Pancreatic Cancer UK

Virtual National Study Sessions

October 2020

Treatment | Dietetic Management | Emotional Support

#PCUKStudyDay

ESPAC-5F and Neoadjuvant Chemotherapy

Thursday 8th October 2020, 09.00 – 10.00

Neoadjuvant Chemotherapy in Pancreatic Cancer: Glasgow experience

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Glasgow Precision Oncology Laboratory
University of Glasgow
Glasgow Royal Infirmary

Pancreatic Cancer UK
Virtual National Study Session
8th October 2020

DISCLOSURE INFORMATION

Cancer Research UK Clinician Scientist

Outline

Glasgow experience neoadjuvant chemotherapy

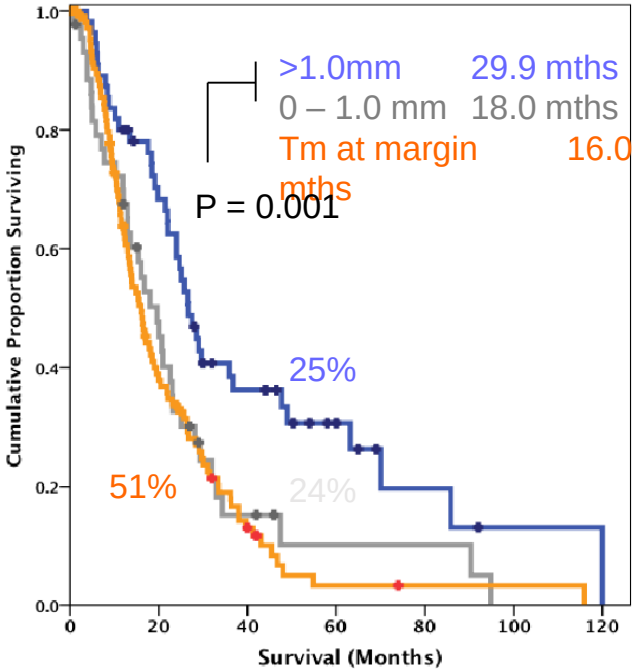
- Rationale
- Experience
- Challenges
- Current Trials and the future

Pancreatic Cancer a true adversary

Despite optimised surgical technique traditional management has resulted in:

- **High complications rate** often limiting adjuvant chemotherapy allocation
- Disappointing **resection margin positivity rate (80%)**

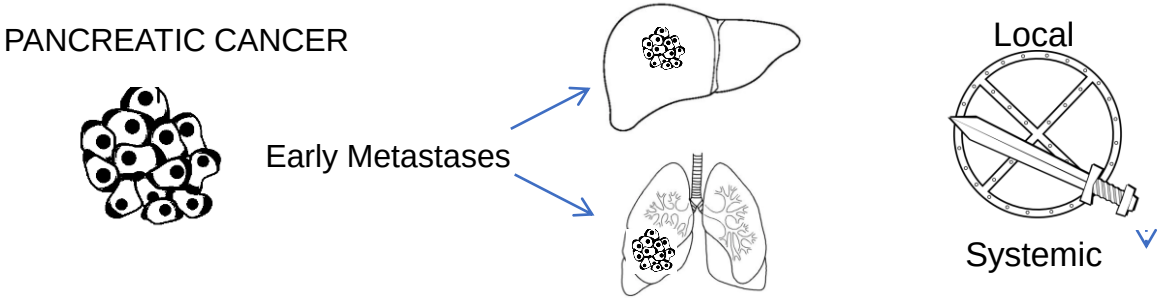
Survival despite resection and adjuvant therapy for localised PDAC remains at **best** 20% at 5 years.



R0 resection - median survival of **30 months**

Jamieson et al. 2009. Annals of Surgery

Pancreatic Cancer is a Systemic Disease



Multimodality therapy is **VITAL** to management of pancreatic cancer

50% of patients did **NOT** receive Adjuvant Chemotherapy

Rationale for Pancreatic cancer Neoadjuvant Therapy

University of Glasgow

For

- Multimodality Therapy better Tolerated without physiological and Immunological derangement of Surgery
- More easily administered preoperatively
- Patients with aggressive biology progress therefore avoid operation
- Risk of early recurrence < 6months avoided
- No significant increase in Morbidity and mortality

