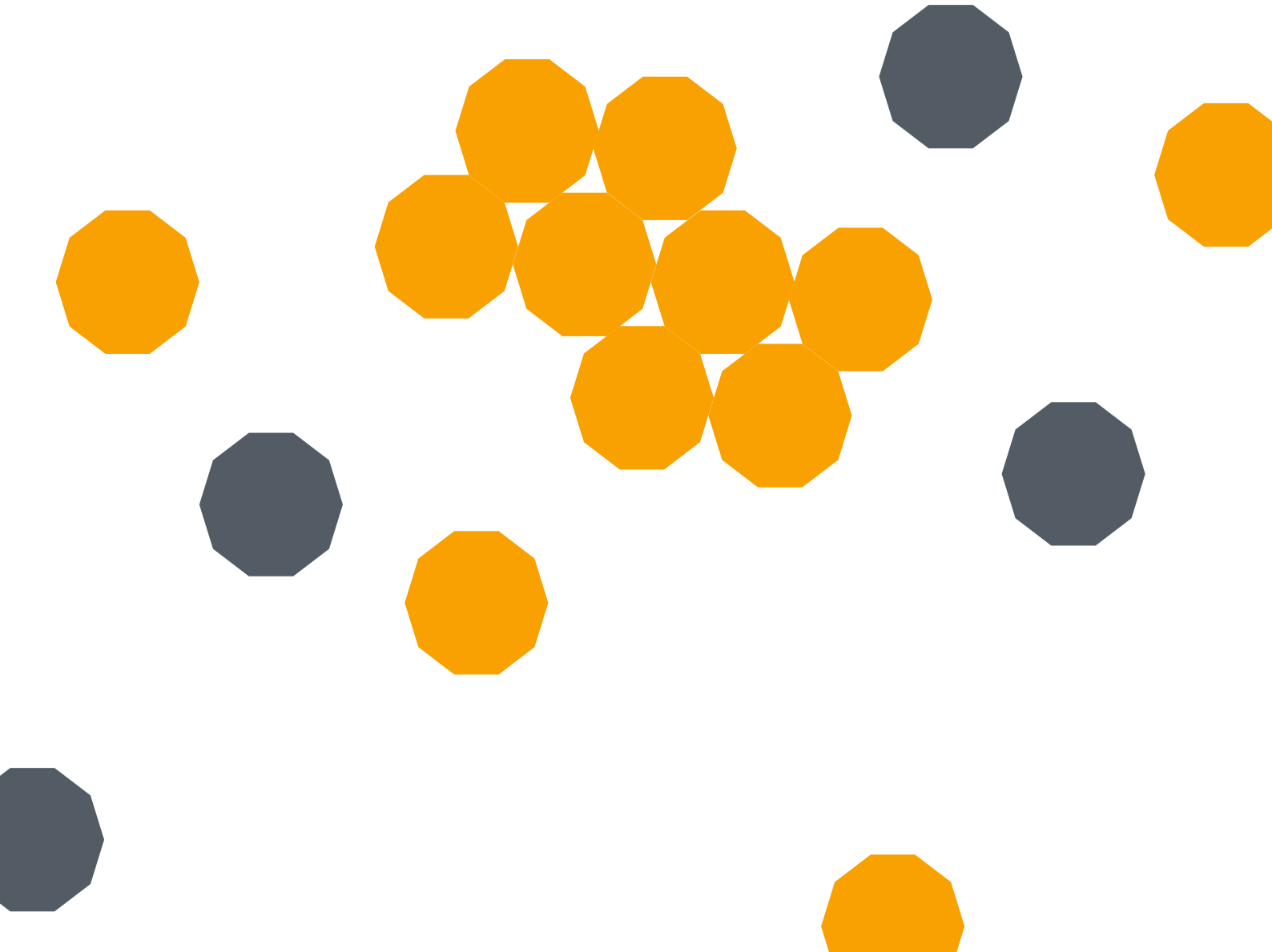
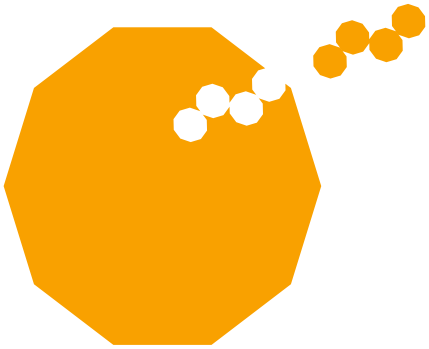
ICR The Institute of Cancer Research

Creating cancer treatments

Designing and trialling new medicines



Introduction



This video and accompanying resource pack from The Institute of Cancer Research, London, explain how researchers discover new cancer drugs and develop them for patients.

