



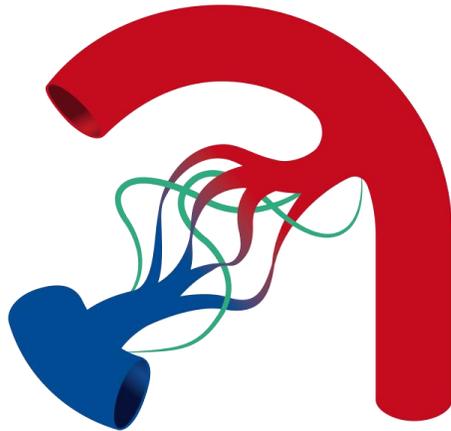
**European
Reference
Network**

for rare or low prevalence
complex diseases



Network

Vascular Diseases
(VASCERN)



Kaposiform Hemangioendothelioma KHE

VASCERN VASCA working group Members

Paolo Gasparella, Emir Haxhija, Rune Andersen, Maria Barea, Eulalia Baselga, Miguel Bejarano Serrano, Sigurd Berger, Petra Borgards, Annouk Anne Bisdorff, Olivia Boccara, Maria Bom Sucesso, Laurence M Boon, Anca Maria Cimpean, Andrea Diociaiuti, Veronika Dvorakova, May El Hachem, Sofia Frisk, Nader Ghaffarpour, Annegret Holm, Alan D Irvine, Mikkel Kaltolf, Friedrich G Kapp, Olga Koskova, Kristiina Kyrklund, Miguel Madureira, Darius Palionis, Przemysław Przewratil, Bitten Schönewolf-Greulich, Maria-Corina Stanciulescu, Jaroslav Štěrba, Jukka Tolonen, Birute Vaisnyte, Carine van der Vleuten, Dariusz Wyrzykowski, Leo Schultze Kool, Miikka Vikkula

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.

Kaposiform Hemangioendothelioma (KHE) Diagnostic work-up: Overview

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 $<50 \times 10^9/L$),
 Consumptive coagulopathy [hyperfibrinogenaemia (fibrinogen $<1.6 \text{ g/L}$) and elevated D-dimer ($>0.5 \mu\text{g/ml}$)]

