Life as a University Senior Lecturer/ challenges of running clinical trials

Simon Pacey

Academic Consultant in Experimental Therapeutics

Dept. Oncology, The University of Cambridge

Objectives:

- Overview of Academic medicine
- (Personal) career overview
- Life as a “clinical trialist”

Academic Medicine

“Branch of medicine pursued by doctors who engage in a variety of scholarly activities”

Includes:

- Clinical work
- Research
- Teaching
- Management/ representative

Every academic has a different job description

Career Pathway History

- Lack clear entry route
- Lack transparent career structure
- Lack flexibility in balance clinical and academic training and in geographical mobility
- Shortage structured and supported posts on completion of training
- Senior academics carved their own routes (high risk)
- Lack job security
- Concern over pay parity

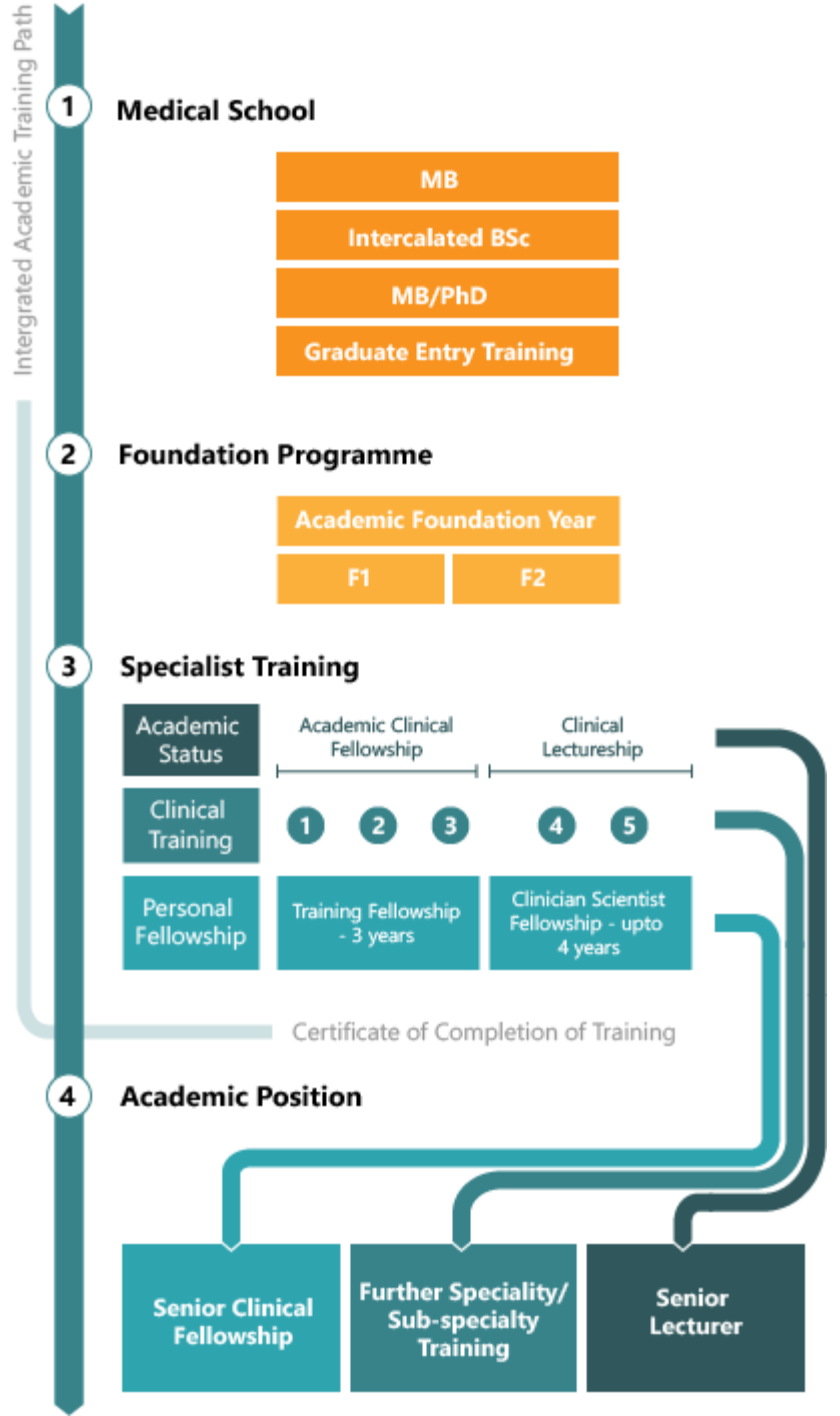
2004 UK Clinical Research Collaboration (gov) recommended a new pathway:

Walport, Tooke and beyond 2005

- Academic career subcommittee of MMC
- FY2 4 month to explore interest
- ACF ST1-3 generally, (25% time research) – generate results to support PhD
- PhD/ MD after ST3
- Return ST4 as academic clinical lecturer/ post doctoral researcher 50% academic
- Work towards senior academic post – clinician scientist

Flexible; NTN(A) and can drop (A) at any stage

Create new CL posts over 5 years



Will it work?

