Cancer Association of South Africa (CANSA)

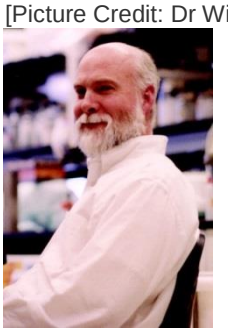
Research • Educate • Support

Fact Sheet on Desmoplastic Small-Round-Cell Tumour

Introduction

Desmoplastic small round cell tumour (DSRCT) was first described in 1989 by Drs William Gerald and Rosai who described a distinct type of small round blue cell tumour with a predilection for serosal surfaces such as the peritoneum and the tunica vaginalis that affected mostly Caucasian males in the second or third decade of life (mean age: 22 years – sex ratio: 4.7 M to 1 F). Dr William Gerald died in 2008 after a long battle with cancer.

[Picture Credit: Dr William Gerald]



DSRCT is generally associated with aggressive features and a poor prognosis. The prognosis for patients with DSRCT remains poor. Despite aggressive therapy, 3-year overall survival has been estimated at 44% and the 5-year survival rate remains around 15%.

DSRCT exhibits a male predominance of 90%, and 85% of patients are Caucasian. Median age at diagnosis has been reported as 14, 19 and 25 years of age in different series. The prognosis for patients with DSRCT remains poor. Despite aggressive therapy, 3-year overall survival has been estimated at 44% and the 5-year survival rate remains around 15%.
(Atlas of Genetics and Cytogenetics in Oncology and Haematology; The Liddy Shriver Sarcoma Initiative).

Desmoplastic Small-Round-Cell Tumour

Desmoplastic Small-Round-Cell Tumour (DSRCT) is considered a childhood cancer that predominantly strikes boys and young adults. The disease rarely occurs in females, but when it does the tumours can be mistaken for ovarian cancer. It is classified as a soft tissue sarcoma. It is an aggressive and rare tumour that primarily occurs as masses in the abdomen.

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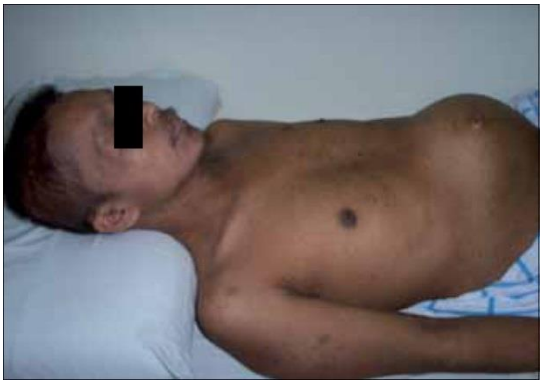
[Picture Credit: Intra-abdominal Desmoplastic Small-Round-Cell Tumour]



Other areas affected may include the lymph nodes, the lining of the abdomen, diaphragm, spleen, liver, chest wall, skull, spinal cord, large intestine, small intestine, bladder, brain, lungs, testicles, ovaries, and the pelvis. Reported sites of metastatic spread include the liver, lungs, lymph nodes, brain and bones.
(Wikipedia).

Incidence of Desmoplastic Small-Round-Cell Tumour
The National Cancer Registry (2011) does not provide any statistics regarding Desmoplastic Small-round-Cell Tumour in South Africa.

Risk Factors and Causes of Desmoplastic Small Round Cell Tumour (DSRCT)
There aren't any known risk factors associated with Desmoplastic Small Round Cell Tumours. The disease is known to pop up from primitive cells during childhood. Chromosomal translocations chromosome 11 and chromosome 22 causes this disease. When this happens, the body is no longer able to suppress tumour growth.
(Know Cancer).

Signs and Symptoms of Desmoplastic Small-Round-Cell Tumour (DSRCT)
Desmoplastic small-round-cell tumour (DSRCT) is a rare disease of children, adolescents and young adults, which begins in the abdominal cavity. Because of the rarity of this disease, little is known about optimal treatment.

These aggressive cancers often form as multiple tumours in the tissue (peritoneum) that lines the inside of the abdomen and pelvis. They quickly spread to other structures within the abdomen.

Patients may present with dozens to hundreds of tumours studding the peritoneal cavity (abdominal cavity). Despite this presentation, it is not primarily considered metastatic but multifocal. It can metastasise to the liver or lung.

Chemotherapy, radiotherapy, and surgical approaches have not been standardised. Neoadjuvant chemotherapy often yields a partial response; however, tumours may remain surgically un-resectable.

An aggressive approach to treatment is required to maximise long-term remission.

Symptoms of desmoplastic small round cell tumour include:

- Pain or a lump in the abdomen
- Cramping
- Nausea
- Vomiting
- Diarrhoea

- Constipation
- Trouble having a bowel movement and/or passing gas
- Abdominal swellingBack pain
- Gastrointestinal blockage
- Lack of appetite
- Weight loss
- Fatigue
- Fluid in the abdomen (ascites)
- Anaemia
- Thyroid or hormone problems

(Hayes-Jordan & Anderson, 2011; Mayo Clinic; St Jude Children's Research Hospital; MD Anderson Cancer Center).