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

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

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

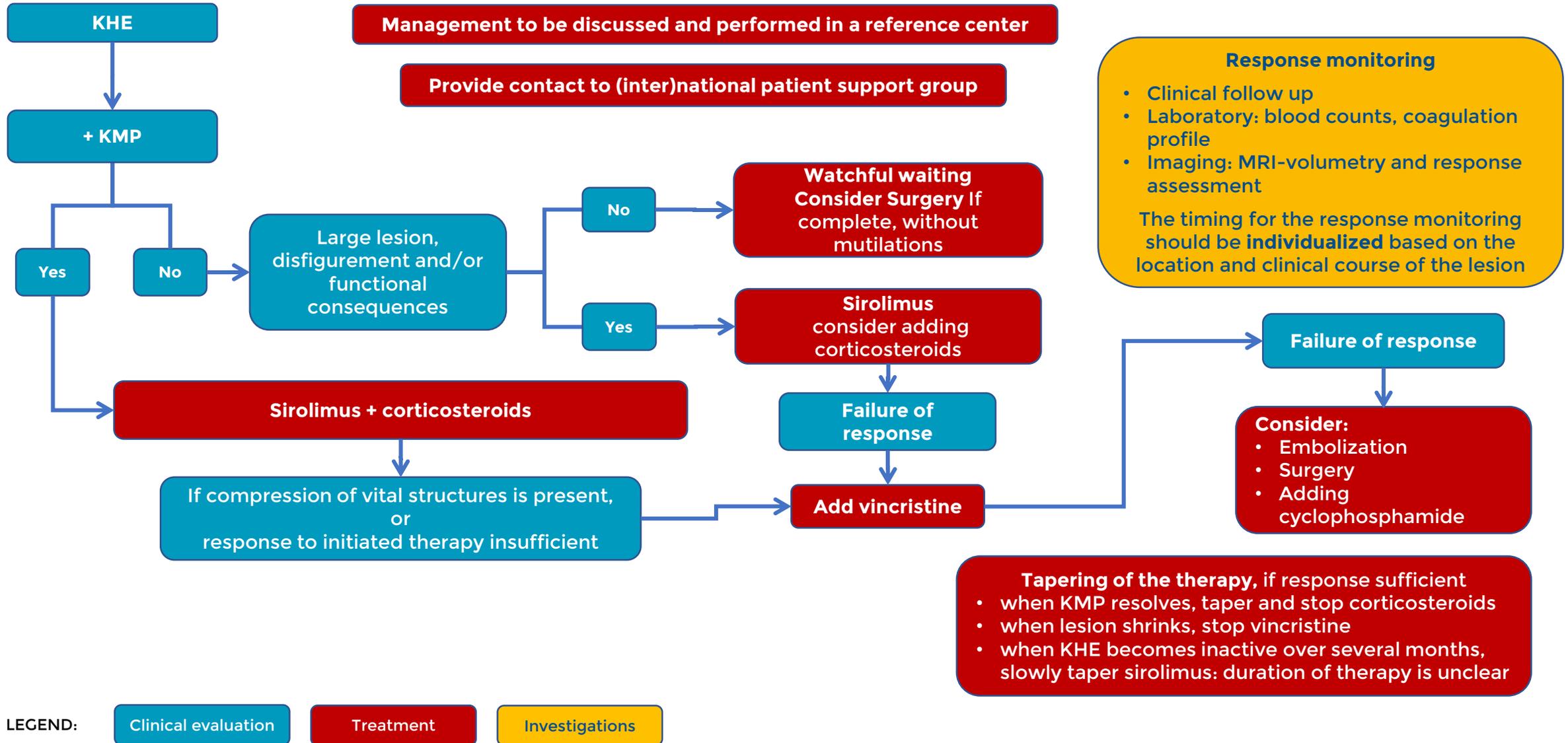
Histological features

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

Kaposiform Hemangioendothelioma (KHE) Management and treatment



Kaposiform Hemangioendothelioma (KHE) Management and treatment

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

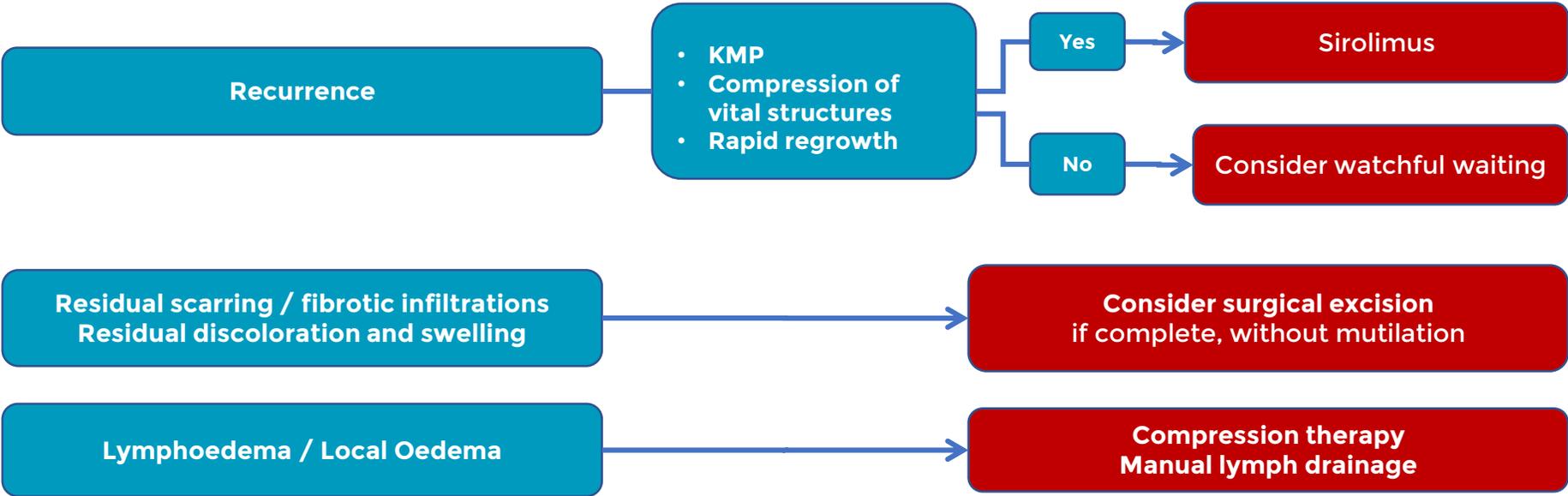
Prednisolone 2 mg/kg/d (oral)

* 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

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



European
Reference
Network

VASCERN

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

Follow us on



Co-funded by
the Health Programme
of the European Union