- How flexible?
- Disadvantage clinicians at later stage in career?
- Binary divide academic and non research clinicians

Best and worst bits

Best

- Achievement
- Recognition for hard work
- Freedom
- Ask q about medical science and solve them

Worst

- 2 jobs: Academia/ NHS
- Feel behind other colleagues if “OOPE”
- Research = marathon with hard slog, deadlines looming

More information:

NIHR website

Academy of Medical Sciences

Deanery

BMA academic sub committee

Funders:

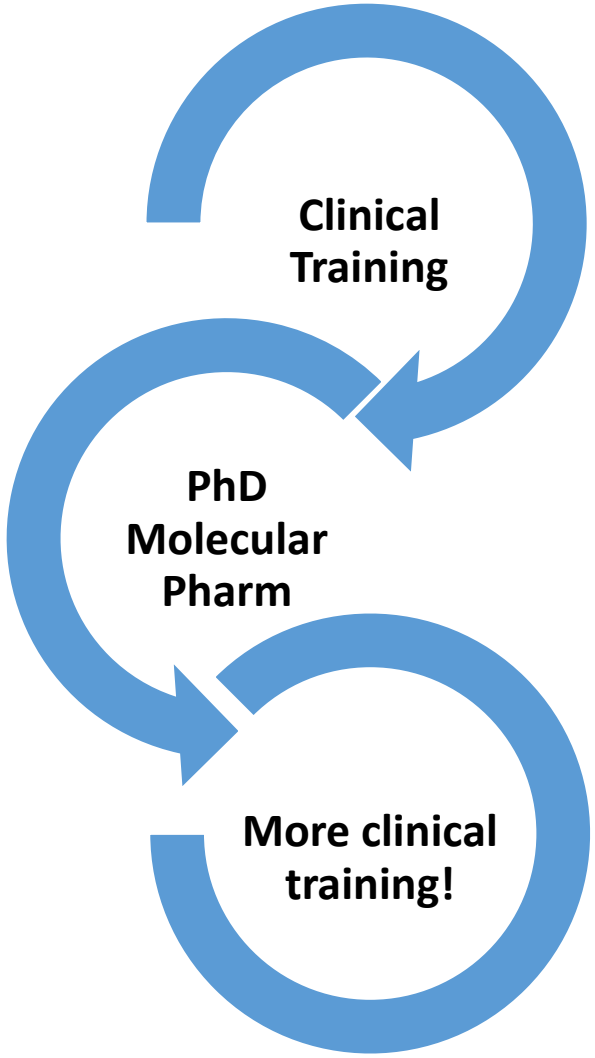
MRC: Wellcome Trust; Cancer Research UK

Career Summary (2002-2011)

RMH/ The ICR DDU
- Clinical fellow

CR-UK PhD student
- Molecular Pharmacology

St Bartholomew's
- Clinical training
- Education
- Management/ leadership
- Phase I design



Goals/ 5-year focus:

Clinical & translational research

Unmet needs eg prostate/ lung

Develop Environment

Staff (recruit, train & retain)

Personal 5-yr aims – interview slide

Short term (0-18 months)

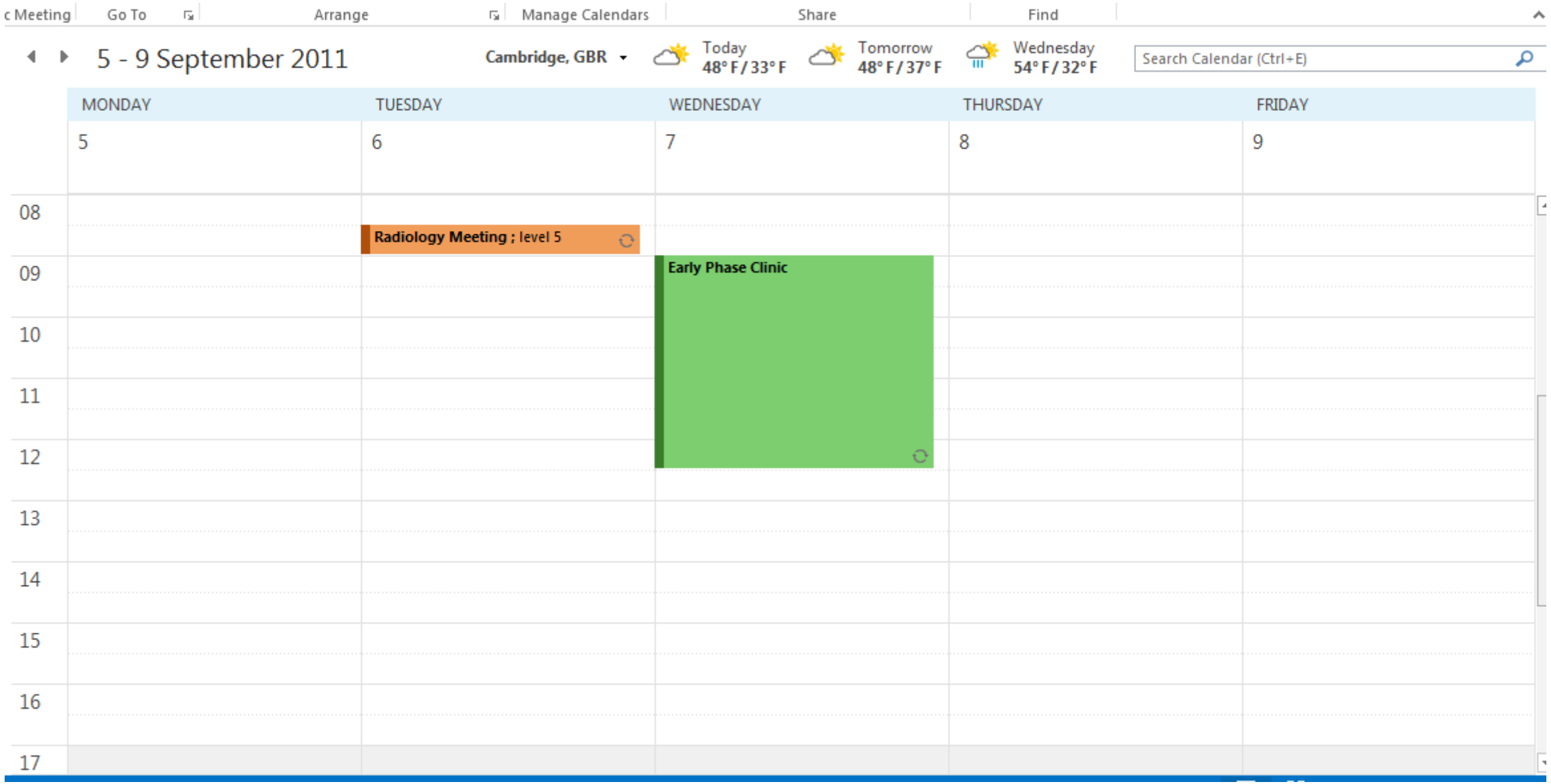
- "Lag" phase used for planning
- Create initial trial portfolio
  - Collaborate on research strength and priorities
  - Work with team to grow "early trials unit"

