ITCC
INNOVATIVE THERAPIES FOR CHILDREN AND ADOLESCENTS WITH CANCER

2,5 years of CTR and CTIS

Experiences from Academic Sponsor Institutions in the ITCC network

Annual workshop of the European network of paediatric research at EMA (Enpr-EMA)

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Introduction

- Anne Elsinghorst – Trial Manager in Princess Máxima Center for Pediatric Oncology, Utrecht, NL
- Part of ECTR Working Group in Trial and Data Center Máxima
- ITCC: Innovative Therapies for Children and Adolescents with Cancer
  - Clinical trials network focused on delivering new treatments for children and adolescents with cancer in the context of Phase I-II clinical trials

Zwaan, Cancer Treat Rev 2010; Moreno, J Clin Oncol 2023; Bautista, J Clin Oncol, 2024;

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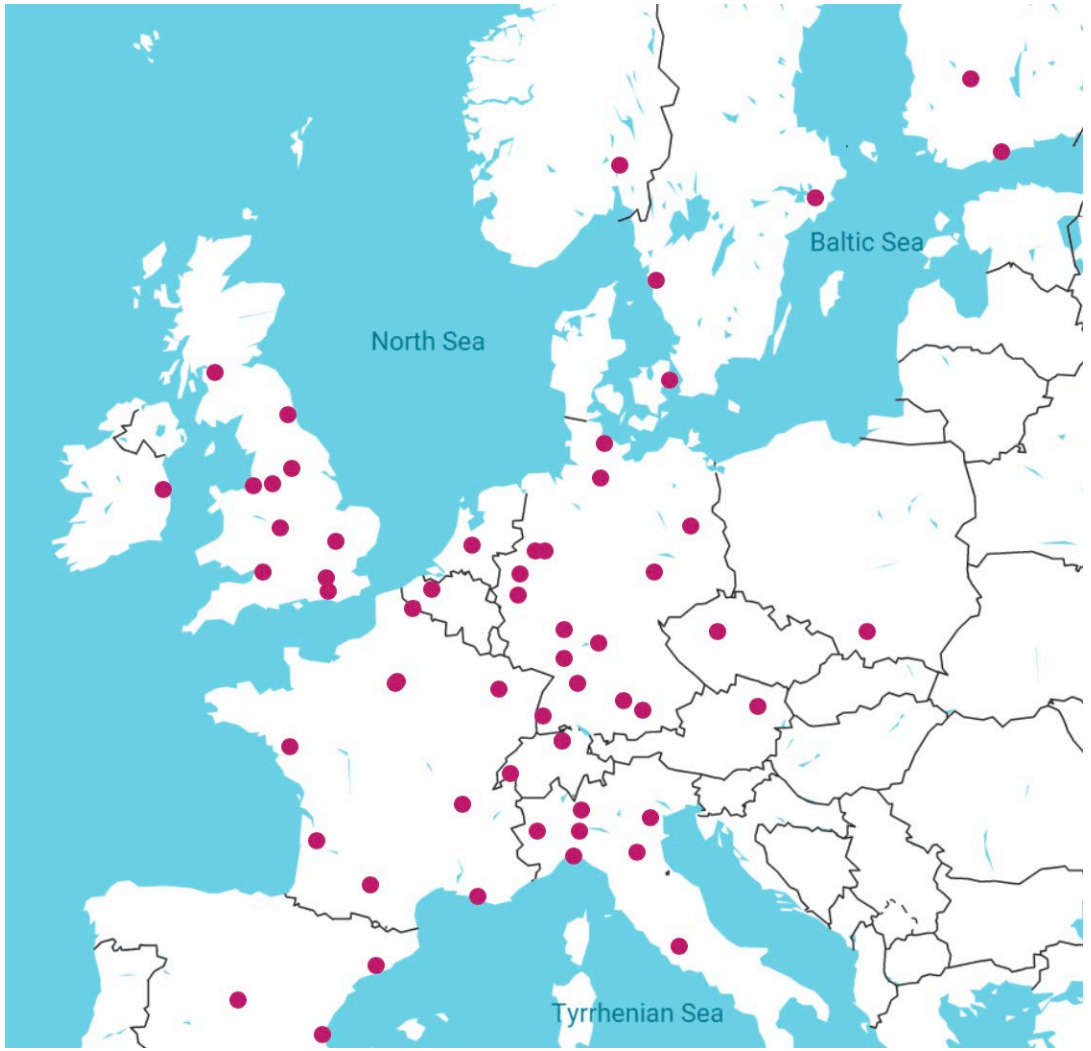
ITCC Trials Network

