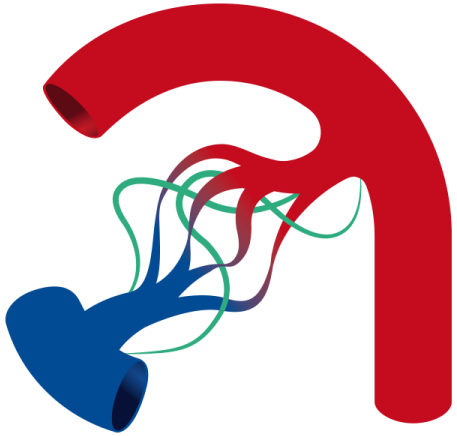
European Reference Network

for rare or low prevalence complex diseases

Network Vascular Diseases (VASCERN)



#VASCERNdays2020

9.45-10.00 coffee break

10.00-11.00
Work Packages

10.00-10.35
Implementation (7' per RDWG Chair)

HHT - Claire Shovlin
HTAD - Julie De Backer
MSA - Leema Robert
PPL - Robert Damstra
VASCA - Miikka Vikkula

10.35-11.00 Q&A, sharing best practices & inter-RDWGs projects

11.00-11.15 Q&A and approval by the Board

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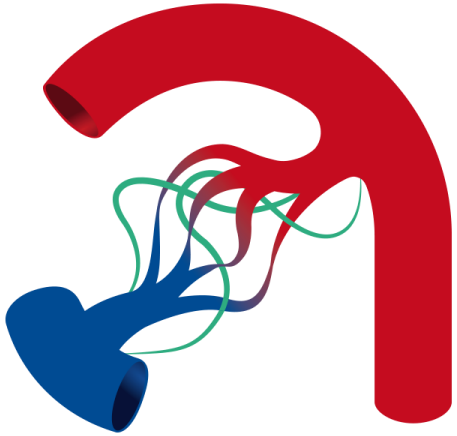


Vascern HHT WG

Claire Shovlin
HHT WG Chair

European Reference Network | Vascular Diseases (VASCERN)

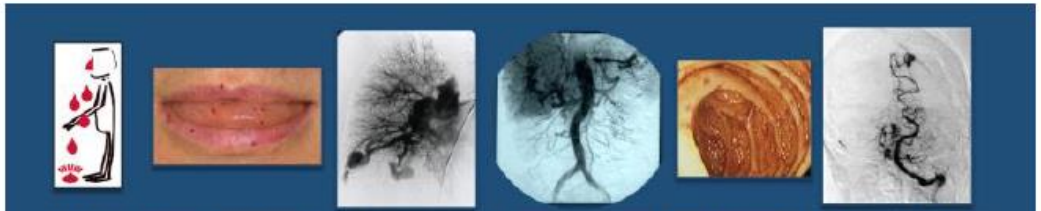
CLS/28.02.2018

Hereditary haemorrhagic telangiectasia (HHT)

- **Affects >85,000 European citizens**
- **Cause of preventable**
  - -Anaemia/blood transfusions
  - -Brain abscess (1 in 16 cases at VASCERN centres)
  - -Ischaemic Strokes (>1 in 8 referrals)
  - -Heart failure
  - -Maternal death in pregnancy (1% of pregnancies)
  - -Venous thromboemboli (VTE)

- **Most cases undiagnosed**
- **Best care demands**
  - -Diagnosis (including by screening)
  - -Nosebleed and pregnancy advice
  - -Iron deficiency anaemia management
  - -Access to multisystemic interventions
  - -Long-term, complex medical care
  - -Wise application in adult and paediatric medicine

VASCERN-HHT Year 1 Impact *(established 9th March 2017)*



HHT, an inherited multisystemic vascular dysplasia that leads to nosebleeds, anaemia due to blood loss, and arteriovenous malformations (AVMs) in organs such as the lungs, liver and brain.

