Children's Cancer and Leukaemia Group | the EXPERTS in CHILDHOOD CANCER

Treatment options for relapsed Wilms tumour in children

An information guide for parents and families

The purpose of this guide is to give information about relapsed Wilms tumour and the treatment options available.

Choosing which treatment is right for your child will depend on a number of things, including what stage their disease was at diagnosis and what treatment they have previously been given. Your child's consultant will be able to give more information on which is the most appropriate treatment for your child at this time.

What is relapse?

Most children diagnosed with Wilms tumour are treated successfully with surgery, chemotherapy and sometimes radiotherapy but for a small number of children, their cancer comes back[1]. Usually this happens after a period of time during which the cancer could not be detected. This is known as **relapse** or **tumour recurrence**.

Sometimes, the tumour starts to grow again before it has been removed. This is known as **tumour progression**. Most relapses (about 80%) occur within two years of diagnosis of the original Wilms tumour, but for a few children it can come back later than this. For children who relapse, their treatment will depend on what treatment they have already had and what their cancer looked like under the microscope (histology)[1].

How many children with Wilms tumour relapse?

In the UK, about 5 to 10 children with Wilms tumour relapse each year[2]. The chance of relapse is greater in children whose original Wilms tumour had already spread (Stage 4) or had 'high risk' histology.

Why and where does the tumour come back?

Wilms tumours are made up of billions of cancer cells. Most of these cells are removed during your child's first operation to take out the tumour. After this, chemotherapy and/or radiotherapy kills any cancer cells that are left.

However, sometimes there are cancer cells that are not killed by your child's treatment. These are known as **resistant** cancer cells and even though the Wilms tumour appears to have gone on scans, undetectable resistant cells can remain and start to grow again.

The original Wilms tumour in your child's kidney can spread to other parts of the body through a process known as **metastasis**. Metastatic and local relapse can occur at the same time.

- **Metastatic relapse** is when cancer cells spread to other parts in the body. The most common areas are the lungs (80%), followed by the liver (15%), and then bone or brain (less than 5%).
- **Local relapse** is when the tumour grows back in the abdomen, usually near the original tumour site[1].
- **Metachronous relapse** is when Wilms tumour appears in the other kidney. It is thought that this is a new Wilms tumour rather than the original tumour returning.

How do we decide which treatment type is best?

Chemotherapy

Chemotherapy is the most common treatment option used and can be given as a single drug, multiple drugs, or in combination with radiotherapy, surgery, or immunotherapy. It can be given by mouth (orally) or intravenously (through a vein).

Currently, no specific chemotherapy combination has been shown to be the best for initial treatment of Wilms tumour[1]. For disease that has recurred in more than one place or has returned distant to where it first started (metastatic relapse), a patient will be treated with chemotherapy that is different to what they received when first diagnosed.

Immunotherapy

Immunotherapy stimulates the patient's own immune system to recognise and attach to specific molecules produced by cancer cells to alter their behaviour. A patient's Wilms tumour cells may have to be tested to see if they have specific changes that can be targeted by immunotherapy drugs because not everyone's cancer cells will have the same genetic changes. Immunotherapy has not been tested in many patients, therefore there is not yet any evidence that it works.

What influences the choice of treatment options?

The choice of treatment options for your child will depend on a number of different factors:

The original stage of your child's tumour and the type of cells it is made up of

Children with 'high risk' cancer cells (anaplastic or blastemal type Wilms tumour) or more advanced tumour stage (Stages 3 and 4) can be more difficult to treat at relapse[1].

How many chemotherapy drugs were used to treat your child's original Wilms tumour

If more than two chemotherapy drugs were needed when your child was treated initially, this can impact how well the tumour responds again.

If radiotherapy was used to treat your child's original tumour

If relapse occurs in an area where radiotherapy was used to treat your child's tumour, it may be difficult to treat.