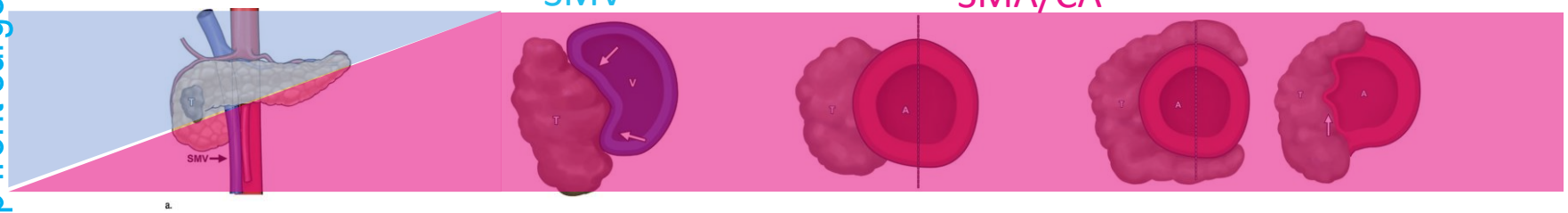
Against

- Potentially operable disease may have local progression or stent related complication
- Preoperative CT assessment not useful
- Concern that vascular resections/reconstructions common
- More challenging operative environment
- Intraoperative fluid shifts, Chyle leaks

