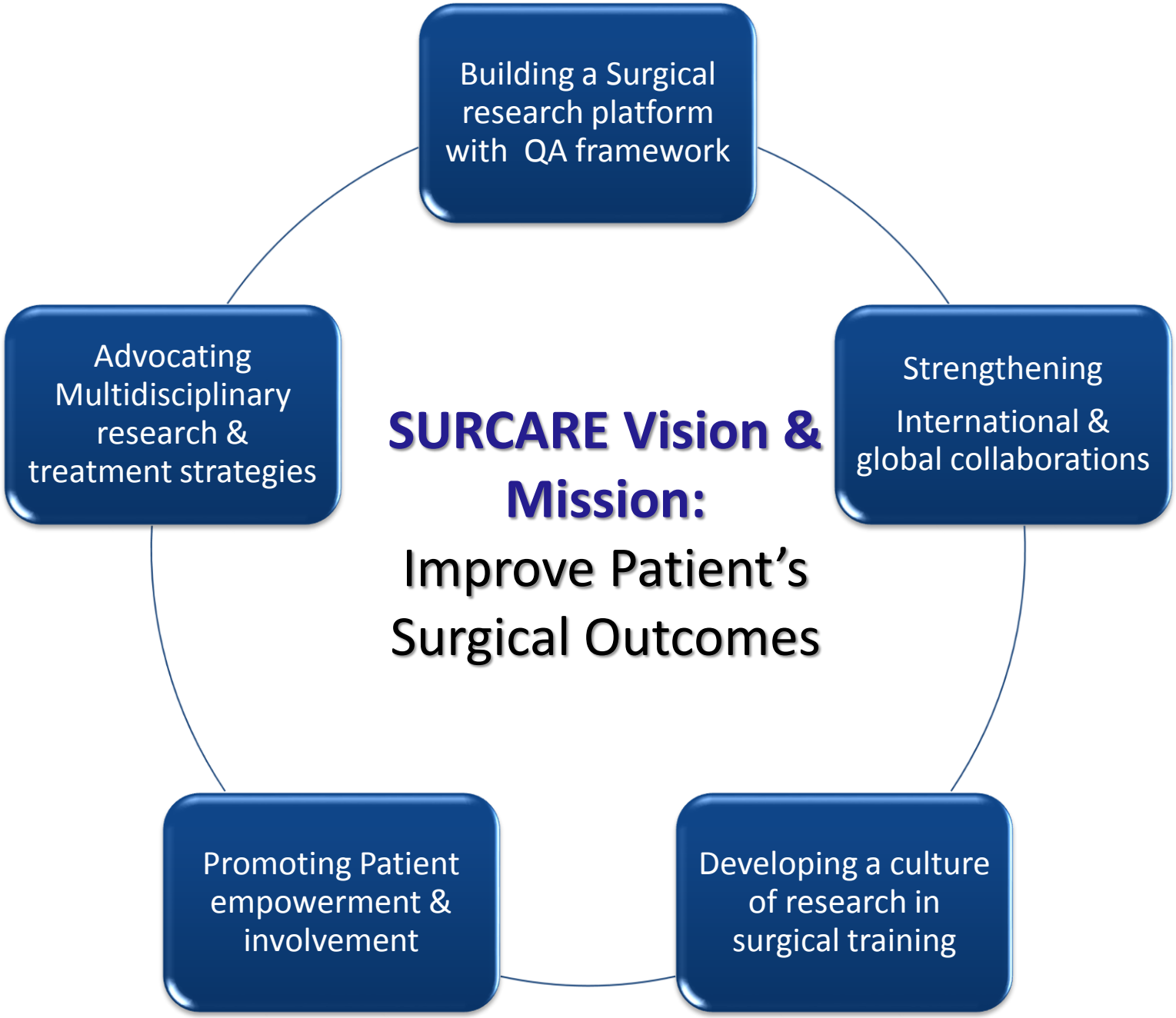
Budgeting

- Finality of the data justifies the means:
  - Professional quality and infrastructure up to the standards as they evolve
- Under estimation of:
  - Resources needed for international coordination
  - Passthrough costs: insurance, on site monitoring, ICOMs, drug supplies, etc.
  - Per patient budgeting is sub-optimal for international trials
  - 4- part budgets: fixed costs/per patient/passthroughs/ICOMs

Funding

- European calls rarely meet the needs
- National funds remain the countries
- Challenges to fund central coordination:
  - Surcare: coordination of the national leagues
  - Rando-discontinuation melanoma: coordination of the payers
  - The sum of the national fundings do not support international efforts