Medium term (18-48 months)

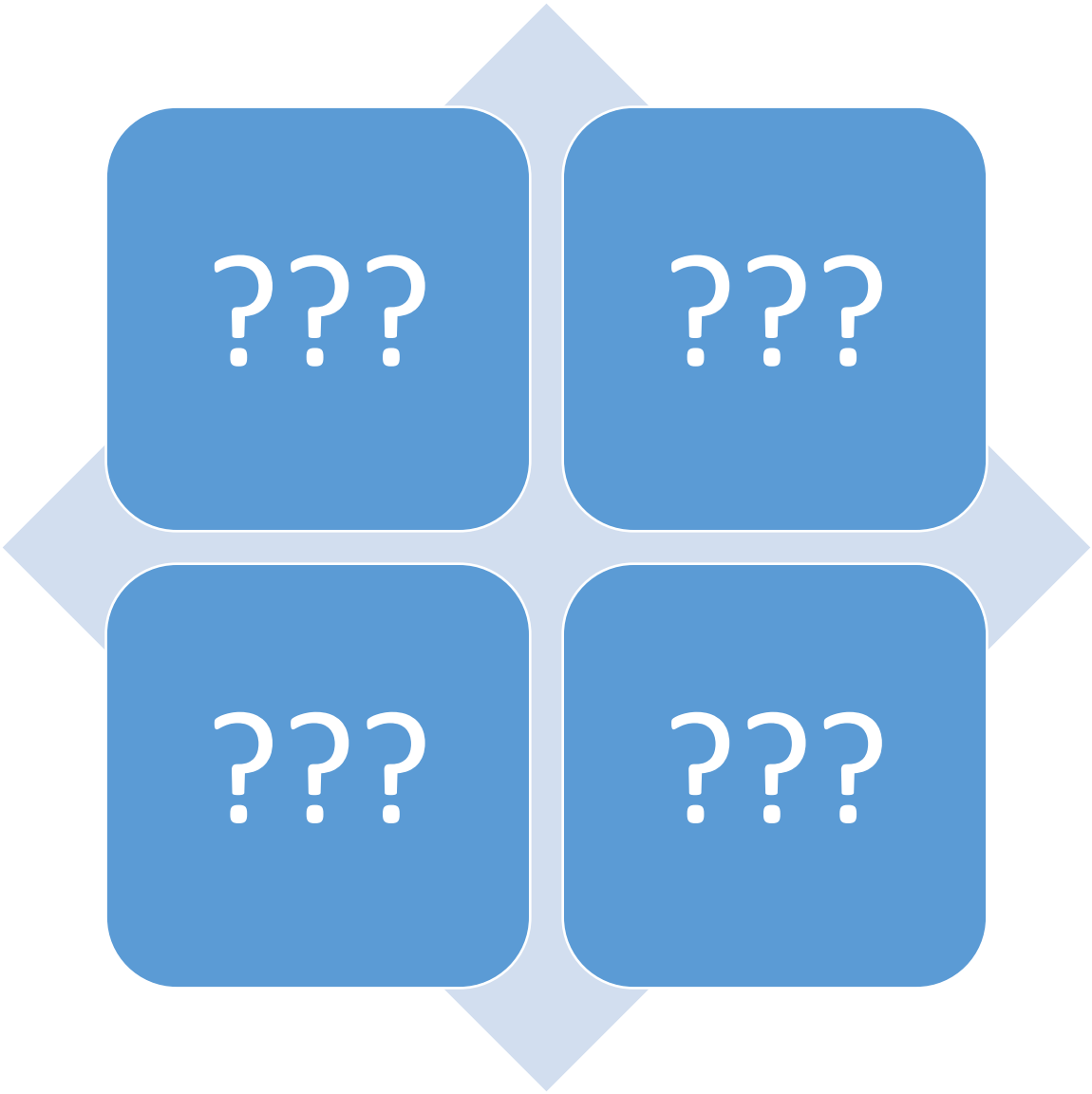
- "Pump prime" agents to tumour site teams
- Grant funding and publications
- Critical mass to unit
- Education and training

Longer term (>4 years)

