

Osteosarcoma clinical landscape and challenges- lessons from EURAMOS-1

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Before EURAMOS-1

- UK commitment to clinical trials before and through European Osteosarcoma Intergroup

Study	Details	Ref
MRC Working Party on Bone Sarcoma study	n=235 1975-1981 VCR + MTX vs VCR + MTX + Dox	Br. J. Cancer (1986), 53, 513-518
BO02	n=198, AP vs AP + M, 1983-1986	Bramwell et al JCO (1992) 10, 1579-91
BO03	n=407, AP vs T10	Souhami et al Lancet (1997) 350, 911-17
BO06	n=497, 1993-2002, AP q2w vs AP q3w	Lewis et al JNCI (2007), 99, 112-28

21st Century catalysts to collaborative efforts in osteosarcoma

- Survival not improving
- Study groups at an impasse

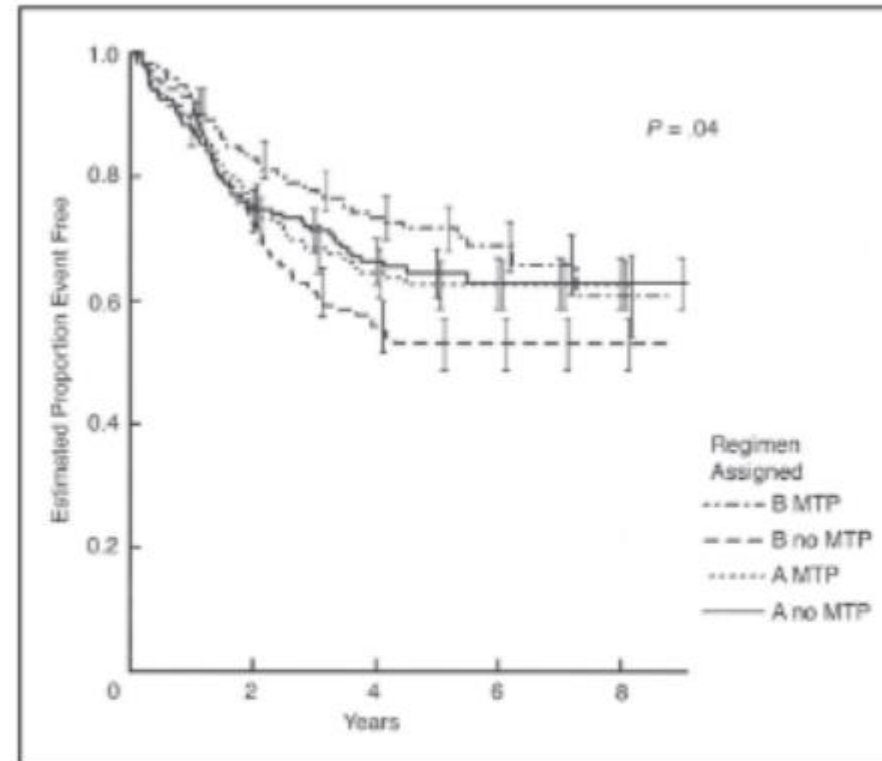
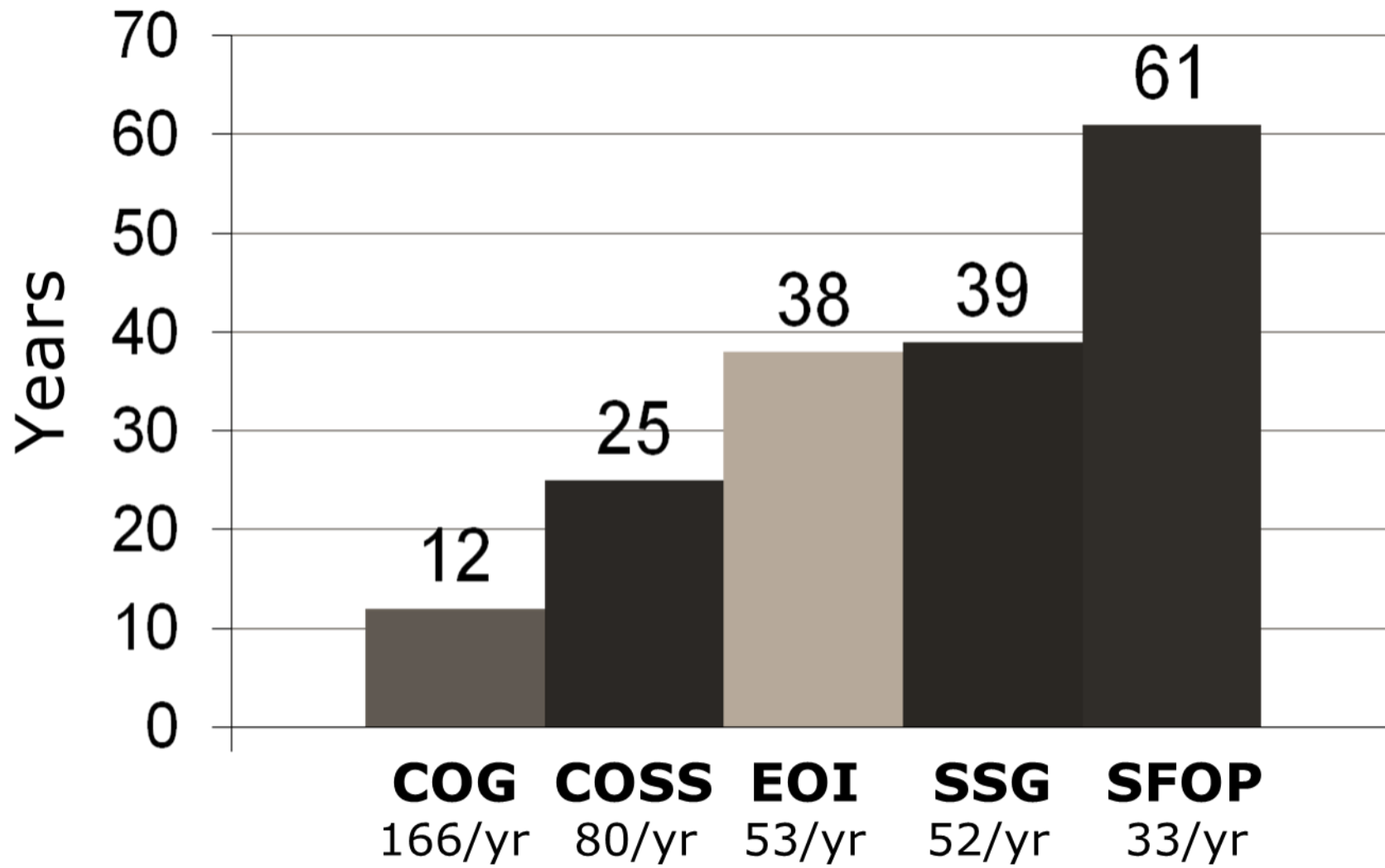


