

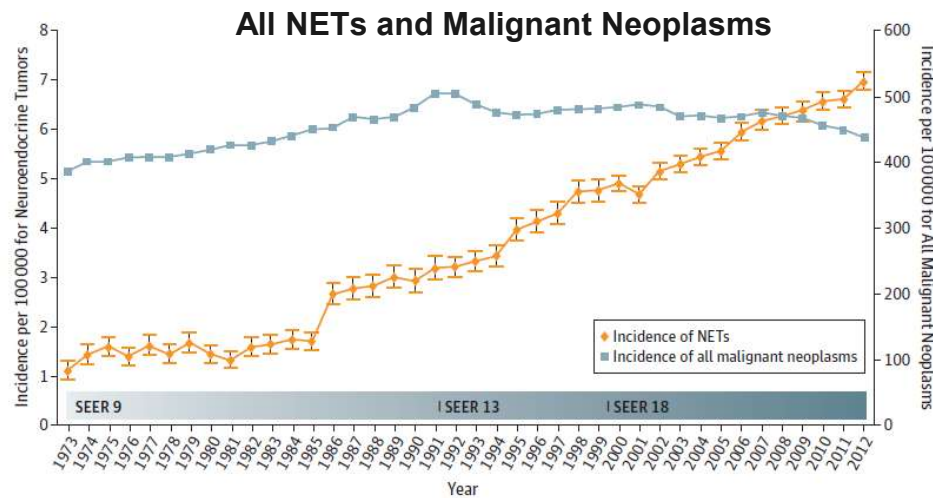


A proposal for a Collaborative Research European Platform in NETs

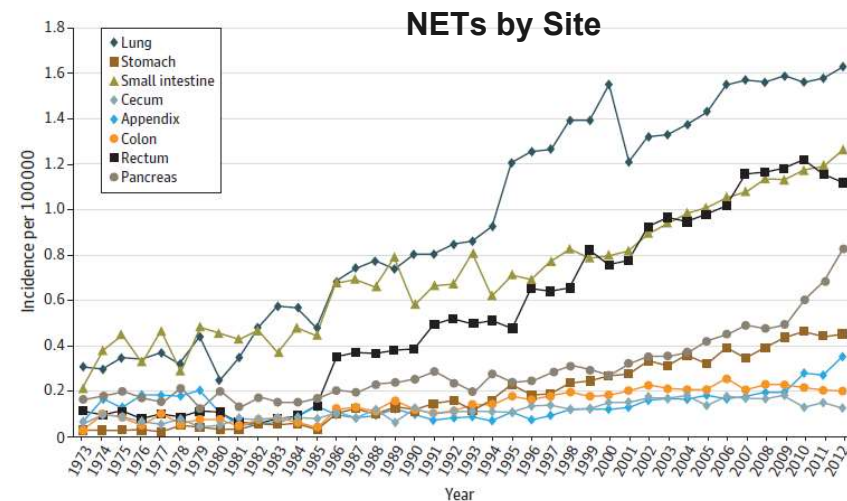
Juan W Valle
23 Nov 2020

- Rare by incidence; not so rare by prevalence

SEER* Data



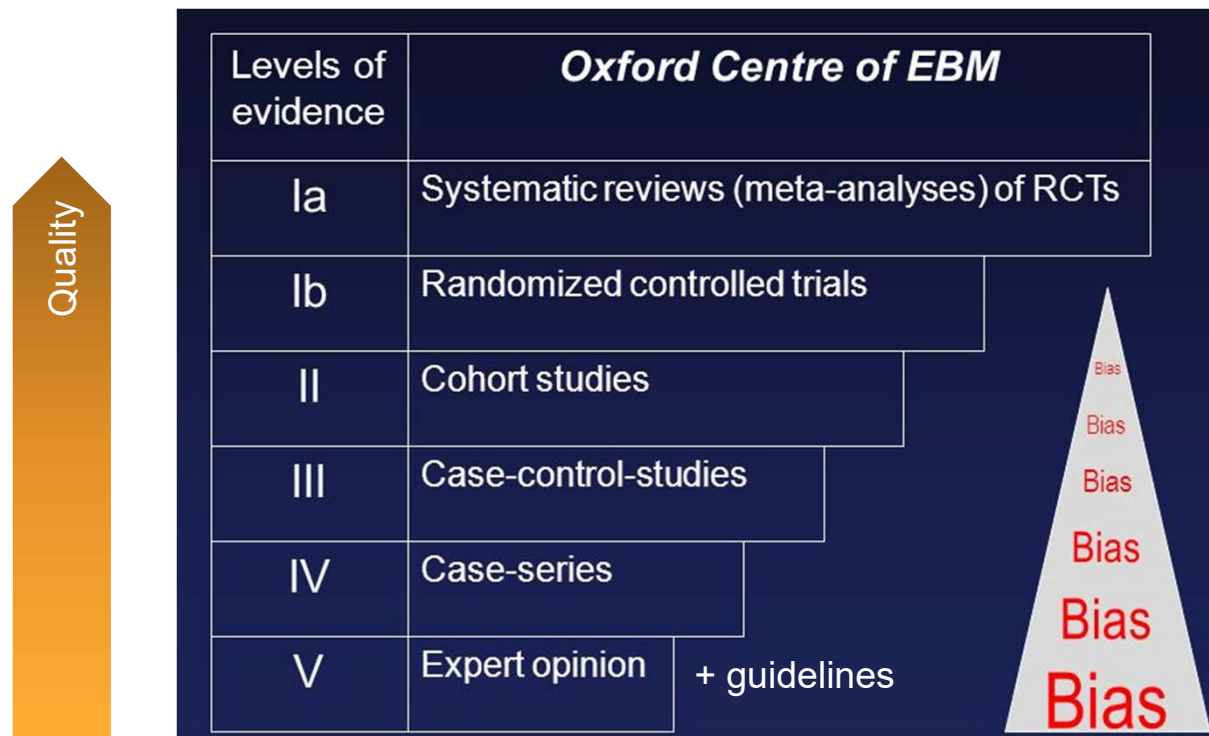
*SEER = Surveillance, Epidemiology, and End Results



