

Non Surgical Treatments of Pancreatic Cancer

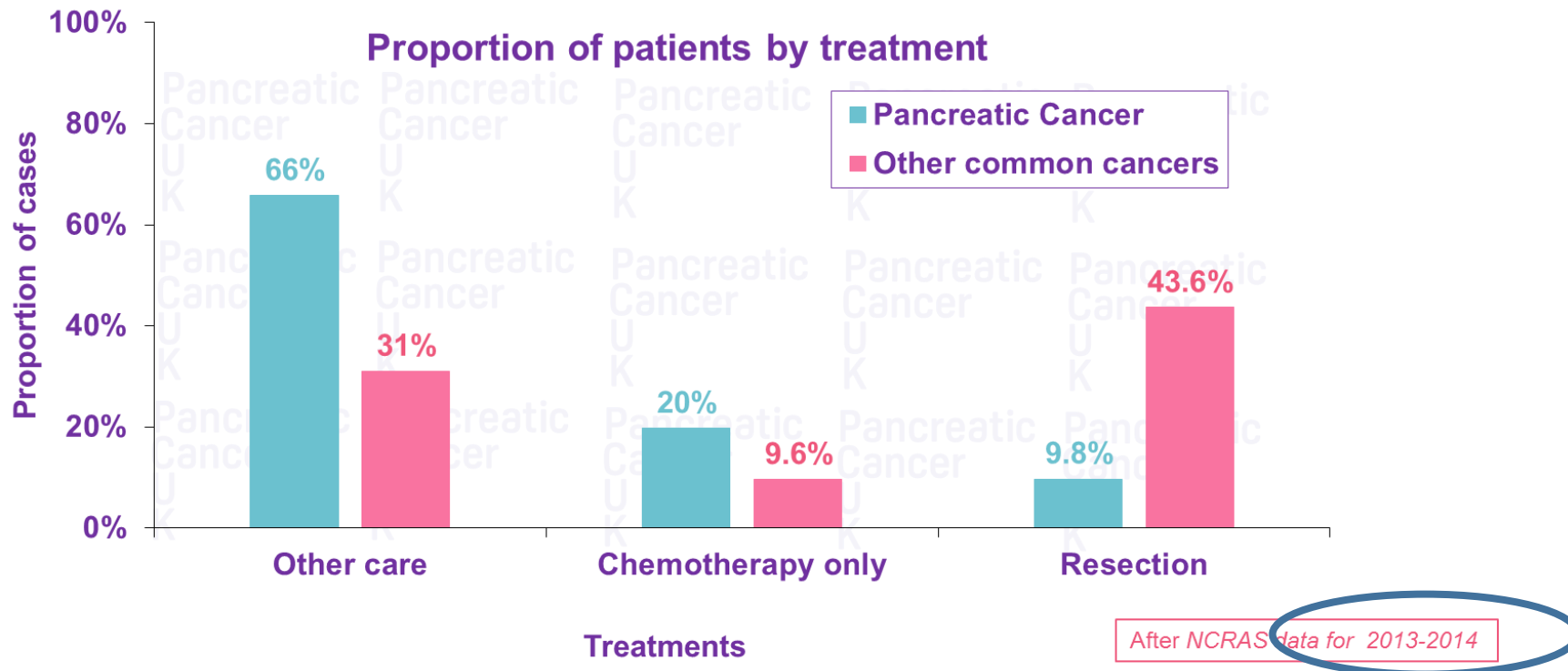
Learning objectives

- **Learn more about the challenges of treatment in pancreatic cancer – who, when and why we offer treatment.**
- **Explore the different anti-cancer treatments for pancreatic cancer**
 - **Chemotherapy**
 - **Radiotherapy/IRE**
 - **Clinical Trials & genomic profiling**
- **How might Pancreatic Cancer UK support you in supporting your patients**

Pancreatic cancer is undertreated

- ✓ 28.3% of people with pancreatic cancer have any form of chemotherapy
- ✓ Across cancer alliances the proportion of people receiving chemotherapy ranges from 25% - 35%

(Jewell 17th September 2020 Variation in Access to Chemo – virtual presentation)



Early diagnosis is essential to increase survival

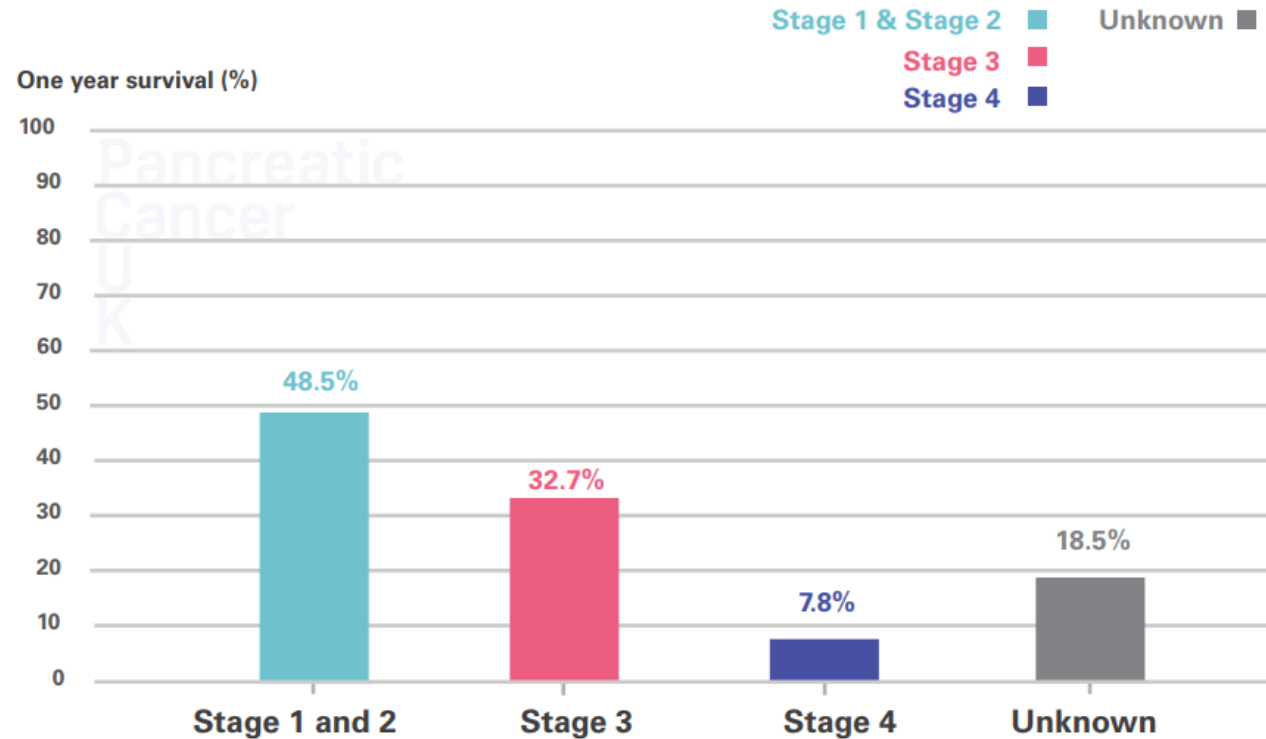


Figure 1: One year survival for people with exocrine pancreatic cancer diagnosed at each stage

When & Who to Treat?