They have been designed and produced by the ICR – one of the world's most influential cancer research organisations – to support and enrich the GCSE science curriculum.

The ICR's mission is to make the discoveries that defeat cancer, and we are passionate about inspiring a diverse and inclusive next generation of cancer researchers.

To find out more about our work with schools visit www.icr.ac.uk/schools

CONTENTS

Content overview and lesson structure	3	Teachers' notes: activities	14
Activity worksheets (for printing)	5	Activity 1	14
Activity 1 worksheet	5	Activity 2	15
Activity 2 flash cards	7	Activity 3	17
Activity 3 worksheet	9	Teachers' notes: word-fill worksheets	18
Word-fill worksheets (for printing)	10	Part 1	18
Part 1	10	Part 2	20
Part 2	12	Part 3	21
Part 3	13	About us	22

About this resource

This video and resource pack are designed to help students explore how researchers discover new cancer drugs and develop them for patients.

They support the GCSE science curriculum in several areas: how medicines are made, clinical trials, cancer and chemical analysis. The content goes beyond the curriculum, introducing new concepts involved in the development of drugs to enrich learning and facilitate a deeper understanding of the subject.

We developed the video with drug discovery and clinical trials researchers at The Institute of Cancer Research (ICR). Some of these researchers present the video, and we have included animations to help explain complex concepts.

The video is 10 minutes long and is divided into three sections. It covers finding a drug target, optimising molecules to improve their activity, and designing clinical trials to show that a new treatment is more effective than the current treatment available.

Each section of the video has an accompanying worksheet for students to complete while it is playing. There are two classroom activities to take place at activity breaks in the video and a third activity which can be given as homework.

We have also provided teachers' notes in this pack, containing answers to the worksheets and information to help you lead discussions.

Although we have designed the video and resource pack with this approach in mind, they can be used flexibly and adapted to suit your needs. The video can be used as a standalone resource and any combination of activities can be used in the classroom or as homework. Please feel free to use the resources in a way that works best for you and your students.

Video

The video is approximately 10 minutes long. It is split into three parts, which cover the following:

Part 1

An introduction to cancer and the initial stages in cancer drug discovery:

- finding a target for a drug
- screening a library of drugs
- the chemical properties that make a good drug

Part 2

- preclinical testing in cells and animals
- the phases of clinical trials

Part 3

- randomised controlled trials
- double-blind trials
- how trials for cancer differ from those for other diseases

At the end of the first two parts a screen indicating an activity break will appear. The third activity takes place at the end of the video or as homework.

Activities

There are three activities contained in this pack. They have been designed for students to complete after each section of the video has been played.

1. The first activity is a worksheet. Students will have to match up new words covered in the video with their definitions and complete a word-fill activity. They will then have to put the stages of drug discovery and development into the right order.

2. The second activity is a flash card activity. Students are split into groups of four and each is given one card from a set, which contains information relating to a drug molecule. Students should discuss their drug molecule with the group and work together to rank the drug molecules according to which would be most likely to progress onto the next stage of development, based on the information about the drug molecule's efficacy, dosage and toxicity, which is provided on the card.

3. In the third activity, students will design a clinical trial for a new drug using the information in the third section of the video.

Depending on time in the lesson, any of these activities can be completed as homework.

Word-fill worksheets

The word-fill worksheets have been designed for the students to complete while the video is playing. All answers to the questions on the word-fill worksheets are covered in the video.

Feedback and results

The answers to the word-fill worksheets and activities are in this pack. You can also use the PowerPoint presentation to provide answers and feedback during the class.

Lesson plan

Here we provide a suggested lesson plan that you could use, but feel free to adapt to suit your needs.