Increasing opportunity for research



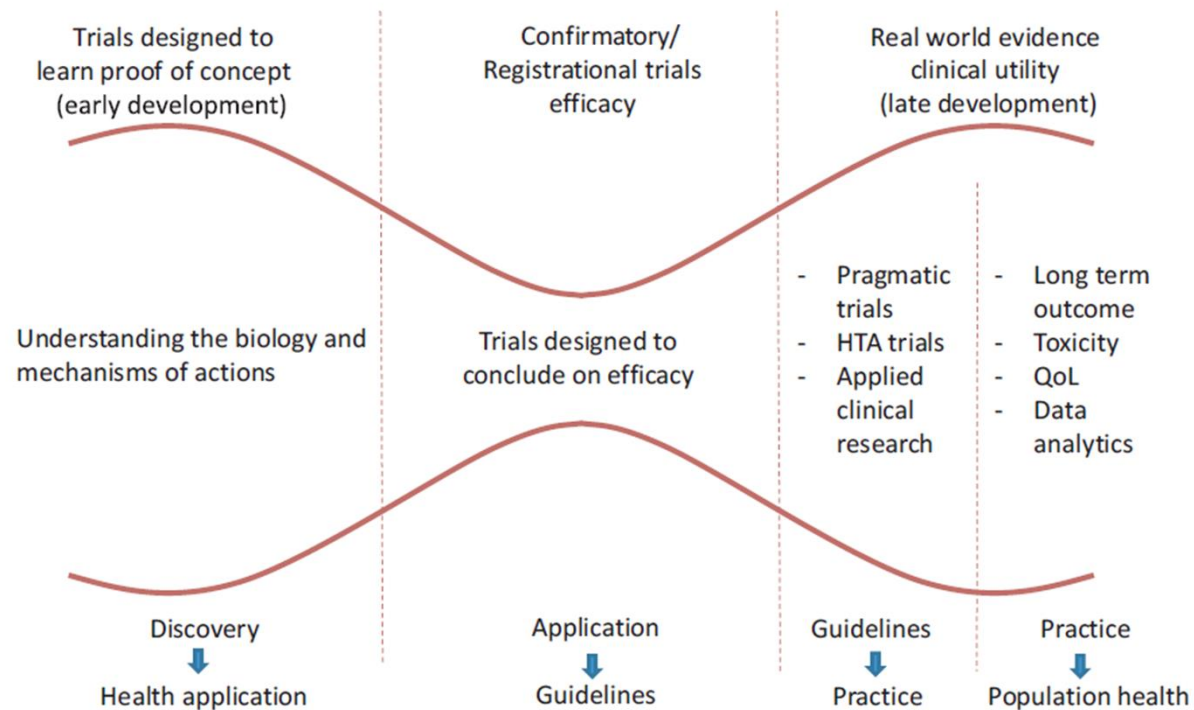
- Levels of evidence



