Your next steps

Find a specialist
All patients should be seen in a clinical genetics department or consultation.

Follow medical guidelines
Bi-annual review should be undertaken by a specialist. Surveillance meansures depend on the age.

Monitor symptoms
Keep track of new or changing health issues

Consider treatment options
Discuss available therapies and potential surgical interventions.

Stay updated on Constitutional Mismatch Repair Deficiency research
Clinical trials may offer new treatment or prevention possibilities.

Find a patient organisation
They can provide guidance and support.

Visit **www.genturis.eu** for medical guidelines and treatment centres.

About ERN GENTURIS

ERN GENTURIS is a European expert network for hereditary tumour syndromes. While we do not offer direct treatment, we provide patients and healthcare professionals with trusted information, guidance, and connections to specialists.

More info and contact

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European Reference Network

Funded by the European Union

Patient information

Constitutional Mismatch Repair Deficiency (CMMRD)

If you or a family member has been diagnosed with Constitutional Mismatch Repair Deficiency, this guide provides clear medical information and practical next steps.

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

ERN GENTURIS
With every diagnosis we can help an entire family

What is Constitutional Mismatch Repair Deficiency (CMMRD)

CMMRD is a very rare inherited condition that causes a very high risk of cancer. CMMRD is particularly associated specific brain tumours, blood cancers and bowel cancers with the first cancer diagnosed often already during childhood or young adulthood.
The risk of developing cancer is estimated to be over 90% by age 20, with the first tumour on average occurring around 7–8 years of age.
Many people with CMMRD also have non-cancerous features, such as café-au-lait skin patches and certain benign skin or brain changes.
Early diagnosis is important so that appropriate cancer treatment and surveillance as well as genetic counselling can be offered.

How is CMMRD inherited?

CMMRD is inherited in an autosomal recessive manner. A person has CMMRD when they inherited from each of their parents a copy of the same mismatch repair (MMR) gene that is each altered by a disease-causing variant. Hence, parents are, usually healthy, carriers of one altered gene copy. This condition is called Lynch syndrome and is associated with a lower cancer risk during adulthood with specific surveillance recommendations. If a child has CMMRD, their siblings may also be affected or may carry one altered copy of the gene. Genetic counselling and testing can help determine the risk for other family members.

What causes CMMRD?

CMMRD is caused by disease-causing variants in both copies of one of four MMR genes: *MLH1, MSH2, MSH6* or *PMS2*. In more than half of CMMRD cases, both copies of the *PMS2* gene are altered.

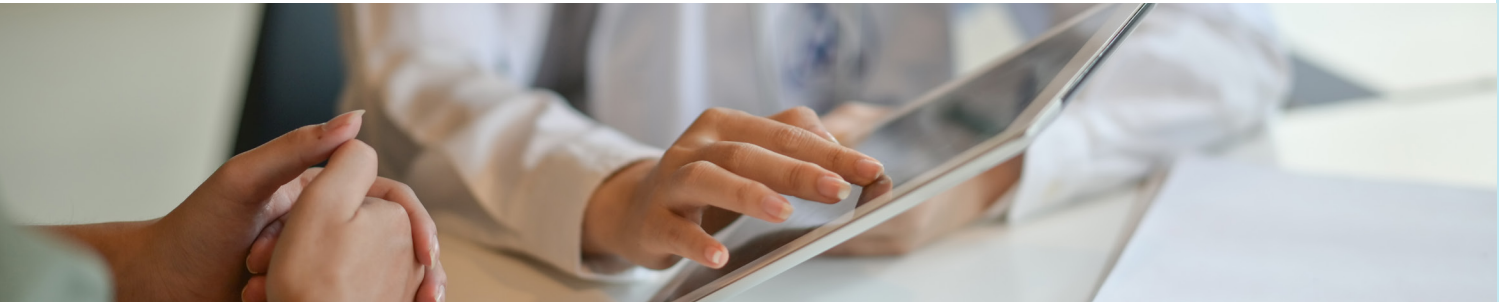
What are the diagnostic/ testing options?

Diagnosis may include: review of the patient's personal and family history; clinical examination for features associated with CMMRD; analysis of the tumour tissue; genetic testing of the *MLH1, MSH2, MSH6* and *PMS2* genes; constitutional microsatellite instability (C-MSI) testing when genetic testing is inconclusive.
Genetic counselling is recommended to explain the results and assess risks for family members.

What are the surveillance recommendations?

Because cancers can develop early, intensive and regular surveillance is recommended:

- Clinical examination: every 6 months from diagnosis.
- Brain MRI: every 6–12 months from at least 2 years of age.
- Ileocolonoscopy: every year from 6 years of age.
- Upper gastrointestinal surveillance: every year from 10 years of age.
- Additional examinations: may be recommended depending on individual risk, including surveillance for gynaecological and urinary tract cancers.



How this diagnosis affects you?

Receiving the genetic diagnosis CMMRD requires intensive medical supervision. Here are key points to consider:

How will CMMRD and the associated tumour risk impact your (your child's) health?

- The condition varies from person to person, but for all close medical surveillance throughtout life is crucial.
- Since CMMRD is genetic, family members should also consider genetic testing and surveillance.

What medical steps should I take?

- **Step 1:** Schedule an appointment with a specialist.
- **Step 2:** Discuss options for genetic testing of relatives.
- **Step 3:** Develop a personalised long-term surveillance plan with your (your child's) doctor.

ERN GENTURIS provides information and resources to help you understand this condition and guide your medical team toward the best possible care.

More information on **CMMRD:**