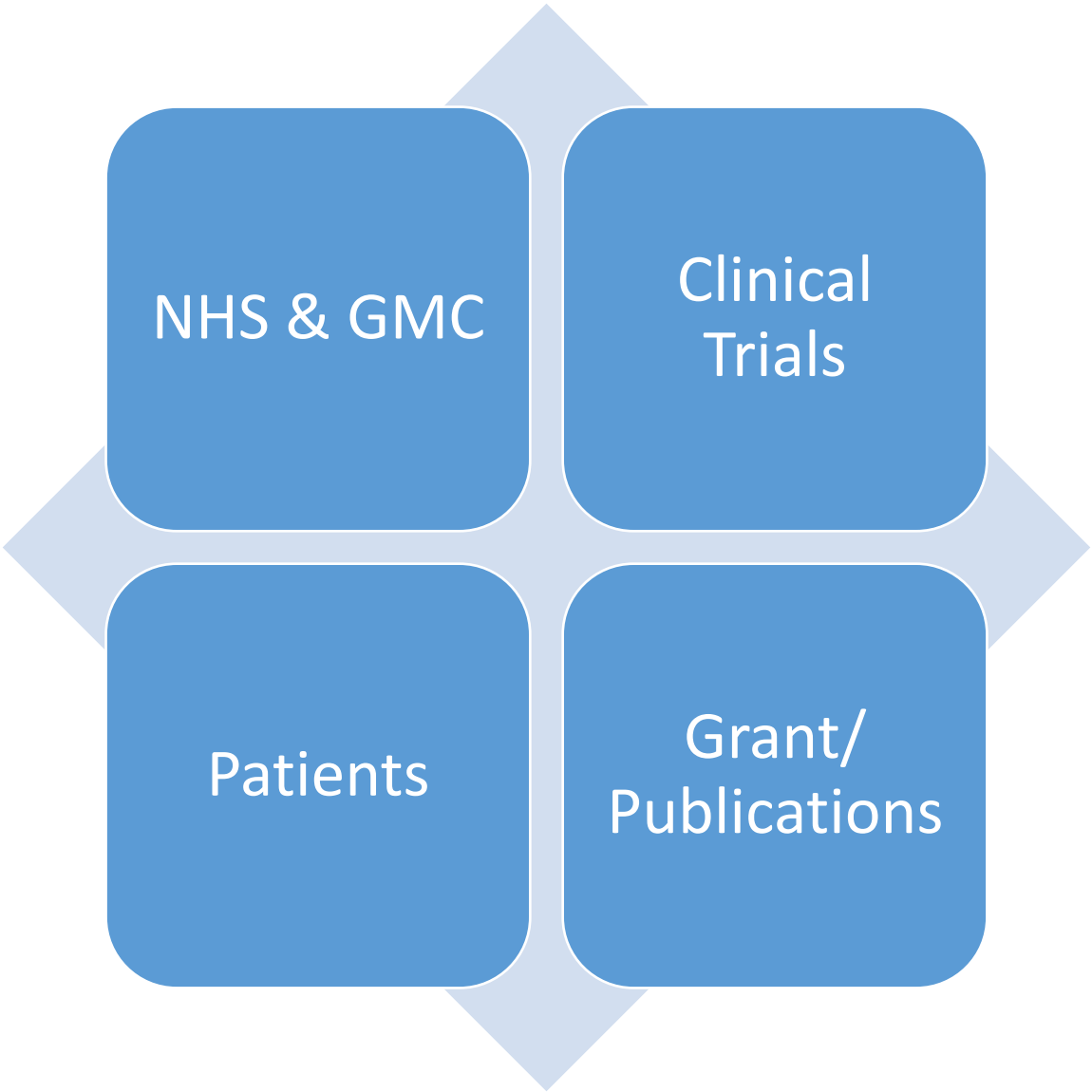
- Ensure post funded and tenured
- Establish links with others eg clinical oncologists, surgical teams & palliative care (supportive therapy)


c Meeting
Go To
Arrange
Manage Calendars
Share
Find
5 - 9 September 2011
Cambridge, GBR
Today
48° F / 33° F
Tomorrow
48° F / 37° F
Wednesday
54° F / 32° F
Search Calendar (Ctrl+E)
MONDAY
TUESDAY
WEDNESDAY
THURSDAY
FRIDAY
5
6
7
8
9
08
09
10
11
12
13
14
15
16
17
Radiology Meeting ; level 5
Early Phase Clinic

