IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES

PRIMARY **IMMUNODEFICIENCIES**

PIDs AND **CANCER**

INTRODUCTION

This booklet explains the types of cancer that can affect people with primary immunodeficiencies (PIDs) and how they can best be managed.

Primary immunodeficiencies (PIDs) are rare diseases that occur when certain parts of the immune system are either not present or are not working normally. When the immune system is not working properly, patients with PIDs are more likely to get a variety of different conditions and are more vulnerable to infections, which potentially can be life-threatening.

People affected by PIDs may have an increased risk of developing some kind of cancer compared with people who do not have a PID.

The following sections review the increased risk of cancer among patients with PIDs, the causes of the increased risk and the ways in which patients should be managed so that any cancer can be identified early and treatment managed appropriately.

ABBREVIATIONS

CVID	Common variable immunodeficiency
IPOPI	International Patient Organisation for Primary Immunodeficiencies
PID	Primary immunodeficiency
NHL	Non-Hodgkin's lymphoma
SCID	Severe combined immunodeficiency

Primary immunodeficiencies and cancer (1st edition).

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PIDs

To date, over 430 different PIDs have been identified ranging from the very rare (e.g. severe combined immunodeficiency [SCID]) to the relatively common (e.g. selective immunoglobulin A deficiency).

Whilst PIDs are generally recognised as rare disorders, some are more common than others and overall they profoundly impact the lives of persons with this condition. PIDs can be diagnosed throughout the lifespan of a person with the most severe forms of PIDs usually being diagnosed in childhood. However, others are often recognised during adulthood because of their late onset or because they have previously been misdiagnosed or have gone undiagnosed. PIDs can vary in severity from relatively mild to life-threatening. Some PIDs develop over time and worsen as late symptoms or complications appear.

People with PIDs are more susceptible to infections, allergies and complications resulting from infections. Often many persons with PIDs go undiagnosed for several years and are repeatedly treated with antibacterial drugs with no permanent cure or long-term positive outcome. In addition, people affected by PIDs have an increased risk of developing some types of cancer compared with people who do not have a PID. In fact, cancer is the second highest cause of death (infection being the first) among children and adults with PID. Your doctor/clinician will check for any early signs of cancer so, should it be detected, it can be treated early.

PIDs AND CANCER

There is some suggestion from registry data that patients with a PID may be at increased risk of developing certain types of cancer including lymphoma (a type of blood cancer that affects white blood cells called lymphocytes), skin cancer, thyroid cancer, gastric cancer, liver cancer (linked to non-alcoholic cirrhosis), bladder and cervical epithelial cancer.[1,2] The exact incidence rates for malignancies occurring with PIDs are difficult to determine because of the rarity of PIDs. Also, having a PID does not mean you will definitely develop cancer. Many people with a PID will remain unaffected by cancer throughout their lives.

There is a great range of PIDs that have an increased risk of cancer. Common variable immunodeficiency (CVID), ataxia telangiectasia (where a person is uncoordinated and has enlarged blood vessels that appear as tiny, red, spider-like veins), Wiskott–Aldrich syndrome and X-linked lymphoproliferative disease, which is also called Duncan's syndrome, are some of them. The table shows malignancy patterns in various PIDs.[3] That said, the great majority of people with CVID, for instance, will never have a problem with cancer.

[1] Mayor PC, et al. Cancer incidence in the US Immune Deficiency Network registry. J Allergy Clin Immunol 2018;141:1028-35

[2] Jonkman-Berk BM, et al. Primary immunodeficiencies in the Netherlands: national patients data demonstrate the increased risk of malignancy. Clin Immunol 2015;156:154-62

MALIGANCY PATTERNS IN VARIOUS PIDS

PID	Predominant tumour type	Specific reported malignancies
CVID	Lymphoma, GI cancer	NHL, stomach, breast, bladder, cervical cancer
X-linked lymphoproliferative disease	Lymphoma	NHL, Hodgkin's lymphoma
Wiskott-Aldrich syndrome	Lymphoma	Diffuse large B-cell lymphoma, NHL, leukaemia, Kaposi sarcoma
Ataxia-telangiectasia	Lymphoma	Lymphoid leukaemias, T prolymphocytic lymphomas, epithelial tumours