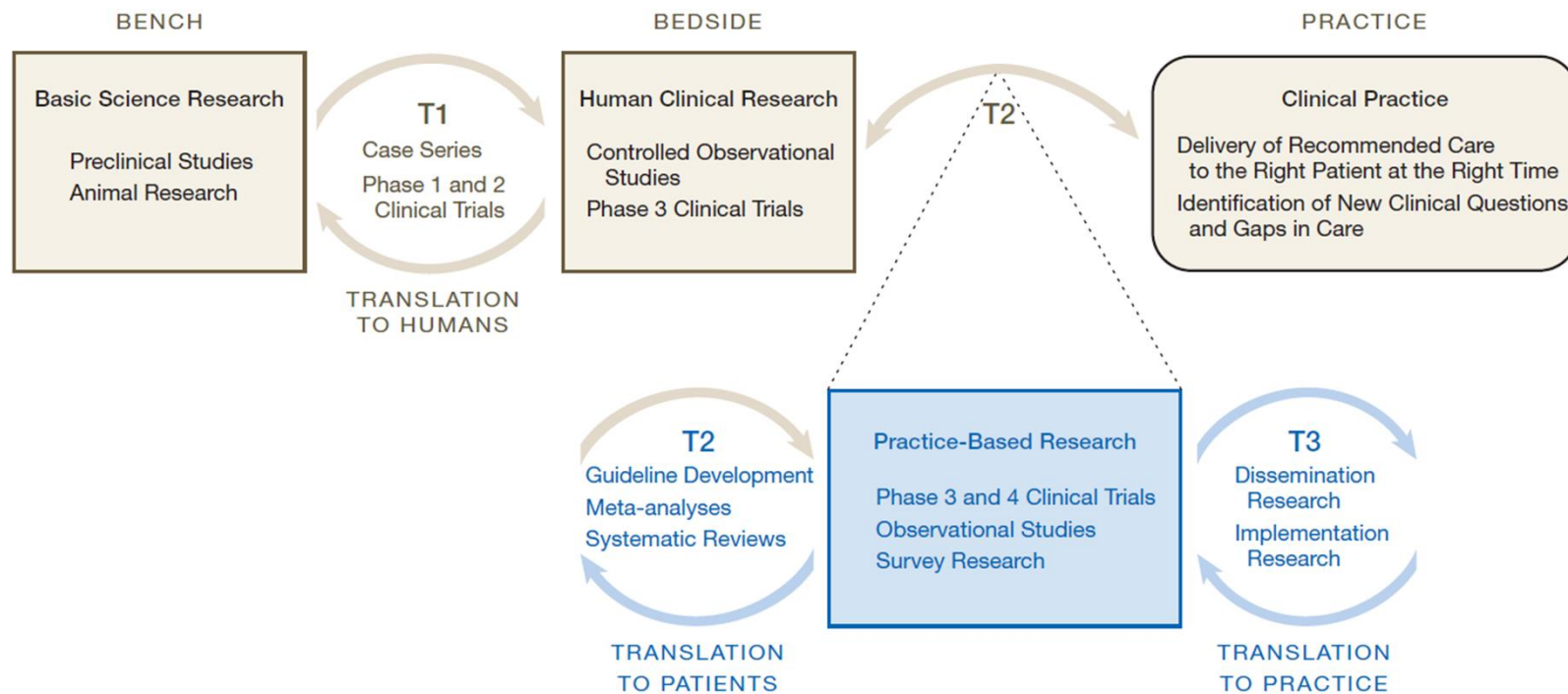
Adapted from Oxford Centre of Evidence Based medicine; <https://www.cebm.net/>