Estimated time: 60 minutes

Group size: ~ 30 Students (split into groups of four for activity 2)

Video part 1 and optional word-fill worksheet (5 minutes)

Activity 1 (10 minutes)

Video part 2 and optional word-fill worksheet (5 minutes)

Activity 2 (20 minutes)

Video part 3 and optional word-fill worksheet (5 minutes)

Feedback and results (15 minutes)

Running the lesson

To deliver the lesson as outlined above you will need:

- Video
- Word-fill worksheets x3 (one for each section of the video per student)
- Activity 1 worksheet (one per student)
- Activity 2 flash cards (one set per group of four students)
- Activity 3 worksheet (one per student)
- Teachers' notes

Activity 1a

Match up the keywords with their definitions and fill in the gaps using the words at the bottom of the page.

Keyword	Definition
CANCER	a technique used to work out the _____ of a molecule
TUMOUR	an organic compound made of _____
DRUG	a group of diseases characterised by uncontrolled _____
TARGET	ability to dissolve in a _____
ABIRATERONE	a lump of _____ caused by uncontrolled cell division
PROTEIN	ability to pass through cell _____
X-RAY CRYSTALLOGRAPHY	a _____ that is intended to cause a change to the body
COMPLEMENTARY	a _____ molecule that a drug binds to
SOLUBLE	_____ that fit together like two pieces of a puzzle
PERMEABLE	a _____ cancer drug discovered and developed at the ICR

prostate
amino acids
substance
liquid
cell division
shapes
biological
cells
structure
membranes

Activity 1b

Put the stages of drug discovery in order.
The first stage has been done for you.

Order Number	Stage
	Test a library of molecules to see if they bind to the target
	Test how well the molecule works as a drug in cancer cells
	Find out as much as we can about the target, including its structure
	Identify a molecule that binds to the target
1	Identify a target by comparing cancer cells and normal cells
	Make changes to the molecule to improve the way it fits the target
	Use bacteria to make copies of the target

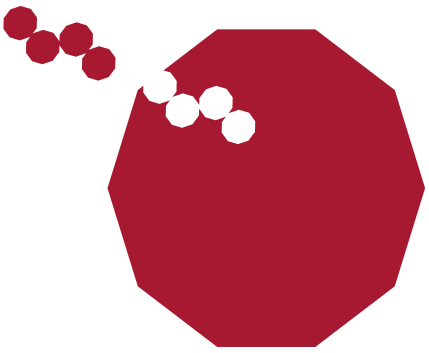
Activity 2

The cards you have been given contain information about a new drug molecule being tested. For each drug molecule, the efficacy, dosage and toxicity of the drug have been marked out of 10.

Think about the advantages and disadvantages of each drug molecule, and how likely it would be to progress onto the next stage of testing. Rank them in order.

What the marks out of 10 mean

Efficacy	A mark of 10 means that the drug treats the disease extremely effectively. So, *higher is better* for efficacy.
Dosage	A mark of 10 means that a high concentration is needed to have any anti-cancer effect, and so a high dosage must be given to the patient. So, *lower is better* for dosage.
Toxicity	A mark of 10 means that it is highly toxic. So, *lower is better* for toxicity.



Drug molecule A	
Efficacy	7
Dosage	6
Toxicity	9

Drug molecule B	
Efficacy	4
Dosage	4
Toxicity	2

Drug molecule C	
Efficacy	10
Dosage	5
Toxicity	3

Drug molecule D	
Efficacy	5
Dosage	9
Toxicity	9

Activity 3

Overview

Drug X is a newly discovered drug at the ICR. It has successfully passed through phase 1 and phase 2 trials, so you know that it is safe to give to people and isn't too toxic for them. You have confirmed the dosage of drug X to use and you know that it has efficacy against the disease you are treating.

Your brief

Imagine you are a cancer researcher at the ICR. You are designing a phase 3 clinical trial to build up strong statistical evidence that drug X works in a particular group of patients. In the trial you are comparing it with drug Y – the standard of care for this disease.

Using the third section of the video to help you, summarise how you would approach setting up and running the phase 3 clinical trial in the boxes on the right:

Things to think about	Your ideas
The type of trial you will conduct	
How patients will be split into two groups and why this is important	
What each of the groups in the trial will take	
Who is allowed to know what each group has taken	
What sort of tests are used to analyse the results of clinical trials	

Word-fill 1

Watch part 1 of the video and answer the questions.

How does cancer occur?

Name three ways of treating cancer:

1.

2.

3.

How does the ICR discover new drugs?

They identify _____ between _____ and _____ cells.

