Developments in Cancer research
– viruses, vaccines and radiotherapy

Health and Care Research Wales conference 2021

Mererid Evans
14 October 2021
Cancer-causing viruses

• Viruses cause ~15% of the global cancer burden

• 1911 Peyton Rous
  - cell free transmission of sarcoma

• 1964 Anthony Epstein & Yvonne Barr
  - discovered Epstein Barr virus (EBV) virus in Burkitt’s lymphoma

• 1983 Harald zur Hausen
  - isolated HPV16 from cervical cancer

• Others include Hepatitis B and C (Liver cancer)

• Cancer usually occurs years or even decades after primary infection
HPV – a significant cause of cancer worldwide

Age standardised incidence rates (per 100,000) of cervical cancer attributable to HPV

Age standardised incidence rates (per 100,000) of head & neck cancers attributable to HPV

HPV-associated head and neck cancer: a virus-related cancer epidemic

screening

vaccination

The “HPV Throat Cancer Epidemic” in Wales

Oropharyngeal Cancer in Wales 2001-2015

Age Standardised Rate (per 100,000)

Source: Welsh Cancer Intelligence and Surveillance Unit, Health Intelligence Division, Public Health Wales

55-80% positive for HPV
Our work in Wales informed the JCVI advice to extend UK HPV vaccination programme to include boys (07/2018), preventing future cancers.

[Evans, Powell et al. BMC Cancer 2013; Schache, Powell, Evans et al Cancer Res 2016]
Cancer vaccines – promise for the future

1. Tumour selective Oncolytic virus
2. Virus infects tumour cell which dies
3. Immune response

UK Lifesciences vision 2021: Healthcare Mission “enabling immune therapies such as cancer vaccines”
A good time to be involved in cancer research in Wales

- CReSt themes:
  - Precision and mechanistic oncology
  - Immuno-oncology
  - Radiotherapy
  - Cancer clinical trials, including experimental therapeutics
  - Supportive and palliative oncology
  - Cancer prevention, early diagnosis, primary care and health service research

Linear Accelerator – produces X-Rays

Targeted at a cancer (in the tonsil)

Causes DNA damage which (if not repaired) leads to cell death
Wales - leading clinical radiotherapy research in different cancers

Upper Gastrointestinal

Head & Neck cancer

Brain cancer

Prostate cancer

Wales is 1 of 4 UK RTTQA centres – ensuring the best radiotherapy is delivered to patients every time
HPV positive head & neck cancer → Minimally invasive surgery (laser or robot)

Co-primary endpoints: swallowing function and Overall Survival
"Developing kinder treatments for patients with head and neck cancer"

A1 Radiotherapy – standard dose (control)
A2 Radiotherapy + Chemotherapy (control)
B1 Radiotherapy – standard dose (test)
B2 Radiotherapy – low dose (test)
C1 Radiotherapy + Chemotherapy (test)
C2 Radiotherapy only (test)

No post-operative treatment

Low risk
Intermediate risk
High risk

Pathology assessment
Randomise
Randomise
Randomise
PATHOS – UK & International

584 patients recruited by 11 Oct 2021 (target 1100 patients by Oct 2023)

Open in 36 UK sites

Open in 8 international sites (USA [Florida, Stanford], Australia [Brisbane], 6 in France).
In set-up in 18 international sites (5 in France, 10 in Germany, 2 in Switzerland and 1 in Hong Kong).

Could establish a new international standard of care for the treatment of HPV-positive head & neck cancer

“Developing kinder treatments for patients with head and neck cancer”
PEARL: PET based Adaptive RT Trial

Week 1-3 of radiotherapy

Weeks 4-6 of radiotherapy

Plan based on PET-active cancer at baseline

Adapted plan based on biological response

Tongue base cancer seen on FDG-PET-CT scan

Aim: to reduce high dose treatment volume in responding patients to reduce toxicity

“Developing kinder treatments for patients with head and neck cancer”

Co-Cl: Dr T Rackley, HCRW Clinical Research Time Awardee
SABR_IT Study
[Awen Gallimore, Andy Godkin, Tom Rackley, Cath Pembroke]

- Blood taken at 5 time points (before, during and after RT and at recurrence)
- Enzyme-linked immunospot (ELISPOT) assay
- Flow Cytometry
Neurocognitive function study

[James Powell, Sahar Iqbal, Richard Wise]

40 patients with brain oligo-metastases, mpMRI pre and post Stereotactic Radiosurgery (SRS)

Diffusion tractography
tumour

Superior Longitudinal fasiculus tract (green) displaced medially

T1 weighted

Arterial spin labelling cerebral blood flow

Orange/yellow = high blood flow. Tumour core has low blood flow [associated with poor outcome], with a high flow border.
**Immunology**

Turning immunologically ‘cold’ tumours into ‘hot’ tumours with radiotherapy

[Ruckert et al, Stem Cells 2021]

**Radiotherapy**

**Imaging**

Using world-class imaging to understand the microstructural & biological effects of radiotherapy

[3T Microstructural MRI
1 of only 3 in the world
Cell size imaging]

**Data, Automation and AI**

Using AI to select cancers for RT & automation to improve efficacy

**Innovation**

**Novel agents including Cancer Vaccines**

Combining RT with tumour selective oncolytic viruses = radioimmunovirotherapies

[Courtesy of Prof Alan Parker]
Developing new infrastructure for research in Wales

- **Increasing patient access to research** - including Early Phase Trials (EPTs) and Advanced Therapies for solid cancer and haematology-oncology

- **Strengthening the translational pipeline** → enabling scientists to bring new discoveries through to the clinic & encouraging new scientific discovery

- **Developing a focus for cancer research excellence in Wales** → enhancing reputation and attracting future funding, partners & staff

- **Enabling training, education & innovation**

- **Housing Welsh research infrastructure, hub for industrial partnerships.**
Priorities for Cancer Research in Wales

• Build a sustainable, internationally competitive portfolio of cancer research in Wales, **focused on thematic areas of research excellence** where Wales can make a unique or significant contribution and build critical mass

• Work together as a ‘**One Wales’** team of researchers, across different institutions, disciplines & diverse skills

• Look outwards to establish effective research partnerships and networks **across the UK and internationally**

• Enable the **translational pipeline** between the laboratory and clinic → developing new infrastructure and people

• Inspire and establish career pathways for **future research leaders** → Clinical, Academic and Clinical Academic.
What we can achieve....

• A thriving, connected cancer research community in Wales

• An identity, focus & enhanced reputation for cancer research in Wales

• Inward investment, ensuring sustainability and benefitting the Welsh economy

• A positive legacy to hand onto the next generation of researchers & cancer patients in Wales

• Health benefits for cancer patients and the public across the whole of Wales

→ Realising these benefits is a collective endeavour (individual, institutional, governmental….)
The Wales Cancer Research Centre

- WCRC is an established & valued part of the cancer research infrastructure in Wales which makes people feel part of something bigger. It is a vehicle to:

  - Influence a harnessed approach for a joined up ‘One Wales’ for cancer research
  - Realise opportunities to develop new infrastructure to benefit cancer research & patients in Wales
  - Champion the cancer research workforce in Wales which needs urgent investment & development of career pathways to build critical mass & a thriving cancer research community for the future
  - Promote and drive the implementation of CReSt for patients and researchers in Wales, working closely with HCRW and with institutions across Wales to ensure its success.
Thank you - Diolch yn fawr

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