HHT WG Meeting # 8, Paris 14.10.2017
12 monthly telecons; more than 1,000 emails

First, a reminder of what we had achieved by the 2019 VASCERN Days

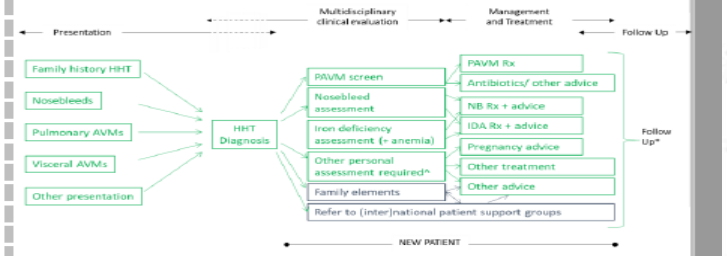
VASCERN-HHT Year 1 Outputs

- Patient pathway defined and revised
- Priorities defined by 61 patients/professionals
- Drug Registry designed and first data published
- 5 Outcome Measures defined and applied
- 11 cross-border clinical cases discussed
- 1 Guideline (Clinical Statement) produced*
- 13 Do's and Don'ts for General Care produced
- 8 research projects with >1 VASCERN HHT centre
- 2 YouTube Videos (published online 2018)
- 2 Educational workshops (published 2017)

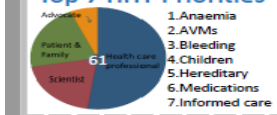
in addition to VASCERN members' existing activities, e.g.

- 3 HHT clinical trials completed/in progress (Dupuis Girod)
- 17 PubMed-publications; >40 research projects

HHT Patient Pathway



Top 7 HHT Priorities



1.Anaemia
2.AVMs
3.Bleeding
4.Children
5.Hereditary
6.Medications
7.Informed care

HHT Drug Registry

- Separate questions for patients, scientists and doctors
- Prioritised antiangiogenic drugs **Thalidomide** and **Bevacizumab (BZB, Avastin)**
- >100 patient responses in review

HHT Outcome Measures

Population		Outcome Measure	Target
HHT (clinical or molecular diagnosis)	1	Screen for pulmonary AVMs	≥ 90%
	2	Receive nosebleed advice in writing	≥ 90%
	3	Assessment of iron deficiency at each consultation	≥ 70%
Pulmonary AVMs (PAVMs)	4	Receive written advice on antibiotic prophylaxis prior to dental and surgical procedures	100%
HHT or PAVMs, and pregnant	5	Receive written advice on PAVM/HHT pregnancies	100%

The metrics identify healthcare providers of good care and encourage care improvement by all healthcare providers details in Guidance Statement- *manuscript in review, Feb 2018*

HHT Do's and Don'ts

1. Physical Activity
2. Breast feeding
3. Contraindicated medications
4. Antiplatelets/ anticoagulants
5. Venous thromboemboli (VTE)
6. Haemorrhagic stroke
7. Brain abscesses:
8. Heart failure
9. Kidney failure
10. Multiple traumatic injuries
11. Bronchoscopies
12. Aortic dissection
13. Pneumothorax

For publication, March 2018
>15 more in preparation, 2018

Other 2017-8 Formal HHT Education

YouTube Minipills of Knowledge (5 minute videos)

An Overview of Hereditary Haemorrhagic Telangiectasia (SHOVLIN) https://youtu.be/z2gALD8xSNE
An introduction to HHT explaining aetiology and main features.
What an ENT doctor needs to know about HHT and why (KJELDSEN) https://youtu.be/k2V92g87NhE

12th HHT International Conference Dubrovnik, June 2017

Workshop on Management of Hepatic AVMs (DUPUIS GIROD & BUSCARINI),
Workshop on Inflammation, Immunity and Injury in HHT (SHOVLIN & BOTELLA)
VASCERN HHT PRIORITY EVALUATIONS 2016-2017 (SHOVLIN ET AL ON BEHALF OF THE VASCERN-HHT WORKING GROUP)
VASCERN HHT Survey 2: drug registry part 1 (BUSCARINI ET AL ON BEHALF OF THE VASCERN-HHT WORKING GROUP)
https://www.ncbi.nlm.nih.gov/pubmed/29147802

Core Values:

- "Patient first, Safety First"
- "Combining evidence and experience to work together"

Pan-VASCERN-specific investment

(excludes local HCP activity eg patient reviews, ERN application)
>500 hours by Board (Shovlin, Dupuis Girod, Buscarini)
>150 hours by the Leads of the 5 other HHT WG Centres
(Note the still very small number of clinical experts)

VASCERN-HHT Year 2-3 Outputs

VASCERN HHT OUTPUT

ORPHANET DEFINITION:
Hereditary haemorrhagic telangiectasia
www.orpha.net/consor/www/cgi-bin/OC_Exp.php?lng=EN&Expert=774