Fig 4. Event-free survival for patients according to treatment arm. Regimen A consisting of cisplatin, doxorubicin, and high-dose methotrexate was the standard arm of this study. Regimen B included the same agents with the addition of ifosfamide. Regimens A+ and B+ also included the investigational agent muramyl tripeptide (MTP). Overall trend for difference was significant ($P = .04$).

Accrual to 2,000 pts at previous rates



European and American Osteosarcoma Study Group

- **Established Oct 2001**
- **Participating groups - COSS, COG, EOI, SSG**
- ***Aim***
 - **to improve survival from OS**
- ***Objectives***
 - **to carry out large international randomised trials**
 - **to facilitate biological research**
 - **to seek new therapeutic approaches**
 - **to develop common understanding and methodologies for staging, pathology etc.**

European and American Osteosarcoma Study

COG

Childrens' Oncology Group



COSS

Cooperative Osteosarcoma Study Group



EOI

European Osteosarcoma Intergroup



SSG

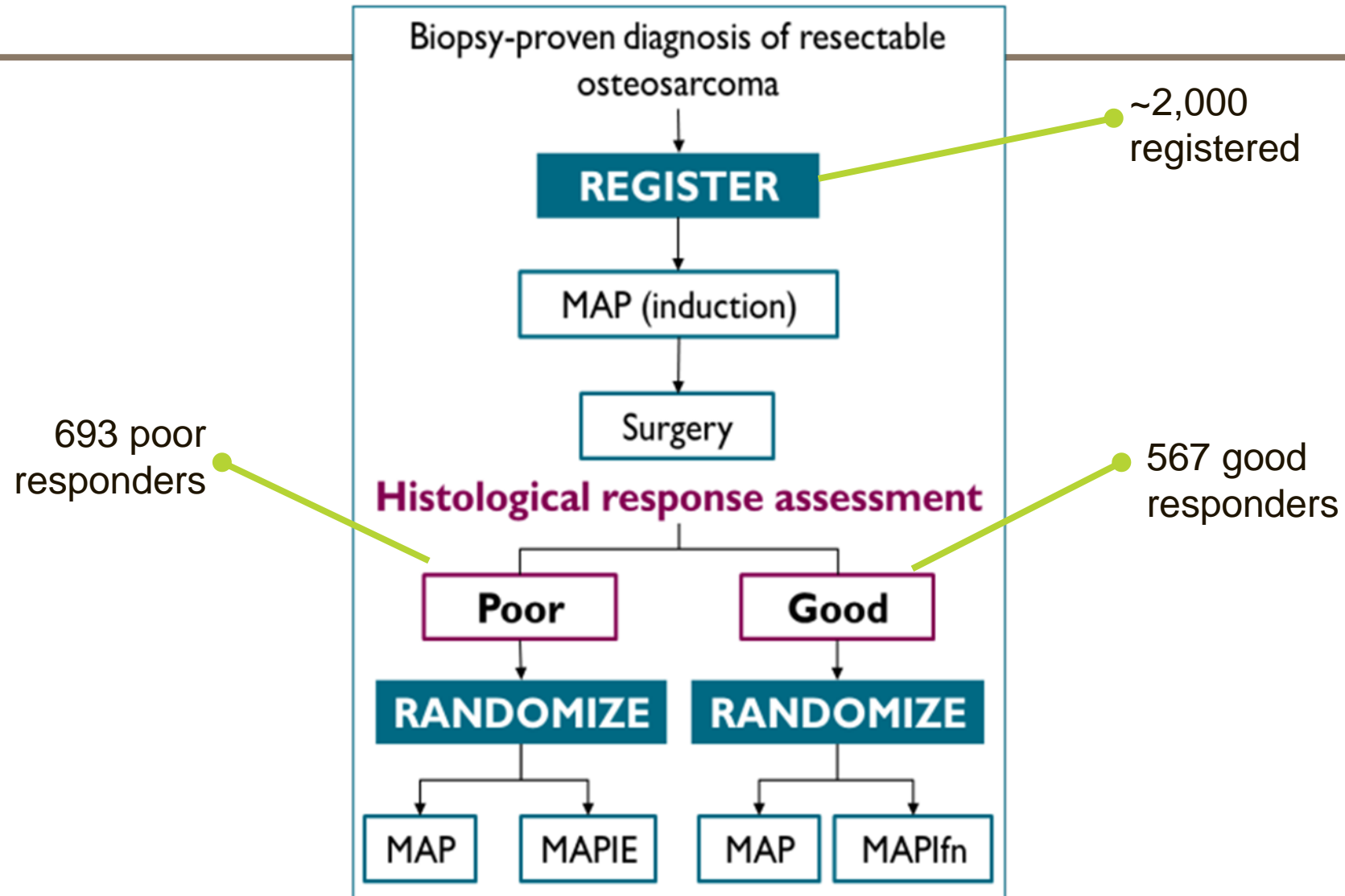
Scandinavian Sarcoma Group



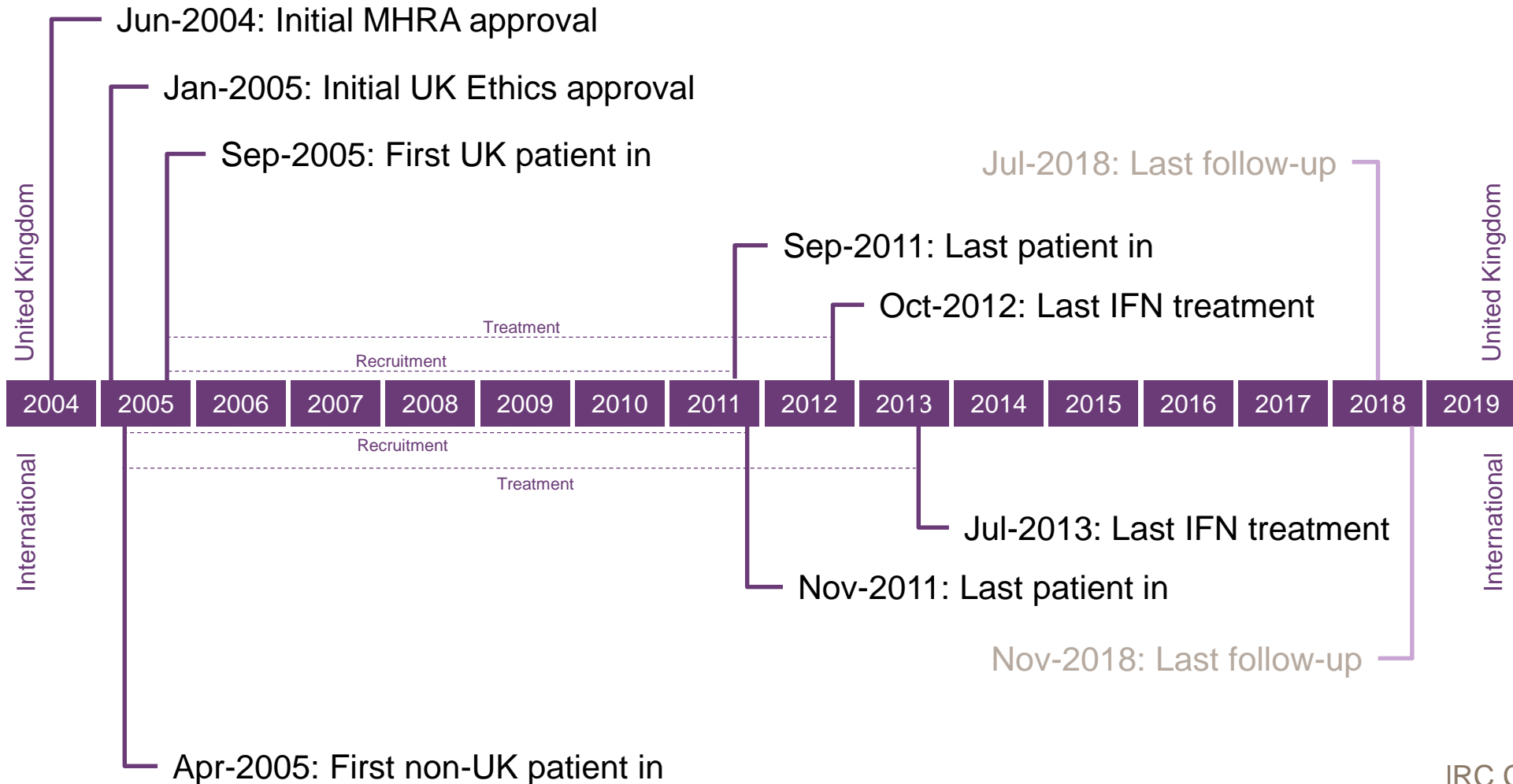
EURAMOS

The EURAMOS logo is located on the right side of the slide, enclosed in a purple bracket that groups the four study groups. The logo consists of the word "EURAMOS" in a blue, sans-serif font, with a white swoosh underneath it, all set against an orange rectangular background.