- From discovery to improved population health




- “Blue Highways” on the NIH Roadmap





- Current ENETS research



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HOME	MEMBERSHIP	EDUCATION/CME	ENETS ANNUAL CONFERENCES	ENETS REGISTRY	RESEARCH
ABOUT US	ENETS GUIDELINES		GRANTS AND AWARDS	CENTERS OF EXCELLENCE	NET NURSE

RESEARCH
ENETS Research
ENETS Research Projects
Researcher Platform
ENETS Excellence Academy Project

ENETS Research

ENETS strives to stay on top of latest findings in NET for improving therapies, diagnostics and treatments for patients all around the world.

ENETS supports and collaborates with important NET research projects in various disciplines.

Important research projects and trials listed have been introduced and further developed since the society's founding in 2004.

ENETS aims to further research collaborations, especially within the ENETS CoE and ENETS Young researcher community by

1. selecting annually one common ENETS EXCELLENCE ACADEMY Project, and
2. providing researchers with a platform on which they can find collaborators by giving a short outline of their project.



- Recruiting projects

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RESEARCH

- ENETS Research
- ENETS Research Projects
- Researcher Platform
- ENETS Excellence Academy Project

ENETS Research - Recruiting Projects

After a thorough selection process, ENETS Advisory Board has approved several research initiatives addressing so far unmet medical needs. ENETS is supporting the following trials, which are still recruiting.

ASPEN STUDY - ASYMPTOMATIC SMALL PANCREATIC ENDOCRINE NEOPLASMS.

