Hereditary Breast and Ovarian Cancer syndrome: *PALB2*
CARE PATHWAY

*The **Patient Clinical Pathway** is "the whole care pathway from identification, diagnostics, and multidisciplinary case discussions to surveillance and preventive surgery", so indeed a pathway in time, focusing on **HOW***

Periodic Review Recommended

Women with a heterozygous *PALB2* pathogenic variant face on average a high lifetime risk of breast cancer, (range between 30%-70%), and an increased risk of ovarian cancer, around 5% (range between 2.5-10%). Female carriers have an increased risk of second primary breast cancer.

Pancreatic cancer lifetime risk may be increased up to 3%. There is also some evidence that *PALB2* pathogenic variants may confer increased risk of male breast cancer and predispose specifically to aggressive prostate cancer.

All individuals identified as carriers of a pathogenic variant in *PALB2* should be offered genetic counselling early in their patient journey.

Periodic review should be undertaken by a specialist in *PALB2* (clinical geneticist and/or other physicians including oncologist, surgeon, gynaecologist). Surveillance should be continued if the person is in good health. Surveillance may depend on the level of the risk. Guidelines can differ in different EU countries. (Marmolejo et al, European Journal of Medical Genetics 2021, PMID 34606975)

HBOC-PALB2
Review Checklist—Adults (25+)

	WHAT TO LOOK FOR	WHEN TO REFER
BREASTS	Promote breast awareness: women should be familiar with their breasts and promptly report changes to their health care provider. Follow country-specific recommendations starting between age 25 and 30 years of age or starting 5-10y earlier than breast cancer in the family with yearly MRI of the breasts in women. Breast mammogram can also be used (in addition) starting from age 25-40 years. Addition of ultrasound should be considered if MRI is not possible or if requested by the radiologist. Information on the possibility of risk reducing mastectomy including the pros (decreased risk of cancer) and cons (surgical complications, cosmetic, sensitivity, etc). Discussion at multidisciplinary team consisting of at least a representative from clinical genetics, oncology, breast surgery and possibly also plastic surgeon, radiologist and gynaecologist.	In case of an abnormal mammography or MRI of the breasts and if signs or symptoms associated with breast cancer, refer to breast centre for investigation.

OVARIES	Information on prophylactic bilateral salpingo-oophorectomy (BSO) between 45 and 50 years (or earlier considering ovarian cancer history in first and second degree relatives) including the pros (highly reduced cancer risk) and cons (long- and short-term side effects). After individual case discussion depending on family history and (non-genetic) risk factors, BSO to be performed after menopause for *PALB2* carriers.	Refer to gynaecologist familiar with *PALB2* between the age of 45-50 years. Refer to diagnostic unit investigation if signs or symptoms associated with ovarian cancer.
PROSTATE	Follow country-specific recommendations as in some EU countries, men with a *PALB2* pathogenic variant may be offered PSA measurements every year from the age of 40-45 years.	Refer to urologist if PSA levels are increased. Refer to a diagnostic unit if signs or symptoms associated with prostate cancer.
PANCREAS	Preferably under a research protocol; Annual pancreatic surveillance with endoscopic ultrasound or MRI can be considered in *PALB2* carriers with family history, starting at age 50 years or 10 years before youngest onset in the family.	Refer to a diagnostic unit if signs or symptoms associated with pancreas cancer.
PSYCHOLOGICAL BURDEN	Despite a short-term increase in anxiety scores when a pathogenic variant is identified, most studies show a good emotional response at mid and long term.	Consider referral to an appropriate counselling service, if increased anxiety or difficulty to cope with the genetic condition.
PREGNANCY	Prenatal diagnosis is usually not requested. Pre-implantation genetic testing (PGT) is an option available in some European countries. PGT relies on pre-pregnancy genetic work up and that the family fulfils the requirements for IVF (e.g. adequate ovarian reserve). Testing of *PALB2* variants in partners of carriers is possible, especially if there is a positive family history or both may be somehow related.	Carriers (both male and female) who are planning pregnancy can be referred to clinical genetics, if reproductive counselling is requested.

Hereditary Breast and Ovarian Cancer (HBOC)
PALB2 Clinical Pathway

European Reference Network for rare or low prevalence complex diseases
Network Genetic Tumour Risk Syndromes (ERN GENTURIS)

Faculty: .....

Family name:

Given name(s)

Address:

Date of Birth: Sex: ☐ M ☐ F ☐ I

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HBOC *PALB2* Review Checklist — Adults 25+

Clinical Presentation:

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Other symptoms:

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Genetic counselling completed ☐

Date Completed: .....

Clinical diagnosis

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Genetic Test '+'ve ☐

Diagnosis Date: .....

General Health Check:

Please record the follow as soon as possible and then annually:

Height

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Weight

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Notes:

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Doctor: .....

Review date: .....

Faculty: .....

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