First ever guidelines on pancreatic cancer

Set best care standards to reduce variations and transform care for people with the disease

This guideline includes recommendations on:

- diagnosis
- monitoring for people with an inherited high risk of pancreatic cancer
- staging
- psychological support
- pain and nutrition management
- **management for resectable, borderline resectable and unresectable cancer**

Full guideline at <https://www.nice.org.uk/guidance/ng85>

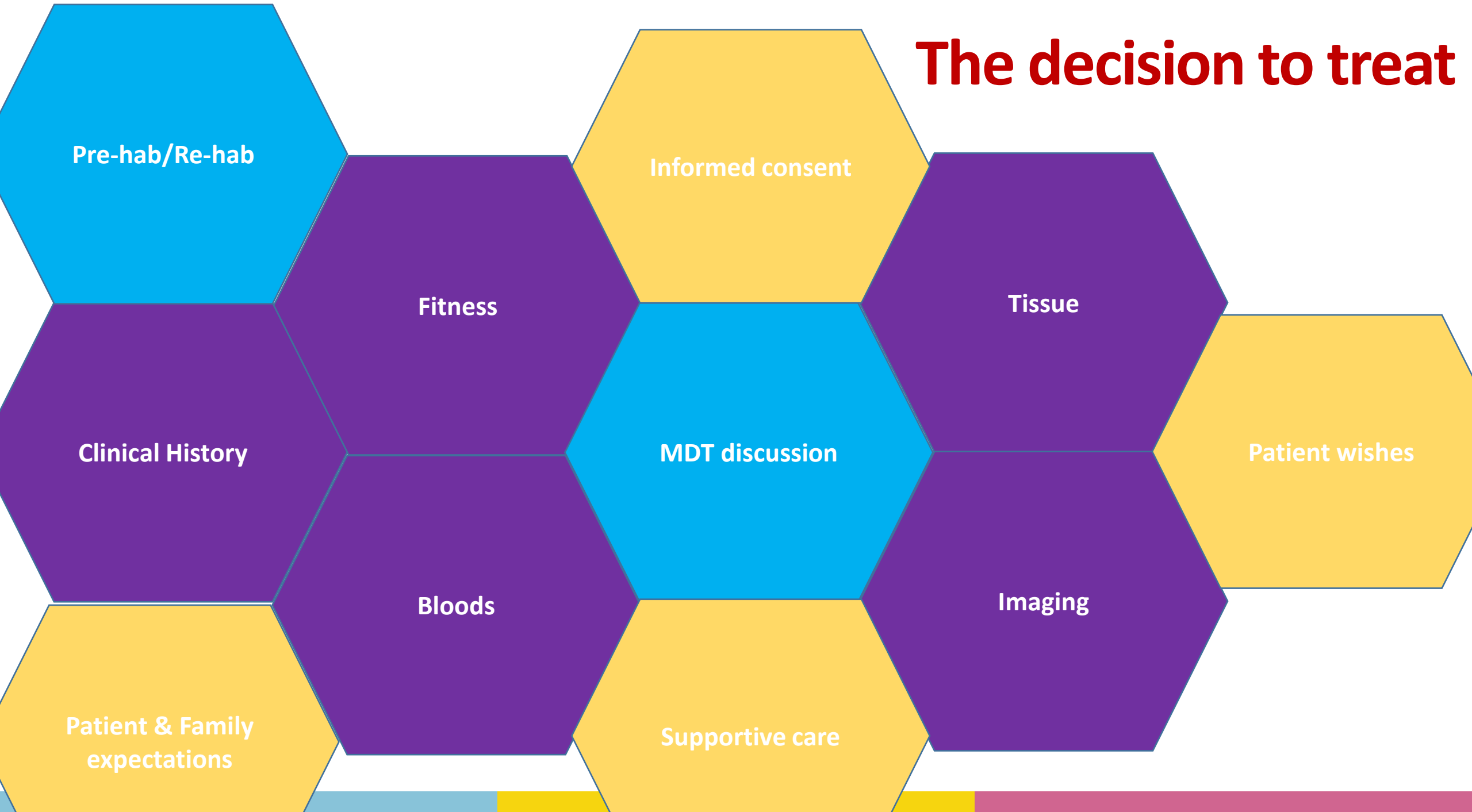
Pancreatic cancer in adults: diagnosis and management

NICE guideline

Published: 7 February 2018

[nice.org.uk/guidance/ng85](https://www.nice.org.uk/guidance/ng85)

The decision to treat



To assist us in deciding how fit people are we use a numerical scoring system called a **performance status or PS**

PS0 = Fully active, able to carry on all pre-disease performance without restriction.

PS1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.

PS2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.

PS3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.

PS4 = completely disabled, cannot carry on any self-care. Totally confined to bed or chair.

(PS0 -1 might be considered for Folfirinox; PS2 or below they may be considered for one of the other chemotherapy regimens that are possibly tolerated better. Treatment does become more difficult to give for those individuals who are PS3 and would not be considered for those PS4.)



- What type of treatment will I have?
- Why am I having this type of treatment?
- What are the aims of the treatment?
- What hospital will I have my treatments in? Will I need to travel?
- How long will my course of treatment take?
- How often will I need to have treatment?
- How often do I need bloods and scans?
- What are the likely side effects of the treatment?
- Are there other types of treatment I could have?
- Are there clinical trials that I could have?
- How will the treatment affect my life?
- Will I have follow-up appointments? If so, how often and who will they be with?
- Who should I contact if I need more information or have questions about my treatment?**



Chemotherapy

Chemotherapy for pancreatic cancer

This fact sheet is for anyone who wants to know more about treating pancreatic cancer with chemotherapy. It explains how chemotherapy is given, and the different drugs that may be used. It also explains the main side effects of chemotherapy and how these can be managed.

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What are the advantages and disadvantages?	6
How is chemotherapy given?	7
Check-ups before and during treatment	8
How does chemotherapy affect the blood?	9
Other side effects of chemotherapy	11
Diet and chemotherapy	15
What happens after my chemotherapy finishes?	16
Coping with chemotherapy	16
Further information and support	18

This information is for people with the most common type of pancreatic cancer, pancreatic ductal adenocarcinoma. People with pancreatic neuroendocrine tumours (NETs) may have different chemotherapy. The NET Patient Foundation has more information at – www.netpatientfoundation.org

Each hospital may do things slightly differently, and treatment will vary depending on your cancer. Speak to your doctor or nurse about your treatment.



You can also speak to our specialist nurses on our confidential Support Line. Call them free on **0808 801 0707**, or email nurse@pancreaticcancer.org.uk

Chemotherapy can be used:

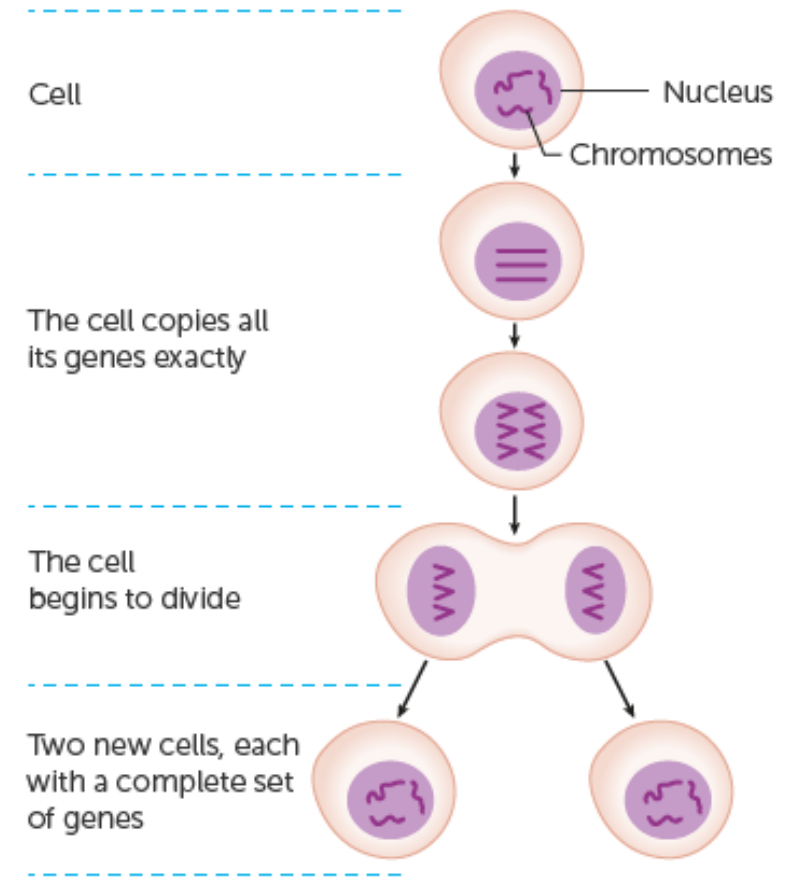
- Neo-ADJUVANT (before surgery to try to shrink the cancer so that there's a better chance of removing it) ?borderline resectable
- ADJUVANT (after surgery to try to reduce the chances of the cancer coming back)
- LOCALLY ADVANCED (to slow down the growth of cancer that has spread to nearby structures, such as the blood vessels around the pancreas, still classes as palliative)
- PALLIATIVE (when the cancer has spread beyond the pancreas to other parts of the body)