This helps them find _____ for new drugs. A target is a biological molecule, like an _____

or a receptor. Their aim is to discover a drug that _____ to the target and _____ how it works.

Answer the following questions about abiraterone:

1. Which type of cancer does it treat? _____

2. What is the target of abiraterone? _____

3. What does abiraterone do to the target _____

Word-fill 1 continued

Proteins are biological molecules made up of which components?

Glycerol Amino acids Saccharides

What three steps occur when a target is identified?

1. _____ the target using x-ray crystallography, to show _____ .

2. _____ of the target using bacteria, to test the new _____ .

3. _____ for a new drug that will _____ .

What is the name for a large collection of potential molecules that are tested to see if they bind to the target?

When a molecule binds to a target like a lock and key, they are said to be:

When a molecule binds to a target like a lock and key, they are said to be:

Soluble	Travels through cell membranes
Stable	Dissolves in blood stream
Permeable	Won't be destroyed by stomach acid or liver enzymes

Word-fill 2

Watch part 2 of the video and answer the questions.

Why do we test new drugs?

We test new drugs to see if they are _____ at killing _____

and to test whether it is _____ to give to _____

Name two animal species that we test new drugs on:

1. _____

2. _____

Define the words below:

Toxicity _____

Dosage _____

Efficacy _____

Fill in the gaps:

There are three different stages, or _____ , of clinical trials; phase _____ , _____ and

_____ . A new drug must usually successfully _____ each phase of clinical trials before

it can _____ onto the next.

Match up the phases of clinical trials:

Phase 1	Aims to find the efficacy of a drug and confirm the dosage
Phase 2	Aims to build up strong statistical evidence that a drug works in a given group of patients
Phase 3	Focusses on the toxicity of a drug including any side effects

Word-fill 3

Watch part 2 of the video and answer the questions.

Who are the first people to take a new drug in most clinical trials?

_____

What do the groups in a randomised controlled trial receive?

Control group _____

Treatment group _____

Fill in the gaps:

_____ are used to _____ patients into different _____

so that we can be sure it's a completely _____ process.

What is a placebo?

a new drug being tested the current best treatment an inactive form of a drug

What are the difference between cancer clinical trials and clinical trials for other diseases?

1. _____

2. _____

Why are statistical tests used to analyse data in clinical trials?

_____

What do we mean by 'sample size' in clinical trials?

the number of drugs being tested the number of people in the trial the number of statistical tests used

Teachers' notes: Activity 1

This activity sheet has been designed for the first break in the video – once the students have learned about:

- what cancer is
- finding a target for a drug
- screening a library of drugs
- the chemical properties that make a good drug.

In the first part of this activity, students match keywords with their definitions. They also fill in the missing words in the definitions, selecting from a collection of missing words provided. In the second part, the students put the stages of drug discovery in order.

We estimate that this activity will take **10 to 15 minutes** to complete.

ACTIVITY 1a

Keyword	Definition
CANCER	a group of diseases characterised by uncontrolled **cell division**
TUMOUR	a lump of **cells** produced by uncontrolled cell division
DRUG	a **substance** that is intended to cause a change in the body
TARGET	a **biological** molecule that a drug binds to, to have its effect
ABIRATERONE	a **prostate** cancer drug discovered and developed at the ICR
PROTEIN	an organic compound made of **amino acids**
X-RAY CRYSTALLOGRAPHY	a technique used to work out the **structure** of a molecule
COMPLEMENTARY	**shapes** that fit together like two pieces of a puzzle
SOLUBLE	ability to dissolve in a **liquid**
PERMEABLE	ability to pass through cell **membranes**

ACTIVITY 1b

Number	Stage
1	Identify a target by comparing cancer cells and normal cells
2	Find out as much as we can about the target, including its structure
3	Use bacteria to make copies of the target
4	Test a library of molecules to see if they bind to the target
5	Identify a molecule that binds to the target
6	Make changes to the molecule to improve the way it fits the target
7	Test how well the molecule works as a drug in cancer cells

Teachers' notes: Activity 2

This activity has been designed to support learning after the second part of the video, which covers preclinical testing in cells and animals and the phases of clinical trials.

In groups, students are given a set of drug molecule flash cards. In the groups, they should compare the drug molecules on the cards and discuss which of the four drug molecules is the most likely to progress through testing and why. They should think about the efficacy, dosage and toxicity of the drug molecules on the cards.