The above factors are used to decide your child's '**risk group**' and help doctors to select the best treatment for your child. Studies show that the time from your child's first diagnosis to relapse, and the site where the cancer has returned, do not influence the success of treatment.

What are the risk groups and what do they mean?

Three risk groups are used to help doctors decide the best treatment for your child and predict the chance of successful treatment.

Risk group	Description of treatment given at your child's first diagnosis of Wilms tumour	Proportion of children predicted to be successfully treated at relapse
STANDARD	• Your child received vincristine with or without actinomycin D only. No radiotherapy was given • Usually your child's original tumour was low stage (Stages 1 or 2) and low or intermediate risk histology	70-80%
HIGH	• Doxorubicin already given and/or radiotherapy already given • Usually, your child's original tumour was localised (Stages 1, 2 or 3) with intermediate risk histology. Some relapsed Stage 4 tumours are also in this group	50%
VERY HIGH	• Four or more chemotherapy drugs already used in your child's treatment so far • Your child's original tumour had high risk histology	10%

What treatment is your child likely to have?

The treatment your child receives will depend on which risk category your child is in (see previous page) and how their original tumour was treated.

The information provided in this factsheet is based on current UK treatment strategies for relapsed Wilms tumours. These strategies are based on internationally recommended treatments by the International Society of Paediatric Oncology (SIOP) Renal Tumour Study Group.

Generally, treatment for relapsed Wilms tumours will include chemotherapy drugs that have not already been used to treat your child's original tumour. However, in some cases of metachronous relapse (which is when a tumour appears in the opposite kidney), the same drugs can be used successfully, as this is considered a 'new' tumour rather than a relapse of the previous one.

TREATMENT FOR STANDARD RISK	The recommendation for children with standard risk relapsed Wilms tumour is treatment with chemotherapy (cyclophosphamide, doxorubicin, etoposide and carboplatin), surgery if appropriate and radiotherapy. This treatment is successful in about 70-80% of children with standard risk relapsed Wilms tumour[1].
TREATMENT FOR HIGH RISK	Children with high risk relapsed Wilms tumour are treated with more intensive chemotherapy (ifosfamide, carboplatin, etoposide and cyclophosphamide) followed by high-dose chemotherapy (melphalan) with autologous stem cell transplant (see below) for those with adequate partial or complete response. Surgery may be necessary before the high-dose chemotherapy. Radiotherapy is usually given afterwards[4]. The current evidence suggests that this treatment can be successful for around 66% of children[3].
TREATMENT FOR VERY HIGH RISK	This risk group is difficult to treat as the tumour is likely to have developed resistance to treatment and no longer responds to available chemotherapy drugs. If your child is in the very high risk group, they may have their treatment as part of a clinical trial which investigates new drugs or new combinations of treatments to treat relapsed Wilms tumours[1].

Autologous stem cell transplants

An autologous stem cell transplant stores your child's own blood stem cells while they have high-dose treatment. This means that your child can have higher doses than usual to treat the cancer.

It is an intensive process and your child will need to stay in hospital for a few weeks. At least two weeks before starting high-dose treatment, your child's own healthy stem cells will be collected and stored to avoid them being damaged by treatment. Once treatment has finished, your child's healthy stem cells are put back into your child's body through a drip (IV infusion).

The cells will then make their way to your child's bone marrow to start making new healthy blood cells after intensive treatment.

Testing your child's tumour cells

Your child will be offered molecular testing of their tumour sample taken at relapse to look for changes in the tumour's genetic make-up (DNA, gene sequencing, and epigenetics). Any changes found can be matched to available drugs that may be active against the particular genetic change (or combination of changes) found in each child's tumour. A sample of your child's relapsed tumour may also be sent to research laboratories to test which drugs are most suitable to treat it [5,6,7,8]. These tests are not guaranteed to guide choice of therapy but may be helpful.

Your child's doctor is the only one who knows your child's individual condition and will be in the best position to tell you about developments and discoveries in cancer medicine that could help your child - they will be more than happy to explain anything to you.