Glasgow Experience

2012 onwards consideration given to a neoadjuvant treatment pathway

Resectable	Borderline Resectable	Locally Advanced
	Venous	
	Arterial	

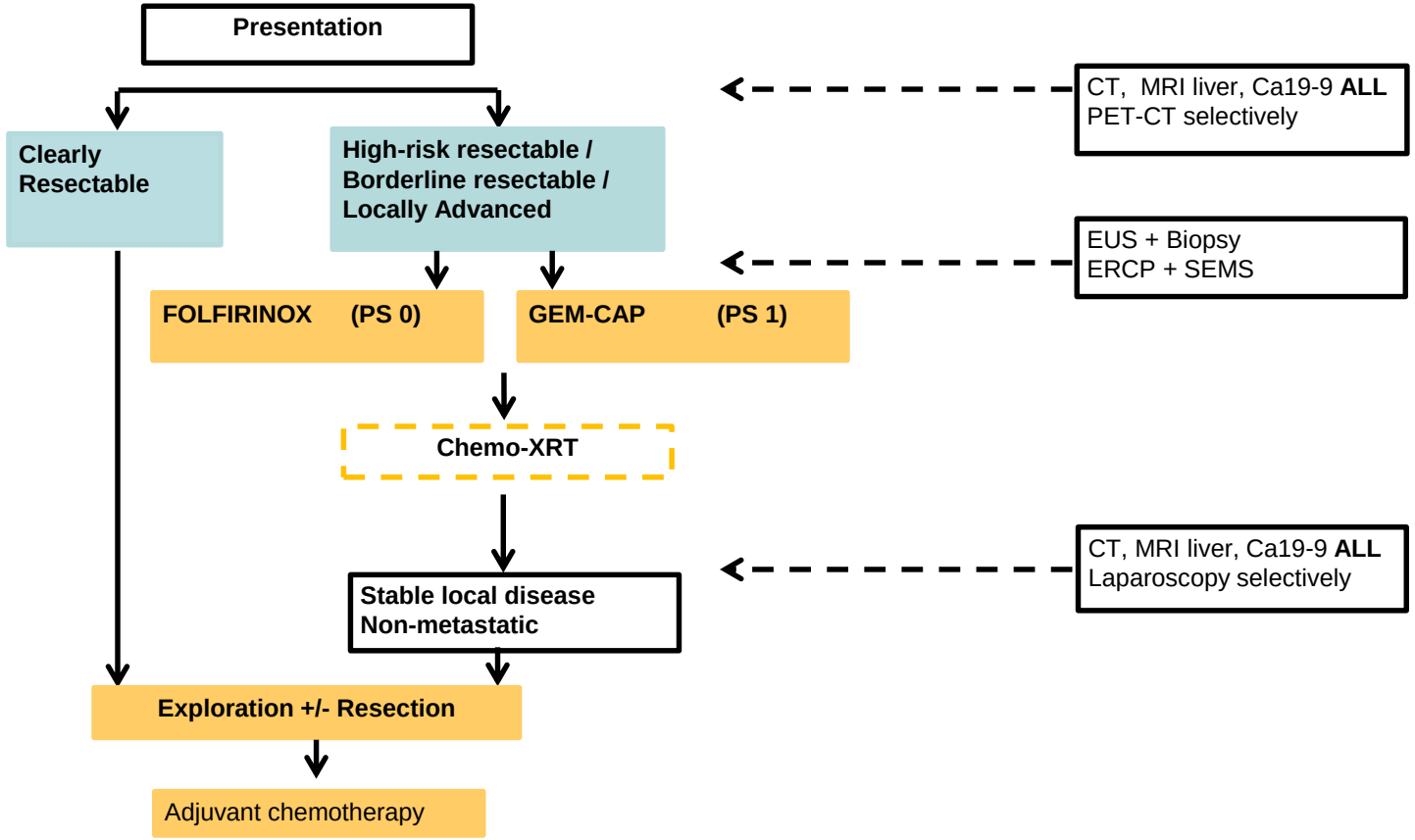


Up front surgery

Unreconstructable Vein

Neoadjuvant therapy

NCCN guidelines *J Natl Compr Canc Netw*
Tempero MA *et al 2017*


Presentation
Clearly Resectable
High-risk resectable / Borderline resectable / Locally Advanced
CT, MRI liver, Ca19-9 ALL
PET-CT selectively
EUS + Biopsy
ERCP + SEMS
FOLFIRINOX (PS 0)
GEM-CAP (PS 1)
Chemo-XRT
CT, MRI liver, Ca19-9 ALL
Laparoscopy selectively
Stable local disease
Non-metastatic
Exploration +/- Resection
Adjuvant chemotherapy

Practicalities of patient selection

Multi-disciplinary Team
Localised pancreatic cancer
Resectable / Borderline / Localised Advanced

ANATOMY — CT scan

BIOLOGY — Ca19-9, MRI liver, Suspicious pulmonary nodules

COMORBIDITY — Optimise, Diabetes, CVD

Glasgow Experience

Almost 275 patients given Neoadjuvant / induction chemotherapy +/- radiotherapy

Over 100 patients resected

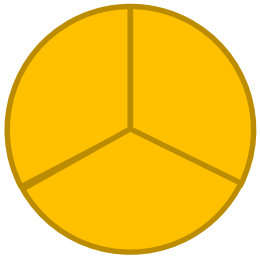
Despite challenging operative field, morbidity profile is not significantly different

Mortality occurred – High BMI, Context of High Dose Radiotherapy

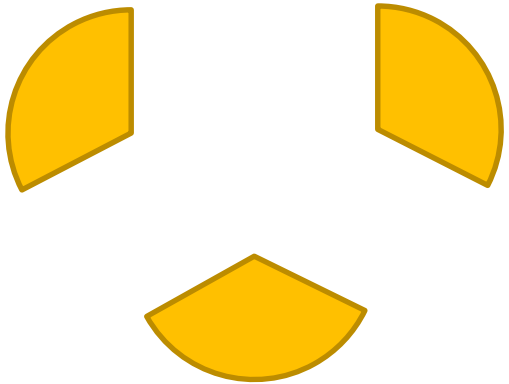
68% adjuvant chemotherapy

Experience

Neoadjuvant Treatment Pathway



Experience



Surgical Exploration

For **Resectable** PDAC – 30% Metastatic progression

Evans DB, et al JCO 2008

ANATOMY

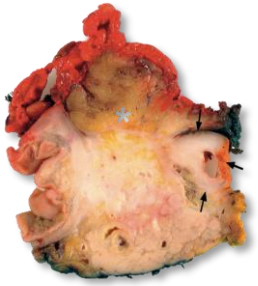
BIOLOGY

COMORBIDITY

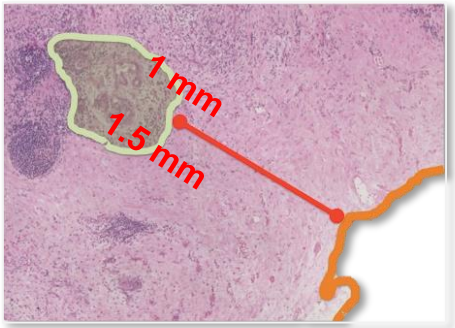
- Patients with stable disease should be offered exploration
- Consider risk benefit carefully
- Trust Neoadjuvant Therapy
- Often operation required is the same one as FIRST CT Scan

Neoadjuvant therapy

Pathology comparison results



N = 310	Surgery First	Neoadjuvant	
Lymph Node Involved	79%	56%	P<0.0001
Perineural Invasion	84%	68%	P<0.0001
Resection margin Involved (1mm)	72%	47%	P<0.0001