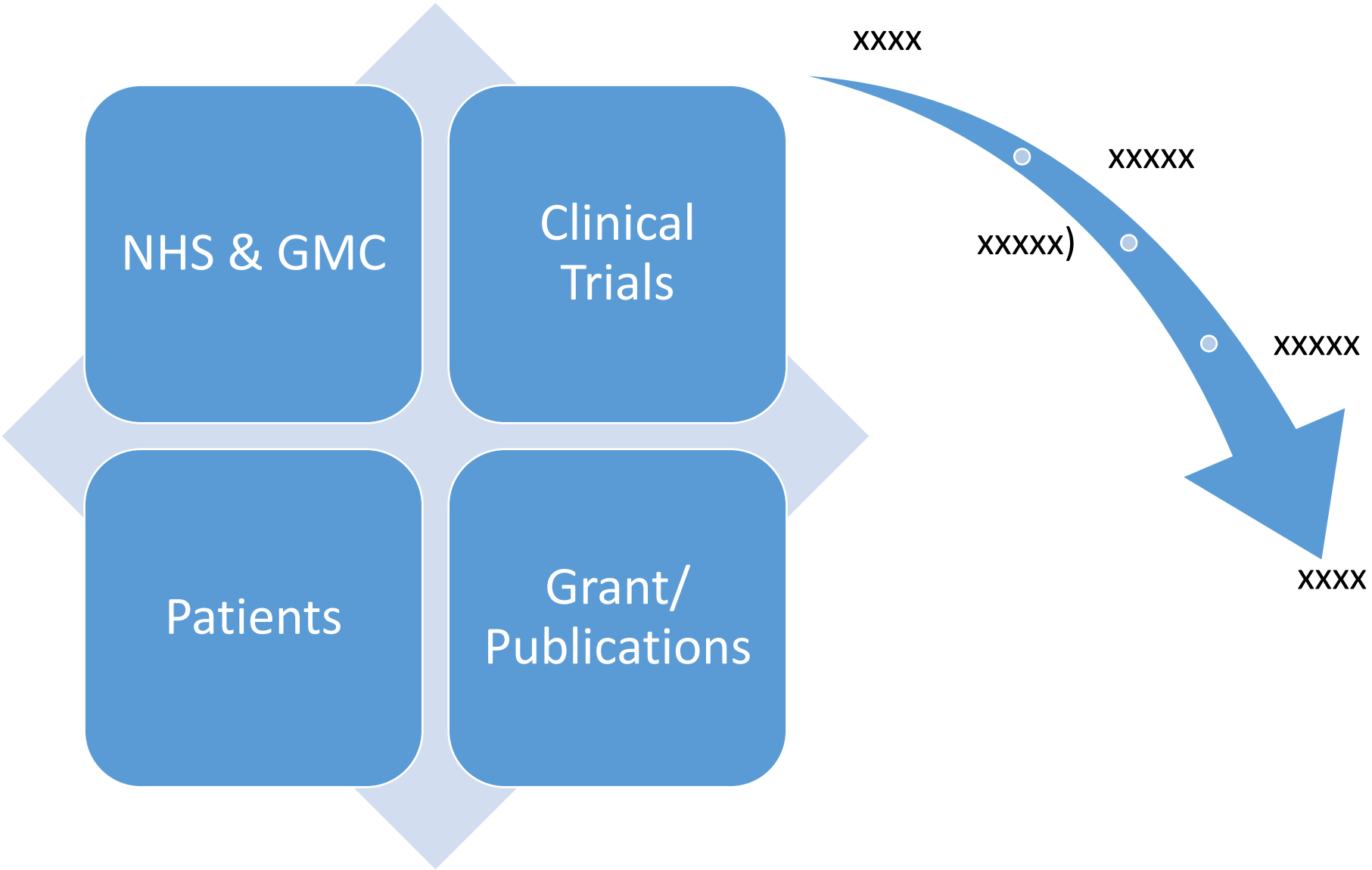
Challenges of running clinical trials – Deliverables?



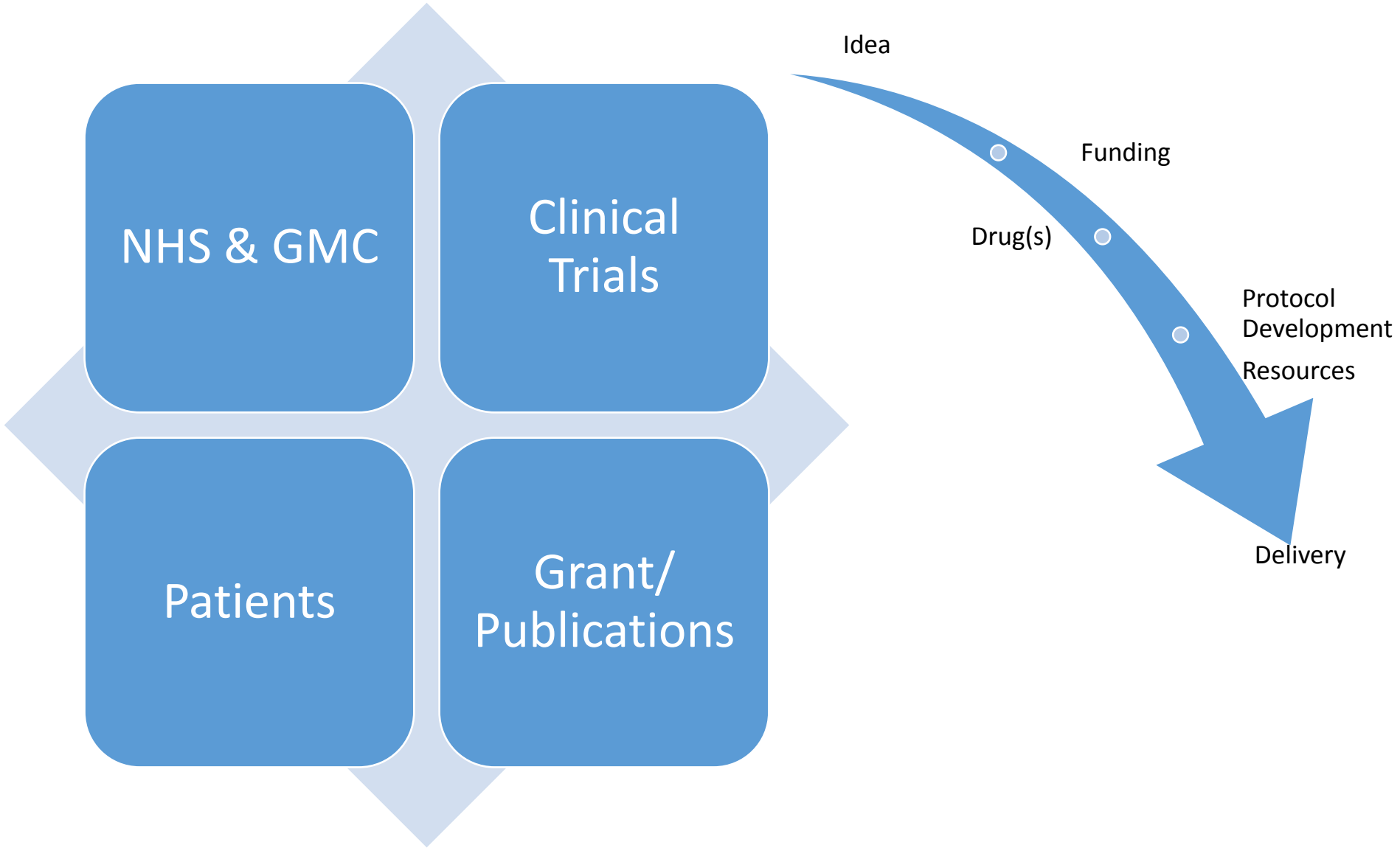
Challenges of running clinical trials?



