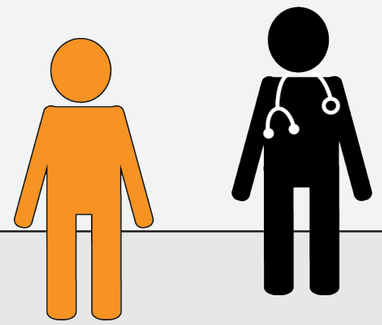
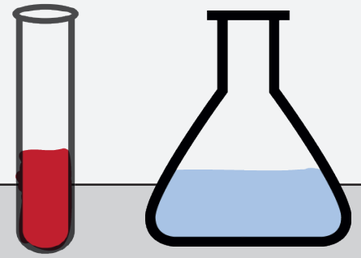
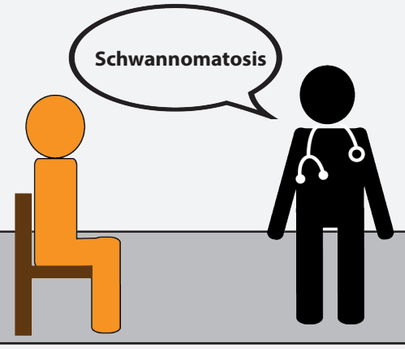
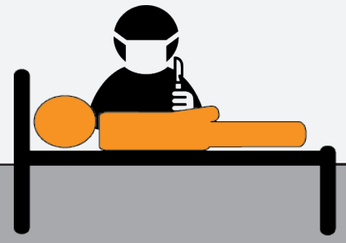
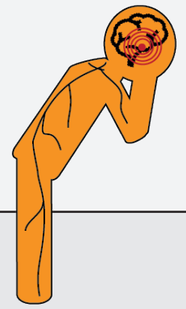
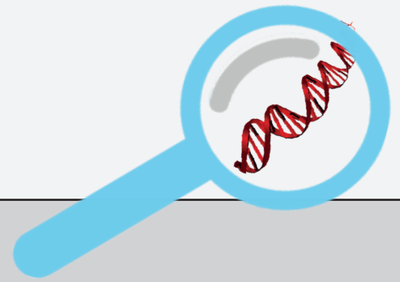
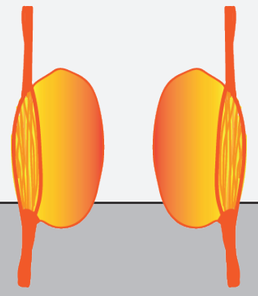
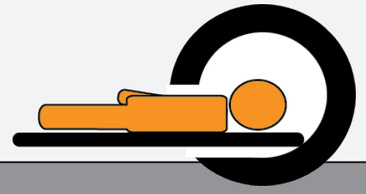
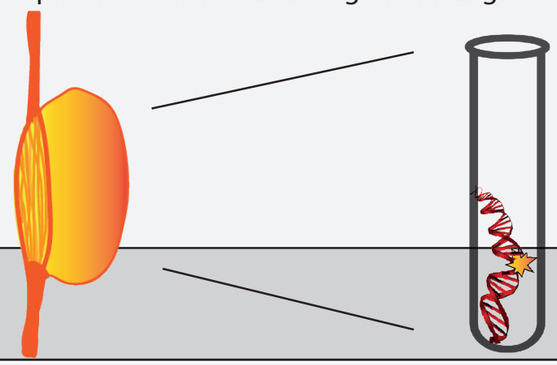
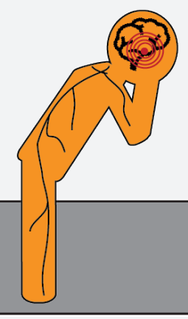
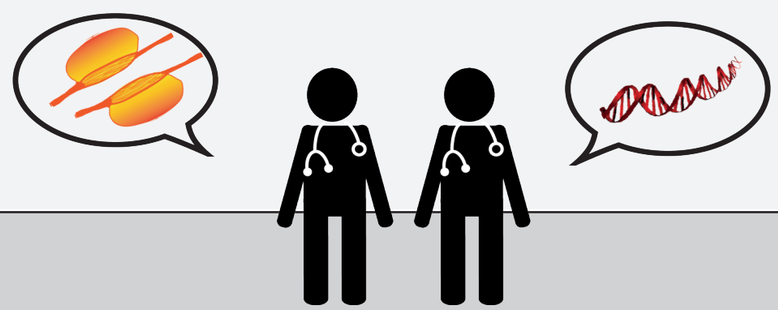
Patient Journey for non-*NF2*-related schwannomatosis

	1st symptoms	Pre-diagnosis	Diagnosis	Treatment	Follow-up
Disease					
Clinic	Neurological pain 	Currently only two genes identified: *SMARCB1* and *LZTR1* 	Diagnostic criteria 	Treatment and surgery 	Wait and scan 
Challenge	Awareness of non-*NF2*-related schwannomatosis 	Neoplastic tissue needed for genetic diagnosis 	Expert neurosurgeons 	Common treatment inefficient for neuropatic pain 	
Goal		Education of non-*NF2*-related schwannomatosis 		Increase quality of life 	

European Reference Network

Genetic Tumour Risk Syndromes (ERN GENTURIS)

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Patient Journey for non-*NF2*-related schwannomatosis

Disease

1st symptoms

Symptoms appear at >20 years of age
Hallmark: neuropathic pain
Other symptoms:
- Numbness
- Tingling
- Weakness
- Difficulty urinating or bowel dysfunction
- Facial weakness
- Headaches
- Vision changes
- Lumps or swollen areas under the skin

Pre-diagnosis

Mosaic schwannomatosis makes it hard to identify the underlying mutation in blood samples.