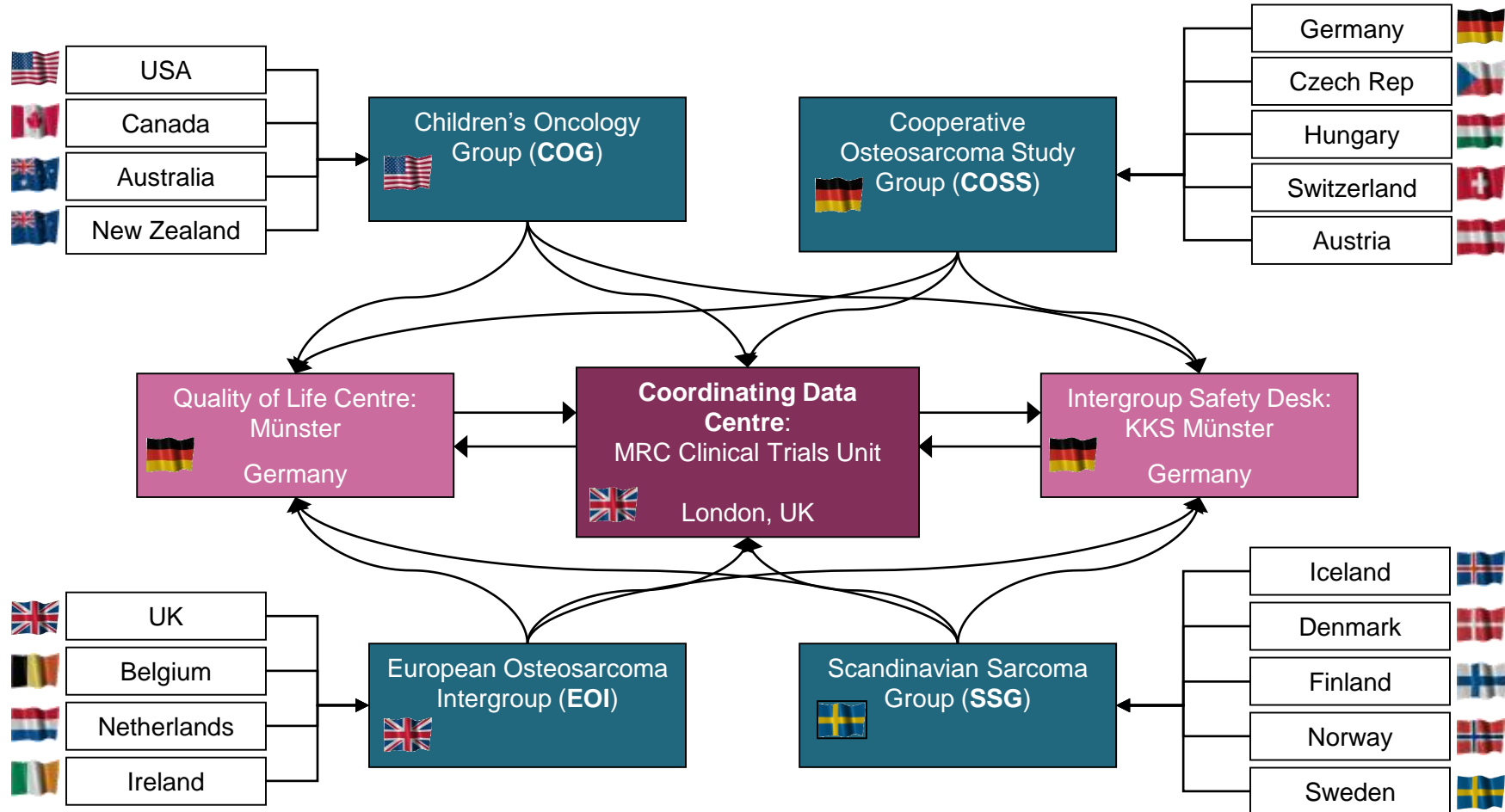
EURAMOS-1 Trial Design



Key dates: Recruitment, treatment



Trial set-up



Recruitment: The value of collaboration

- EURAMOS-1 is the largest trial completed in osteosarcoma
- On average per year,
 - 405 patients were registered
 - 238 were randomised
- Compare with previous EOI trial,
 - 504 patients randomised over 9 years
 - 56 per year
- From the EOI alone,
 - To recruit ~2000 patients would take 40 years

Is EURAMOS-1 a firm foundation for future studies?

- Outputs from EURAMOS-1...
 - Model for collaborative research in rare cancers
 - Participated in EU-level consultations on trials in rare cancers
 - Huge international enthusiasm for further collaborative studies
 - EURAMOS STRATEGY GROUP (ESG)
 - Expanded membership inc. the EORTC, French, Italian, Spanish, Japanese and Australasian Sarcoma Groups
 - Infrastructure to build on for future studies put in place
 - 1st future trials planning meetings held in 2009

• So...

Where is EURAMOS-2?

