The Challenges of Data Access for Historical Clinical Trials: A user experience

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Biomarkers and Companion Diagnostics Group

- Formerly known as the Endocrine Cancer Group
- Established in 2006
- Tissue banking, image analysis and biomarker analysis for phase III breast cancer clinical trials
- Currently 4 staff, 3 in tissue banking and 1 RA
- Based in Edinburgh Cancer Research Centre, Western General Hospital

Changing face of trials

Completed trials

- Prospective (e.g. 2007-2023)
- Informed patient consent
- Tissue collection as standard
- Computerised records

Current trials

- Retrospective (e.g. 1985-1991)
- No consent signatures
- No tissue collection at time
- No computerised records

Why go back?

- Primary end points were disease free survival, overall survival, recurrence free survival etc. *but only for 5-10 years of follow-up*
- Can now go back to archived tissue blocks and apply novel sequencing technology
- Use 25 years + of follow-up data so can capture those patients who recurred/ died in years 11-25.
- More data used for analysis → more robust conclusion
- Bring test to market quicker

Trial 1: Radiotype DX (RDX)

- Collect tissue samples from patients from two historic radiotherapy trials: Scottish Conservation Trial and Prime 1.
- SCT: 585 patients recruited between 1st April 1985- 2nd October 1991
- Retrieve tissue blocks from archives
- Process tissue at BCD → shipp to PFS Genomics
- RNA extraction + sequencing to validate novel signature
- Update outcome data and publish a follow-up paper
- Signature validated lead to patenting/ marketing of novel prognostic test

RDX challenges

Tissue challenges

- Location of blocks
  - Off site storage
- Retrieval of blocks
  - Pre-computerised records, logbook system
  - Not all pathology numbers available
- Processing
  - Quality of tissue after this long in storage

Data challenges

- No explicit consent for future use of data
- Collection of data
- Data requirements of sponsor
- Storage of data
- Transfer of data
- Analysis of data

RDX data collection challenges

- No official Informed Consent
  - Patients given PIS but no signatures obtained.
- Data originally entered onto Microsoft Access 95
  - Now practically obsolete!
  - “Future Proofed” data- exported into CSV file
- CRFs & path forms- scanned onto CD as images
  - view with Document Explorer (time consuming)
- Path forms- faxes & photocopies- scanned
- Accessing medical records – who does it?

RDX data usage challenges

- Data requirements of funder
  - Subject information
  - Tumour information
  - Treatment information
  - Outcome information
  - Molecular information *

* Newly generated data

- Storage of data
  - Safe haven? Cloud device? Locked room? USB stick?
- Transfer of data
  - Site to trials Office
  - Trials office to PFS Genomics
  - Trials office to UoE
  - PFS Genomics to statistician
- Analysis of data

Public Benefit and Privacy panel

“The Public Benefit and Privacy Panel for Health and Social Care is a governance structure of NHSScotland, exercising delegated decision-making on behalf of NHSScotland Chief Executive Officers and the Registrar General. The panel operates as a centre of excellence for privacy, confidentiality, and information governance expertise in relation to Health and Social Care in Scotland, providing strategic leadership and direction in this area to NHSScotland Boards, the research community, and wider stakeholder groups.”

Ethics & PBPP

- No patient consent required for tissue collection as pre-HTA
- Ethical approval obtained on 13th May 2016 (REC) with 1 condition
- Submitted to PBPP 20th September 2016
- Tier 3 committee review 18th April 2017
- Comments: Cloud arrangements? EU-US security shield? Location of data analysis?
- Tier 3 committee refused to grant approval unless data analysis happened within UK

Trial 2: Trans-ATTOM

- Collect tissue samples from patients from a historic tamoxifen trial – aTTOM adjuvant Tamoxifen Treatment offer more?
- Tissue blocks retrieved from archives
- Serial sections cut at BCD and shipped to BioTheranostics Inc.
- RNA extraction and sequencing of ER positive patients
- Opportunity to collect longer term follow-up data for the trial and publish a follow-up paper
- Signature validated lead to patenting/ marketing of novel prognostic test

Trans-ATTOM Challenges

Tissue block retrieval

- Location of blocks
  - Off site storage
- Retrieval of blocks
  - Pre-computerised records, logbook system
  - Not all pathology numbers available
- Processing
  - Quality of tissue after this long in storage

Data challenges

- Collection of data
- Data requirements of sponsor
- Storage of data
- Transfer of data
- Analysis of data

Trans-ATTOM data collection challenges

- Informed Consent given for trial entry
- Patients were aware data would be accessed
- Only patients who have not withdrawn will be selected for extended follow-up – CAG approval to access patient information on trial database for selection
- Follow-up data will be obtained through CHI linkage/National registry
- Possible access to CHI database for those patients where CHI number is unknown using patient identifiable information.

Trans -ATTOM data usage challenges

- Data requirements of funder
  - Subject information
  - Tumour information
  - Treatment information
  - Outcome information
  - Molecular information *
- Storage of data
  - Safe havens
- Transfer of data
  - Safe havens
- Analysis of data
  - UK based

* Newly generated data

Where are we now?

- RDX
  - Reopened negotiations with the funder to change data flow and analysis plan.
  - Requires amendments to protocol (ethics) and contracts (lawyers)
  - Original ethics approved May 2016. Hope to get first block in July 2018.
  - PBPP v2 submitted 7th November
  - Approval will take 18 months, project duration is 24 months.
- Trans-ATTOM
  - PBPP application to be submitted in December 2017.
  - Hoping to use RDX as an example of how ‘not to do it’

On a side note…..

- Patient focus group was held for RDX in April 2017
- Feedback form patients sought on issues raised by PBPP
- Overwhelmingly supportive of the trial and had no issue with
  - Patient data leaving UK
  - Commercial sponsorship of trial
  - Use of cloud storage devices for patient trial data
  - Open access of genomic data generated from trial samples

Conclusions

- Historic trials are an attractive prospect for future research
- Combining new methodologies with long term follow-up
- Careful planning at the initial stages is essential!!
- Issues to be considered: data requirements, access, locations, transfer, storage, analysis.
- New GDPR regulations coming into enforce May 2018
  - Call for explicit consent on what data will be collected and how it will be used.
  - These will also apply to non-EU organisations who use data on EU subjects

Contact details

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