Learn from every patient

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PCUK National Study Day
9am – 4pm, Monday 15th October 2018
Hyatt Regency, Birmingham B1 2JZ
Are patients willing to enter clinical trials?

Aim of NCRN:
- double trial accrual from 3.75% (2001) to 7.5% (2004)

Audited 2004 patients:
- N=137
- median age 65 years (range 46 – 84)
- 52% male
- 99% Caucasian
- Stage: adjuvant 11%, advanced 89%

Board RE et al Pancreas 2007;34(2):269-70
Are patients willing to enter clinical trials?

- Offered clinical trial: 38%
- Chemo not appropriate (Dr): 4%
- Chemo not appropriate (Patient): 4%
- No histology: 7%
- Prior malignancy: 15%
- Prefer treatment locally: 19%
- Poor performance: 4%
- No trial available: 4%
- Reason not known: 5%

n=137
Are patients willing to enter clinical trials?

- n=137
  - Accepted invitation: 38%
  - Declined (anxiety/concern): 19%
  - Avoid delay: 15%
  - Refused further treatment: 7%
  - Prefer treatment locally: 4%
  - Reason not known: 4%

- n=52
  - Accepted invitation: 68%
18% of the patients referred entered a clinical trial.
Patients are willing to enter clinical trials

Barriers

– Lack of histology
– Delays in protocol-driven tests
– Patient concerns
– Nature of studies
  • Chemotherapy
  • Epidemiology
  • Psychosocial
  • Nursing
  • Dietary
  • Radiology
  • Biomarkers...

69% of patients with pancreatic cancer are willing to take part in clinical trials...

...however, a study was only offered to 38% of patients
PanDA
Pancreatic cancer Dietary Assessment study

Lindsay Carnie | Research Dietitian
Prospective observational study of prevalence, assessment and treatment of pancreatic exocrine insufficiency in patients with inoperable pancreatic malignancies
Pancreatic Exocrine Insufficiency (PEI)

**Symptoms**
- Abdominal pain
- Weight loss
- Steatorrhea

+ Faecal elastase

**PERT | Pancreatic Exocrine Replacement Therapy**
Importance of diagnosing & treating PEI

PDAC
- Diagnosis of cancer (advanced stage)
- Assessment of fitness for treatment (chemotherapy)
- Treatment (aim of improving patient’s outcome)

PDAC + untreated PEI
- Diagnosis of cancer (advanced stage)
- Assessment of fitness for treatment (chemotherapy)
- Treatment (aim of improving patient’s outcome)

- PEI can impact negatively on patient’s quality of life and fitness, affecting treatment delivery and even response to treatment
- By securing an adequate nutrition, patients may tolerate and benefit more from treatment.
Audit on our previous clinical practice (2014)

- 183 patients with PDAC or panNETs
- 63% of patients had symptoms in keeping with PEI
- Diagnosis based on symptoms; no specific diagnostic technique was used
- Not everyone with symptoms was treated with PERT
- Importance of dietitian input for ALL patients

Patients who received a nutritional intervention were more likely to receive chemotherapy (65.8% vs. 50%; p-value 0.03).

Nutritional intervention was associated with longer survival (10.2 (95%-CI 7.5-13.3) vs. 6.9 months (95% CI 5.5-9.9))

40% reduction in risk of death (HR 0.6 (95%-CI 0.4-0.9), p-value 0.015 in multivariable analysis.)
PanDA | Study plan and objectives

- Prospective observational study (150 pts)
- Patients diagnosed with PDAC and pNETs
- **Demographic cohort:** How frequent is PEI?
- **Diagnostic cohort:** Breath test. FE1. Which is the best way for diagnosing PEI? Can we design a diagnostic panel?
- **Follow-up cohort:** Validation of diagnostic panel. QoL. Pts outcomes

**Year 1**

- **Fact-finding**
  - **The demographic cohort**
    - N=50 evaluable patients
    - Assessed at baseline for symptoms of pancreatic enzyme insufficiency (PEI) and nutritional status using data from a standard of care panel of blood tests.
  - **The diagnosis cohort**
    - N=50 evaluable patients
    - Assessed at baseline for symptoms of PEI and nutritional status using data from a standard of care panel of blood tests and a faecal elastase measurement.
    - A breath test will test for PEI.