- Chemotherapy is one word to describe lots of drugs, often used in many different combinations to treat cancer.
- It is '**systemic treatment**'
- It is **cyto-toxic**, meaning cell killing

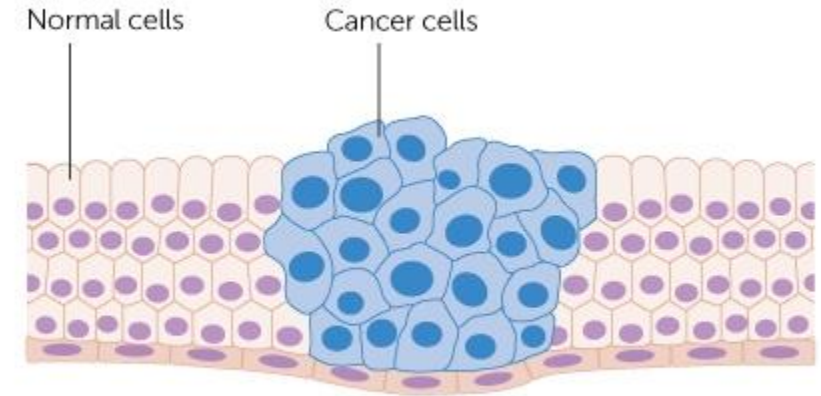
How Chemotherapy Works

- Our bodies are made of billions of individual cells. Once we are fully grown, most of the body's cells don't divide that much, often only divide if they need to repair damage.
- In the centre of each living cell is the nucleus. The nucleus is the control centre of the cell. It contains chromosomes, which are made up of genes.
- As 1 cell divides into 2 each cell will contain the same set of genes, these 2 will split to make 4 and so on and so forth.

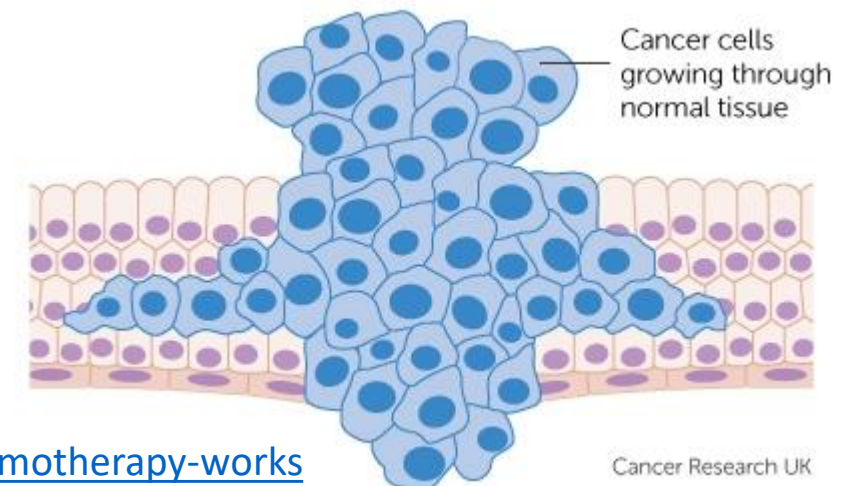


Cancer Research UK

- In cancer the abnormal cell keeps dividing till there is a mass of the abnormal cells and this mass become a tumour
- Chemotherapy damages the genes inside the nucleus of the cells
- Cancer cells divide much more often than normal cells and this is why chemo is much more likely to kill them.
- We often use combinations of chemotherapy drugs as different drugs have different actions; some damage the control centre that makes the cells divide others interrupt the chemical processes of cell division.



Cancer Research UK



Cancer Research UK

Common Chemotherapy Drugs in PDAC

Gemcitabine

Capecitabine

Fluorouracil (5FU)