MANUSCRIPT:
European Reference Network For Rare Vascular Diseases (VASCERN) Outcome Measures For Hereditary Haemorrhagic Telangiectasia (HHT).
Orphanet J Rare Dis. 2018;13(1):136.
https://ojrd.biomedcentral.com/articles/10.1186/s13023-018-0850-2 *(1,373 accesses)*

MANUSCRIPT:
Safety of direct oral anticoagulants in patients with hereditary hemorrhagic telangiectasia
Orphanet J Rare Dis. 2019 Aug 28;14(1):210.
https://ojrd.biomedcentral.com/articles/10.1186/s13023-019-1179-1 *(1,143 accesses)*

MANUSCRIPT:
Safety of thalidomide and bevacizumab in hereditary hemorrhagic telangiectasia.
https://ojrd.biomedcentral.com/articles/10.1186/s13023-018-0982-4 *(424 accesses)*

MANUSCRIPT:
Prevention of serious infections in hereditary hemorrhagic telangiectasia: roles for prophylactic antibiotics, the pulmonary capillaries-but not vaccination.
http://www.haematologica.org/content/104/2/e85.long *(360 accesses)*

3rd pill of knowledge
HHT from VASCERN HHT: An Introduction to Hereditary Haemorrhagic Telangiectasia
https://www.youtube.com/watch?v=0YjWf7Agn40&feature=youtu.be *(543 views)*

And preparing Year 4 Outputs

<u>>1,200 views for each of our three HHT videos, >12,000 views combined</u>

- **An Overview of Hereditary Haemorrhagic Telangiectasia** https://youtu.be/z2gALD8xSNE **(9,067 views *since* 23 Jan 2018 upload)**
- **What an ENT doctor needs to know about HHT and why** https://youtu.be/k2V92g87NhE **(2,274 views *since* 23 Jan 2018 upload)**
- **HHT from VASCERN HHT: An Introduction to Hereditary Haemorrhagic Telangiectasia** **(1,329 views *since* 8 March 2019 upload)**
  https://www.youtube.com/watch?v=0YjWf7Agn40&feature=youtu.be

2020 A: REGISTRY PREPARATION: SELECTION OF CIROCCO

HCP	Approximate number of cases – on existing HCP database	Local / Web	Funding for extra workload to import to CIROCCO	Consent for upload to European platform	Likelihood of obtaining consent
Lyon	5-6,000	Web	Yes (to modify the database)		
London	>2,000 HHT/PAVM	Local	No	No	Unknown
Crema	~1,300	Local	No	No	Low
Bari	800	Local	No	No	Unknown
Essen	>300	Local	no	no	unknown
Odense	600	Web	No	No	Low to zero
St Antonius	~3,000 including controls	Local	No	Maybe	Unknown

2020 B: COVID-19 Statement, March 2020

European Reference Network
for rare or low prevalence complex diseases
Network Vascular Diseases (VASCERN)

Hereditary haemorrhagic telangiectasia (HHT)

/

VASCERN HHT Statement on COVID-19

A statement from the European Reference Network for Rare Multisystemic Vascular Diseases (VASCERN) for people with hereditary haemorrhagic telangiectasia (HHT) and their doctors:

1. **People with HHT should follow the standard Public Health Measures as recommended in their specific country.**
   - 1.1. These are directed at reducing the spread of infection, and strategies differ slightly between countries.

2. **People with HHT should be no more and no less concerned about COVID-19 than the general population without HHT.**
   - 2.1. There is no reason to think people with HHT [1] will be at higher or lower risk of infection [2,3] , or complications if they become infected.
   - 2.2. Some people with HHT, as for some people in the general population, may be less able to tolerate the extra demands placed on their bodies if they suffer infection with complications, but this will be a small group and should not be applied to all HHT patients.

3. **The presence of HHT or AVMs in someone who currently has a normal or high exercise tolerance should not limit their access to medical treatment compared to someone without HHT or AVMs of the same age.**
   - 3.1. People with HHT have normal life expectancy managed in Europe,[4,5] likely attributed to the beneficial effects of reduced cancer, reduced rates of cancer [4,6,7] and fewer heart attacks [8]
   - 3.2. Anyone with normal or high exercise tolerance (able to walk uphill quite briskly without stopping) will have good cardiorespiratory reserve [9,10].