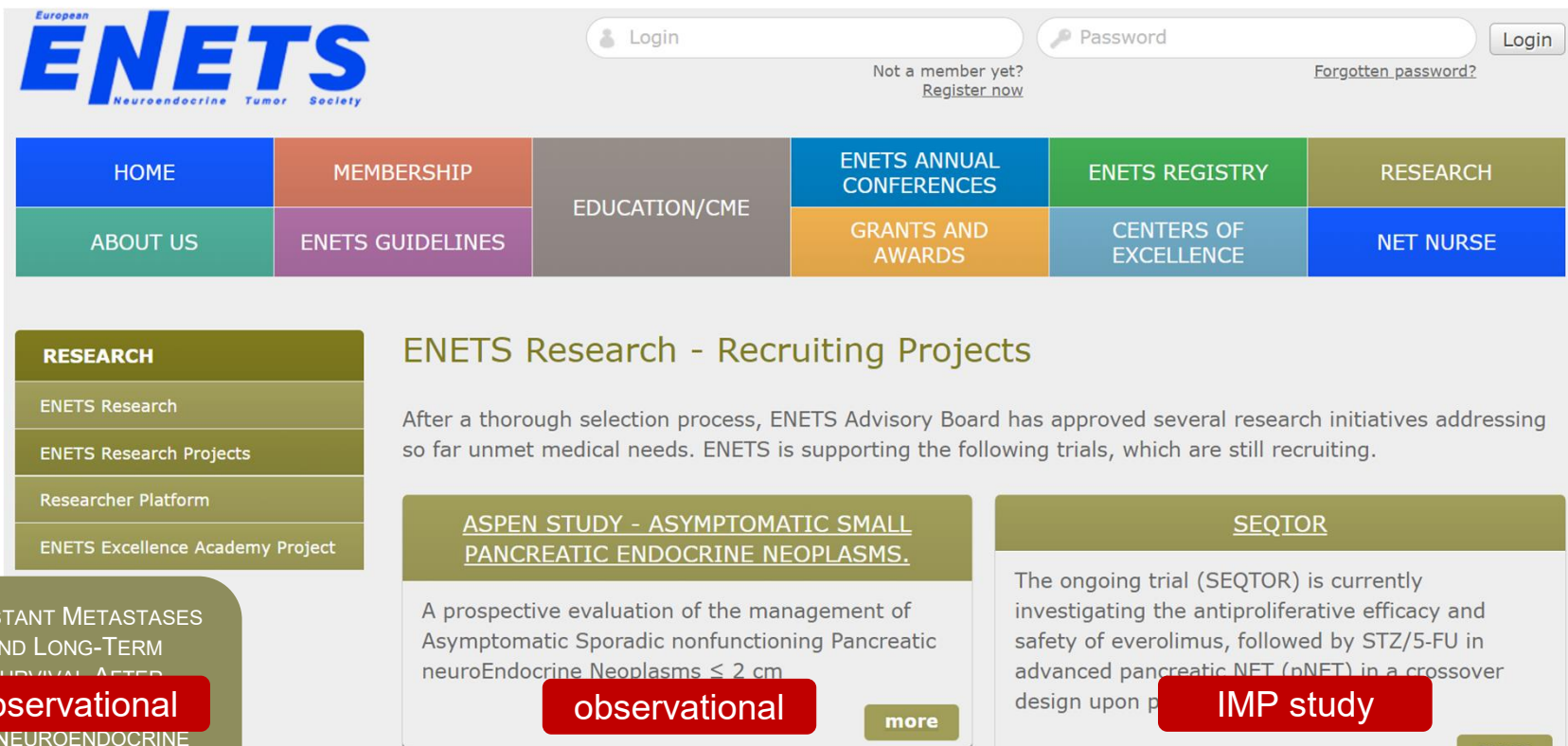
A prospective evaluation of the management of Asymptomatic Sporadic nonfunctioning Pancreatic neuroEndocrine Neoplasms ≤ 2 cm

SEQTOR

The ongoing trial (SEQTOR) is currently investigating the antiproliferative efficacy and safety of everolimus, followed by STZ/5-FU in advanced pancreatic NET (pNET) in a crossover design upon progression

+ DISTANT METASTASES AND LONG-TERM SURVIVAL AFTER COMPLETE RESECTION OF NEUROENDOCRINE TUMORS OF THE APPENDIX (SURVIVAPP)

- Recruiting projects



The screenshot shows the ENETS (European Neuroendocrine Tumor Society) website. At the top, there is a navigation bar with links: HOME, MEMBERSHIP, EDUCATION/CME, ENETS ANNUAL CONFERENCES, ENETS REGISTRY, RESEARCH, ABOUT US, ENETS GUIDELINES, GRANTS AND AWARDS, CENTERS OF EXCELLENCE, and NET NURSE. Below this, a section titled "ENETS Research - Recruiting Projects" is displayed. It includes a sidebar with links to ENETS Research, ENETS Research Projects, Researcher Platform, and ENETS Excellence Academy Project. The main content area features two project cards: "ASPEN STUDY - ASYMPTOMATIC SMALL PANCREATIC ENDOCRINE NEOPLASMS" and "SEQTOR". The ASPEN study is described as a prospective evaluation of the management of Asymptomatic Sporadic nonfunctioning Pancreatic neuroEndocrine Neoplasms ≤ 2 cm. The SEQTOR study is described as an ongoing trial investigating the antiproliferative efficacy and safety of everolimus, followed by STZ/5-FU in advanced pancreatic NET (pNET) in a crossover design upon p. Both study cards have a red "observational" label. A third red label, "IMP study", is placed over the SEQTOR card. A legend at the bottom right states: "IMP = Investigational Medicinal Product".