Challenges to collaboration

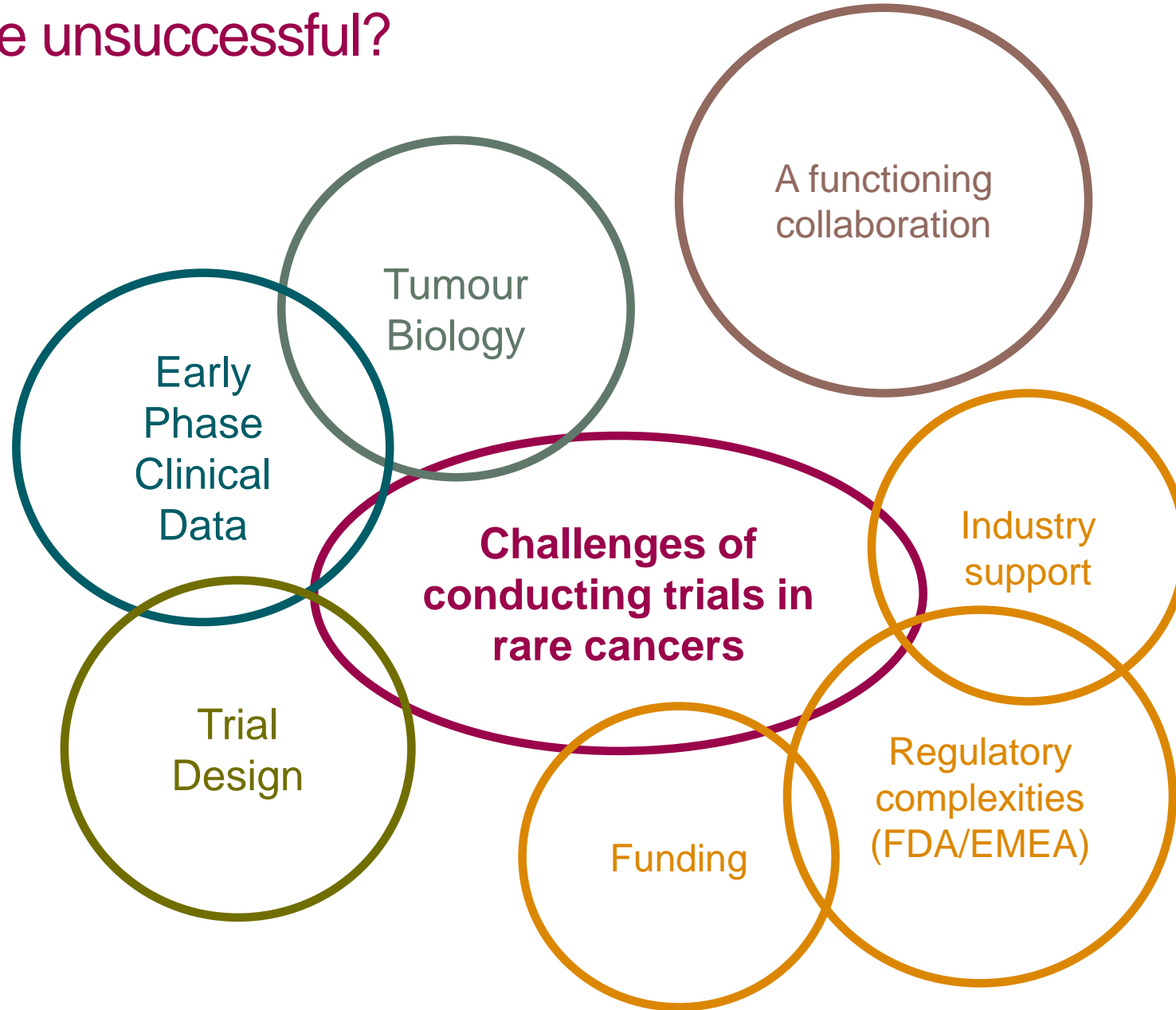
Clinical and personal

- Differing practices: pragmatism and compromise
- Buy-in and ownership
- Less recognition for principal investigators

Practical

- Sponsorship
- Infrastructure requirements
- Differing regulations by jurisdiction
 - Knowledge
 - Local processes and national regulations
- Funding support
- Indemnity

Why were we unsuccessful?



Key learning

- EURAMOS-1 shows that large randomised controlled trials in osteosarcoma can be done **but**
- Clinical trials are hard and need firm foundations as well as answerable questions
 - Underlying biological rationale and possibly good early phase evidence
 - Need to use efficient trial designs
 - Rarely have resources or opportunity to do confirmatory trials
- Young adults were still less likely to be registered in the trial and subsequently randomized than younger age-groups.
- Participant involvement in planning, design and conduct of trials in rare cancers is essential and should be promoted
- Since closure, potentially 2,500 patients could have been included in EURAMOS-X

Key Questions

- Major challenges prevent repetition of EURAMOS-like trials. But do we need such trials?
- Why cant we or how do we make use of 'signal' from new drugs – to influence clinical practice and clinical trials?

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