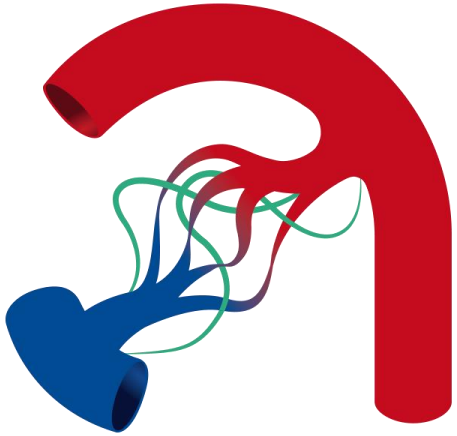
European Reference Network

for rare or low prevalence complex diseases

Network Vascular Diseases (VASCERN)



Kaposiform Hemangioendothelioma KHE

VASCERN VASCA working group Members

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Disclaimer

- This document is an opinion statement reflecting strategies put forward by experts and patient representatives involved in the Vascular Anomalies (VASCA) Rare Disease Working Group of VASCERN.
- It is preferable that patients be evaluated in a multidisciplinary centre specialized in the diagnosis and management of vascular anomalies.
- This pathway is issued on 20.11.2024 and will be further validated and adjusted as needed.
- Responsibility for care of individual patients remains with the treating physician.
- Multidisciplinary team should re-evaluate treatment decisions regularly.

Dieses Dokument wurde am 10.09.2025 von PD Dr. Friedrich Kapp für das Zentrum für Gefäßfhelbildungen (Uniklinik Freiburg) für das FZSE Freiburg geprüft und kommentiert. Eine gemeinsame Überprüfung und Diskussion wir unabhängig hiervon in der VASCA-WG erfolgen.

Kaposiform Hemangioendothelioma (KHE)
Diagnostic work-up: Overview

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VISIBLE LESIONS

Solitary firm tumour of the skin, soft tissue.
Red-purple tumours or plaques
Ill-defined margins, Ecchymosis with/without telangiectasia

NONVISIBLE LESIONS

Visceral KHE may be without superficial involvement
Patients may present with or without coagulation changes

Children under 1 year of age (90%)
Superficial / Deep (9:1)
Lateral Neck, Axilla, Groin, Extremities
Intrathoracic, Intra-abdominal, Retroperitoneal

KASABACH MERRIT PHENOMENON (KMP)
Severe thrombocytopenia (platelet count <50 x 10^9/L),
Consumptive coagulopathy [hyperfibrinogenaemia (fibrinogen<1.6 g/L) and elevated D-dimer (>0.5 µg/ml)]

→ Tumour becomes purpuric, warm on palpation, sudden increases in size and painfulness
Petechiae appear elsewhere

- Blood tests: check for severe thrombocytopenia and coagulopathy (KMP)
- Doppler ultrasound: ill-defined vascular tumour
- Contrast enhanced MRI: first assessment of size and infiltration of structures, follow-up during therapy

- Biopsy for confirmation of the diagnosis is recommended, especially in cases **without** KMP
- Additional procedures, if necessary to rule out differential diagnoses

LEGEND: Clinical evaluation | Investigations

Kaposiform Hemangioendothelioma (KHE)
Diagnostic work-up: differential diagnoses and histological features

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VISIBLE LESIONS

Tufted angioma
Congenital haemangioma
Kaposiform lymphangiomatosis
Malignant tumours (e.g. congenital fibrosarcoma, rhabdomyosarcoma, rhabdoid tumour, neuroblastoma)
Venous malformation

KMP and NO VISIBLE LESION

Leukaemia
Sepsis
Immunthrombocytopenia (ITP)
Other causes of DIC

Histological features

Infiltrating, ill-defined, rounded and confluent nodules, composed of spindled endothelial cells, forming channels and slit-like lumina containing erythrocytes, along with platelet thrombi, eosinophilic hyaline bodies, red-cell extravasation and hemosiderin deposits
KHE lesions are positive for CD31, CD34, VEGFR3, D2-40, LYVE-1 and PROX-1.
Negative for GLUT-1

KHE and Tufted angioma are part of the same clinicopathological spectrum

No characteristic somatic genetic signature has yet been identified. Biopsy for somatic mutations if biopsy indicated or safely feasible

LEGEND: Diff. Diagnosis | Histological features | Associated Genes

Kaposiform Hemangioendothelioma (KHE)
Management and treatment

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Kommentar FK 09/2025:Behandlung sollte an einem kinderonkologischen Zentreum erfolgen, Rücksprache mit einem Referenzzentrum für Gefäßanomalien sollte gehalten werden.

KHE

+ KMP

Management to be discussed and performed in a reference center

Provide contact to (inter)national patient support group

Yes

No

Large lesion, disfigurement and/or functional consequences

No

Watchful waiting
Consider Surgery If complete, without mutilations

Yes

Sirolimus
consider adding corticosteroids

Failure of response

Add vincristine

Failure of response

Consider:
- Embolization
- Surgery
- Adding cyclophosphamide

Sirolimus + corticosteroids

If compression of vital structures is present, or
response to initiated therapy insufficient

Response monitoring
- Clinical follow up
- Laboratory: blood counts, coagulation profile
- Imaging: MRI-volumetry and response assessment

The timing for the response monitoring should be **individualized** based on the location and clinical course of the lesion

Tapering of the therapy, if response sufficient
- when KMP resolves, taper and stop corticosteroids
- when lesion shrinks, stop vincristine
- when KHE becomes inactive over several months, slowly taper sirolimus: duration of therapy is unclear