RESEARCH

- ENETS Research
- ENETS Research Projects
- Researcher Platform
- ENETS Excellence Academy Project

ENETS Research - Recruiting Projects

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A prospective evaluation of the management of Asymptomatic Sporadic nonfunctioning Pancreatic neuroEndocrine Neoplasms ≤ 2 cm

observational [more](#)

SEQTOR

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IMP study

IMP = Investigational Medicinal Product

- EORTC – an introduction



Mission

AIM: To increase cancer patients' survival and quality of life

Do this through:

- **Generating robust medical evidence**: design, coordinate and conduct **multidisciplinary, clinical and translational** trials, leading to therapeutic progress and new standard of treatment in care
- **Setting Standards**: being a **reference** for methodological research and an **authority** in establishing the standards of treatment in care

- EORTC – an introduction



Missions EORTC Headquarters

- To provide an optimal infrastructure for carrying out multicenter cancer clinical trials
- To provide expertise in clinical research management
- To ensure independence and objective conduct, analysis and reporting of trials
- To promote and conduct internal research projects
- Education role: courses / manuals / PhD / fellowships

- EORTC – an introduction



EORTC is unique

Independent

- **Not for Profit organization** where research is done with **unwavering independence** and accountability for making all results public

Multidisciplinary

- Our research spans **all aspects of cancer management**: medical, radiation, surgical, imaging, and translational research

Multi-tumour

- Network of **over 5.300 oncology experts**. Our research is solution-driven, for all types of cancers, leaving no-one behind

International

- A network of **over 930 institutions** in **31 countries**; coordinated and managed from headquarters in Brussels with over **200 core staff**

Regulatory compliance

- Our experts ensure our activities meet the **strictest regulatory standards and quality assurance requirements**

- Peer review of protocol by internal and external Protocol Review Committee
- Database in control of independent organization
- Access to primary endpoint by the pharmaceutical industry only at maturity
- Database ownership & use as per sponsor setting
- Strict control of biological material by academia
- IDMC, final analysis and publication under the control of academia

- EORTC – an introduction



EORTC Research Fields

- Tumor specific:

Brain Tumor
Breast Cancer
Lung Cancer
Leukemia
Lymphoma
Melanoma
Soft Tissue and Bone Sarcoma

Gastro-Intestinal Tract
Cancer
Genito-Urinary Cancer
Gynecological Cancer
Head and Neck Cancer
Endocrine Tumor Group
Cutaneous Lymphoma

Neuroendocrine and
hepato-pancreato-
biliary

- Cross-discipline:

Quality of Life
Radiotherapy
Elderly Task Force
Imaging
Translational Research

- EORTC – an introduction



EORTC Research Fields

- Tumor specific:
 - Brain Tumor
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 - Lung Cancer
 - Leukemia
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 - Soft Tissue and Bone Sarcoma

- Cross-discipline:
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hepato-pancreato-
biliary



- Neuroendocrine neoplasms - therapies emerging in the more common subgroup

Subgroups with approved therapies

- Pancreatic NET
- Small intestinal NET
- Other GI
- Lung

**Busy space with industry-
sponsored studies**



- Neuroendocrine neoplasms - therapies emerging in the more common subgroup

Subgroups with approved therapies

- Pancreatic NET
- Small intestinal NET
- Other GI
- Lung

Busy space with industry-sponsored studies

Rarer subgroups – unmet need

- NET-G3
- Thymus
- MEN-1-related
- Paraganglioma / pheochromocytoma
- Genito-urinary
- Breast
- Prostate
- etc...