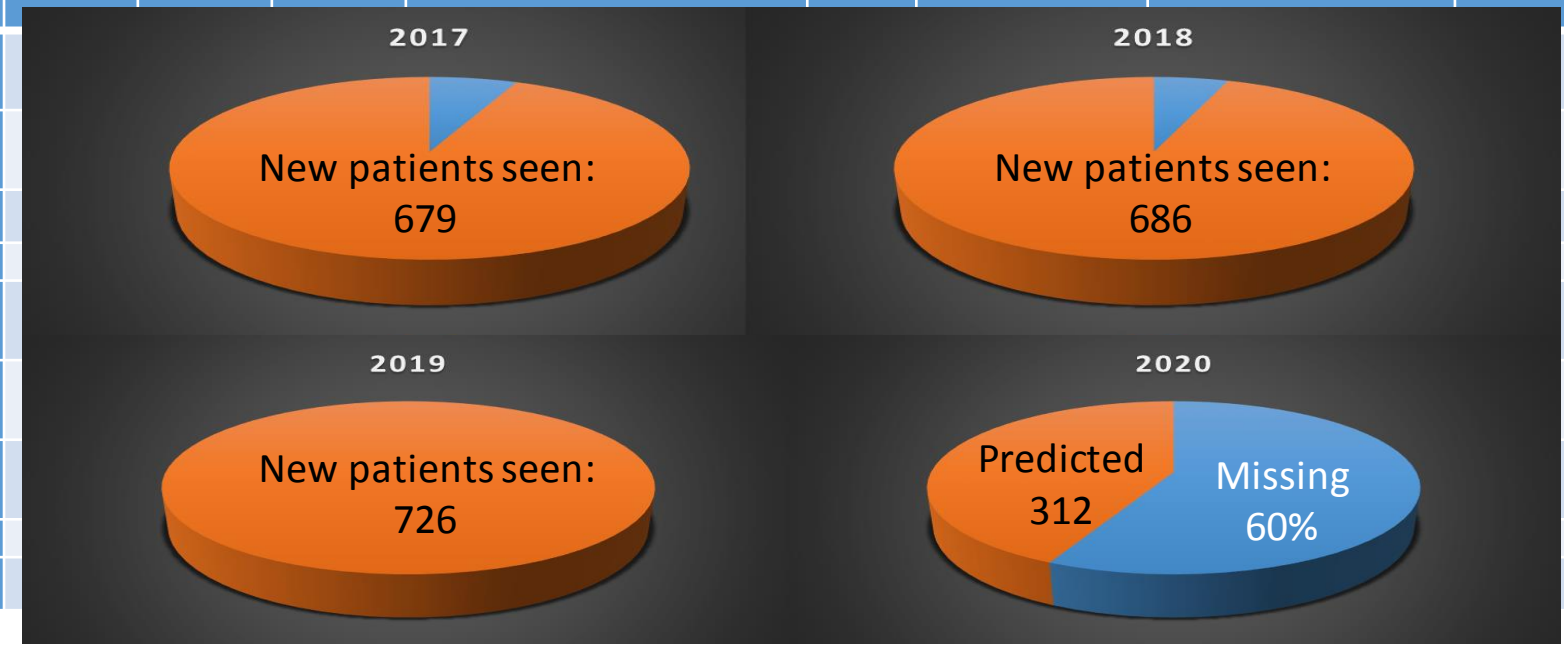
4. **For those who are obliged to self-isolate because of the general situation**
   - 4.1. Maintain normal treatment regimes if possible. **It is very important that iron supplements for anaemia are continued.**
   - 4.2. Avoid sedentary states- exercise is recommended as discussed further for the general population [11]

AUTHORS:
Claire L. Shovlin, Carlo Sabba, Hans Jurgen Mager, Anette Kjeldsen, Ulrich Sure, Elisabetta Buscarini and Sophie Dupuis-Girod
VASCERN HHT Centre Leads in Denmark, France, Germany, Italy, the Netherlands and the UK, on behalf of VASCERN HHT

During the current epidemic, reference centres may be unable to perform elective diagnostic/therapeutic procedures for people with HHT but they continue to assist urgent/emergency presentations

A reminder of the devastation wrecked by COVID-19 on the HHT WG HCPs……

	2017	2018	2019	2020 estimate	2020 est. no	Period with no new cases	Now able to see new cases?	Usual patient willingness to be seen	Clinical research
Odense University Hospital								No	Yes
University Hospital Essen								No	Yes
Azienda Ospedaliero-Universitaria								No	No
Maggiore Hospital, ASST Crema								No	No
Hammersmith Hospital, Imperial College Healthcare NHS Trust London								No	No
St. Antonius Hospital								No	Yes
Hospices Civils de Lyon								No	Yes
OVERALL									