Margin Clearance

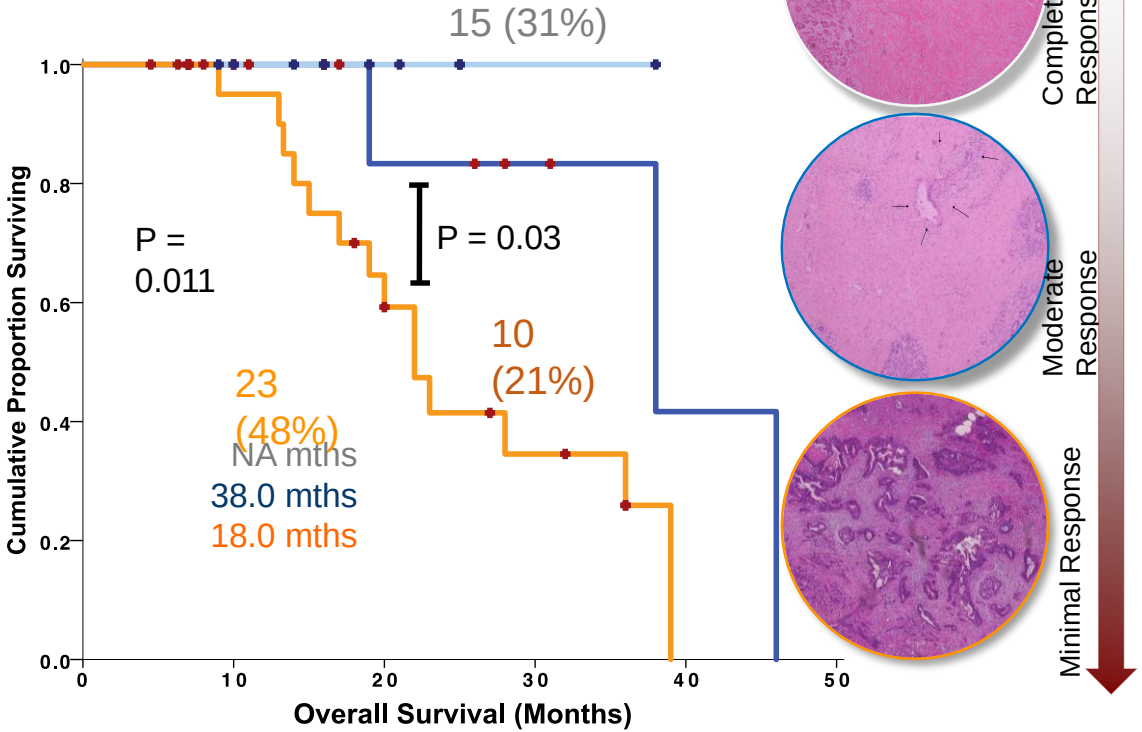
Variable	Primary resection	Neoadjuvant	P value
Lymph node examined	22 (14-55)	22 (13-70)	0.67
Lymph node positive	3 (0-26)	1 (0-9)	<0.001
Resection margin clearance (mm)	0.5 (0-7)	1.2 (0-30)	<0.001

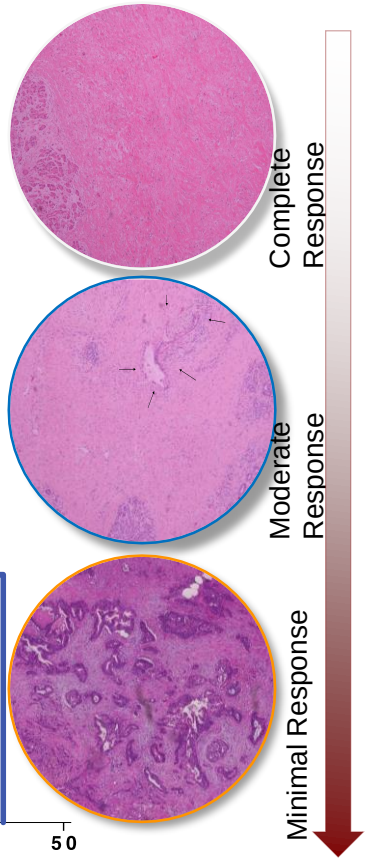
Median (Range)

Tumour Regression: Implications

Patients categorized into 3 subgroups:

- Complete or near complete response
- Moderate response
- Minimal response





CPR/Near CPR (12.5%)

isolated tumor cells

More common with FFX and XRT

Includes true locally advanced

Lessons learned

Prehabilitation

Ensuring nutritional and diabetic optimization during neoadjuvant journey

Avoid deconditioning

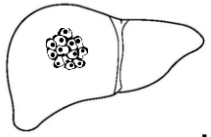
Patient Journey

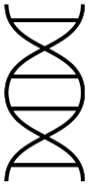
Appropriate patient expectations

Disease progression

Communication between oncology and surgery

Lessons learned





Staging

Anatomy - CT scan and MRI liver (PET scan)