Challenges of running clinical trials:



Challenges of running clinical trials:



Building Trial Portfolio

- Collaborations/ colleagues
- Cancer Research UK
  - Centre for Drug Development
  - Cancer Research UK centres
    eg Belfast, RMH, GKT, UCH, & Barts
- Pharmaceutical/ Biotech
- ECMC network
  - Collaborative alliance (Astra Zeneca, other)
- Other networks

Cambridge Portfolio

Trial Name	PI	Agent (s)	Investigational drug target (s)	Population	Trial Type	Company Involved	Sponsor / CTU	Phase
CURRENT								
VANSEL	Pacey	Vandetanib + Selemetinib	EGFR / VEGF + MEK	Advanced solid tumours	Investigator-initiated, collaboration	AstraZeneca	Cancer Research UK DDO	Ib
NOTCH	Jodrell (Basu)	MK0752 + gemcitabine	Notch	Stage IV pancreatic cancer	Investigator-initiated, Cambridge-led	Merck	Cancer Research UK DDO	I/II
HYPAZ	Jodrell/ Cheryian	Pazopanib	VEGF	Advanced solid tumours	Investigator-initiated, Cambridge-led	GlaxoSmithKline	GSK	Mechanism of toxicity
Immunocore (IMCgp100)	Jodrell	IMCgp100	Immunotherapy (gp100 / CD3)	Advanced malignant melanoma	Commercial	MedImmune	MedImmune	I
OPARATIC	Jefferies	Olaparib + temozolamide	PARP	Recurrent Glioblastoma	Investigator-initiated, collaboration	AstraZeneca	Cancer Research UK DDO	I
ToTem	Pacey	Temsirolimus, gemcitabine +cisplatin	mTORC	Advanced solid tumours expansion in urothelial malignancy	Investigator-initiated, collaboration	Pfizer	Wales CTU	I/II
RADICAL	Baird	Aromatase inhibitor +/- AZD4547	FGFR	Advanced ER+ breast cancer	Investigator-initiated, collaboration	AstraZeneca	Imperial CTU	I/II
Millennium	Corrie							
SGI-110-02	Basu	SGI-110	Methylation	Platinum resistant ovarian cancer	Commercial/Partnership (translational)	Astex	Astex	II with Ph I run in
TAX-TORC	Basu	Weekly paclitaxel + AZD2014	mTORC1/2	All-comers expansion in platinum resistant ovarian cancer	ECMC/AZ alliance	AstraZeneca	RMH / ICR	Ib
PiSARRO	Basu	Carboplatin / Caelyx +/- APR-246	p53 reactivation	Platinum-sensitive and p53 mutated epithelial ovarian cancer	Commercial/Partnership (translational)	Aprea	Aprea	I/II
PAKT	Baird	Weekly paclitaxel +/- AZD5363	AKT	Advanced triple-negative breast cancer	Investigator-initiated, collaboration	AstraZeneca	Barts CTU	II
TRAP	Pacey	ADIPEG-20, pemetrexed and cisplatin	Arginine metabolism	ASS negative solid tumours, including mesothelioma +NSCLC	Investigator-initiated /partnership	Polaris	Barts CTU	I
iBET	Jodrell	iBet	Bromodomain	Haematologic malignancies	Investigator-initiated /partnership	GlaxoSmithKline	GlaxoSmithKline	I
CALIBRATE	Baird / Pacey	Tumour and ctDNA profiling for patients on early phase trials	Biomarker	Patients on early phase clinical trials	Investigator-initiated, Cambridge-led	AstraZeneca	Cambridge CTU	Biomarker
DARPins	Baird	MP0250	MET / VEGF	Advanced solid tumours	Commercial/Partnership (translational)	Molecular Partners	Molecular Partners	I
CANCAP02	Pacey	AZD2014	mTOR	Window pre-prostatectomy	Investigator-initiated, Cambridge-led	AstraZeneca	Cambridge CTU	Biomarker
POSEIDON	Baird	Tamoxifen +/- GDC-0032	PI3K	Advanced ER-positive breast cancer	Investigator-initiated, Cambridge-led	Genentech	Netherlands Cancer Institute	I/II