Irinotecan

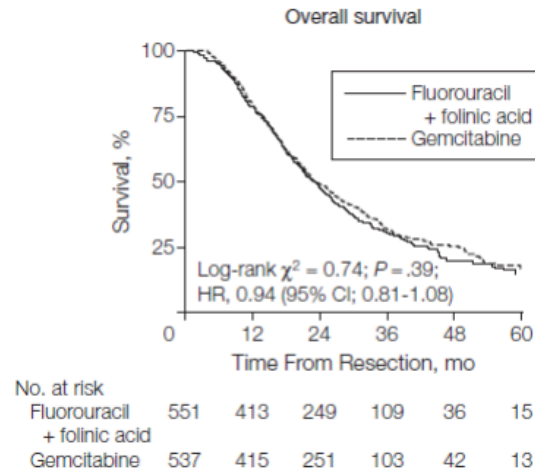
Oxaliplatin

Nab-paclitaxel (Abraxane) **only licenced for 1st line metastatic use**

**Maybe used in combination FOLFIRNOX, GEM/CAP, GEM/CISP,
Gem/Abraxane,**

Combination treatments

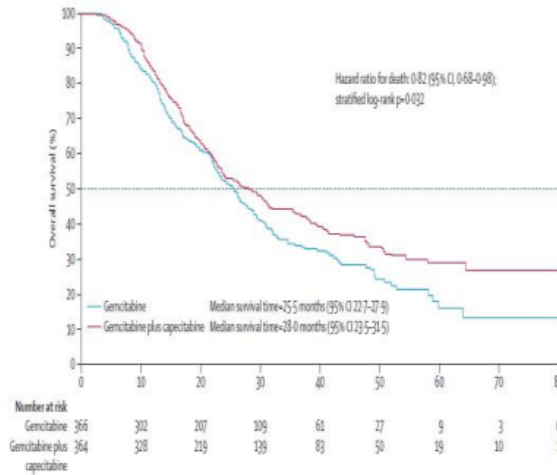
Adjuvant Treatment



ESPAC-3

Gemcitabine or 5FU:
same results but
gemcitabine less toxic

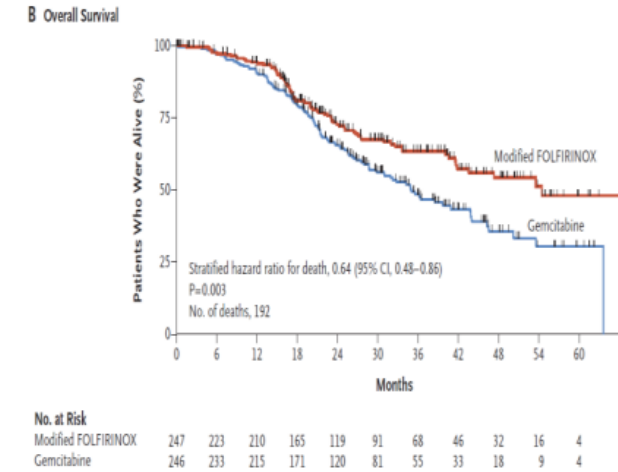
Neoptolemos et al JAMA 2010



ESPAC-4

Gemcitabine and 5FU:
improved 5-year survival,
more side-effects

Neoptolemos et al Lancet Oncol 2017

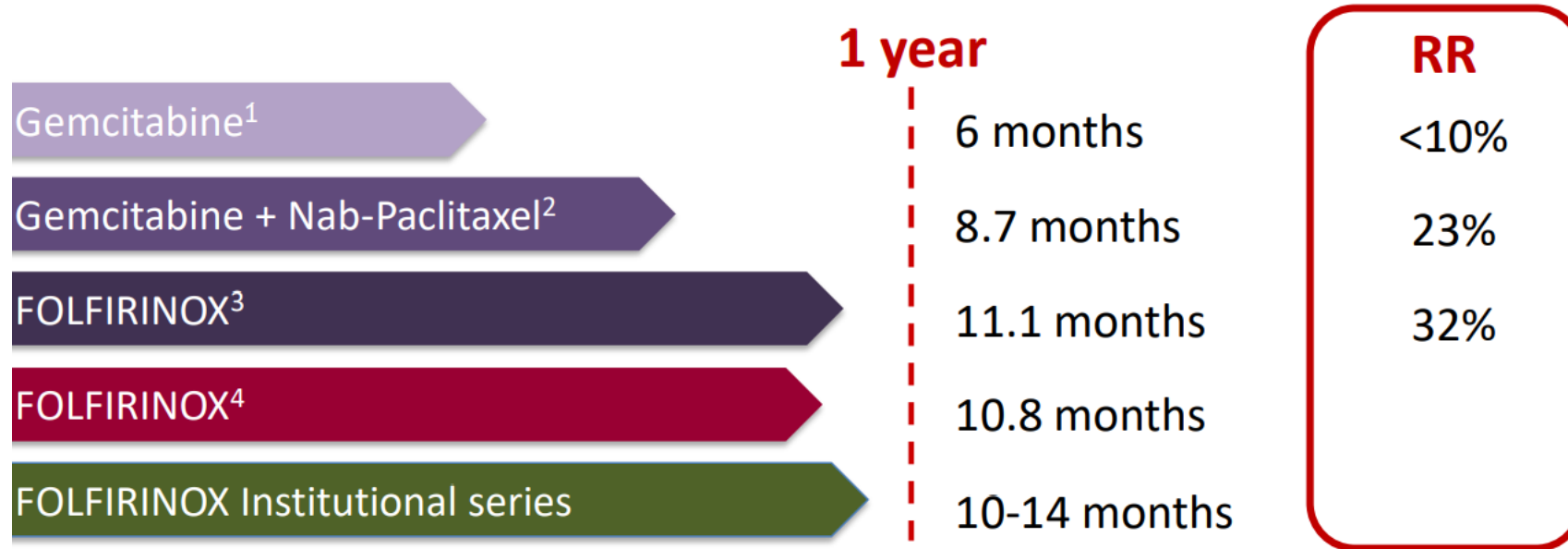


PRODIGE-24

FOLFIRINOX improved
survival compared with
gemcitabine...more toxic

Conroy et al NEJM 2018

Palliative Treatment



Treatment with FOLFIRINOX is applicable in ~25% patients⁵

¹ Burris et al, J Clin Oncol 1997, ²Von Hoff et al N Engl J Med 2013, updated Goldstein D et al GI Cancers Symposium, abstract 178, ³Conroy et al N Engl J Med 2011, ⁴Singhal ESMO abstract 617PD; ⁵ Gill et al. ASCO 2012 abstr. e14588

The results of this trial provide evidence for neoadjuvant short-course chemotherapy in borderline resectable pancreatic ductal adenocarcinoma

Favoured neoadjuvant chemotherapy rather than neoadjuvant chemoradiotherapy.

The survival advantage of neoadjuvant therapy was seen despite no significant difference being noted in resection rate.

Immediate surgery compared with short-course neoadjuvant gemcitabine plus capecitabine, FOLFIRINOX, or chemoradiotherapy in patients with borderline resectable pancreatic cancer (ESPAC5): a four-arm, multicentre, randomised, phase 2 trial

Paula Ghaneh, Daniel Palmer, Silvia Cicconi, Richard Jackson, Christopher Michael Halloran, Charlotte Rawcliffe, Rajaram Sripadam, Somnath Mukherjee, Zahir Soonawalla, Jonathan Wadsley, Ahmed Al-Mukhtar, Euan Dickson, Janet Graham, Long Jiao, Harpreet S Wasan, Iain S Tait, Andreas Prachalias, Paul Ross, Juan W Valle, Derek A O'Reilly, Bilal Al-Sarireh, Sarah Gwynne, Irfan Ahmed, Kate Connolly, Kein-Long Yim, David Cunningham, Thomas Armstrong, Caroline Archer, Keith Roberts, Yuk Ting Ma, Christoph Springfield, Christine Tjaden, Thilo Hackert, Markus W Büchler, John P Neoptolemos, for the European Study Group for Pancreatic Cancer



Side effects

Chemotherapy affects healthy body tissues where the cells are constantly growing and dividing, such as:

- your hair, which is always growing
- your bone marrow, which is constantly producing blood cells
- your skin and the lining of your digestive system, which are constantly renewing themselves

Therefore side effects may include,

- Nausea and vomiting
- Diarrhoea
- Fatigue
- Mucositis
- Alopecia
- Neutropenia
- Anaemia
- Risk of bleeding
- Plantar Palmar Erythema
- Rash
- Cold sensitive parathesia /neuropathy

**Proactive side effect
management is key**

Considerations

- Studies show that there is no benefit from starting adjuvant treatment earlier than 8 weeks post-op
 - Recommendation is to start treatment at 8-12 weeks
 - This can allow people a chance to recover from surgery
 - There is a role for pre-hab and re-hab to actively manage symptoms post operatively to maximise wellbeing and increase likeliness of being able to have **and** tolerate treatment
 - It is more important to finish chemo than start early
 - The role of pre-hab/re-hab **for all those with pancreatic cancer**
-
- Proactive side-effect & symptom control support benefits all
 - Dose reduction/escalation is a useful tool to allow people to complete their treatment regimes



This can lead to people staying well on treatment, maintain QoL and open up 2nd/3rd line treatment opportunity

Radiotherapy and IRE

Radiotherapy for pancreatic cancer

- External beam radiotherapy is used to kill cells
- It is a **localised** therapy
- Given with oral chemotherapy, this creates the potential for tumour selectivity and enhanced therapeutic index.
- Therefore the cancer cells are more sensitive to the radiotherapy, making it more effective.
- Given to those with borderline resectable and locally advanced disease. (About 30-40% of patients have a locally advanced pancreatic cancer, which is not treatable with surgery. The main treatment for LAPC is chemotherapy)



Advantages of radiotherapy

- Each treatment session will take about 30 minutes
- You won't usually need to stay in hospital.
- You may be able to carry on with your daily life, such as going to work, if you feel up to it.
- If you have advanced cancer, radiotherapy can help control symptoms and relieve pain.

Disadvantages of radiotherapy

- Radiotherapy can cause side effects, including tiredness, sickness and runny poo (diarrhoea). But these are often mild.
- If you have chemoradiotherapy, you may also get side effects from the chemotherapy. There are ways to manage side effects.
- If you have borderline resectable or locally advanced cancer, you may have to go to hospital five days a week for several weeks for your treatment

Radiotherapy for pancreatic cancer

This fact sheet is for people with pancreatic cancer who are having radiotherapy to treat their cancer, or to manage pain. Family members may also find it helpful. It explains what radiotherapy is, how it is used depending on your diagnosis, how it is given, and the possible side effects and ways to manage these.