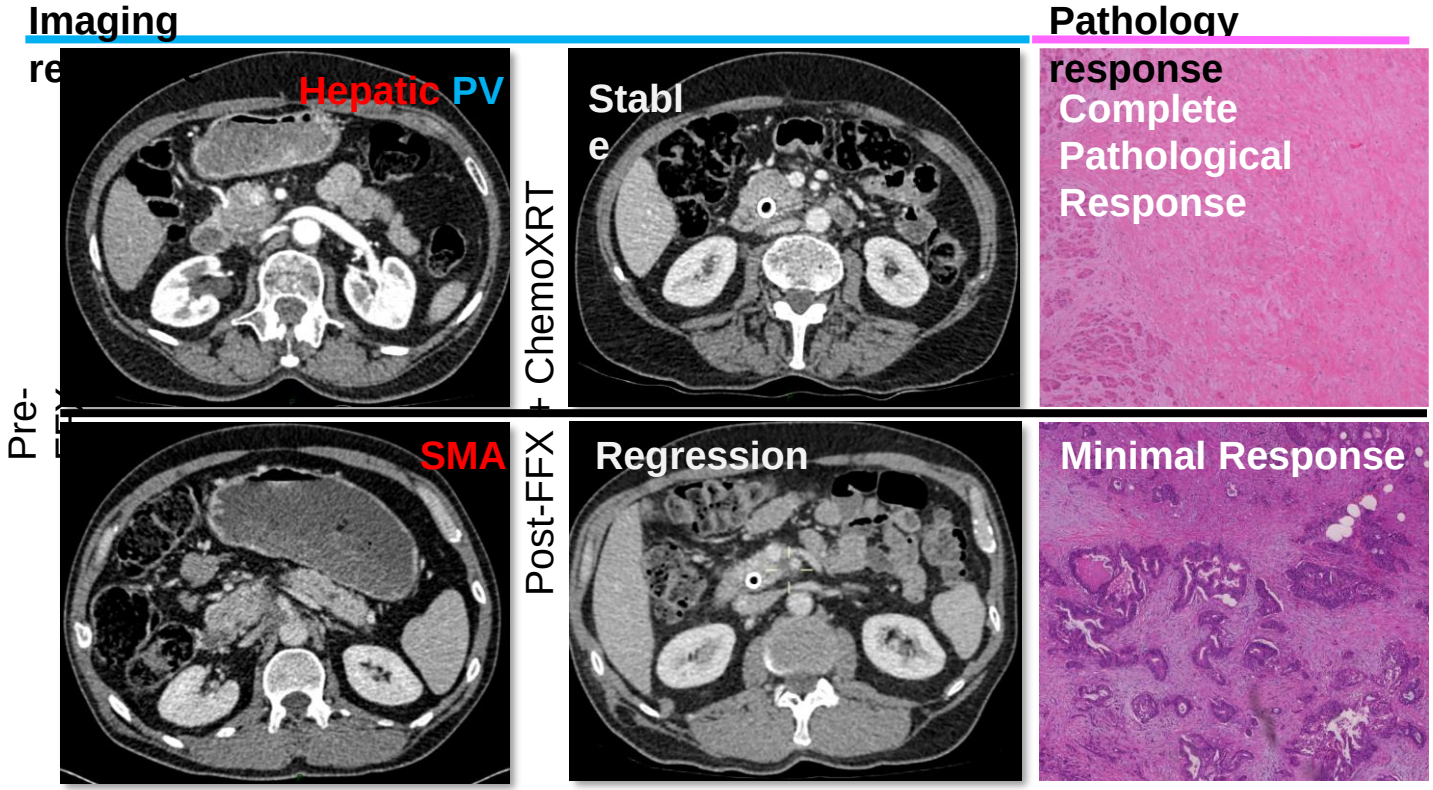
CT scan does not predict response

Initial CT can overcall – pancreatitis

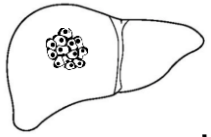
Biology - **Ca19-9 stable or falling**

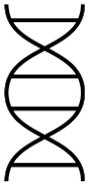
Clinical **– Optimise comorbidity, CPET, Weight loss**

Predicting Pathological Response



Lessons learned





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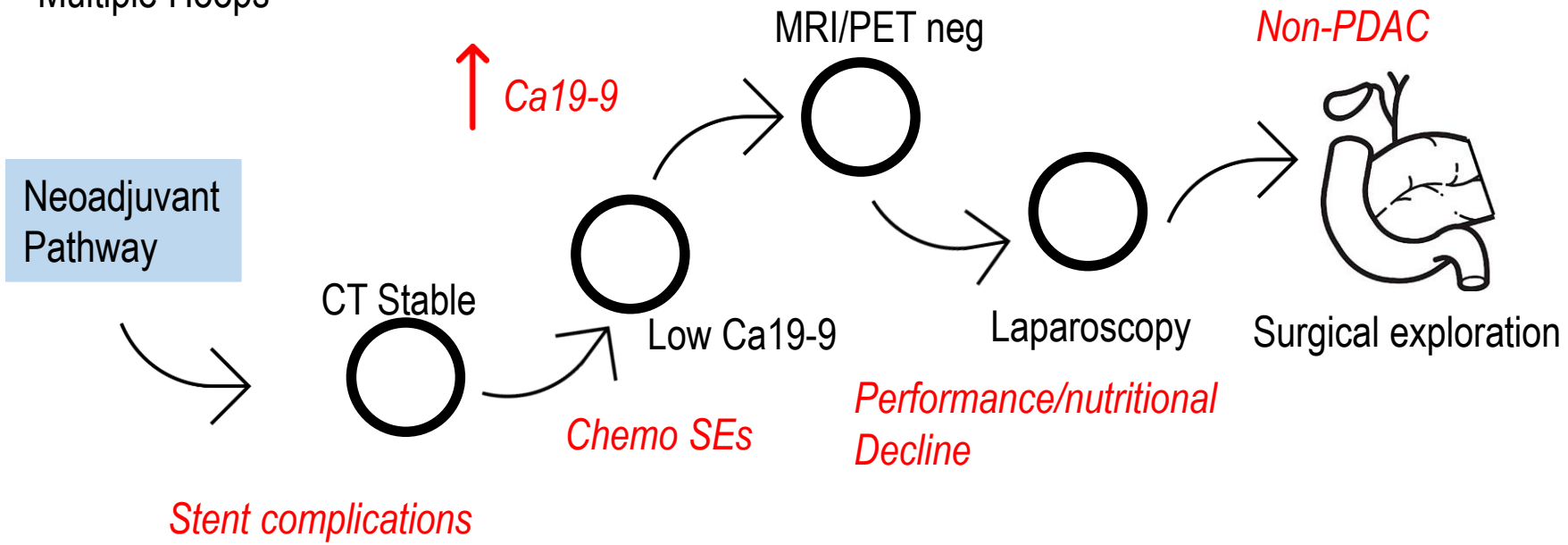
Lessons learned