Portfolio

Trial Name	PI	Agent (s)	Investigational drug target (s)	Population	Trial Type	Company Involved	Sponsor / CTU	Phase
CURRENT								
VANSEL	Pacey	Vandetanib + Selemetinib	EGFR / VEGF + MEK	Advanced solid tumours	Investigator-initiated, collaboration	AstraZeneca	Cancer Research UK DDO	Ib
NOTCH	Jodrell (Ba	MK0752 + gemcitabine	Notch	Stage IV pancreatic cancer	Investigator-initiated,	Merck	Cancer Research	I/II
HYPAZ	Jod Che							chanism of city
Immunocore (IMCgp100)	Jod							
OPARATIC	Jeff							
ToTem	Pac							
RADICAL	Bai							
Millennium	Cor							
SGI-110-02	Bas							ith Ph I run
TAX-TORC	Bas							
PiSARRO	Bas							
PAKT	Bai							
TRAP	Pac							
iBET	Jod							
CALIBRATE	Bai Pacey	patients on early phase trials		trials	Cambridge-led			marker
DARPins	Baird	MP0250	MET / VEGF	Advanced solid tumours	Commercial/Partnership (translational)	Molecular Partners	Molecular Partners	I
CANCAP02	Pacey	AZD2014	mTOR	Window pre-prostatectomy	Investigator-initiated, Cambridge-led	AstraZeneca	Cambridge CTU	Biomarker
POSEIDON	Baird	Tamoxifen +/- GDC-0032	PI3K	Advanced ER-positive breast cancer	Investigator-initiated, Cambridge-led	Genentech	Netherlands Cancer Institute	I/II

- High proportion investigator initiated studies
- Developed collaborations nationally and internationally
- Increasing number of first in man/ first in class studies

Year one: in one slide

EPCTT	Urology	CR-UK CI	Academic projects
• **OPEN TRIALS**: • VANSEL-1 • ToTem (set up) • AT13387 (set up) • **CONCEPTS**: • ADIPEG20 + pem/cis (PS/ Polaris) • ArQule – Akt i	• PROSTATE: • High risk men pre surgery • Linked to imaging, metabolism & lab pathways (ER stress now included)	• Neal Group: window concept • AZ collaboration • Aki + taxane (DJ)	•TNFR2, 180k grant • ctDNA/ molecular characterisation •PhD supervision •ER stress

Seminar series
Anglia research meeting
DDU advisory board
Anglian prostate r/ group (VG)

Trial methodology course for ACF
Onc R&D, CTU
CTU Management Committee

External collaborations:
Astra Zeneca, Seattle (RJ)- ctDNA

Combined (Academic/ NHS) Job Plan:

Day	AM	PM
Monday	Academic/ research	14.00 – 15.30 Urology MDT 15.30 - 16.00 EPCTT Training updates (alt weeks)
Tuesday	08.30 X ray Meeting 09.30 – 12 Departmental Meetings 12 – 13.00 CRI Seminar Series	13.15 – 14.00 Oncology R&D/ preparation for R&D alt weeks 14.30 Fellows education/ trial methodology Academic/ Research
Wednesday	09 – 13.00 EPCTT OPD	Audit/ clinical management & administration
Thursday	09 – 12.30 EPCTT CIW/ CRF (OPD)	13.30 - 17.30 Urology Trials OPD
Friday	09.30 – 10.30 PDDG Lab meeting 10.30 – 11.30 Project meeting 11.30 – 12.00 Trial coordinator	Academic/ research

“what do you actually do in the academic time”

Delivery

Timing:

45% of pharmaceutical-led projects completed on time

32% of non-commercial studies,

24% of projects led by other commercial organisations

Budget:

68% of pharmaceutical-led projects completed on budget,

64% of non-commercial studies

48% of projects led by other commercial organisations

Quality

Uni Warwick online data

Delivery

- Plan for Growth 2011
- Benchmark < 70 days from valid application to FPFV
- Future NIHR funding linked

2014-15 Quarter 1:
Clinical Trials Receiving NHS Permission in the 12 Months to 30/06/2014

Data is represented for the 51 providers of NHS services subject to the requirement for at least 4 quarters

	Adjusted Trials Total *	Adjusted Trials Meeting the Benchmark	% of Adjusted Trials Meeting the Benchmark	Adjusted Trials Not Meeting the Benchmark
	A	B	C	D
			=B/A	
TABLE SUMMARY - TOTAL FOR ALL 51 PUBLISHED PROVIDERS	1811	1203	66.4%	608
Alder Hey Childrens NHS Foundation Trust	8	7	87.5%	1
Barts Health NHS Trust	90	59	65.6%	31
Bradford Teaching Hospitals NHS Foundation Trust	38	30	78.9%	8
Brighton and Sussex University Hospitals NHS Trust	28	14	50.0%	14
Cambridge University Hospitals NHS Foundation Trust	74	52	70.3%	22
Camden and Islington NHS Foundation Trust	6	3	50.0%	3
Central Manchester University Hospitals NHS Foundation Trust	59	42	71.2%	17
Cumbria Partnership NHS Foundation Trust	-	-	-	-
East London NHS Foundation Trust	2	2	100.0%	0
Great Ormond Street Hospital for Children NHS Foundation Trust	18	14	77.8%	4
Guys and St Thomas NHS Foundation Trust	104	77	74.0%	27
Hertfordshire Partnership NHS Foundation Trust	2	0	0.0%	2
Homerton University Hospital NHS Foundation Trust	#	#	#	#
Imperial College Healthcare NHS Trust	77	39	50.6%	38
Kings College Hospital NHS Foundation Trust	66	39	59.1%	27
Leeds Community Healthcare NHS Trust	6	4	66.7%	2
Leeds Teaching Hospitals NHS Trust	79	49	62.0%	30
Manchester Mental Health and Social Care Trust	3	2	66.7%	1
Moorfields Eye Hospital NHS Foundation Trust	10	8	80.0%	2
North Bristol NHS Trust	24	21	87.5%	3

