At a glance

**Background:** The majority of pancreatic cancer cases are unresectable as they are not diagnosed early enough to receive curative surgery. Chemotherapy gemcitabine (alone or in combination) and Folfirinox are commonly used for unresectable pancreatic cancer treatment. Despite the progress in chemotherapy drugs seen in the last 20 years, survival still remains poor. It is therefore critical to implement a treatment pathway to improve disease outcomes for patients with unresectable pancreatic cancer.

**Implemented centralised care protocol:** This showcase presents a retrospective study led by Dr Faluyi and Dr Palmer and their team in Clatterbridge Cancer Centre in Wirral. The aim of the study was to compare disease outcomes of advanced (unresectable) pancreatic cancer patients between those that received centralised care (dedicated pancreatic cancer oncology) and those that received care in devolved (general oncology) clinics.

**Outcomes:** Centralisation of care was associated with initiation of chemotherapy treatment 10 days earlier than in devolved care clinics. About 25% more patients received chemotherapy in centralised care compared to devolved care clinics. Median survival for all advanced pancreatic ductal adenocarcinoma (PDAC) patients was five months in centralised care clinics compared to three months in devolved care clinics. For metastatic PDAC, median survival was 4 months in the centralised care clinics that was higher by 1 month compared to devolved care clinics. Survival of patients with lower performance status was improved when care was delivered in centralised care clinics; median survival was 1 month longer and one-year survival was 13% for low performance status patients in centralised care clinics, whilst there was no one-year survivor in the group of the devolved care patients.

**Conclusions:** Centralised care oncology clinics for unresectable pancreatic cancer was associated with better disease outcomes especially for patients with metastatic disease and for those who had lower performance status. Development of centralised clinics can provide better access to treatments and supportive care that can improve quality of life, care experience and potentially survival of these patients.
**Quick Facts**

A study contacted by the Cancer Survival Group led by Professor Michel Coleman in the London School of Hygiene and Tropical Medicine (LSHTM) showed that in England:

- 27,529 patients were diagnosed with PDAC in the period 2010-2013 from which only 2,086 had curative surgery, i.e. 7.6% of the PDAC cases.
- The five-year survival of PDAC patients who did not receive surgery was 1.7% (unpublished data).

**Background**

It is estimated that the majority of patients diagnosed with pancreatic ductal adenocarcinoma (PDAC) in England cannot undergo curative surgery, the only potentially treatment for longer survival. 10-20% of patients with pancreatic cancer are diagnosed with locally advanced pancreatic ductal adenocarcinoma (LPDAC) and 50-60% of patients are diagnosed with metastatic or systemic disease. Patients with advanced pancreatic cancer typically receive first-line treatment and a small proportion will also receive second-line chemotherapy. Radiotherapy is also sometimes given to manage pain and prevent pathological fractures. Gemcitabine (Gem) chemotherapy for advanced pancreatic cancer has shown modest median survival benefits (5.65 vs 4.41 months) and improved quality of life (23.8% vs 4.8% improvement). Longer median survival (up to 11.2 months) has been demonstrated in more recent trials using combination chemotherapy (gemcitabine plus a targeted agent). Folfirinox has been shown to have a survival advantage over gemcitabine (11.2 vs 6.8 months) and it is widely used in clinical settings.

In a recent meta-analysis study, patients with advanced LPDAC had a 24.2 months overall survival; longer than what has been reported with gemcitabine (6-13 months). Nevertheless, a systematic study in Wales in a cohort of patients with locally advanced non-metastatic and metastatic PDAC in the period 2002-2005 reported median survival of 7.4 and 2.8 months, respectively. Moreover, a recent study in pancreatic cancer outcomes in Germany and the United States reported little improvement in overall survival of advanced pancreatic cancer, i.e. from 4.8% to 5.7% in periods 2000/02 and 2010/12, respectively, suggesting that outcomes achieved in trials described above are not replicated in real life.
Case for change

Advanced pancreatic cancer is associated with increased morbidity and poor prognosis. The alarming statistics place the need for development of non-surgical treatment regimens for advanced pancreatic cancer patients to drive improvements in disease outcomes. Centralised care with the introduction of Hepato-Pancreatic Biliary (HPB) specialist centres has been proved a key development for improvement of resection outcomes for early PDAC patients. Moreover, high-volume centres are associated with reduced peri-operative mortality and better median survival\textsuperscript{11,12}. Increased surgeon specialisation and peri-operative supportive care are considered important factors that contribute to better management of resectable PDAC cases. Therefore, it is plausible to hypothesise that care of unresectable PDAC patients in dedicated oncology clinics can enable delivery of best chemotherapy protocols by specialist oncologists and could potentially improve supportive care, survival and care experience for this group of patients. This report presents a systematic study led by Dr Faluyi, Consultant in Medical Oncology and Dr Palmer, Chair in Medical Oncology in Clatterbridge Cancer Centre (CCC) in Wirral and the University of Liverpool\textsuperscript{1}.