‘Multiple Hoops’



Multiple MDT visits – risks **MDT inertia**

Clinical Trials

PRECISION PANC

Personalising treatment for pancreatic cancer

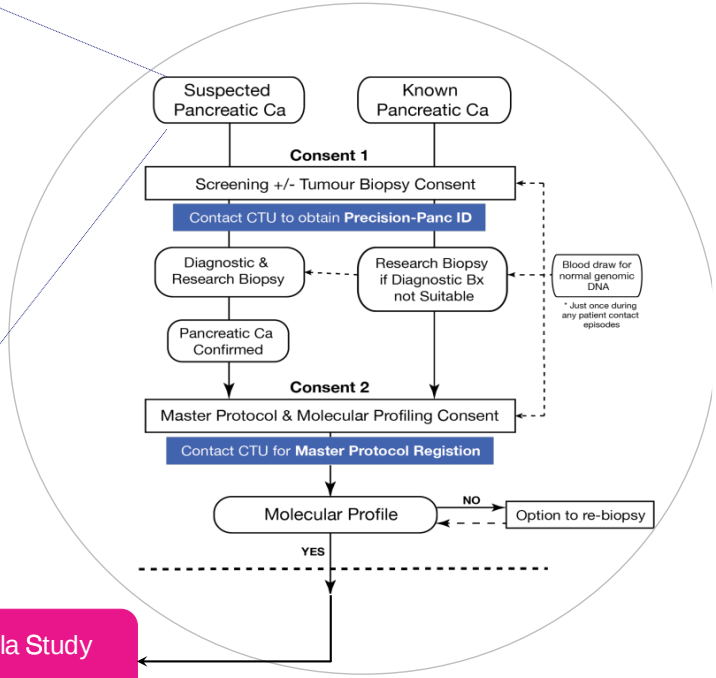
CANCER RESEARCH UK

Patient Recruitment

All patients with pancreatic cancer hoping to access a PRIMUS trial need to 1st be screened and registered into the Precision-Panc Master Protocol to allow either:

- Extra tissue to be taken from their diagnostic study
- Material to be released from their diagnostic biopsy
- Undergo additional research biopsy

Precision-Panc Master Protocol



Pancreatic canceR Individualised Multi-arm Umbrella Study (PRIMUS) Porfolio

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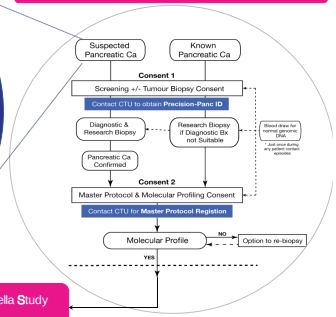
Precision-Panc Master Protocol



Pancreatic cance**R** Individualised **M**ulti-arm **U**mbrella **S**tudy (**PRIMUS**) Porfolio

1st line

PRIMUS 001 — Open / Recruiting

Metastatic

Adaptive phase II study:
FOLFOX-A (FOLFOX + nab-paclitaxel) versus Gem-Abraxane (nab-paclitaxel + gemcitabine)
In patients with metastatic pancreatic cancer, with integrated biomarker evaluation

1st line

PRIMUS 002 — Open / Recruiting

Resectable / Borderline

An umbrella phase II study:
Examining two **neo-adjuvant** regimens (FOLFOX-A and AG) in resectable / borderline resectable pancreatic cancer, focusing on biomarker and liquid biopsy development