- 62 European Paediatric Oncology Departments across 17 countries with expertise in conducting early phase trials in children and adolescents



ITCC trials in CTIS - experience

- 4 large Sponsor centers of ITCC (University of Birmingham, Gustave Roussy, KITZ Heidelberg, Princess Maxima)
- Responsibilities of Sponsor center:
  - Implementation of multicenter early phase clinical trials
  - Overall submission coordination and delegation of tasks
  - Finally responsible for all activities in CTIS

	Approved	In preparation or under evaluation in CTIS
Transition studies	35	22
Initial applications	24	22

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Content of presentation

- Implementation of Regulation
- Benefits
- Harmonization across countries
- Complex clinical trials
- Technical issues/shortcomings
- Case study
- Conclusion

Implementation of Regulation

- Working group assigned in Trial and Data Center PMC
  - 3 core members
  - Responsible for training colleagues (~30 persons)
  - Responsible for communicating updates/changes

- Information and updates
  - Newsletters
  - Website Dutch Competent Authorities
  - Progressive insight from RFIs

→ Sources of information scattered, difficult to keep on top of changes

Benefits

- Insight in approval timelines
- CTIS serves as a reference for study documents
  →Especially useful when a CRO is involved
  → Insight in latest versions approved, status of submissions etc.
- Multiple accesses possible -> people can prepare national dossier at same time and for separate parts in the dossier
- EMA is actively improving the system and guidelines
  → e.g. updated transparency guidelines

Harmonization across countries

- Heterogeneity is observed in national guidelines and requirements in both transitional and initial applications
- Differences in national templates compared to EMA template
  - E.g. content of cover letter
- Q&A annex provides some guidance, but overview is missing
  - Challenge to instruct CROs and NCCs
- Cases where MSCs requested changes in protocol (part I), while the application was to add a member state.
  - Consequence: amendment part I needed, 2/3 months delay in start recruitment in this country

Complex clinical trials

- E.g. master protocol with multiple sub-trials (with different IMPs)
- The current CTIS design is not suitable for submitting complex clinical studies
  - →All protocols to be submitted separately
  - →Not possible to submit master in itself, needs to be accompanied with 1 sub-protocol
- Consequence: high costs for separate submissions
  - → Not clear if master protocol is only assessed 1 time
- How to proceed in case a country is not part of submission of first sub-protocol with master
  - → solution: master protocol submitted for reference only

Technical issues/other shortcomings

- No alerts or notifications by email, only in system
- Not possible to submit NSM in parallel to ongoing Part II assessment of DIFFERENT member state
- Difficulties in creating substantial modification because of bug in CTIS
- Multiple examples where Help Desk did not respond timely (solution took > 4 weeks)
- Cancel button too accessible (initial applications were deleted right before submission)
- Part II viewer/preparer access on country-level not possible
- Not always clear who is assessing the dossier, communication possibility with EC/CA is limited

Case: HEM-iSMART trial

- Complex clinical trial – master protocol with 3 sub-protocols
  - Separate EU-CT numbers
- One sub-protocol approved under CTD and transitioned
- 2 sub-protocols added as initial application after transition

Case: HEM-iSMART trial

- Master could not be submitted separately
- Pharmaceutical company refused to cooperate in IMPD-Q only submission

  → no liquid formulation available (important for pediatric patients)
- No NSM possible during ongoing assessment of other MSC
- Wrong RMS invertedly selected in IMPD-Q only submission

  → rigid system, only solution to withdraw whole application
- Bug in system when submitting substantial modification

  → in some cases rapid solution is essential, difficult to emphasize urgency to Help Desk

Conclusion

- Quite early to conclude on improved approval process
- There is a need for further harmonization of country-specific requirements OR better overview of differences between countries
- Important to evaluate a few years after transition period

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  - Princess Máxima Center