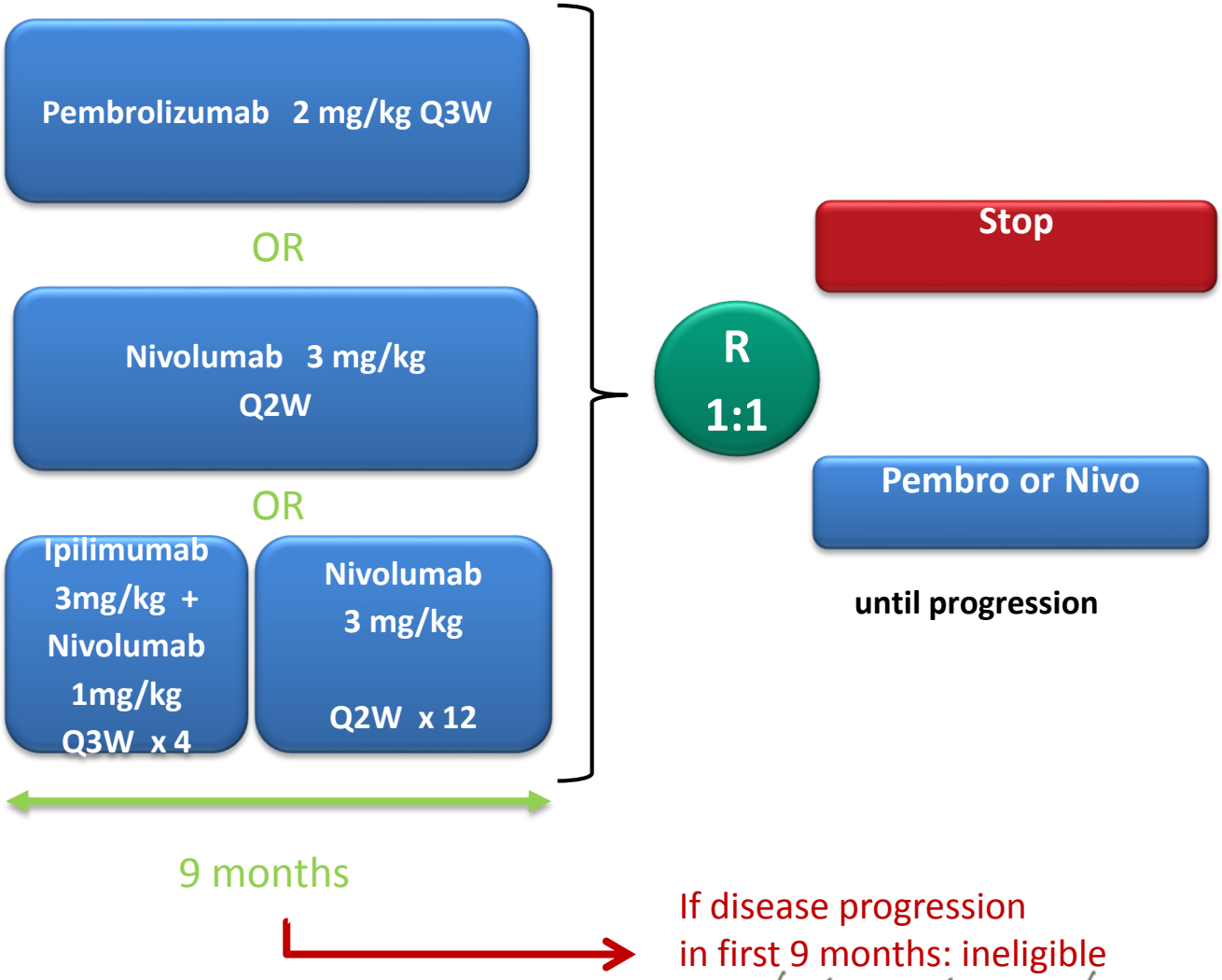
SURCARE: Framework for Integrated Quality Assurance


Building a Surgical research platform with QA framework
Strengthening International & global collaborations
Developing a culture of research in surgical training
Promoting Patient empowerment & involvement
Advocating Multidisciplinary research & treatment strategies
SURCARE Vision & Mission:
Improve Patient's Surgical Outcomes

