Current challenges in translational science & their application in early phase trials requiring regulatory input

ECMC Annual Network Meeting 10th May 2017
Ruth Challis – Southampton ECMC, QATS steering committee

- Regulatory challenges with novel biomarkers
- Regulation around secondary and tertiary end points
- Outputs following the QATS conference

Who is the QATS Network Group?

Quality Assurance Translational Science

We support translational research, with a focus on high levels of quality and regulatory compliance.

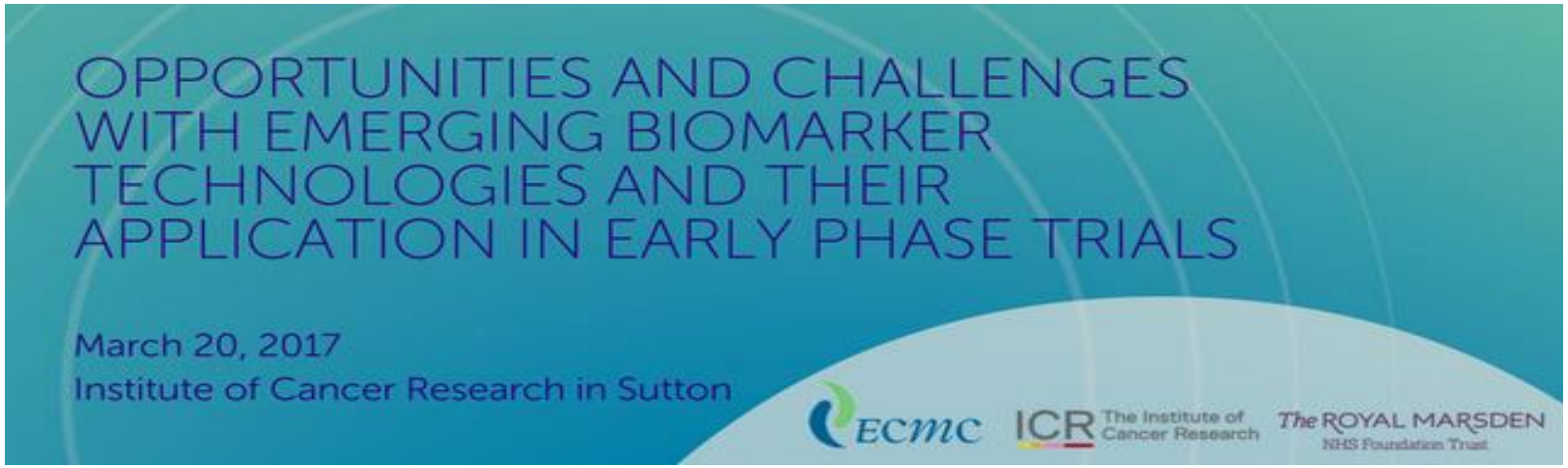
Mission Statement

The ECMC QATS Network Group supports and enables ECMCs to conduct translational research to the appropriate levels of quality and regulatory compliance, utilising validated, cutting-edge techniques.

Quality Assurance Subgroup
Chair: Alex MacLellan, Edinburgh
Co-chair: Sara Yeats, Southampton

Translational Science Subgroup
Chair: Karen Swales, ICR
Co-chair: Fiona Thomson, Glasgow

QATS conference – 20th March 2017:



Conference aims:

1)To learn about novel technologies being used for translational science across the Network

2)To discuss the challenges of application of novel biomarker analysis in early phase oncology trials

3)To network with other QATS members

QATS conference – 20th March 2017:

Afternoon parallel workshops:

Workshop 1: The future of translational science in early stage oncology trials: How will the ECMC Network continue to deliver high quality biomarker research?

Workshop 2: Challenges for translational science analytical validation in early phase oncology trials

Regulatory challenges with novel biomarkers

Common themes emerging from network - **Suggestions / improvements**

- Lack of predictive biomarkers
  - **increased use of transferable validations/ biomarkers across trials**
- Lack of appropriate specimen collection
  - **more lab input in study design / Lab guidance on standardised collection protocols**
- Poor understanding of specificity
  - **improved communication/ training across network**
- Variable practices across network on biomarker validation process
  - **improved communication/ training across network & creation of Biomarker Centres of Excellence**
- Variable practices across network on Quality Assurance process
  - **improved focus on *laboratory* QA with increased communication/ training**
- Variation in sponsor expectations for extents of validation – regulatory guidance open to differing interpretation
  - **improved communication of existing guidance documentation**

Primary, secondary and tertiary end points

- Primary endpoints – key patient safety / screening tests
- Secondary endpoints – informing safety / dose decisions
- Tertiary/exploratory endpoints – research endpoints

Regulation around secondary and tertiary end points

❖ MHRA Good Clinical Practice guide:

Section 13.3.1 on Method Validation states:

"The nature of the necessary validation will be dictated by the complexity and type of technique(s) being employed and will need to be assessed on a case-by-case basis. In all cases, the aim will be to show that the method can be used to generate reproducible and reliable data."