2nd line

PRIMUS 003 — Completed

Metastatic

A phase Ib and II open-label, multi-centre study of $CXCR2_{inh}$ + Check point inhibitor evaluated in patients with metastatic pancreatic cancer

2nd line

PRIMUS 004 — Awaiting Final Approval

Metastatic

An Umbrella phase II study:
Testing combinations that target DNA Damage Repair deficiency and replication stress in molecularly selected patients with metastatic pancreatic cancer

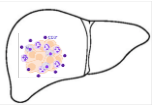
10 centres recruiting

75 patients enrolled

Aiming to improve pancreatic cancer survival by

'Finding the right trial for the right patient'

Pancreatic canceR Individualised Multi-arm Umbrella Study (PRIMUS) Porfolio



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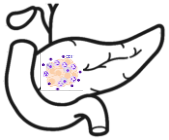

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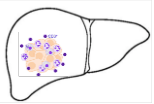

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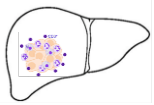

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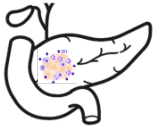

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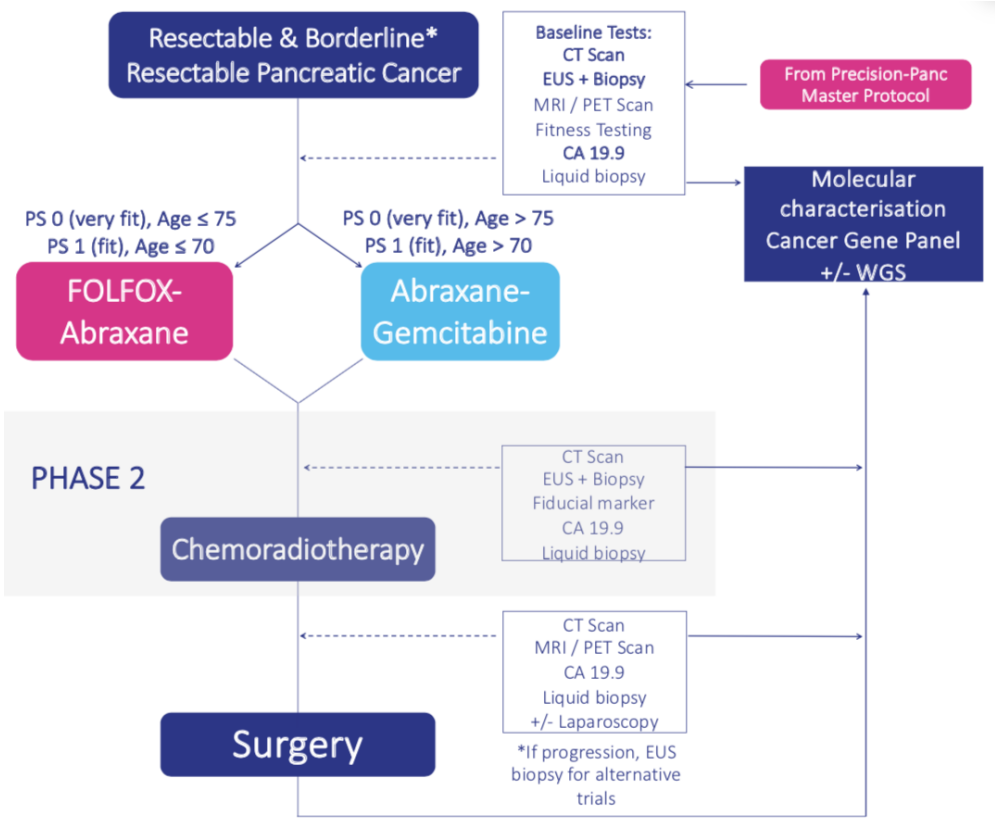
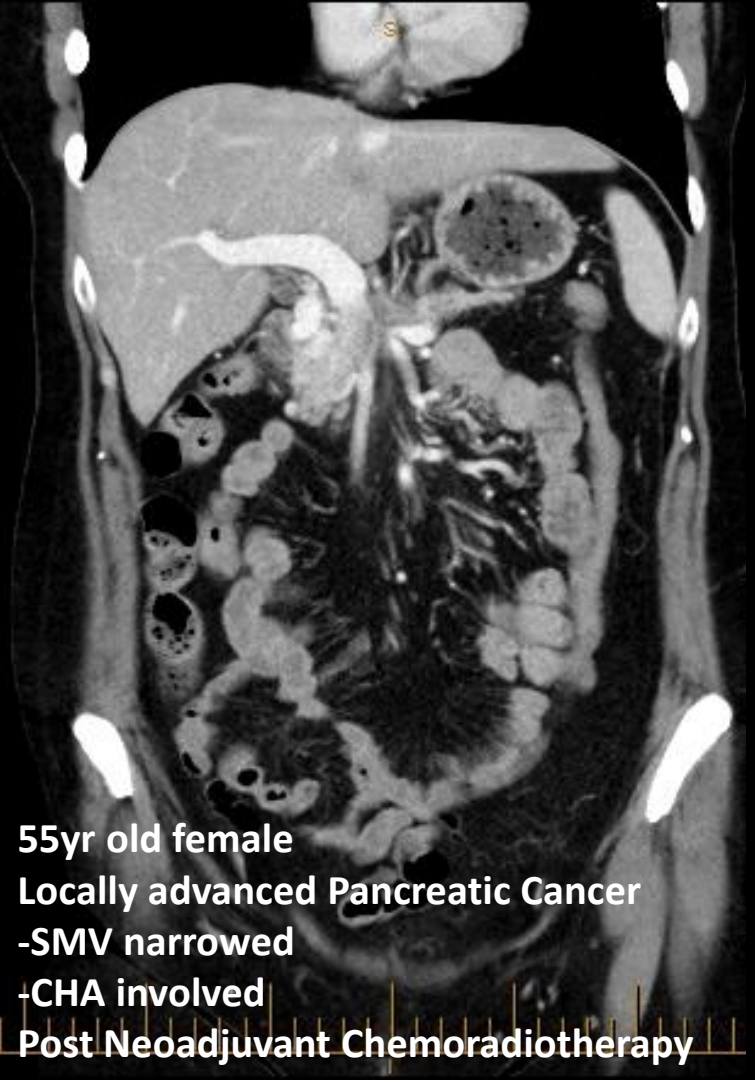