2020 C: Neurovascular-led Position Statement on cerebral screening in HHT

Eker *et al. Orphanet Journal of Rare Diseases* (2020) 15:165
https://doi.org/10.1186/s13023-020-01386-9

Orphanet Journal of Rare Diseases

POSITION STATEMENT Open Access

European Reference Network for Rare Vascular Diseases (VASCERN) position statement on cerebral screening in adults and children with hereditary haemorrhagic telangiectasia (HHT)

Omer F. Eker[1*], Edoardo Boccardi[2], Ulrich Sure[3], Maneesh C. Patel[4], Saverio Alicante[5], Ali Alsafi[4], Nicola Coote[4], Freya Droege[3], Olivier Dupuis[1], Annette Dam Fialla[6], Bryony Jones[4], Ujwal Kariholu[4], Anette D. Kjeldsen[6], David Lefroy[4], Gennaro M. Lenato[7], Hans Jurgen Mager[8], Guido Manfredi[5], Troels H. Nielsen[6], Fabio Pagella[9], Marco C. Post[8], Catherine Rennie[4], Carlo Sabbà[7*], Patrizia Suppressa[7], Pernille M. Toerring[6], Sara Ugolini[9], Elisabetta Buscarini[5*], Sophie Dupuis-Girod[1] and Claire L. Shovlin[10*]

European Reference Network
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Network Vascular Diseases (VASCERN)

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First, we summarised the published literature on prevalence and bleeding risk in 6 different types of vascular abnormalities encountered in people with HHT, and in general population.
- See Eker et al OJRD 2020 Table 2

Second, the neurosurgical and neurovascular intervention Lead authors provided a discussion on the treatments available, including risks and benefits.

Third, we summarised published and unpublished data from across the VASCERN HCPs, including genotype distinctions, and according to how the vascular abnormalities were classified
-See Eker et al OJRD 2020 Table 3

Fourth we generated statements with 100% consensus from the VASCERN HHT Clinicians:

At least 6 of the 8 HCP Leads were able to share not only academic experience but also decades of discussing these critical decisions with patients
- Individually (hundreds per HCP Lead), and
- at Patient Meetings.

This enormously wide experience was what allowed 100% consensus to be reached amongst the HHT clinicians.

European Reference Network
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1. If neurological symptoms, or malformation found accidentally → Manage as in general neurological and emergency care

2. The current evidence base does not favour the treatment of unruptured AVMs → Cannot be used to support widespread screening of asymptomatic patients

3. Individual situations and conflicting advice from non neurovascular experts → All HHT patients should have the opportunity to discuss knowingly brain screening issues with their HHT healthcare provider, including informed choice of scan

4. Before any scan, informed, pre test review of the latest evidence →
a) Regarding potential efficacy
b) Explicitly stating possibility of harm
due to detection of, or intervention on, a vascular malformation that would not have caused any consequence later in life.

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Fifth and finally, we summarised current practice across the ERN HCPs:

	ADULT SCREEN		ANTE/NEONATAL SCREENS a	
HHT Centre *Country*	**Discuss**	**Perform**	**Discuss**	Perform
Bari *Italy*				
Crema *Italy*				
Essen *Germany*		69.80%		
London *UK*	c	8.1% (49/603) [20]		
Lyon *France*				
Nieuwegein *Netherlands*		80-90% HHT1, ~50% HHT2		
Odense *Denmark*				
Pavia *Italy*				

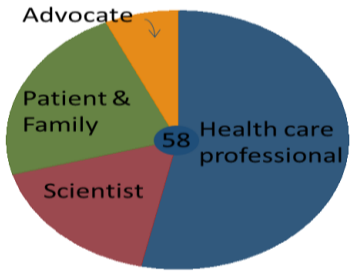
More Homogeneous than people think

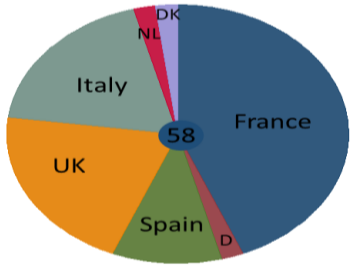
Huge difference between discussing for all and recommending a screening scan to all