This activity will enable students to reflect on the properties that make a good drug and gain an understanding of the complex factors that have to be taken into account.

You may wish to revisit the definitions of efficacy, toxicity and dosage with the class before starting this activity, which can be found at 05:39 in the video.

We estimate that this activity will take **15 to 20 minutes** to complete.

Activity preparation

The flash cards need to be printed and cut out before starting this activity. One set of cards is required for each group of students (four students in each group).

Background

Finding a new drug is a balancing act between making sure it works against the disease, while ensuring that it doesn't harm the patient.

The ideal new drug would have a high efficacy, meaning that it would treat the disease very effectively. It would do this at low concentration, meaning that patients could be given a low dosage of the drug. Finally, it would cause minimal side effects for the patient.

In other words, the drug would have a high efficacy, low toxicity and be effective at a low dosage.

Unfortunately, this is very difficult to achieve, especially with cancer drugs, which often have considerable side effects.

Scientists and doctors have to find the drug with the best combination of properties – efficacy, dosage and toxicity.

Teachers' notes: Activity 2 (continued)

Answers

N.B. Scores on the flash cards are out of 10. Please take this to mean the following:

- A mark of 10 for efficacy means that the drug treats the disease extremely effectively. Therefore, higher is better for efficacy.
- A mark of 10 for dosage means that a high concentration is needed to have any anti-cancer effect, and so a high dosage must be given to the patient. Therefore, lower is better for dosage.
- A mark of 10 for toxicity means that it is highly toxic. Therefore, lower is better for toxicity.

Drug molecule A:

This drug has a high efficacy, low dosage and high toxicity. This means that is destroys cancer cells very effectively and patients don't have to take high doses of it. However, it has severe side effects.

This drug is neither the best nor the worst. It is in the middle, along with Drug molecule B.

Drug molecule B:

This drug has a low efficacy, high dosage and low toxicity. This means that it isn't very effective at destroying cancer cells and patients have to take high doses of the drug. However, it has few side effects.

This drug is neither the best nor the worst. It is in the middle, along with Drug molecule A.

N.B. Drug molecule A and B are purposely difficult to distinguish, so there may be differences in opinion in the class. There is no right answer – it is aimed to stimulate discussion about the balance of efficacy, dosage and toxicity of new drugs. The take-home message is that discovering and developing new drugs is extremely complicated as there are lots of factors to consider.

Drug molecule C:

It has a very high efficacy with low toxicity and low dosage. This means that the drug would be very good at destroying the cancer cells, the patient wouldn't have to take high doses of the drug and they wouldn't have severe side effects.

This drug has the most favourable properties out of the four.

Drug molecule D:

It has a low efficacy and very high toxicity and dosage. This means that the drug wouldn't destroy cancer cells very well, the patient would have to take very high doses of the drug to get any anti-cancer effects, and they would have severe side effects.

This drug has the least favourable properties out of the four.

Teachers' notes: Activity 3

This activity has been designed to support the content in the final section of the video (04:24 to 06:51). It covers the different types of clinical trials, and how cancer clinical trials differ from clinical trials for other diseases.

Individually in class or as homework, students should use the content of the final section of the video to design a phase 3 clinical trial for a new drug.

We estimate that this activity will take **20 to 25 minutes** to complete.

As an additional activity, students can present their ideas in a poster or presentation.

Answers

The type of trial you will conduct:

- *A randomised controlled trial or a double-blind trial*

How patients will be split into two groups and why this is important:

- *Using computer programs to ensure that it is a completely random process*

Which of the groups will be the control and treatment groups:

- *The control groups takes drug Y – the standard of care/current, best treatment*
- *The treatment groups takes drug X – the new drug we are testing*

Who is allowed to know what each group has taken:

- *In a double-blind trial neither the doctors nor the patients know which group is taking the new drug or the control*
- *Other types of randomised controlled trial can be blind, where only the participants on the trial don't know which group they are in but the doctors do, or open label, where both the trial participants and the doctors know who is in which group (not covered in the video)*

What sort of tests are used to analyse the results of clinical trials:

- *Statistical tests are used to show that the results have not happened by chance*

Teachers' notes: Word-fill 1

Watch part 1 of the video and answer the questions.

How does cancer occur?

Cells continue to divide without stopping, producing cells when the body doesn't need them.