Each hospital may do things slightly differently, so use this fact sheet as a general guide. If you have any questions, speak to your doctor, nurse or another member of your radiotherapy team.

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Stereotactic ablative radiotherapy (**SABR**) or stereotactic body radiotherapy (SBRT) is a type of very precise radiotherapy. You may have heard it called **Cyberknife®**. SABR delivers higher doses of radiation in a shorter time, which reduces the number of treatments.



England

Stereotactic ablative body radiotherapy (SABR) is recommended to be available as a treatment option through routine commissioning for adults with locally advanced, inoperable, non-metastatic pancreatic carcinoma (LANPC) within the criteria set out in this document.

November 2021

<https://www.england.nhs.uk/wp-content/uploads/2021/11/2011-stereotactic-ablative-body-radiotherapy-policy-statement-1.pdf>



Ste

prec

radia

The clinical commissioning policy statement recommends the use of SABR as a treatment option for adults with locally advanced, inoperable, nonmetastatic pancreatic carcinoma where the disease remains localised following >3months of systemic chemotherapy. The use of SABR as an alternative option for chemo/rad means that the patients require fewer daily hospital visits for their radiotherapy and, as concurrent daily oral chemotherapy is not required, are also spared the side effects of the chemo.

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r doses of



England

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treatment option through routine commissioning for adults
with locally advanced, inoperable, non- metastatic pancreatic carcinoma
(LANPC) within the criteria set out in this document.

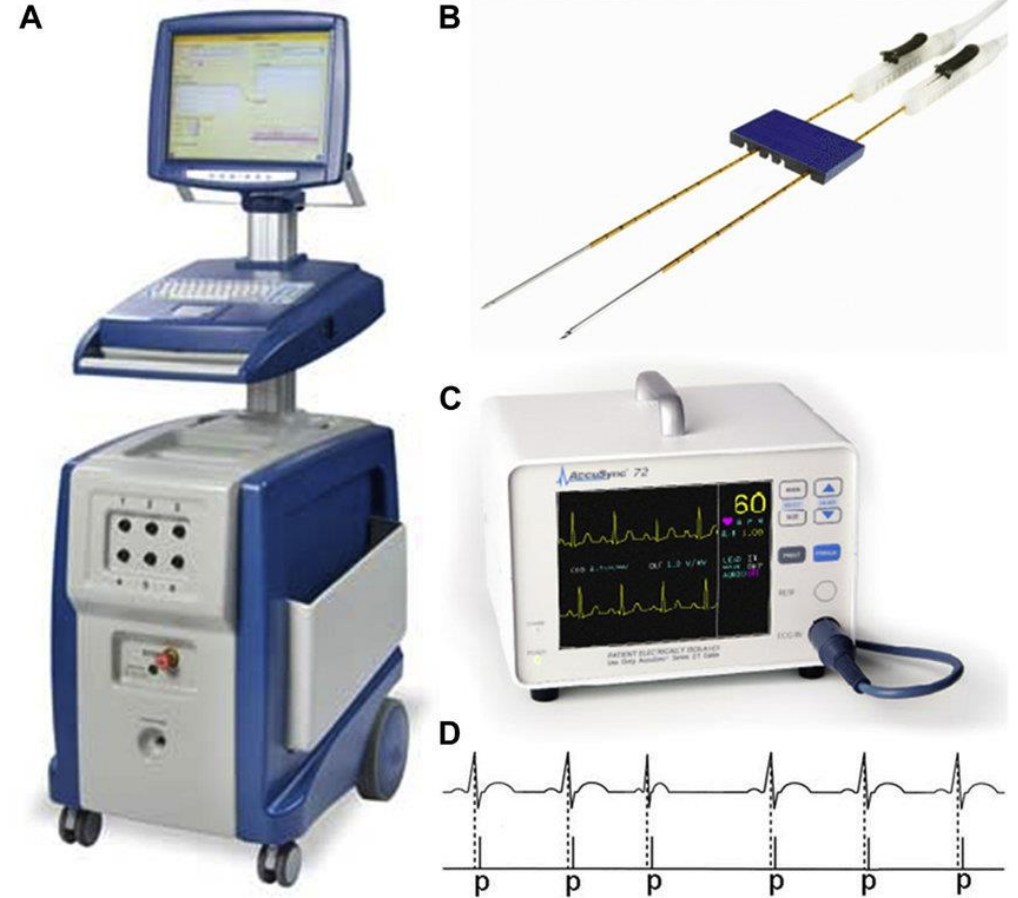
November 2021

<https://www.england.nhs.uk/wp-content/uploads/2021/11/2011-stereotactic-ablative-body-radiotherapy-policy-statement-1.pdf>

Irreversible electroporation (NanoKnife®) for pancreatic cancer

Irreversible electroporation (IRE) is a treatment that uses electrical currents to damage and destroy cancer cells. It known as **NanoKnife**

IRE for pancreatic cancer involves inserting thin needles around the cancer. Electrical currents are passed between the needles. These currents damage and destroy the cancer cells.



Irreversible electroporation (IRE) for pancreatic cancer

This fact sheet is for people who want to know more about irreversible electroporation (IRE) for pancreatic cancer. It explains what the treatment is, who it might be suitable for, what happens during treatment and possible side effects.

IRE is sometimes known as NanoKnife®. This is the brand name for the machine used to deliver the treatment.



You can speak to our specialist nurses on our confidential Support Line about IRE. Call free on **0808 801 0707** or email nurse@pancreaticcancer.org.uk

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The aim of irreversible electroporation (IRE) is to destroy cancerous cells using a series of short electrical pulses using high-voltage direct current. This creates multiple holes in the cell membrane, irreversibly damaging the cells' homeostatic mechanisms and leading to cell death.

In pancreatic cancer, IRE is usually done to increase survival in people with locally advanced disease, or to treat resection margins to increase the success of curative surgical resection.

Current evidence on the safety and efficacy of irreversible electroporation for treating pancreatic cancer is **inadequate in quantity and quality**.

Therefore, this procedure should only be used in the context of research.

Further research, preferably in the form of randomised controlled trials, should assess the effect of the procedure on local tumour control, patient survival, pain control and quality of life.