Aim

- To adopt a transition from devolved to centralised care for advanced PDAC patients within the Merseyside and Cheshire Cancer Network (North West England)
- To evaluate the impact of such a transition in delivery of care
- To improve survival for unresected PDAC patients.
Transition from devolved to centralised care of unresected pancreatic cancer patients took place in the period 1st of October 2009 and 31st of December 2010

A prospective database with clinical patient records was generated by statisticians of the Clinical Effectiveness Team (CET) in CCC

Ethical approval was obtained to review the database and access patient data

Patients with resectable PDAC were excluded from the database

The study group comprised patients with unresectable PDAC and were grouped as follows:

i) Devolved care group (D). Patients who were managed as part of the devolved care, i.e. between 1st October 2009 and 31st December 2010 (n=121 patients treated in devolved care)

ii) Centralised care group (C). Patients who were managed following centralisation of care, i.e. between 1st January 2013 and 31st March 2014 (n=115 patients treated in centralised care)

Devolved care group (D) was managed by five different oncologists in any of five clinics distributed throughout the Merseyside and Cheshire region which had accommodated mostly patients with non-HPB malignancies

Centralised care group (C) was managed by two oncologists in two dedicated clinics specialised in HPB malignancies

Ad-hoc pathways for referral to dietitians, palliative care and other HPB medical specialists was available to both D and C groups with more direct referral pathways for such care in the C group
The model of care practice (continued)

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| **8** | Data was recorded as follows:  
  i) Histological diagnosis was recorded in CET database and cross-checked with pathology results  
  ii) Cancer stage was monitored by radiology reports, which were updated by pancreatic cancer multi-disciplinary team (MDT) reviews |
| **9** | Survival analysis was measured as per status of patients on the 30th of September 2015, permitting sufficient follow-up to calculate median and one-year survival for all patients and ensure enough cases in both devolved (D) and centralised (C) care to compare survival between the two groups. Overall survival was taken as the interval between first visit in a CCC clinic and the date of death |
| **10** | Statistical analysis was performed by CET statisticians who managed the CCC database and all cofounding factors (e.g. demographics, smoking, comorbidities) were taken into account |

This is a schematic summary showing differences between devolved (D) and centralised (C) care setting for advanced PDAC patients

**Devolved care (D)**
- **D group**  
  - n=121 patients  
  - x5 oncologists  
  - x5 non-HPB clinics

**Centralised care (C)**
- **C group**  
  - n=115 patients  
  - x2 oncologists  
  - x2 HPB-dedicated clinics
Timeline

Devolved care group (D). Patients managed in devolved care clinics:
1st October 2009 and 31st December 2010

Centralised care group (C). Patients managed in centralised care clinics:
1st January 2013 and 31st March 2014

Survival analysis was measured as per status of patients on the
30th of September 2015
Outcomes

Treatment characteristics of patients

In the centralised (C) group, 67% (77 out of 115) patients received first-line chemotherapy as opposed to 43% (52 out of 121) in the devolved (D) group (Figure 1). From these patients, 1.9% (1 out of 52) from the D group received second-line chemotherapy, whereas in the C group 23.4% (18 out of 77) patients received second-line chemotherapy. However, it should be noted that it is likely that the highest proportion of patients who received second-line chemotherapy was due to Folfirinox being available as a first-line treatment in the centralised care group. Folfirinox was introduced after 2011 when it was shown that it has better survival outcomes than gemcitabine.5

Distribution of chemotherapy treatment among patients (%)

Figure 1: Chemotherapy treatment in devolved (D) and centralised (C) care patient groups. Data is expressed as % proportion of patients who received first-line chemotherapy in devolved (D; purple bar) and centralised (C; pink bar) patient groups (left panel) and % proportion of patients who underwent second-line chemotherapy (right panel).
Treatment times

The time to commencement of chemotherapy after initial review was on average 10 days less in the centralised care group of patients (Figure 2). Treatment initiated within 18 days on average for C group and 28 days on average for D group.

Figure 2: Average number of days of initiation of treatment from the time that patients were first reviewed. Data is expressed as mean number of days between patients who were managed in devolved care (D; left panel) and patients who were managed in centralised care clinics (C; right panel).
**Survival**

**Survival by clinical evaluation**

Overall, median survival for patients with advanced LPDAC was improved (7 months) compared to the survival of patients with metastatic disease (3 months) that was lower by 4 months, regardless of the care setting they were in (Figure 3A). However, overall median survival for patients with advanced PDAC who were managed in centralised (C) care clinics had a median survival of 5 months that was 2 months longer compared to patients seen in devolved (D) care clinics. This was mainly attributed to higher survival of metastatic patients in the C group, as there was no difference in survival of LPDAC patients between devolved and centralised care clinics (data not shown). Precisely, C group of patients with metastatic cancer had a median survival of 4 months as opposed to patients in the D group that survived 1 month less (Figure 3B).