**Year 2**

- **Active treatment**
  - **The follow-up cohort**
    - N=50 evaluable patients
    - Pancreatic enzyme replacement therapy (PERT) prescribed (as req)
    - PEI diagnostic panel from Step 1 (Diagnostic Cohort) will be validated

Dietitian input for ALL patients
## PanDA | Schedule of events

<table>
<thead>
<tr>
<th>Demographic cohort  N=50</th>
<th>Diagnosis cohort  N=50</th>
<th>Follow-up cohort  N=50</th>
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<tbody>
<tr>
<td><strong>First (and only) appointment</strong>&lt;br&gt;• Symptoms, concomitant meds, PS, comorbidities</td>
<td><strong>First appointment as per demographic cohort</strong>&lt;br&gt;1-2 weeks after baseline appointment&lt;br&gt;• Every activity detailed in the Demographic cohort&lt;br&gt;• <strong>¹³C Breath test</strong>&lt;br&gt;• Collect data from standard of care Faecal elastase-1 test&lt;br&gt;• Test acceptance evaluation&lt;br&gt;• Cancer treatment follow-up (rate of starting treatment &amp; dose intensity)&lt;br&gt;• Survival follow-up</td>
<td><strong>First appointment</strong>&lt;br&gt;• Baseline assessment (symptoms, concomitant meds, PS, comorbidities)&lt;br&gt;• <strong>Use of designed diagnosis panel for PEI</strong>&lt;br&gt;• Dietitian assessment (including weight, BMI, MUAC, handgrip strength, SC-test and FAACT–A/CS (with VAS)) and intervention (PERT treatment if required)&lt;br&gt;• QoL questionnaires (QLQ-C30 and QLQ-PAN26 +/- QLQ-GLNET21)&lt;br&gt;<strong>Follow-up appointments</strong>&lt;br&gt;• Dietitian review (including weight, BMI, MUAC, handgrip strength SC-test and FAACT–A/CS (with VAS))&lt;br&gt;• Symptom monitoring (diary and clinic review)&lt;br&gt;• PERT treatment &amp; toxicity monitoring (compliance diary and clinic review)&lt;br&gt;• QoL questionnaires (QLQ-C30 and QLQ-PAN26 +/- QLQ-GLNET21)&lt;br&gt;• Test acceptance questionnaire&lt;br&gt;• Feedback questionnaire (4-6 weeks later by post)&lt;br&gt;• Cancer treatment follow-up (rate of starting treatment and dose intensity) and survival follow-up</td>
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### Data from standard of care blood tests
- Haemoglobin, MCV, INR
- Serum total protein, albumin, pre-albumin, retinol binding protein
- Cholesterol; inc Total, LDL & HDL, triglycerides
- Amylase
- Vitamins A, D & E
- HbA1C
- Transferrin, ferritin
- Magnesium

### Dietitian assessment (including weight, BMI, MUAC, handgrip strength, SC-test and FAACT–A/CS (with VAS)) + (PERT treatment if req)
- Cancer treatment follow-up (rate of starting treatment and dose intensity)
- Survival follow-up
• Protocol fully developed (with support from dietitian) and approved by REC (November 2017)

• First patient recruited 17/09/2018

• 27 patients recruited to date

• Due preliminary results (demographic and diagnostic cohort by June 2019)
OBSERVATIONAL STUDY | RELEVANT
RELEVANT study | Patient and physician perspectives on clinically-meaningful outcomes in advanced pancreatic cancer

Rille Pihlak, MD

Supervisors: Dr Mairéad McNamara and Prof Juan Valle

Dr Rille Pihlak is funded by the Collins Clinical Research PhD fellowship and by Pancreatic Cancer UK
What is meaningful?