Not all schwannomatosis genes have been identified.

Diagnosis

Diagnosis is based on clinical features and molecular testing:
- MRI on brain, spine and peripheral nerves determines schwannomatosis diagnosis
- Pathology and histology confirm tumour type: schwannoma
- molecular testing on blood and frequently also on tumours

Diagnostic criteria

A diagnosis of *SMARCB1*- or *LZTR1*-related schwannomatosis can be made when an individual meets one of the following criteria:
- At least one pathologically confirmed schwannoma or hybrid nerve sheath tumour AND a SMARCB1 (or LZTR1) pathogenic variant in an unaffected tissue such as blood#.
- A common SMARCB1 or LZTR1 pathogenic variant in two schwannomas or hybrid nerve sheath tumours.

#if a likely pathogenic variant is identified, tumour analysis may aid upward classification.
See guideline on www.genturis.eu

Treatment

Neurosurgery or peripheral nerve surgery is the treatment of choice; only if necessary, based on:
- Position
- Volume
- Speed of growth

Often tumours are already too large or in a risky part of the nervous system, to be removed without iatrogenic consequences.

Follow-up

MRI of the brain and spine every two to three years beginning at age 12-14y.

For symptomatic patients a whole-body MRI examination at baseline, and increasing surveillance can be recommended with yearly clinical visits.

Need for **MRI radiologist** for tumour observation and management.

Clinic

Neurological pain

Schwannomas develop along the nervous roots and central nerves.
Neurological pain results from subcutaneous nodules, i.e. schwannomas, along peripheral nerves or spinal tumours.
Other symptoms of schwannomas, vary depending on the location and the volume of the tumour.

Currently only two genes identified: *SMARCB1* and *LZTR1*

Molecular diagnosis is hard:
- DNA blood tests are unreliable
- Two different Schwannomatosis genes have been identified: *SMARCB1* and *LZTR1*
- 50% of patients with clinical symptoms, that do not have a mutation in one of these two genes.

Treatment and surgery

Choice for surgery depends on:
- Position
- Volume
- Speed of growth

When a tumour cannot be removed or there is no immediate need to go through a risky surgery, there are non-operative treatment options:
- Observation
- Periodic imaging
- Pain management

Wait and scan

New tumours may develop throughout life. Wait and scan small tumours.

After each MRI risk of tumour versus risk of surgery are assessed based on:
- Position
- Volume
- Speed of growth

Challenge

Awareness of non-*NF2*-related schwannomatosis

Clinicians and GPs are aware of non-*NF2*-related schwannomatosis.

They know about their characteristics:
- presence of multiple schwannomas
- sometimes meningiomas
- sometimes unilateral vestibular schwannoma.

Since 2005 non-*NF2*-related schwannomatosis is officially recognised as a new entity.
Non-*NF2*-related schwannomatosis is very similar to *NF2*-related schwannomatosis.
Mild cases of *NF2*-related schwannomatosis require genetics test for the differential diagnosis.

Neoplastic tissue needed for genetic diagnosis

Genetic diagnosis is important for patients and their relatives.

To get a reliable genetic diagnosis, neoplastic tissue is mandatory.

Neurosurgeons should be aware of this need and should send resected neoplastic tissue for genetic testing.

Expert neurosurgeons

Need for expert neurosurgeons and specialised schwannomatosis centers

Good quality centers are realized in:
- -United Kingdom
- France
- Spain
- Germany.

In other countries care is not organised/specialised.
To go to a specialised neurosurgeon, patients have to go abroad and arrange their own funding.

All patients are entitled to good care and expert surgery.

Common treatment inefficient for neuropatic pain

Schwannomatosis patients experience neurological pain, which is resistant to common drugs.

Need for improved pain management.

Goal

Education of non-*NF2*-related schwannomatosis

Clinicians and GPs are educated on patients' signs and symptoms.
Quick referral to MRI – the gold standard for diagnosis.

Surgeons should be aware of the need of the genetic test on resected neoplastic tissues.
Genetic tests are positive for *SMARCB1* or *LZTR1* in less than 50% of the cases:
currently, not all schwannomatosis genes are identified.

Increase quality of life

More and effective options to relieve neurological pain.

Psychological follow-up to avoid depression, learn how to live with surgery sequels and to deal with uncertainty of disease evolution.

Social help for patient inclusion in society.

All of the above will improve quality of life.

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