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**Figure 3: Median survival by clinical evaluation.**
A) Median survival (months) between localised advanced (LPDAC) and metastatic PDAC. B) Median survival between all advanced PDAC and metastatic PDAC between devolved (D) and centralised (C) care groups.
Survival by performance status

No difference was observed in survival of patients who had a high fitness status between the devolved and centralised care clinics (data not shown). In contrast, among patients who had a lower fitness status, patients in the centralised care (C) group (n=30) had a median survival of 4 months (Figure 4, right pink bar) with 13% surviving beyond one year (Figure 4, right yellow triangle) as opposed to patients in devolved care (D) group (n=40) whose median survival was 1 month less (Figure 4, left purple bar) with no survivor within a year (Figure 4, left yellow triangle) (Figure 4).

Survival in lower fitness patients

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<th>Patient group</th>
<th>Median survival (months)</th>
<th>One-year survival</th>
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<tr>
<td>D - devolved care</td>
<td>3</td>
<td>2%</td>
</tr>
<tr>
<td>C - centralised care</td>
<td>4</td>
<td>14%</td>
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Figure 4: Median and one-year survival of lower fitness patients.
Data is expressed as median (column bars; left y axis) and absolute one-year (triangles; right y axis) survival.
Conclusions

The current study shows that management of patients by oncologists specialised in pancreatic cancer has better disease outcomes. From the current data, it is unclear whether the survival benefit of patients seen in centralised care clinics has been impacted by the use of Folfirinox as a first-line chemotherapy as this drug was not available in 2009-2010 when outcomes for patients seen in devolved care clinics were studied. However, the results presented in this report demonstrate that other factors might also play a role in better outcomes of centralised care clinics. Firstly, around 25% more patients received chemotherapy in centralised care (67% as opposed to 43% in devolved care). Second, patients in centralised care started treatment 10 days earlier than patients who attended the devolved care clinics. This might well have contributed to the 1 month longer survival observed in patients with metastatic PDAC. Moreover, the survival benefit of patients with lower fitness status in centralised care clinics might be attributed to better and earlier supportive care of these patients. Notably, in the lower fitness status patients, the one-year survival was 13% when received centralised care, whereas there was no survivor in the group of patients with low fitness status who attended the devolved care clinics after one year from diagnosis. Differences in care outcomes between centralised and devolved care clinics are summarised in the schematic below.
Key care outcomes in devolved (D) and centralised (C) care clinics

**Devolved (D) care**

- D group
  - n=121 patients
  - 43% of patients received first-line chemo
  - 1.9% of patients received second-line chemo
  - Initiation of treatment 28 days post-diagnosis
  - Survival:
    - i) All advanced PDAC: 3 months
    - ii) Metastatic PDAC: 3 months
    - iii) Low fitness: 3 months median survival and 0% one-year survival
  - x5 oncologists
  - x5 non-HPB clinics

**Centralised (C) care**

- C group
  - n=115 patients
  - 67% of patients received first-line chemo
  - 23.4% of patients received second-line chemo
  - Initiation of treatment 18 days post-diagnosis
  - Survival:
    - i) All advanced PDAC: 5 months
    - ii) Metastatic PDAC: 4 months
    - iii) Low fitness: 4 months median survival and 13% one-year survival
  - x2 oncologists
  - x2 HPB-dedicated clinics
Recommendations and future directions

Dedicated oncology clinics for unresectable pancreatic cancer should be considered for faster treatment initiation and access to better supportive care. Development of tools to evaluate performance status and treatment efficacy and tolerance should be implemented to rehabilitate patients for chemotherapy. Conditioning of patients to tolerate the most efficient treatment regimens is important so that patients can receive sequential chemotherapy to prolong survival with minimum impact on their daily life. Introduction of dedicated oncology clinics for advanced pancreatic cancer could improve quality of life and early supportive care for better symptom management such as weight loss, nutrition deprivation and pain. Expanding the capacity and infrastructure to manage patients with advanced pancreatic cancer in dedicated clinics might open new avenues in non-surgical life-extending cancer care and treatments that could overall improve patient and disease outcomes. Future evaluative studies to measure impact on quality of life in patients from these two models of care will establish better benefits that centralised care may have.

References


This report will be reviewed in January 2019.