Irreversible electroporation for treating pancreatic cancer

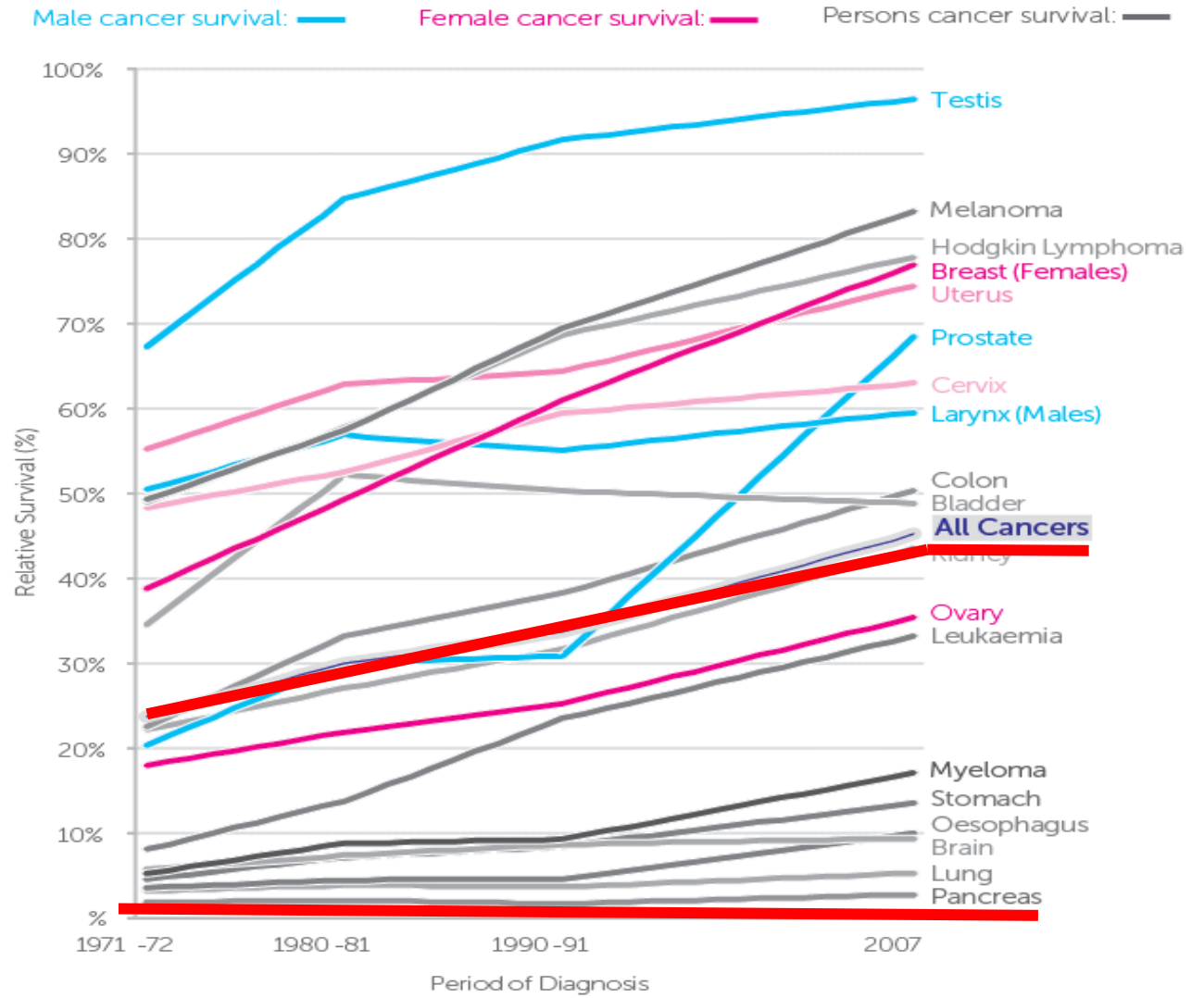
Interventional procedures guidance

Published: 3 May 2017

www.nice.org.uk/guidance/ipg579

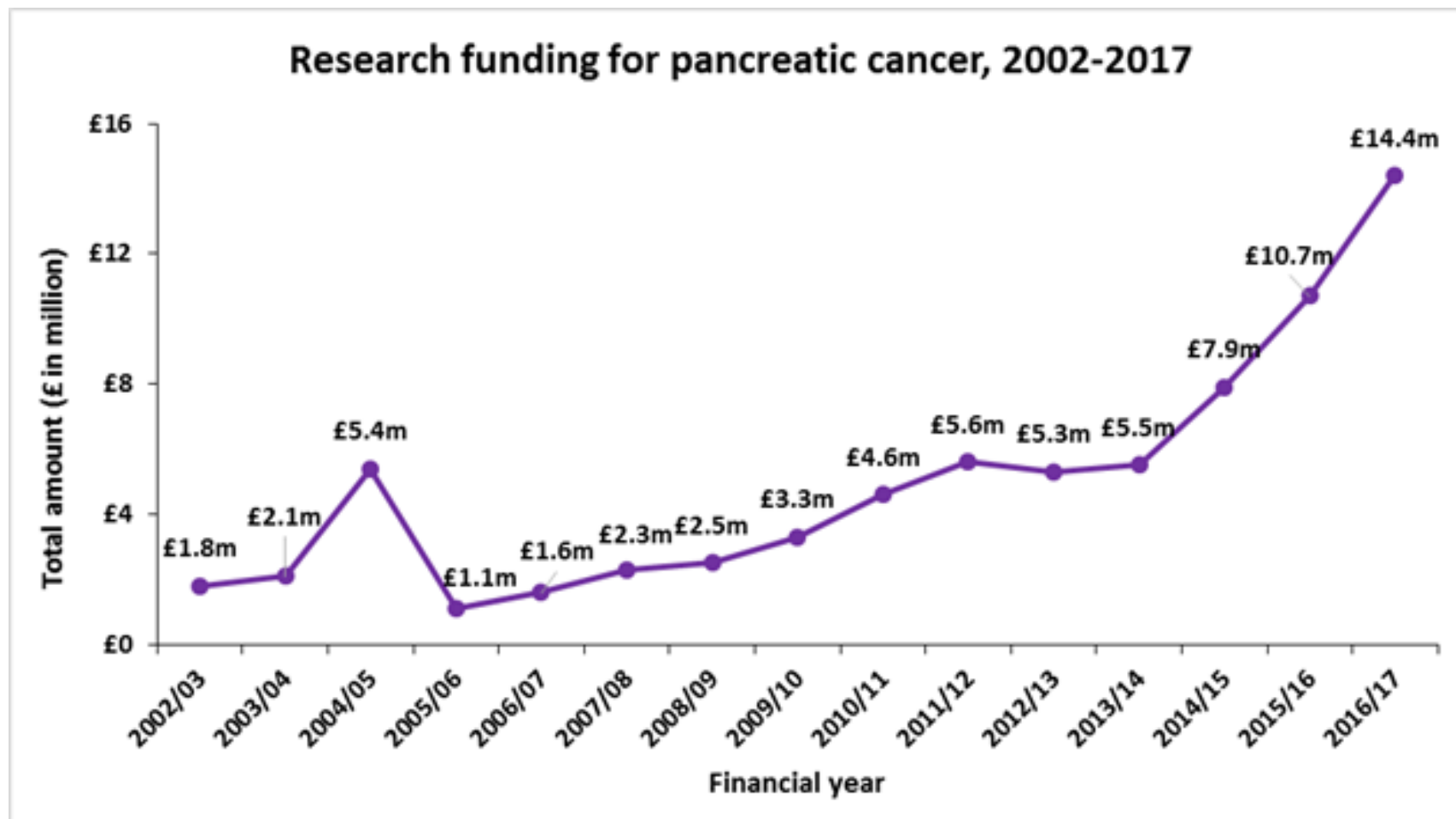
Clinical Trials

5 year survival rate hasn't improved in last 40 years



http://www.cancerresearchuk.org/sites/default/files/cstream-node/cs_surv_common.pdf
(October 2017)

Pancreatic Cancer UK



The screenshot shows the ClinicalTrials.gov website. At the top, there is a navigation bar with the NIH logo and the text "U.S. National Library of Medicine". Below this is the "ClinicalTrials.gov" logo. A blue banner below the logo contains the text: "ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world." Below the banner, there is a search section titled "Find a study (all fields optional)". This section includes a "Status" filter with two radio button options: "Recruiting and not yet recruiting studies" (unselected) and "All studies" (selected). Below the status filter is a "Condition or disease" filter with a text input field and a small "X" button to clear the input. To the left of the search section, there is a text block that says "Explore 451,538 research studies in all 50 states and in 221 countries." followed by a button that says "See listed clinical studies related to the coronavirus disease (COVID-19)". At the bottom left, there is a note: "ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine." and an "IMPORTANT" notice: "Listing a study does not mean it has".

www.clinicaltrials.gov

Checked 10th May 2023 – recruiting trails in adults, includes diagnostic, screening, chemo, radiotherapy, surgery

