Breast cancer research and a changing treatment pathway

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What is the breast surgeon’s role in 2016?

- Surgery is a medieval treatment in a molecular era
- Breast cancer outcomes are determined by disease biology, tumour burden and response to therapy, not extent of surgery
- The surgeon’s role is to maximise breast and axillary conservation
- The breast surgeon underpins much clinical breast cancer research

More is better
Radical surgery only treatment – “one size fits all”

Minimum required – for effective disease control - “personalised surgery”
A changing treatment strategy: From the traditional....

Surgery is no longer the *de facto* primary treatment for breast cancer

- remains key to successful treatment
...to the contemporary Surgery as adjuvant treatment

Shift driven by clinical, scientific and translational research
Benefits of pre-surgical treatment

• Patient benefits
  • Downstaging of surgery
    • More breast conserving surgery, less mastectomy
    • “response-adapted surgery”
  • Treatment modification
    • “is it working?”
    • If not – change it!

• Research benefits
  • evaluation of new treatments and strategies
    • Easy to monitor response
    • Serial biopsies and blood samples
      • Study disease in situ
      • Monitor effects of treatment
Neoadjuvant and “window of opportunity” studies in breast cancer

Multiple cycles or prolonged course of treatment, 18 – 24 weeks

Short course of treatment

Short duration (2 – 4 weeks) treatment before surgery
Neoadjuvant studies...a Belfast example
The Neo-DDRD study

• DDRD assay
  • Developed by Almac Diagnostics
  • Uses tumour tissue
  • Predicts response to certain chemotherapy types
    • Both before and after surgery

• Neo-DDRD study
  • Feasibility study
  • Assess the possibility of using the assay in routine practice
  • Strong translational science component
    • Sample collection during treatment
    • Research to understand pathways underlying the signature
NeoDDRD study – a neoadjuvant feasibility study

- Integrated into standard neoadjuvant treatment
- Two additional research breast biopsies at diagnosis
- Blood samples at diagnosis
- Standard neoadjuvant treatment
  - Serial tissue and blood samples during treatment and at surgery
Neo-DDRD study

• Open since May 2014 in BCH
• Recently opened in UHD
• 25 patients recruited
• Excellent rates of sample donation
• Trial extended to 50 patients
• Example of successful collaborative working
• Scientific studies on samples will be used to support phase II studies
  • Neoadjuvant and window studies
CIBRAC – Chemoprevention in BRCA Carriers

• BRCA1
• 80% lifetime risk of breast cancer
  • Majority of cancers oestrogen receptor negative
  • But oestrogen appears key
    • Tumours in breast and ovary
    • Removal of ovaries reduces breast cancer risk
    • Pregnancy may increase breast cancer risk
• By-products of oestrogen metabolism in cells may cause DNA damage
• Role of BRCA1 is to respond to DNA damage

Molecular and Cellular Pathobiology

BRCA1 Deficiency Exacerbates Estrogen-Induced DNA Damage and Genomic Instability

Kleenan I. Savage, Kyle B. Matchett, Eliana M. Barros, Kevin M. Cooper, Gareth W. Irwin, Julia J. Gorski, Katy S. Orr, Jekaterra Vokhodina, Joy N. Kavanagh, Angelina F. Madden, Alexander Powell, Lorenzo Manti, Simon S. McDade, Ben Ho Park, Kevin M. Prise, Stuart A. McIntosh, Manuel Salto-Téllez, Derek J. Richard, Christopher T. Elliott, and D. Paul Harkin

Cancer Research
CIBRAC

• Does reducing circulating oestrogen levels reduce DNA damage in breast tissue?
  • Confirm link between oestrogen exposure and DNA damage
  • Better understand how oestrogen and metabolites initiate tumour development
  • Provide evidence to support a larger clinical study looking at chemoprevention in BRCA1 mutation carriers
Planned pilot clinical window study

- DNA damage (comet assays and Immunofluorescence)
- Plasma and urine metabolite & DNA adduct levels