2 centres

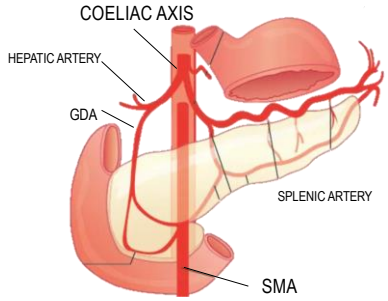
18 registered
7 resected

Pushing The Boundaries…



55yr old female
Locally advanced Pancreatic Cancer
-SMV narrowed
-CHA involved
Post Neoadjuvant Chemoradiotherapy

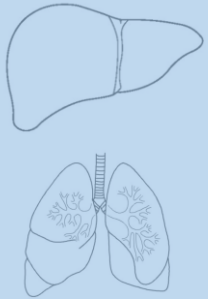
Total pancreatectomy
- Low Ca19-9
- Excellent PS



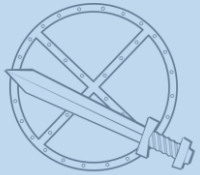
Neoadjuvant Chemotherapy for Pancreatic Cancer

PANCREATIC CANCER

Early Metastases

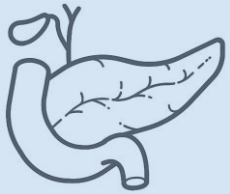


Local



Systemic

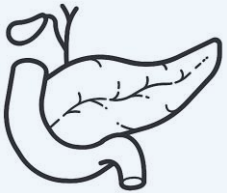
Surgery First



Adjuvant

Multimodality Therapy	Median Survival
50%	30mths

NEOAdj

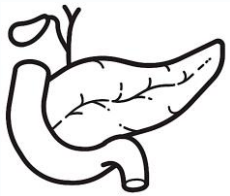


Surgery Last

Multimodality Therapy	Median Survival	Near/Complete Response
100%	38mths	12%

Targeted preoperative

NEOAdj



Surgery Last

? Increased Complete Pathological Response

SUMMARY

Neoadjuvant strategy can be applied safely

Staging and preoperative assessment are logistically challenging

True multi-displinary approach required.

Pathological features are improved, with tumour regression the most important prognostic feature

Future benefits may be derived from

Tailored neoadjuvant strategies

Integration of tumour biology

Operate Less but on the Right Patients

University of Glasgow

CANCER RESEARCH UK

PRECISION PANC

Glasgow Royal Infirmary

Euan Dickson
Ross Carter
Colin J Mckay
Maria Coats
David Chang
Abdullah Al-Adhami

GPOL

Andrew Biankin
David Chang
Susie Cook
Philip Beer
Stephan Dreyer
Selma Rebus
Holly Leslie
Assya Legrirni

Beatson Oncology Centre

Janet Graham
Derek Grose
David McIntosh
Amy Martin

Royal North Shore Sydney

Jas Samra
Anubhav Mittal
Anthony Gill

Patients and family

25 Centres currently recruiting

@precisionpanc

www.precisionpanc.org

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University of Glasgow

CANCER RESEARCH UK

PRECISION PANC

Thank you

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