Pancreatic Cancer 31

Breast Cancer 102

Lung Cancer 141

Colorectal Cancer 62

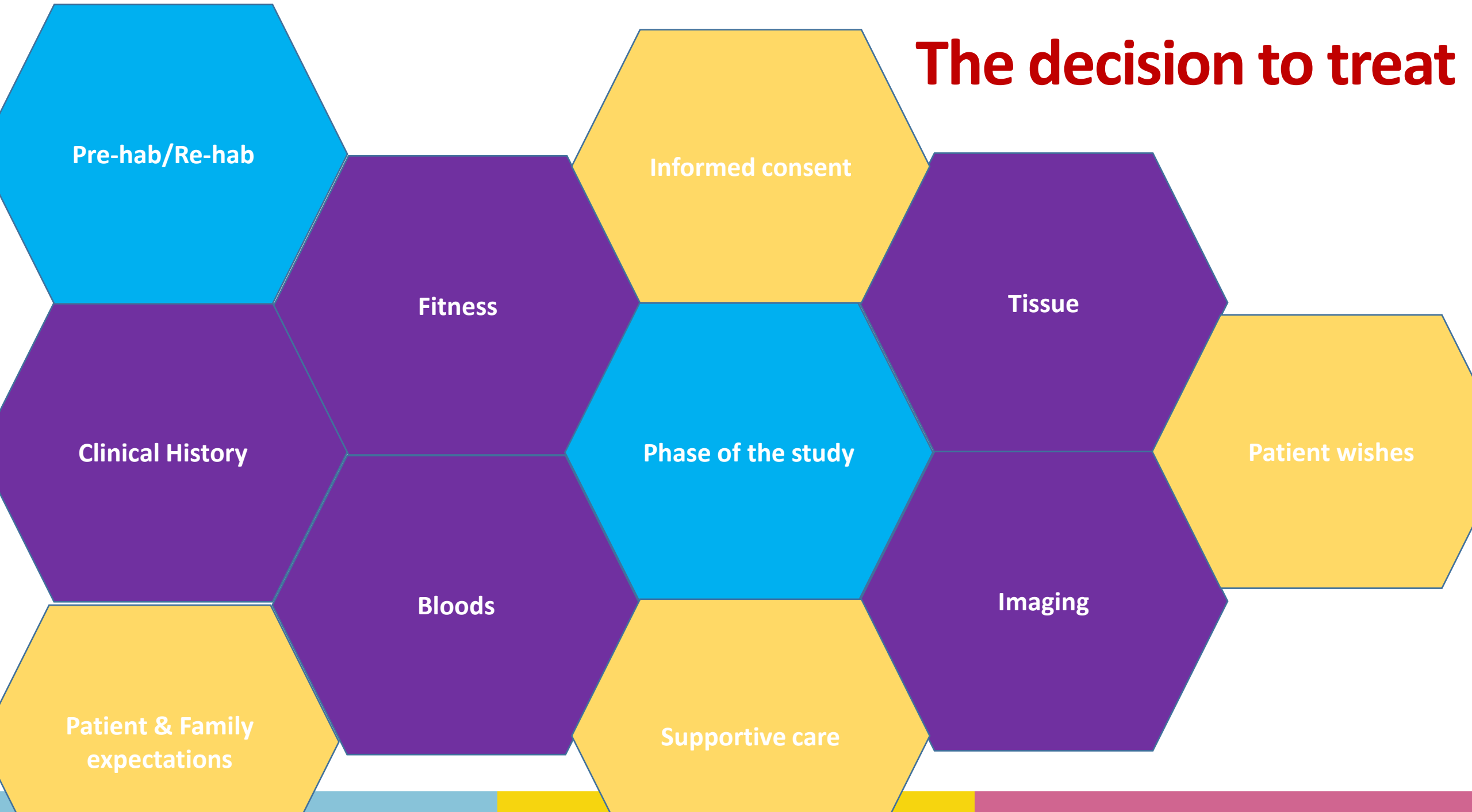
There is excellent evidence that participation in clinical trials is associated with better outcomes for patients.

What clinical trials can offer a person is the opportunity to have novel therapy (so a new drug), a new treatment regime (a new way of using known drug/s), or a combination of the two but what we don't know is if these treatments are helpful for those with pancreatic cancer.

The **advantages** of being part of a clinical trial is this access to new treatments or regimes, there may be fewer side effects compared to standard treatment, you often have more frequent reviews and blood test and your participation can improve future pancreatic cancer treatments.

However there are **disadvantages** too, the new drugs or regimes might not be better than standard therapy, there could be worse side effects and the trial might not be available locally to you so the travel, extra visits and bloods can be burdensome. There is also some uncertainty with clinical trials which some people might find difficult to deal with.

The decision to treat





- What type of trial is relevant for me?
- What phase of research is this trial? (what are the aims of the trial?)
- Why am I being offered this trial?
- What hospital will I have my trial in? Will I need to travel to get onto the trial?
- How long will my course of treatment take?
- How often will I need to come to clinic?
- How often will I need bloods and scans?
- What are the likely side effects of the treatment?
- Are there other types of standard treatment I could have?
- How might the trial affect my life?
- Who should I contact if I need more information or have questions about my treatment?**



Keyword(s) i

Country

Age group

Trial status i

Study type i

<https://clinicaltrialfinder.pancreaticcancer.org.uk/>

Clinical Trials for pancreatic cancer

This fact sheet is for anyone who would like to find out more about clinical trials for pancreatic cancer. Clinical trials can be an important treatment option for people with pancreatic cancer. This factsheet explains what clinical trials are, why they are important and what they involve.

You can also speak to our specialist nurses on our confidential Support Line. Call free on 0808 801 0707, or email nurse@pancreaticcancer.org.uk

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How do I decide if I want to take part in a clinical trial?.....	7
What happens if I do decide to take part in a clinical trial?.....	8
What happens with the results of a pancreatic cancer clinical trial?.....	9
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Phase 1 – small group recruited, aimed at finding out how safe a drug is

Phase 2 – larger group recruited, aim is to better understand safety and side effect profile. Does the drug benefit people?

Phase 3 – larger groups still, usually international so multicentred Compared standard of care, so how well does this drug work? Helps to understand more about S/E, the long term risks and problems associated with new drug