Opportunity space for ENETS Collaborative studies needed

- ENETS has many strengths

- Network with large global footprint
- Specialist expertise
- Multidisciplinary
- Pooled ability to deliver on rare patient subgroups
- Centres of Excellence
- Oversight/governance structure
- Iterative process through society meetings
 - Annual meeting
 - Advisory board
 - Next-gen meetings



- ENETS limitations

- Unable to sponsor studies
- Unable to fund studies
- Quality of life methodology
- Health economic methodology
- No CRO function





- Operational functions vs. academic co-development

Operational
Database
Data management
Monitoring / QA
Regulatory submissions
Drug distribution
Sample collection
Pharmacovigilance
Annual reports/registrations*
* complex, by country-level



- Operational functions vs. academic co-development

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Academic collaboration
Methodology
Protocol development
Quality of life group
Health economics
Statistical methods
BioBanking
Pharmacology (early phase)



- Operational functions vs. academic co-development

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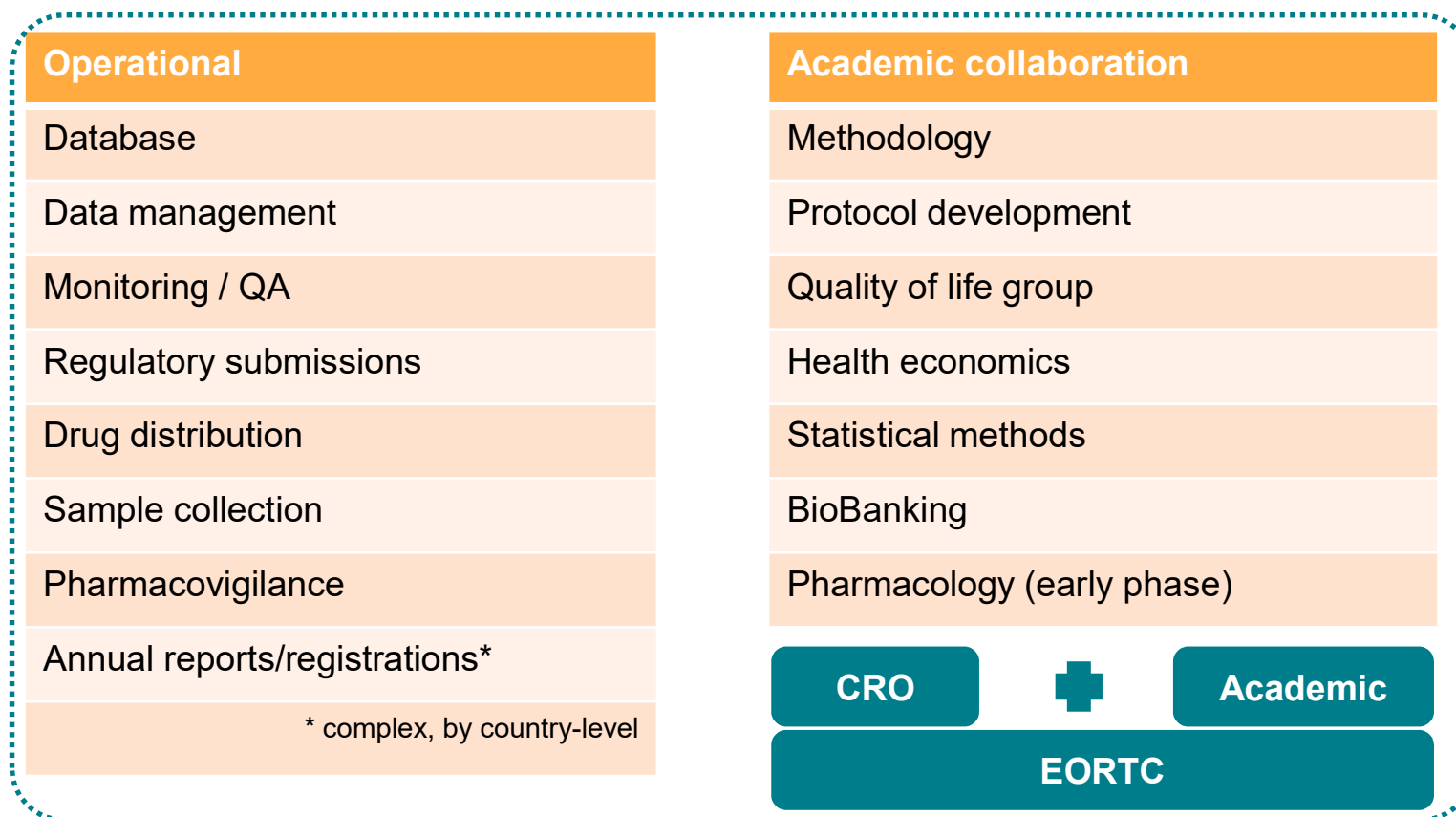
CRO