Setting up a study:

Trial Set UP Summary Notes

TRUST R&D DOCS

All current Trial documentation

- Protocol
- Localised:
  - Patient Information Sheets,
  - Consent Forms
  - GP Letter

IRAS documentation

- NHS REC Form
- NHS R&D Form
- Draft NHS SSI Form – list of Depts. authorisation is being sought from

Approvals

- REC
- MHRA

Personnel Documentation - CV/GCP

- Draft Contracts (if non-commercial, if Commercial these go direct to Priya usually in advance)
- Any other documentation e.g. Insurance Certificates, Sponsor Letters

SSI Authorisations

One per Dept from which assistance is required, Trial Name and REC number to be added to each form, including:

- Cancer Division and
- Radiation Protection where Radiology involvement
- Others

Documentation to be sent:

- Protocol
- Patient Information Sheet
- Draft SSI Form
- Authorisation Form (shared drive)
- REC Form
- Lab Manual – Tissue Bank Only

CCTC needs to record the date the authorisations where sent out and the date they were returned (EPIC)

Other Forms

- Lab Registration Form (generates):
  - Reference Ranges
  - Lab Accreditations
  - Lab Director CV
  - Lab Orderset
- ACRC Application Form
- Site Information Form (SIF) Commercial Trials Only
- ARSAC Application Form / PET Proforma for PET/CT
- CRN Application for Service Support Costs

SPONSOR DOCUMENTS eg

- Finance Disclosure Forms
- Data Protection Consents
- FDA1572
- Delegation Log
- Training Log
- Supply all personnel CV's & GCP

What is your “Unique selling point?”

unique

/juːˈniːk/

adjective

1. being the only one of its kind; unlike anything else.
   "the situation was unique in British politics"
   synonyms: distinctive, individual, special, especial, idiosyncratic, quirky, eccentric, isolated; More

noun *archaic*

1. a unique person or thing.
   "some of Lamb's writings were so memorably beautiful as to be uniques in their class"

Academic Career - Advice 1:

- **Stamina** - perseverance in the face of countless rejections...
- **Papers** - focus on getting papers. Be realistic - any paper is better than none. No point working on a big project that will realistically take 4 years when funding is for 2 years. But ultimately also include some high risk big projects in your portfolio that will give the big paper before your senior clinician scientist application
- **Get grants** - initially small but build your cv to show a track record
- **Institution and mentor** - 50-80 percent of the scores in your grant are for the environment. Match your project to the institutions strengths or move to one that is strong in your interest

Academic Career - Advice 2:

- **Follow your passion** in academic medicine. If you don't have one then don't bother wasting your time! Life's too short..
- Learn to play the **game**
- **Publish** quality not quantity
- **Set up collaborations** with a win-win formula (aim to be first or last on everything you do, but sometimes you may need to be in the middle!)
- Work on a **'wow' project**. If it isn't a wow project reconsider whether academic medicine is for you...
- Find something to do **outside** of academic medicine (take up a sport etc).
- Above all **stay focused**, stay on message, and nail that project!

Academic Career - Advice 3:

- Single biggest thing is to get a clear understanding of what you are **expected to deliver** eg minimum income from grants, commercial trials, numbers/IF of publications etc.

- With this, how and when your **performance will be assessed**

- **Speak to others** who have been the process

- Ensure **regular reviews** with your boss

Summary (in no particular order):

- Stamina
- Balance career/ life
- Publish
- Attract funding/ grants
- Collaborate
- Seek advice
- Know your goals (personal/ institutional) – continued funding
- Focus

Acknowledgements

Gert Attard

Peter Szlosarek

Deb Sarker

Thanks and questions…?

Cambridge Early Phase Trials Team

Professor Duncan Jodrell
Early Phase Trials Lead

Academic Consultant Physicians
Dr Bristi Basu
Dr Richard Baird
Dr Simon Pacey

Senior Research Nurse
Teresa Lockett

Early Phase Pharmacist

Research Nurses (4.5 whole time)

Trial coordinators

Clinical Fellows: Research (ACCI) wards

Speciality trainees: Med Oncology Joint CR-UK CDD Academic Lecturer

Data / Lab practioner

Data Managers

Quality Assurance Manager

Experimental Therapeutics in Cambridge

Cambridge Early Phase Trials Team, Department of Oncology:
Professor Duncan Jodrell
Dr Bristi Basu, Dr Richard Baird, Dr Simon Pacey

Cambridge Cancer Centre: Achievements To Date

Strength of Science

- Average: 1 publication per week in journals with IF > 20

Partnership with NHS

- Outcomes across multiple cancers are excellent
- Cancer is a key priority for the NHS Trust next 10 years
- Consistently in top 3 ‘Cancer Networks’ for trial entry

Recognition

- NHS Biomedical Research Centre – UK leading
- CRUK ‘Major Centre’ designation (1 of 3 – Oxford, Manchester)
- Cancer a Cambridge University ‘Strategic Initiative’
- International: designated an OECI Comprehensive Cancer Centre

Example translational Group: Urological Cancers

Research team

Urology

NGS

QPCR

IHC

Gene profiling

CTC

PD/PK studies

In vivo modelling

Window trial

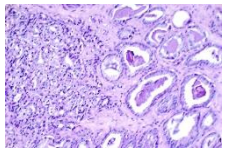
Functional imaging

Targeted biopsies

Serial sampling

Target popln

Radiology



Pathology

Oncology