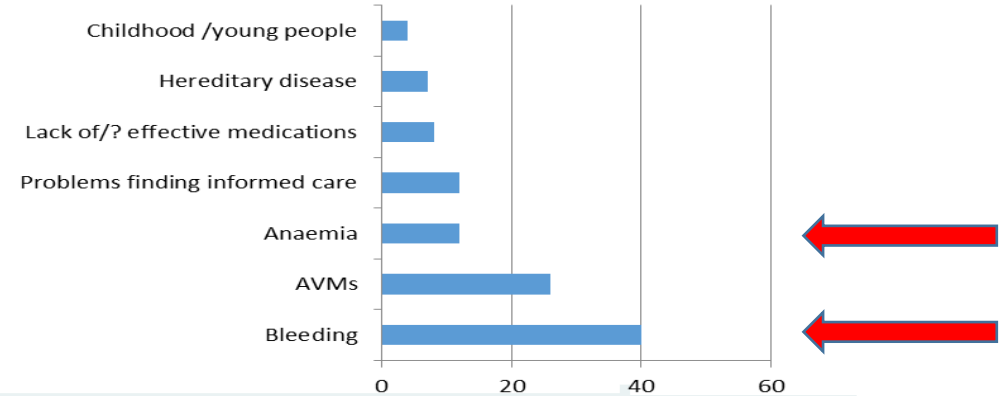
Fig. 1 Current screening practices across the eight VASCERN HHT Centres. Proportions of the cohorts where screening is discussed and performed. 4 colour codes represent 4 broad percentage ranges: Black 90–100%; dark grey 50–90% (adult columns 1 and 2); mid grey 10–50%, light grey < 10%. **a** in addition to population-wide, country specific antenatal screening programmes. **b** Pregnancies are an indication for antenatal screening and transfontanellar Doppler US in perinatal period; MR is discussed on the basis of familial history. **c** as per protocol in [20]. **d** In any setting, discuss first, and have an open door policy for imaging if things change. Aiming too for prenatal scan support. Under 3 months, as no general anaesthetic required for MR, use "feed and wrap"

2020 D: Six HCP LEADS and ePAG CoCHAIR PARTICIPATED IN INTERNATIONAL HHT GUIDELINES

Topics in keeping with our 2017 Survey:

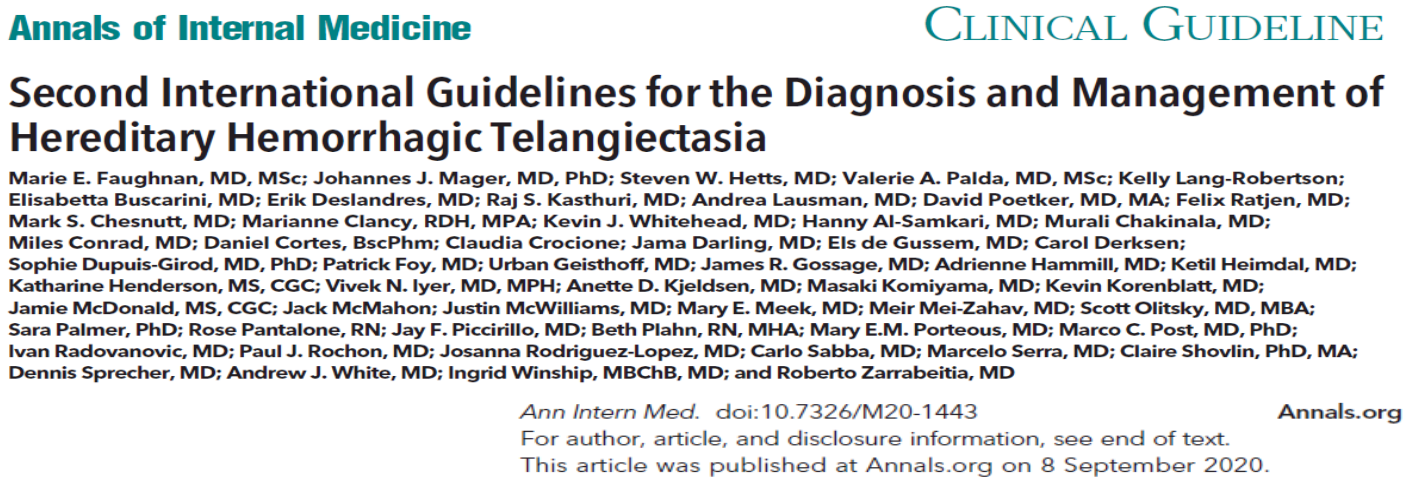






2nd International HHT Guidelines Topics, and VASCERN representation on each panel:

- Nosebleeds (epistaxis) *Geisthoff (D)*
- GI bleeding Sabba (I)
- Anaemia Shovlin (UK)
- Hepatic AVMs Buscarini (Italy, Chair)
- Children Mager (NL, Chair)
- Pregnancy Dupuis Girod (F)
  Crocione (ePAG)



Annals of Internal Medicine

CLINICAL GUIDELINE

Second International Guidelines for the Diagnosis and Management of Hereditary Hemorrhagic Telangiectasia

Marie E. Faughnan, MD, MSc; Johannes J. Mager, MD, PhD; Steven W. Hetts, MD; Valerie A. Palda, MD, MSc; Kelly Lang-Robertson; Elisabetta Buscarini, MD; Erik Deslandres, MD; Raj S. Kasthuri, MD; Andrea Lausman, MD; David Poetker, MD, MA; Felix Ratjen, MD; Mark S. Chesnutt, MD; Marianne Clancy, RDH, MPA; Kevin J. Whitehead, MD; Hanny Al-Samkari, MD; Murali Chakinala, MD; Miles Conrad, MD; Daniel Cortes, BscPhm; Claudia Crocione; Jama Darling, MD; Els de Gussem, MD; Carol Derksen; Sophie Dupuis-Girod, MD, PhD; Patrick Foy, MD; Urban Geisthoff, MD; James R. Gossage, MD; Adrienne Hammill, MD; Ketil Heimdal, MD; Katharine Henderson, MS, CGC; Vivek N. Iyer, MD, MPH; Anette D. Kjeldsen, MD; Masaki Komiyama, MD; Kevin Korenblatt, MD; Jamie McDonald, MS, CGC; Jack McMahon; Justin McWilliams, MD; Mary E. Meek, MD; Meir Mei-Zahav, MD; Scott Olitsky, MD, MBA; Sara Palmer, PhD; Rose Pantalone, RN; Jay F. Piccirillo, MD; Beth Plahn, RN, MHA; Mary E.M. Porteous, MD; Marco C. Post, MD, PhD; Ivan Radovanovic, MD; Paul J. Rochon, MD; Josanna Rodriguez-Lopez, MD; Carlo Sabba, MD; Marcelo Serra, MD; Claire Shovlin, PhD, MA; Dennis Sprecher, MD; Andrew J. White, MD; Ingrid Winship, MBChB, MD; and Roberto Zarrabeitia, MD

Ann Intern Med. doi:10.7326/M20-1443 Annals.org
For author, article, and disclosure information, see end of text.
This article was published at Annals.org on 8 September 2020.

2020 E: Other highlights

Despite COVID

We managed a further 7 meetings in first 10 months of 2020

Meeting number	Date
#34	27th January 2020
#35	28th February 2020
#36	20th March 2020
#37	2nd June 2020 – *in place of Face to Face in Lyon*
#38	24th July 2020
#39	25th Sep 2020
#40	22nd -23rd October 2020 - *VASCERN Days*

-several topics and cases prioritised for discussion

European Reference Network

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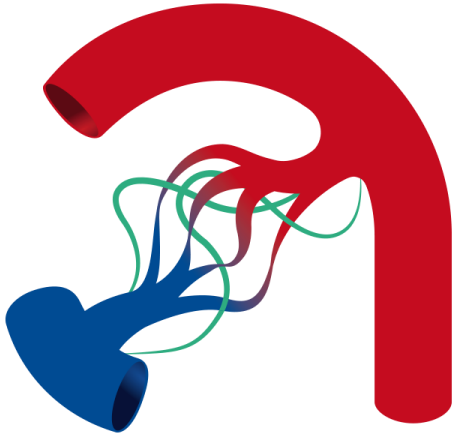