Academic



- Operational functions vs. academic co-development





- (Working) proposal

1. **ENETS Research Workshop**

- Provide peer-review for proposals
- NET expertise
- Identify methodology partners needed
- Feasibility of delivery
- Letter of support for grant applications
- Open to active investigators with core membership/panel
- Representation by national groups (e.g. GETNE, UKINETS, etc.)
- Next-Gen of investigators



- (Working) proposal

1. ENETS Research Workshop
2. **ENETS-badging of studies**

- Formal application process
- Pre-specified criteria (academic quality)
- Definition of eligible studies:
 - Audits – multi-national (≥ 3 countries)
 - Retrospective studies
 - Observational studies
 - Prospective studies
 - Industry studies



- (Working) proposal

1. ENETS Research Workshop
2. ENETS-badging of studies
3. **ENETS-developed studies**

- Pipeline of studies via workshop
- Open to non-workshop studies



●(Working) proposal

1. ENETS Research Workshop
2. ENETS-badging of studies
3. ENETS-developed studies
4. **Ongoing review of portfolio opportunities**

- Retrospective studies
- Prospective studies
- Observational studies
- Interventional studies
 - Non-IMP (e.g. endoscopic surveillance)
 - IMP
- Biomarker
- QoL
- Translational
 - Tissue BioBank
 - Imaging BioBank

- RWE – e.g. application of guidelines
- Community-based studies
- Public health research
- Health policy analysis

IMP = Investigational Medicinal Product; RWE = real world evidence;
QoL = quality of life



●(Working) proposal

1. ENETS Research Workshop
2. ENETS-badging of studies
3. ENETS-developed studies
4. **Establish PPI* group to support research**

- Involve patients and advocates in co-development of research
- Feasibility
- Acceptability
- Promotion of studies
- Platform for dissemination

* PPI = Patient-Public Involvement



- (Working) proposal

1. ENETS Research Workshop
2. ENETS-badging of studies
3. ENETS-developed studies
4. Establish PPI* group to support research
5. **EORTC collaboration**

- For selected studies
- Where synergies can be maximised (cross-cutting groups)
 - Quality of life
 - Radiotherapy
 - Elderly
 - Imaging
 - Translational
- Academic co-development of studies
- Agreements in place
- (not to the exclusion of other academic collaborations)

* PPI = Patient-Public Involvement



- Summary

- Many opportunities for research in the field of NENs
- Improved understanding of molecular biology and immunology is paving the way for innovative pharmacological approaches.
- Academic priorities differ from “marketing authorisation” approach
- Unanswered questions re: quality of life, survival, biomarker-selected groups, treatment duration, sequences and combinations, etc.
- Need for integrated translational research
- This proposal is open for discussion