Clinical Research in Rare Cancers
Friday 10th February 2012
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Rare cancer is a common disease

• “Rare Cancer”: [prevalence <50/100,000] incidence <6/100,000/year

• Together, ‘rare cancers’ account for 22% of all cancer diagnoses in UK/Europe

• This is more than any single common cancer: breast 16%, lung 13%, colorectal 13% and prostate 12%

• Average outcome inferior to common cancers
IRCI - Aims

• To facilitate the development of international clinical trials of treatments for rare cancers

• To identify and overcome barriers to international trials so that agreed IRCI trials can run smoothly
IRCI – partner organisations

Organisational goals
Memo of Understanding
Administrative support
IRCI – partner organisations

Organisational goals
Memo of Understanding
Administrative support
**Expressions of interest**

- incidence <3/100,000/yr
- no existing RCTs
- no existing international trial group
- **rationale, potential and enthusiasm** for an interventional trial (preferably RCT)

**Interest in ≥ 2 member groups?**

**IRCI board meets to select and prioritise new study groups**

- group co-chairs appointed
IRCI rare cancer group

Chairs’ teleconf.

Full group face-to-face
- decide trial plans
- assign CI(s)

Follow-up trial development mtgs

Trial submitted to primary grant funder

Parallel fast-track approval by IRCI partners
IRCI – groups formed in 2011

- Salivary gland cancer & anaplastic thyroid cancer
- Small bowel adenocarcinoma
- Gynaecological sarcoma
- Fibrolamellar hepatocellular carcinoma
- Penile cancer
- Ocular melanoma
- Thymoma
- Relapsed/metastatic anal cancer
IRCI – groups formed in 2011

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IRCI – Salivary gland cancer

- 9 new cases and 2 deaths per million population
- Chemo for advanced disease: RR ~25%, PFS~7months
- Androgen receptors commonly expressed
- Reported responses to androgen deprivation therapy (ADT) in 20-44%, but no RCT

Three studies discussed:

- Androgen deprivation therapy in advanced salivary gland cancer patients
- Axitinib versus placebo study for patients with adenoid cystic carcinoma
- The role of post-operative radiotherapy or post-operative chemoradiotherapy in salivary gland tumours
IRCI – Salivary gland cancer

**Proposed study:** Androgen deprivation therapy (ADT) versus platinum anthracyclin (CT) in patients with androgen receptor (AR) expressing, recurrent &/or metastatic salivary gland cancer

- Recurrent &/or metastatic SGC (1st-line)
- **Chemotherapy** (Cisplatin and doxorubicin)
- **ADT**

n-110 (Korn design); primary endpoint PFS
**alpha = 20%**, power 80% for 15% improvement (60% to 75%) at 6 months
IRCI – Small bowel adenocarcinoma

- ~6 new cases and 4 deaths per million population
- Usually treated as for colon cancer but no good evidence base

**Adjuvant Trial:**
- Patients with completely resected SBA
  - Observation
  - Cap or 5FU/FA
  - Cap/Ox or 5FU/FA/Ox

**Advanced disease trial:**
- Metastatic or unresectable SBA
  - Prior oxaliplatin-based therapy
    - Yes
      - Chemotherapy (FOLFOX)
      - Chemotherapy + bevacizumab
    - No
      - Chemotherapy (FOLFIRI)
      - Chemotherapy + bevacizumab

\( n = 1200 \) over 5 years; 657 DFS events
90% power to detect HR 0.775 (5% alpha) for +/- chemotherapy; 80% power for same HR for +/- oxaliplatin

Sample size not yet determined
IRCI – Gynaecological sarcomas

Four studies discussed:
• Uterine leiomyosarcoma (uLMS) study
• Endometrial Stromal Sarcoma (ESS) study (x2)
• Undifferentiated Uterine Sarcoma (UUS) study

**uLMS study:** A Phase III randomised trial of gemcitabine plus docetaxel followed by doxorubicin versus observation for uterus limited, high grade uterine leiomyosarcoma

- Observation
- Chemotherapy
- high risk uterine leiomyosarcoma

maximum sample size = 218
Alpha 0.05; power 80% for 60% improvement in median OS (30 to 48 months)
One interim analysis; Pampalonia-Tsiatis critical boundaries
IRCI – Penile cancer

Management of Inguinal Nodes in Penis Cancer

Penis cancer with clinical inguinal node disease

- No need for neoadjuvant treatment / clinical LOW risk
  - Therapeutic inguinal node dissection
    - Pathological LOW risk
      - Adjuvant ChemoRT
        - R3
    - Pathological HIGH risk
      - Surveillance

- Clinical uncertainty / INTERMEDIATE risk
  - Definite need for neoadjuvant treatment / clinical HIGH risk
    - Neo-adjuvant Chemo
      - RESTAGE
        - Therapeutic inguinal node dissection
          - Pathological HIGH risk
            - Adjuvant ChemoRT
              - R3
          - Pathological LOW risk
            - Surveillance
          - Pathological HIGH risk
            - Prophylactic Pelvic lymph node dissection
              - R3

Likelihood Bayesian approach, aiming to recruit at least 400 patients with minimum 60 in R1, 200 in R2 and 200 in R3
**Proposed study:** A Randomized Multi-Arm Multi-Stage study

- MAMS design
- 2 intermediate stages, one final
- Increasingly stringent 1-sided alpha of 0.5, 0.2, 0.03
- High power of 93%, 93%, 88%
- Total accrual target 168 patients over 3 years maximum
Proposed study: Phase II/III Study of Induction Chemotherapy followed by surgical resection followed by randomization to post-operative radiation or observation for stage III Thymoma and Thymic Carcinoma

Histologically proven, untreated thymoma (stage III) or thymic carcinoma (stage IIb or III)

Preoperative Chemotherapy → Surgery

Complete resection → PORT

Incomplete resection → Off-study PORT

Observation

Sample size not yet determined
Plans

• Continue to aid existing groups
• Work through the issues of trial setup with first round of trials
• Expressions of interest for round 3 of new groups
• Other cooperative groups considering joining IRCI:
  • NCIC (Canada)
  • INCa (France)
  • Korean NCI
  • Cancer Australia
• Discussing IRCI-Industry Alliance Partnerships