Name three ways of treating cancer:

1. *Surgery*
2. *Radiation/radiotherapy*
3. *Drugs*

How does the ICR discover new drugs?

They identify *differences* between *healthy* and *cancerous* cells.

This helps them find *targets* for new drugs. A target is a biological molecule, like an *enzyme*

or a receptor. Their aim is to discover a drug that *binds* to the target and *affects* how it works.

Answer the following questions about abiraterone:

1. Which type of cancer does it treat? *Prostate*
2. What is the target of abiraterone? *An enzyme*
3. What does abiraterone do to the target *Stop it making hormones that drive the cancer*

Word-fill 1 continued

Proteins are biological molecules made up of which components?

Glycerol | Amino acids | Saccharides

What three steps occur when a target is identified?

1. *Analyse* the target using x-ray crystallography, to show *what it looks like* .
2. *Make copies* of the target using bacteria, to test the new *drugs* .
3. *Search* for a new drug that will *bind to the target* .

What is the name for a large collection of potential molecules that are tested to see if they bind to the target?

A library

When a molecule binds to a target like a lock and key, they are said to be:

Complementary

When a molecule binds to a target like a lock and key, they are said to be:

Soluble	Travels through cell membranes
Stable	Dissolves in blood stream
Permeable	Won't be destroyed by stomach acid or liver enzymes

Word-fill 2

Watch part 2 of the video and answer the questions.

Why do we test new drugs?

We test new drugs to see if they are *effective* at killing *cancer cells*

and to test whether it is *safe* to give to *people*

Name two animal species that we test new drugs on:

1. *Rats*

2. *Mice*

Define the words below:

Toxicity *whether a drug is dangerous for people taking it and what side effects it has*

Dosage *how much of a drug you should give to people*

Efficacy *how well a drug works against a disease*

Answer the following questions about abiraterone:

There are three different stages, or *phases* , of clinical trials; phase *1* , *2* and *3* . A new drug must usually successfully *complete* each phase of clinical trials before it can *progress* onto the next.

Match up the phases of clinical trials:

Phase 1	Aims to find the efficacy of a drug and confirm the dosage
Phase 2	Aims to build up strong statistical evidence that a drug works in a given group of patients
Phase 3	Focusses on the toxicity of a drug including any side effects

Word-fill 3

Watch part 2 of the video and answer the questions.

Who are the first people to take a new drug in most clinical trials?

Healthy volunteers

What do the groups in a randomised controlled trial receive?

Control group *Standard of care*

Treatment group *New drug*

Fill in the gaps:

Computer programs are used to *divide* patients into different *groups* so that we can be sure it's a completely *random* process.

What is a placebo?:

a new drug being tested | the current best treatment | an inactive form of a drug

What are the difference between cancer clinical trials and clinical trials for other diseases?

1. *Cancer drugs aren't tested in healthy volunteers.*
2. *Placebos aren't commonly used in cancer clinical trials.*

Why are statistical tests used to analyse data in clinical trials?

To make sure the results haven't happened by chance.

What do we mean by 'sample size' in clinical trials?

the number of drugs being tested | the number of people in the trial | the number of statistical tests used

About us

The ICR is one of the world's most influential cancer research organisations.

We have an outstanding record of achievement dating back more than 100 years. We provided the first convincing evidence that DNA damage is the basic cause of cancer, laying the foundation for the now universally accepted idea that cancer is a genetic disease. Today, the ICR is a world leader in understanding cancer biology and genetics, discovering new targeted drugs and developing new high-precision forms of radiotherapy.

The ICR is a charity and relies on support from partner organisations, funders and the general public. It is also the UK's top-ranked academic institution for research quality, and provides postgraduate higher education of international distinction.

The ICR's mission is to make the discoveries that defeat cancer. For more information visit www.icr.ac.uk

Daisy Henesy is the ICR's Public Engagement Officer. She led on the development of this video and resource pack with the help of ICR researchers and staff and subject-specialist teachers.

Daisy has a degree in Medical Science and a background in cell biology, having worked in academic research and drug discovery. At the ICR she works with the public and ICR staff and students – connecting them with each other to share knowledge, thoughts and ideas about cancer research.

Much of her work focuses on inspiring a diverse and inclusive next generation of cancer researchers and she works closely with schools and educators to facilitate meaningful outreach opportunities.

Acknowledgements

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ICR The Institute of Cancer Research