https://www.ukcrc.org/wp-content/uploads/2014/03/iCT_Booklet.pdf

Understanding Clinical Trials





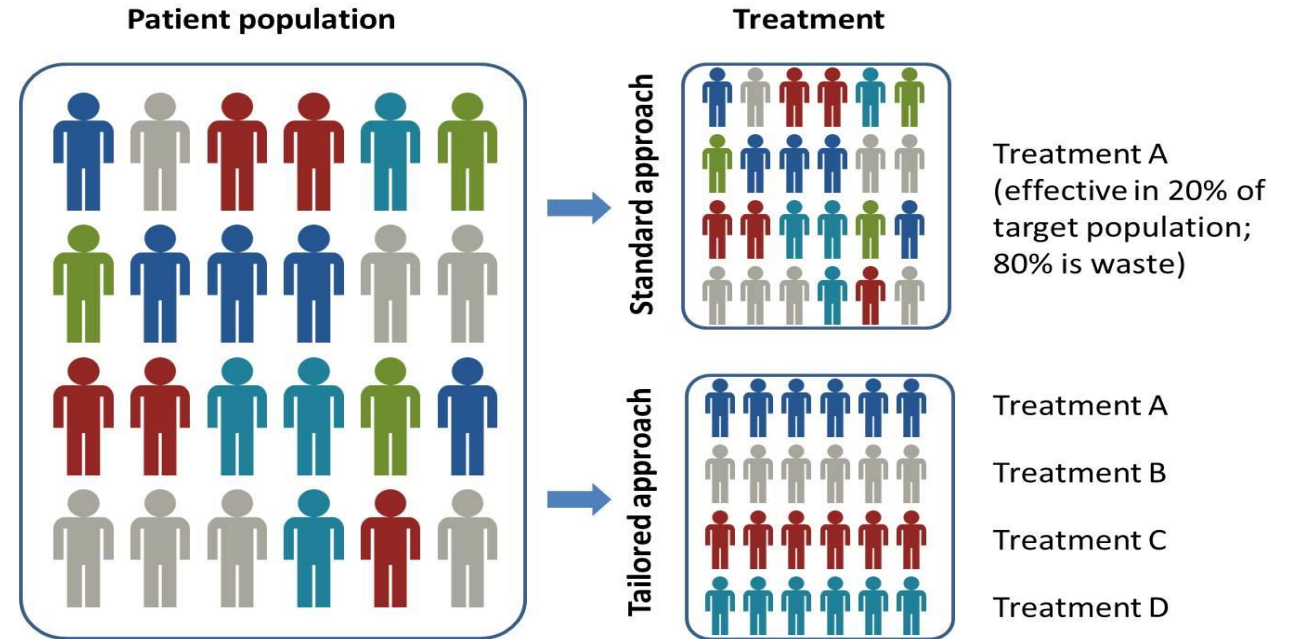
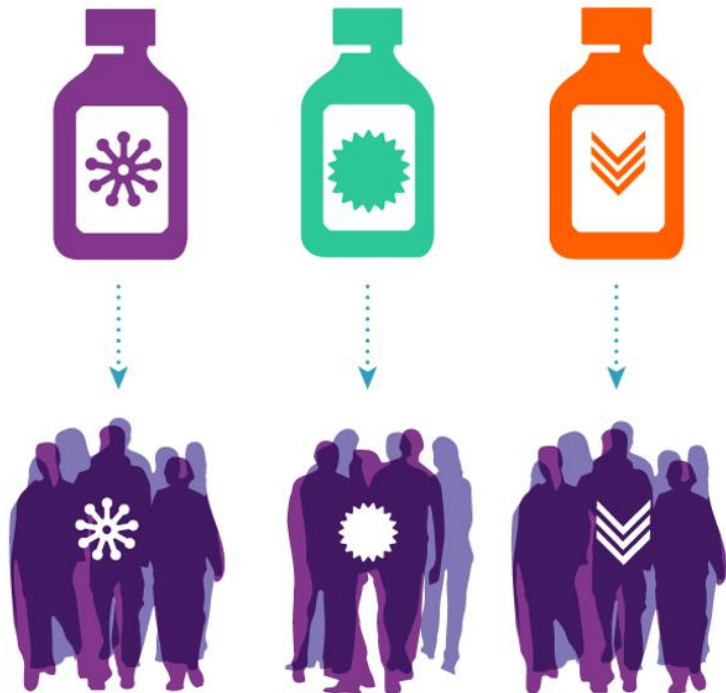
There is a lot of work being done across the country around individualised targeted treatment. The idea behind this is recognising that each person's pancreatic tumour(s) **may** be different and **may** respond to various treatments differently.

This is looking at the genomic sequencing of **individual cancers** of different people with the same disease to seeing if there are any unique mutations in the genomic sequence that present an opportunity to offer specific treatments targeting that particular mutation.

Genomic sequencing **isn't a treatment**

UNDERSTANDING PRECISION MEDICINE

In precision medicine, patients with tumors that share the same genetic change receive the drug that targets that change, no matter the type of cancer.



UNDERSTANDING PRECISION MEDICINE

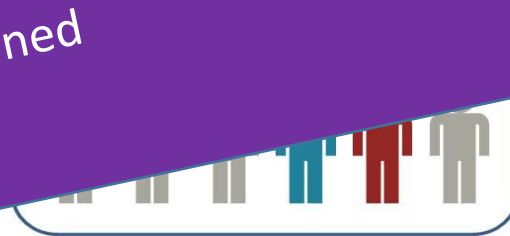
In precision medicine, patients with tumors that share the same genetic change receive the drug that targets that mutation.

PROS

- Covers all options, can put people minds at ease
- One stop shop (why good biopsy is essential)

CONS

- Only a small % of people will have a mutation that is linked to therapy
- Therapy might not be commissioned
- Costly
- Need to manage expectations



Tailored ap



Treatment A
Effective in 20% of
target population;
(rest is waste)

Treatment A
Treatment B
Treatment C
Treatment D

**Olaparib for maintenance
treatment of BRCA
mutation-positive
metastatic pancreatic
cancer after platinum-
based chemotherapy
(terminated appraisal)**

Technology appraisal guidance
Published: 8 December 2021
www.nice.org.uk/guidance/ta750

**Maintenance Olaparib for Germline
BRCA-Mutated Metastatic Pancreatic Cancer**

Talia Golan, M.D., Pascal Hammel, M.D., Ph.D., Michele Reni, M.D.,
Eric Van Cutsem, M.D., Ph.D., Teresa Macarulla, M.D., Ph.D.,
Michael J. Hall, M.D., Joon-Oh Park, M.D., Ph.D., Daniel Hochhauser, M.D., Ph.D.,
Dirk Arnold, M.D., Ph.D., Do-Youn Oh, M.D., Ph.D.,
Anke Reinacher-Schick, M.D., Ph.D., Giampaolo Tortora, M.D., Ph.D.,
Hana Algül, M.D., Ph.D., M.P.H., Eileen M. O'Reilly, M.D.,
David McGuinness, M.Sc., Karen Y. Cui, M.D., Ph.D., Katia Schlienger, M.D., Ph.D.,
Gershon Y. Locker, M.D., and Hedy L. Kindler, M.D.

This article was published on June 2, 2019, at
NEJM.org. N Engl J Med 2019;381:317-27. DOI:
10.1056/NEJMoa1903387

Maintenance Olaparib for Germline BRCA-Mutated Metastatic Pancreatic Cancer

Talia Golan, M.D., Pascal Hammel, M.D., Ph.D., Michele Reni, M.D., Eric Van Cutsem, M.D., Ph.D., Teresa Macarulla, M.D., Ph.D., Michael J. Hall, M.D., Joon-Oh Park, M.D., Ph.D., Daniel Hochhauser, M.D., Ph.D., Dirk Arnold, M.D., Ph.D., Do-Youn Oh, M.D., Ph.D., Anke Reinacher-Schick, M.D., Ph.D., Giampaolo Tortora, M.D., Ph.D., Eileen M. O'Reilly, M.D., Ph.D., M.P.H., Eileen M. O'Reilly, M.D., Ph.D., Katia Schlienger, M.D., Ph.D.,

NICE National Institute for Health and Care Excellence



NICE is unable to make a recommendation about the use of NHS Olaparib for maintenance treatment of BRCA mutation-positive metastatic pancreatic cancer in adults after platinum-based chemotherapy. This is because AstraZenica has confirmed that it does not intend to make a submission for the appraisal. AZ considered that there is unlikely to be enough evidence that the technology is a cost-effective use of NHS resources for this population

based on...
(terminated appraisal)

Conclusion

- Pancreatic cancer remains an area of unmet need.
- Surgery is the cornerstone of curative therapy
- Adjuvant chemotherapy reduces the risk of recurrence
- Promising studies into Neo-adj are ongoing
- Chemotherapy remains the 1st line gold standard treatment for those with LA, BR, Met PDAC
- There is a role for localised therapy for LA, BR PDAC
- Genomic profiling could offer people more targeted treatment options

- Streamlined patient pathway
- Investment in people and places
- Comprehensive structured assessment
- There is a role for pre-hab/Re-hab **for all those with pancreatic cancer**
- Optimise patient physically and mentally

**Pancreatic
Cancer
UK**



Thank you. Any questions?

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