LEGEND: Clinical evaluation | Treatment | Investigations

Kaposiform Hemangioendothelioma (KHE)
Management and treatment

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Treatment options

Medical treatments

First line:
Sirolimus
Corticosteroids

Second line/additive:
Vincristine

Third line:
Other chemotherapeutic agents (e.g. cyclophosphamide)
Re-evaluate differential diagnoses

Supportive treatment of KMP

Should involve haematologist
Fibrinogen, FFP
Platelet transfusions should be avoided
Aspirin* Ticlopidine* (often used but without evidence)

In case of failure of medical treatment consider:

- **Interventional radiology**
  Embolization (performed in a reference Center)
  +/- medical treatment or before surgery
- **Surgery**
  If complete resection without mutilation is feasible (rare) (performed in a reference centre)

Recommended doses

Sirolimus
Target blood concentration: 5-10 ng/ml
Standard doses:
Neonates and infants need a dose reduction e.g. to 2x 0.25 mg/m²/d, depending on age
Children 2x 0.8 mg/m²/d

Vincristine
Per institutional guideline, dosing in mg/kg or mg/m² depending on age and body weight. Dose reduction in neonates, infants and in children with low body weight

Corticosteroids
Prednisolone 2 mg/kg/d (oral)

*** used in KMP treatment protocols at some institutions, yet poor evidence in the literature and platelet function is already reduced in KMP.**

Kaposiform Hemangioendothelioma (KHE)
Management and treatment: Recurrence/Sequelae

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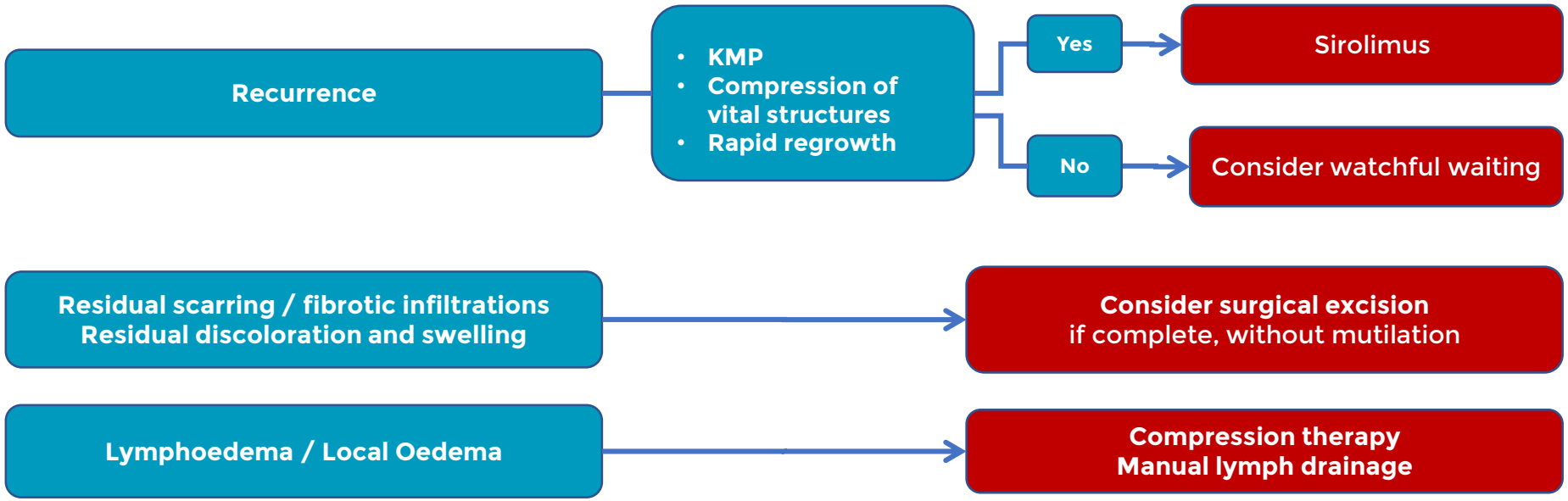
Long-term follow-up
Patients should be followed clinically (with or without MRI studies, depending on KHE location and symptoms)
Watch for:
- **Recurrence**
- **Local sequelae (e.g. scarring, fibrosis, lymphedema)**



LEGEND: Clinical evaluation | Treatment | Investigations

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Gathering the best expertise in Europe
to provide accessible cross-border healthcare
to patients with rare vascular diseases

VASCERN, the European Reference Network on Rare Multisystemic Vascular Diseases, is dedicated to gathering the best expertise in Europe in order to provide accessible cross-border healthcare to patients with rare vascular diseases (an estimated 1.3 million concerned). These include arterial diseases (affecting aorta to small arteries), arteriovenous anomalies, vascular malformations, and lymphatic diseases.

VASCERN currently gathers 48 expert teams from 39 highly specialized multidisciplinary HCPs, plus 6 additional Affiliated Partner centres, coming from 19 EU Member States, as well as various European Patient Organisations, and is coordinated in Paris, France.

Through our 6 Rare Disease Working Groups (RDWGs) as well as several thematic WGs and the ePAG (European Patient Advocacy Group), we aim to improve care, promote best practices and guidelines, reinforce research, empower patients, provide training for healthcare professionals and realise the full potential of European cooperation for specialised healthcare by exploiting the latest innovations in medical science and health technologies.

More information available at: www.vascern.eu

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