Don't worry that your child's doctor will be offended if you turn up with a list of questions about things you have found out online. They will take you seriously and give you honest, balanced advice based on your child's individual situation.

The following CCLG booklets:

'When your child's cancer comes back or does not respond to initial treatment'
'A parent's guide to kidney tumours'

are available FREE of charge from your child's hospital

All CCLG booklets and leaflets can be downloaded or ordered from our website: www.cclg.org.uk/publications

Alice relapsed six months after her first round of treatment when a tumour was found on her lung. Her relapse treatment included surgery, an autologous stem cell harvest and transplant, high-dose chemotherapy and ten sessions of radiotherapy. Since recovering from her relapse treatment, Alice has gone from strength to strength. She is loving school, dancing, Girl Guides and is a massive animal lover; our latest additions are guinea pigs Toffee and Oreo. Check-ups are now every six months and all being well we will reach the big 5-year remission milestone next year!

Jane, mum to Alice who was diagnosed with relapsed Wilms tumour, shares her experience...

Alice in hospital during treatment

Glossary

Anaplastic Wilms tumour

About 5-10% of Wilms tumours have an appearance called anaplasia, which means the cells look very disorganised under a microscope. Considered to be a 'higher risk' type of Wilms tumour.

Blastemal-type Wilms tumour

This group of high-risk tumours cannot be identified by looking at the biopsy because they occur when a particular type of early kidney cell survives the pre-surgery chemotherapy. These cells are known as blastemal cells. Tumours where most of these cells survive chemotherapy are called blastemal-type Wilms tumours.

Chemotherapy

Drug treatment that kills cancer cells.

Histology

The appearance of tissue under a microscope, which helps to determine the diagnosis.

Local relapse

When the tumour grows back in the abdomen, usually near the original tumour site.

Metachronous relapse

When Wilms tumour appears in the other kidney. It is thought that this is a new Wilms tumour rather than the original tumour returning.

Metastasis

Tumours that have spread from the first (primary) tumour into another part of the body. Also known as secondary tumours.

Progression

Where the tumour continues to grow, even during treatment.

Radiotherapy

The use of radiation to treat cancer.

Relapse/recurrence

The return of cancer after previous treatment.

Staging

Categorising the tumour after surgery, based on whether it has spread outside the kidney to help decide on a course of treatment.

Surgery

An operation.

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Notes:

Children's Cancer and Leukaemia Group | the EXPERTS in CHILDHOOD CANCER

Children's Cancer and Leukaemia Group (CCLG) is a leading national charity and expert voice for all childhood cancers.

Each week in the UK and Ireland, more than 30 children are diagnosed with cancer. Our network of dedicated professional members work together in treatment, care and research to help shape a future where all children with cancer survive and live happy, healthy and independent lives.

We fund and support innovative world-class research and collaborate, both nationally and internationally, to drive forward improvements in childhood cancer. Our award-winning information resources help lessen the anxiety, stress and loneliness commonly felt by families, giving support throughout the cancer journey.

Our work is funded by donations. If you would like to help, text 'CCLG' to 70300 to donate £3. This will cost £3 plus a standard rate message.

We are grateful to all those who have contributed to this publication. We make every effort to ensure that information is accurate and up to date at the time of printing. CCLG does not accept responsibility for information provided by third parties, including those referred to or signposted to in the publication. Information in this publication should be used to supplement appropriate professional or other advice specific to your circumstances.

CCLG publications on a variety of topics related to children's cancer are available to order or download free of charge from our website. If you have any comments on this booklet, please contact us at publications@cclg.org.uk.

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This version is published in conjunction with Bethany's Wish, a Special Named Fund at CCLG, dedicated to Bethany Polanco, who sadly lost her life to Wilms tumour, a childhood cancer of the kidney. For more information, please visit www.cclg.org.uk/BethanysWish

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