Cancer Research: the value of partnership

Peter Johnson
Why cancer matters:

CCG Outcome Indicator Set 2014/5
Premature (under 75) deaths by clinical domain:

Deaths <75 - Wessex

- Cancer: 44%
- Heart Disease and Stroke: 22%
- Lung: 9%
- Other: 25%

Wessex is highly active in cancer research

Cancer patients recruited per million population in NIHR: 2016
Why research matters:

Patients treated in research-active hospitals have better outcomes:

Ovarian Cancer:


Colorectal cancer: Downing et al, Gut 2016
Historical perspective: the success of targeted funding in research infrastructure

Overall NIHR CRN Cancer Trial Recruitment as % of Cancer Incidence

![Graph showing recruitment percentage of cancer incidence from 2001/02 to 2012/13. The graph illustrates a steady increase in recruitment rates.]
Funding and activity

NIHR infrastructure funding: 2017

- London: 54%
- Oxbridge: 29%
- Rest: 17%

Recruitment to NIHR studies: Cancer

- London: 23%
- Oxbridge: 12%
- Rest: 65%
Cancer Research UK: Research portfolio of clinical studies

Confirmatory and practice-changing trials:
Outcomes at the population level (this stuff works!)
Systemic therapy and mortality
(similar points could be made about surgery and radiotherapy)

- Cisplatin for testicular cancer
- Imatinib for CML
- Rituximab for lymphoma

Source: cruk.org/cancerstats
Some things have changed

Changes in the research landscape
Our understanding of cancer has also changed

Cancer now has 10 hallmarks

Cancer evolves

Tumours are heterogenous
Making Systemic Treatment Work: then and now

NITROGEN MUSTARDS

ADMINISTRATION

Dosage:
About 0.07 - 0.08 mg/kg, body weight
Course: 4-6 injections given daily
First Dose - 3-5 mgs.; Increase by 1 mg, daily
Course may be repeated in 8 - 10 weeks

Mode of Administration:

Immediate Reactions: Nausea and Vomiting in 1-2 hours
lasting 1 - 3 hours
Occasional chills and fever

Lung cancer with EGFR mutation
CRUK Stratified Medicine Programme – Part 2
Screening lung cancers for clinically relevant molecular signals

PRE-SCREENING

NGS SEQUENCING

NATIONAL LUNG MATRIX TRIAL

Centralised NGS (Technology Hubs)

Bespoke Illumina NGS panel – aligned to requirements for included MPPs
Bespoke tissue pathology where required (e.g. ALK)
DNA extracted from 

Biomarker A: Drug A
Biomarker B: Drug B
Biomarker C: Drug C
Biomarker D: Drug D
Biomarker E: Drug E
Biomarker F: Drug F
The National Lung MATRIX Trial
Designed as a rolling early-phase “signal seeking” programme...

- 2nd line trial is a Phase IIa, single arm, 2-stage Bayesian design (n=30 per arm), with ORR and PFS endpoints
- Mainly monotherapy (combinations possible with dose/schedule)
- Modular design with umbrella protocol to allow drop-in/drop-out
- Single national protocol, single regulatory submission
- Linked longitudinal circulating tumour DNA analysis
Key relationships for the Cancer Centre

Wellcome Trust Clinical Research Facility
Wessex Investigational Sciences Hub
NIHR Biomedical Research Centre

Chemistry
Crystallography
Opto-electronics
Supercomputing
Clinical Research Infrastructure:

• Phase I unit on-site

• Full team of clinical investigators and dedicated research nurses, data managers funded by CRUK and trials income

• Global first patient in several commercial immunotherapy studies

• GCLP-compliant immunomonitoring lab, successfully audited by pharma

![NIHR Wessex Cancer patients recruited annually](image)

70% of commercial studies recruited to time and target

![Recruitment and Number of studies](image)
Immunotherapy for cancer: the next wave of progress

“No recent advance has been more transformative than the rise of immunotherapy, particularly over this past year,” said Julie M. Vose, MD, MBA, FASCO, ASCO President.
Antibody therapeutics
Discovery science into clinical trials

IN VITRO MODELS

Cragg, Blood. 2003; 101:1045-1052

EX VIVO MODELS

Ivanov, J Clin Invest. 2009;119:2143-2159

CLINICAL TESTING


Roche’s Gazyva/Gazyvaro showed superior progression-free survival compared to MabThera/Rituxan in people with previously untreated follicular lymphoma

- Phase III GALLIUM study met primary endpoint early, as determined by independent data monitoring committee

Lim, Blood 2011:118:2530-2540

Roghanian, Cancer Cell 2016:27:473-488

A CANCER RESEARCH UK PHASE II/IIA CLINICAL TRIAL OF BI-1206; AN ANTIBODY TO FCYRIIB (CD32B), AS A SINGLE AGENT AND IN COMBINATION WITH AN ANTI-CD20 ANTIBODY IN PATIENTS WITH CD32B POSITIVE B-CELL MALIGNANCY.

Sponsor protocol number: CRUKD/16/001
EudraCT number: 2015-004999-29
Translational immunotherapy
Novel combinations and complex immuno-monitoring

HNSCC
Oral cavity, oropharynx

TIL (n=41)

N-TIL (n=36)

TIL (n=36)

NSCLC

Lung N-TIL
NSCLC-TIL
HNSCC-TIL

TIL lung Adeno
TIL lung SCC
TIL HNSCC HPV-
TIL HNSCC HPV+

Z-score
-2 0 2

Lung
N-TIL

TIL lung
Adeno
TIL lung
SCC
TIL HNSCC
HPV-
TIL HNSCC
HPV+

Adeno SCC
HPV-
HPV+

4-1BB
PD1
TIM3
LAG3
CTLA4
TIGIT
ICOS
CD27

4-1BB
PD1
TIM3
LAG3
CTLA4
TIGIT
ICOS
CD27

Z-score
-2 0 2

HNSCC

TIL high
TIL mod
TIL low
Unavailable
The Centre for Cancer Immunology (opening 2017...)