Lymphomas associated with CVID are more likely to be a predominance of non-Hodgkin's lymphoma (NHL). A US analysis showed that patients with CVID may be at increased risk for NHL, gastric cancer or skin cancer.[1] These usually occur in persons over 30 years of age and are rarely seen in children.[4]

A Dutch analysis found a 10% increase in risk of cancer in patients with PID, with younger patients being more at risk for lymphoma or leukaemia (a blood cancer that usually affects white blood cells in bone marrow).[2]

An analysis of the Italian Cancer Registry database found that patients with CVID were at increased risk for gastric cancer, which tended to be more aggressive than usual.[5]

[3] Shapiro RS. Malignancies in the setting of primary immunodeficiency: implications for hematologists/oncologists. Am J Hematol 2011;86:48-55.

[4] Mortaz E, et al. Cancers Related to Immunodeficiencies: Update and Perspectives. Front Immunol 2016;7:365.

[5] Pulvirenti F, et al. Gastric cancer is the leading cause of death in Italian adult patients with common variable immunodeficiency. Front Immunol 2018;9:2546

There is no evidence that patients with a PID are at increased risk for the more common kinds of cancer such as lung, breast, ovary, prostate or large bowel cancer. The increased risk appears to be for cancer of the white blood cells (lymphomas), cancer of the gastric tract and some kinds of skin cancer.

WHY IS THERE AN INCREASED RISK OF CANCER FOR PATIENTS WITH PIDs?

This is not fully understood. Clinicians and researchers think this happens because the faulty immune response in PID fails to get rid of potentially cancerous cells before they grow into an established cancer or because these particular kinds of cancer may be caused, at least in part, by infections with viruses or bacteria which are not killed off effectively in someone who has a PID.

CAN DEVELOPMENT OF CANCERS IN PID BE AVOIDED?

In general no, because it isn't possible to tell in advance with any certainty who will, and who will not, get cancer. Your doctor may discuss with you 'risk factors' that are thought to have a role in cancer development and try to address these issues, but the value of doing this is not yet known. Some of these so-called 'risk factors' include getting rid of specific bugs from the stomach that might be associated with stomach cancer and avoiding exposure to large amounts of radiation in X-rays and scans, which is particularly relevant to conditions like ataxia telangiectasia.

It is possible that early treatment of the PID in some patients, before end-organ damage has occurred, may reduce the risk of cancer, but a greater understanding of the pathways responsible for this increased risk is needed. There is no underlying difference in the response to cancer treatment in patients with PID compared with non-immunodeficient patients. However, as patients with PIDs often have widespread tumours that require systemic cytotoxic therapy, which is poorly tolerated, there is an increased risk for infection and end-organ damage.

Patients can also play their part to decrease their general cancer risk by not smoking, drinking, having a healthy diet and avoiding sunburn.

SCREENING FOR AND TREATING CANCER IN PATIENTS WITH PID

Screening and early detection are the best preventive measures, just like for people without a PID. One of the reasons doctors see patients with a PID regularly is to examine them and perform routine blood test monitoring to detect cancer, or any risk factors for cancer, at as early a stage as possible. Patients with a PID should be screened for lymphoma and other cancer types associated with the particular PID that they have.

If cancer is detected, a multidisciplinary team comprising an immunologist and an oncologist (or an haematologist depending on the type of cancer involved) will ensure that timely and appropriate individualised treatment options are discussed, agreed and started, in the context of the ongoing management of the PID.

FURTHER INFORMATION AND SUPPORT

This booklet has been produced by the International Patient Organisation for Primary Immunodeficiencies (IPOPI). Other booklets are available in this series. For further information and details of PID patient organisations worldwide, please visit **www.ipopi.org**.

Provided by

IMMUNO DEFICIENCY UK

Supporting families affected by primary and secondary immunodeficiency

Immunodeficiency UK is a national organisation supporting individuals and families affected by primary and secondary immunodeficiency.

We are the UK national member of IPOPI, an association of national patient organisations dedicated to improving awareness, access to early diagnosis and optimal treatments for PID patients worldwide.

Our website has useful information on a range of conditions and topics, and explains the work we do to ensure the voice of patients with primary and secondary immunodeficiency is heard. If we can be of any help, please email us or call on the number above, where you can leave a message.

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