Diagnosis of Desmoplastic Small Round Cell Tumour (DSRCT)

Diagnostic tests vary, based on location of the tumour. It is often noticed that at diagnosis, the tumour has metastasized to distant organs. Diagnosis of Desmoplastic Small Round Cell Tumour is made using the following tools:

- Physical examination, evaluation of patient's medical history
- Histopathological studies conducted on a biopsy specimen - the specimen is examined under a microscope by a pathologist, to arrive at a definitive diagnosis
- MRI, CT, and PET scans of the affected regions - to aid in obtaining a clear image of the tumour prior to surgery. A solid and firm mass is usually noticed

Many clinical conditions may have similar signs and symptoms. Your healthcare provider may perform additional tests to rule out other clinical conditions to arrive at a definitive diagnosis.
(Dove Med).

Differential diagnosis of Desmoplastic Small-Round-Cell Tumour (DSRCT)

The following conditions are kept in mind when making a diagnosis:

- peritoneal carcinomatosis
- non Hodgkin lymphoma
- malignant peritoneal mesothelioma
- rhabdomyosarcoma
- round cell sarcomas
- Ewing sarcoma/primitive neuroectodermal tumour
    - alveolar rhabdomyosarcoma
    - desmoplastic round cell tumour
    - mesenchymal chondrosarcoma
    - poorly differentiated synovial sarcoma
- lymphomas
- neuroendocrine carcinoma
- neuroblastoma and variants

(Lessnick, *et al*, 2009)

Treatment of Desmoplastic Small-Round-Cell Tumour (DSRCT)
Because DSRCT is so rare, no standard way to treat it has been developed. The following treatment methods have been used:

- Surgery - is used to remove as much of the cancer as possible. Often, DSRCTs have spread too far for complete removal, but surgeons try to remove at least 90 percent of them
- Hyperthermic intraperitoneal chemotherapy (HIPEC) - may be given during the surgery to kill cancer cells that cannot be removed surgically. (The patient also avoids the side effects of standard chemotherapy.)
    - HIPEC is done by circulating a heated, sterile chemo solution through the part of the abdomen where the tumours are found, for up to two hours
- Chemotherapy - uses powerful medicines to kill cancer cells or stop them from growing (dividing) and making more cancer cells
    - Chemotherapy may be injected into the bloodstream, so that it can travel throughout the body
    - Some chemotherapy may be given by mouth
    - Some chemotherapy may be given by mouth
- Radiation therapy - uses high-energy X-rays or other types of radiation to kill cancer cells or stop them from growing
    - External radiation uses machines outside the body to deliver the X-ray dose.
    - Internal radiation uses needles, seeds, wires or catheters to deliver the radiation directly into or close to the cancer.

DSRCT located outside the abdomen without any spread seems to respond better to treatment than DSRCT in the abdomen or than DSRCT which has spread into other parts of the body.

DSRCT is a very aggressive neoplasm with a 5-year survival of less than 15%.

Treatment options include surgery, radiotherapy, chemotherapy with or without stem cell transplantation, and recently introduced molecularly targeted therapies. Unfortunately there is no standard therapeutic regimen described since no modality is clearly superior to any other. Surgery is usually extensive and often includes excision of the omentum, splenectomy and lymph node resections. Due to the invasive nature of this tumour, complete resection with negative margins is usually not possible. Debulking surgery has been described as an attempt to eliminate 90% of the tumour bulk.

In addition to surgery and radiation therapy, local control options for DSRCT (particularly metastatic disease) include radiofrequency ablation, gammaknife, cryoablation, embolisation and chemoembolisation. These are usually performed in academic centres after careful consideration of individual cases.

Treatment Options

Tumour Location	Treatment Options
Peritoneal Disease	Surgery, whole abdominal radiotherapy, continuous hyperthermic peritoneal perfusion
Liver Metastases	Surgery, stereotactic radiosurgery, radiofrequency ablation, cryoablation, 90Y-microspheres
Lung Metastases	Surgery, stereotactic radiosurgery
Mediastinal Lymph Nodes	Radiation therapy
Bone Metastases	Radiation therapy

Chemotherapeutic agents utilised include

- cyclophosphamide
- doxorubicin
- vincristine
- ifosfamide
- etoposide (a combination known as P6 protocol)

as well as:

- cisplatin
- carboplatin
- topotecan
- temozolamid
- vinorelbine
- irinotecan

High-dose chemotherapy with autologous stem-cell rescue has also been attempted, however no significant impact in long-term survival has been achieved after transplant.
Although DSRCTs are generally sensitive to chemotherapy, the response is not enough to achieve cure since patients almost invariably relapse. This could potentially be a reflection of the heterogeneity of the cells within the tumour; where a distinct population of cells ("cancer stem cells") that are less sensitive to chemotherapy and radiotherapy possess the ability to self-renew and retain the capacity to regenerate the tumour bulk after it has been eradicated. This represents a highly attractive hypothesis since it could explain tumour behaviour and lead to the identification of new targets for more effective therapies. Unlike other small round blue cell tumours like Ewing's sarcoma, such a stem cell has not been yet identified in DSRCTs.
(St Jude Children's Research Hospital; Livvy Shriver Sarcoma Initiative).

About Clinical Trials

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

<u>Types of Clinical Trials</u>

Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have

had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer.

Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different "phase" in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or "control" interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial

might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

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