- Open to interpretation and very sponsor dependent
- EMA guidance paper based on ligand binding or small molecule/PK studies
- Use of the phrase ‘fit-for-purpose’ assays/ validations

Regulatory challenges with validation of biomarkers

Common themes emerging from network - **Suggestions / improvements**

- Variation in sponsor expectation of 'fit-for-purpose' validations
  - **Transferable validations/ increased use of biomarkers across trials**
- How should novel technologies be validated?
  - **Increased sharing of successful and unsuccessful validations across the network**
- Different interpretations of primary/ secondary / tertiary endpoints
  - **Standardise definitions across the network**
- How can validation be performed within tight timelines and budgets?
  - **More time allowed for validation / planned overlap of validation work with trial open**
- Are all sponsors / PIs realistic in their choice of Biomarkers?
  - **Involvement of translational scientists at early stages**
- Do all endpoints need the same level of validation?
  - **Increased publication output of validation papers or guidance documents?**

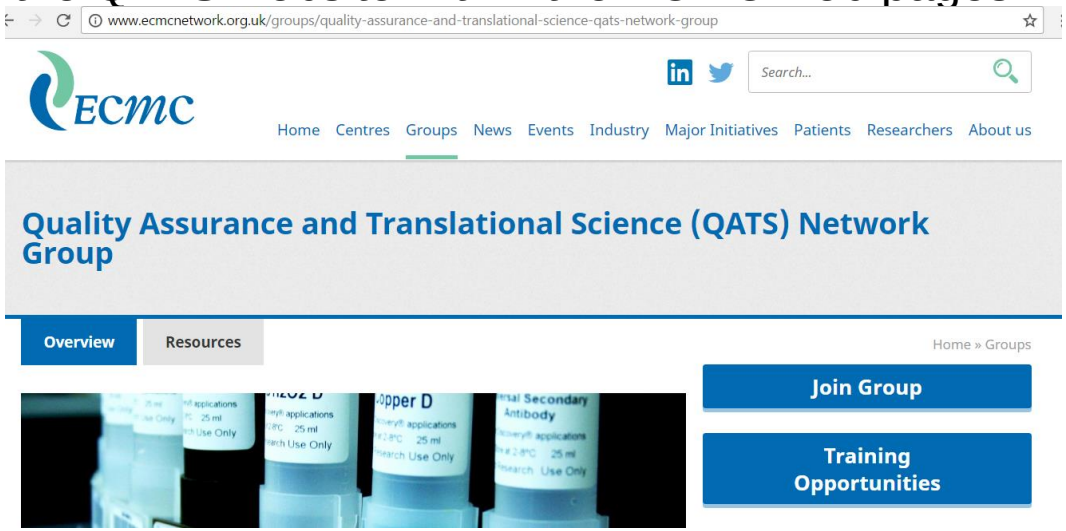
QATS conference outputs / Next steps….

- ❖ Need for improved communication/ training across network
  - **Excellent feedback following our first focused one day conference; plan to run similar event every 2 years hosted by different centres**
- ❖ Request for greater sharing of SOPs, and sharing of successful AND unsuccessful validations
  - **Tensions due to IP; but increased resource / motivation for publication to be considered?**
- ❖Need for more information sharing on existing validation guidance papers
  - **Review existing guidance documentation on validation processes to create information repository**
- ❖ Increased training in laboratory focussed issues and validation workshops
  - **Planning of centre based training / workshops – linked to specific techniques**

Where can you get more information?

- ✓ Join the QATS network for regular updates on activity – email ECMCadmin@cancer.org.uk

- ✓ Look at the QATS website within the ECMC web pages



- ✓ Join the QATS steering committee ECMCadmin@cancer.org.uk

ECMC QATS steering committee

Quality Assurance Subgroup

Alex MacLellan, Edinburgh

Sara Yeats, Southampton

Tony Price, Manchester

Rebecca Gallagher, Belfast

Translational Science Subgroup

Karen Swales, ICR

Fiona Thomson, Glasgow

Stephanie Traub, CDD

Ruth Challis, Southampton

Bill Greenhalf, Liverpool

New members? – please ask one of the existing committee for details or contact ECMCadmin@cancer.org.uk

NIHR/Cancer Research UK
Experimental Cancer Medicine Centre

Southampton NIHR BRC

Southampton NIHR/Wellcome
Trust CRF

Cancer Research UK

University Hospital Southampton