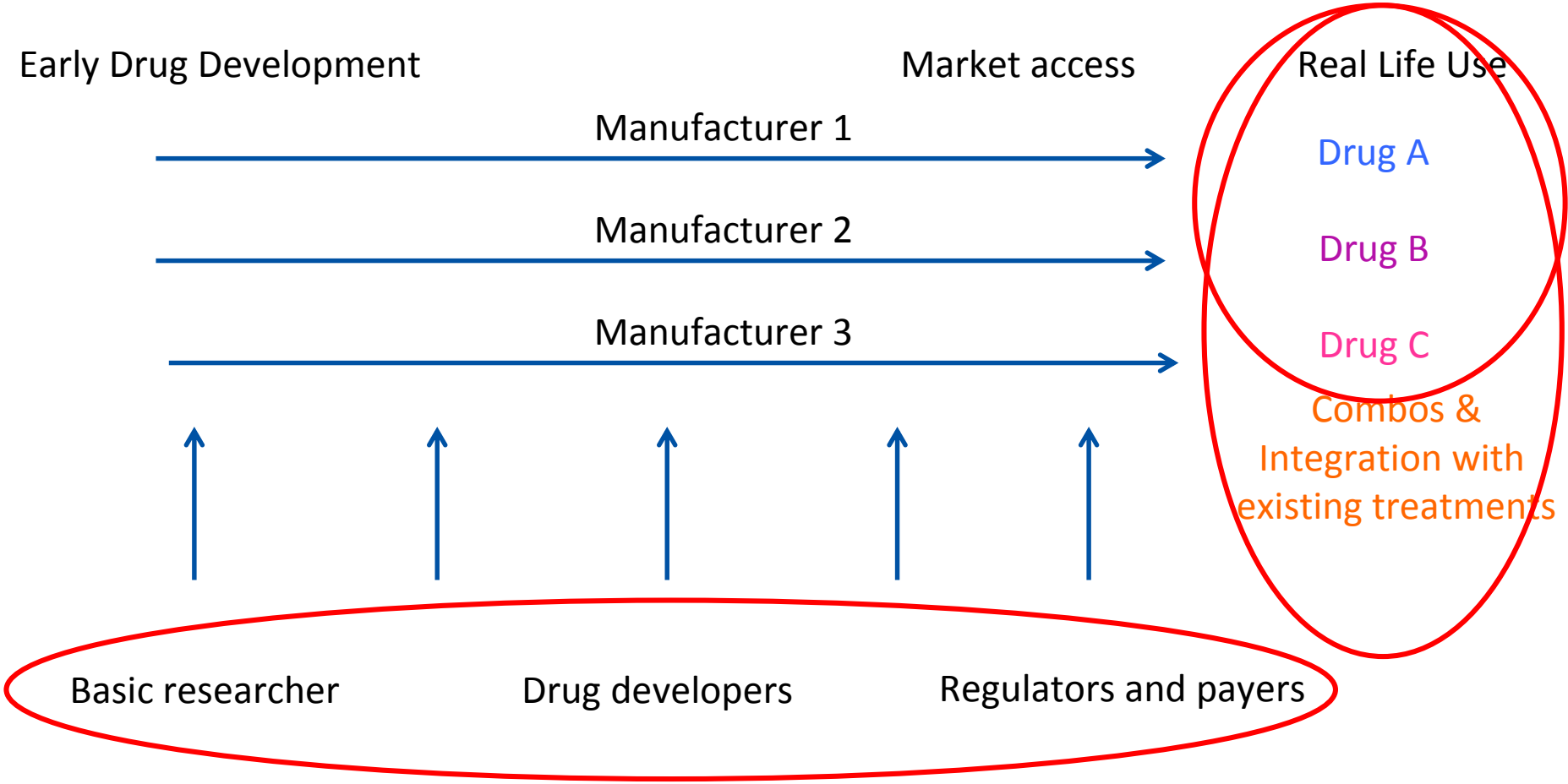
The Global Network of SURCARE

EORTC 1639-MG: Study design

- Unresectable stage III or IV melanoma
- No clinically significant tumor-related symptoms or evidence of rapidly progressive disease
- ECOG PS 0-1
- Eligible to receive or currently receiving (< 9 months) PD-1 inhibitor or combined with a CTLA4 inhibitor as 1st line, which is Health Authority approved and publically-funded



From R&D to real life…



Conducting the study

Need to align on the needs

- Quality assurances programs
- Pharmacovigilance:
  - Safety management and reporting
  - DSURs/regulatory reports
- Risk/benefits and risk based programs:
  - i.e. on-site quality control
- Reporting capacities in all required format:
  - New kid on the block: lay language summaries

Back to the future…

- Getting ready with the triple regulations
- In many ways… back to 2004
- Inconsistencies and conflicts between the 3 regulations (CTR, IVDR and DPR) currently being addressed by EORTC
- New regulatory skills to be developed, will raise challenges for small volume international non commercial sponsors

THANK YOU FOR YOUR ATTENTION