• To patients, **QoL may be more / as important as overall survival**

• **Better assessment** of specific-cancer-related symptoms can help better define clinically-meaningful outcomes

• Using **validated instruments** and shorter cancer-specific surveys may be helpful

• The American Society of Clinical Oncology concluded that a **4-5 month improvement in overall survival**, over standard treatment would be meaningful.

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American Society of Clinical Oncology Perspective: Raising the Bar for Clinical Trials by Defining Clinically Meaningful Outcomes

**VOLUME 27 · NUMBER 33 · NOVEMBER 20 2009**

**JOURNAL OF CLINICAL ONCOLOGY**

Call for Clarity in the Reporting of Benefit Associated With Anticancer Therapies

Why is it important to know what patients want?

- 2 studies with 1193 and 917 patients; non-curative colorectal or lung cancer

- **70-80% of patients had unrealistic expectations** about the likelihood of chemotherapy curing their cancer

- Patients who thought that they were going to live for **at least 6 months** were more likely to favour life-extending therapies compared to BSC, and in turn were more likely to undergo aggressive treatment... **6-month survival was not better** for these patients

- Patients who receive **early palliative care** have better survival (non-curative lung cancer)

• While patients may have unrealistic perceptions of prognosis, it is still not known what difference in survival benefit would be meaningful to them.

• In advanced pancreatic cancer, survival may be less than 6 months.

• Many patients are already in their last months of life when they are first seen by an oncologist.

• Physicians often have very different views on adverse events and quality of life than patients.

• Both physicians and patients may under or over-estimate the potential for treatment benefit and adverse events.

*Burris et al 1997.*
• Survey among patients with advanced pancreas cancer, and their physicians at The Christie

• Patients asked to fill in a survey, in addition to QoL questionnaires, at three time points.

• Physicians are asked to fill in a similar survey at those same time points, after seeing the patient in clinic.

• **Aim** | Understand what patients think about their cancer diagnosis, potential treatment and goals, and determine if their views change over time, due to treatment response or side-effects.
Figure 1: Planned study outline at three timepoints
## Patient study questions

### Background
- Decision making.
- Previous information about chemotherapy.
- Where they received information about the cancer diagnosis.

### Understanding the aims of treatment*
- What patients have been told about aim of their treatment.

### Impact on patients’ life*
- How often they need to come for treatment.
- Chemotherapy effect on QoL and current symptoms.
- Likelihood of the chemotherapy to improve symptoms.

### Treatment outcome*
- Likelihood of chemotherapy to extend life, or keep their cancer stable.
- Minimal extra time that would be meaningful.
- How much side-effects would the patients be willing to accept as trade-off with minimal, and doubled extra time.

### Patient goals*
- Patient personal goals.
- What are the most important ones.

### EORTC QLQ- C30 and QLQ-PAN-26
To evaluate changes in QoL, side-effects and symptoms.
Physician study questions

• Similar to the patient survey, at the same 3 time points.

Aim
• Correlation with the patient answers.

• What physicians view as meaningful outcomes for the patients.

• What physicians think are the patients’ goals.

• How much they think patients are willing to trade-off side-effects for extra time.
• Planned recruitment – approximately 150 patients (and up to 12 physicians/nurse clinicians)

Dates and participant numbers:
• Opened for recruitment 23/05/18.
• 30 patients consented and have filled in time point 1 questionnaires (paired with physicians).
• 9 physicians and nurse clinicians consented.
A BROAD PORTFOLIO
Learning from every (most) patient(s)

BioBank
- 552 consented
- 273 tissue only
- 279 tissue and blood
- 80% advanced

Observational studies
- PanDA

Clinical Trials
- NCRI portfolio studies
- RELEVANT

Big Data Data Mining
- Commercial studies

Scope for many additional studies; including nursing and dietetic studies
• A high proportion of patients are willing to take part in clinical trials

• Interventional clinical trials require a high threshold of fitness

• Observational studies offer opportunity for all patients (including less fit) to get involved

• BioBanking also enables participation…while patients are able to consent

• Big Data studies may yield important information in the future

• “Learning” does not mean it has to be done by someone else…be inspired!
Thank you