Vascern HTAD WG

Julie De Backer, HTAD WG Chair

WP4	Sharing of experience: discussion of difficult clinical cases	Monthly Calls – 1-2 Cases
WP5	Patients Pathways: improvements and updates	Version 2.0 – Under review
WP6	Mobile Application	Criteria for inclusion discussed
WP7	Pills of Knowledge	5 completed by the end of this year
WP8	Registries	HTAD Database under development - ROPAC
WP9	Clinical trials & Research	2 Research studies ongoing
WP10	Availability of videos on YouTube	E3 summit
WP12	Definition of clinical outcomes	2 projects – in progress
WP13	Writing Clinical Practice Guidelines	1 proposal
WP14	Do's and Don'ts factsheets	2 available

European Reference Network

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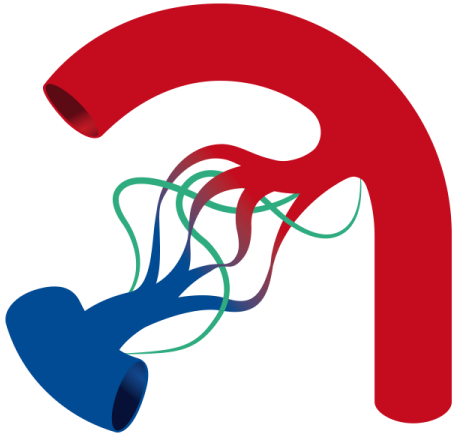


VASCERN-Days 2020

Vascern PPL-WG 22-10-2020

Robert Damstra
PPL WG Chair

WP4	**Sharing of experience: discussion of difficult clinical cases**
WP5	**Patients Pathways: improvements and updates**
WP6	**Mobile Application**
WP7	**Pills of Knowledge**
WP8	**Registries**

Monthly Calls – 1-4 Cases + CPMS: New affiliated member from Slovenia

General pathway: Published
Algorithm will be made
specific pathways proposal

Criteria for inlcusion discussed

Movie from Portugal with personal experience patient
More patients journeys We now have 4: overview PPL; compression in PPL; cellulitis / erysipelas in PPL
6 items have been put in a patient friendly video in several langauges

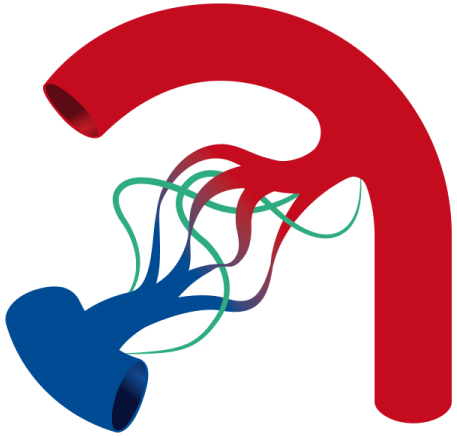
FAIR registry test side

WP9	**Clinical trials & Research**	tuberosus sclerosis and lymphedema bariatic surgery: NS and St. Georges multicenter trial: primary genital lymphedema review VEGF lymphatin in Milroy: controlled+ comparative study MR-lymphography with VASCA group
WP10	**Availability of videos on YouTube**	Proposal for 3 webinars: -Research and genetics / infections / surgery and PPL
WP12	**Definition of clinical outcomes**	From the clinical outcome we generated a core minimal dataset
WP13	**Writing Clinical Practice Guidelines**	3 members joined the ERN-ITHACA for European guideline for Phelan-McDermid syndrome (lymphedema part)
WP14	**Do's and Don'ts factsheets**	13 items: Adjustments by patients with more same style of language and more patiënt based

European Reference Network

for rare or low prevalence complex diseases

Network Vascular Diseases (VASCERN)



VASCERN-Days 2020

Vascern VASCA-WG 22-10-2020

Miikka Vikkula
VASCA WG Chair

The European Reference Network for Rare Vascular Diseases (VASCERN): VASCA-Working Group – towards Better Management of Vascular Anomaly Patients

Miikka Vikkula, Leo Schultze Kool, Alan Irvine, Päivi Salminen, Nader Ghaffarpour, Andrea Diociaiuti, Jochen Rössler, C.T. van den Bosch, Eulalia Baselga, Anne Dompmartin and Laurence Boon

VASCERN virtual Days 22-24/10/2020

BELGIUM

Chair

Pr. Laurence M. BOON
Pr. Miikka VIKKULA
Coordonator Center for Vascular Anomalies
Division of Plastic Surgery
Cliniques universitaires Saint-Luc
Human Molecular Genetics, de Duve Institute
Université catholique de Louvain
Brussels, Belgium

NETHERLANDS

Co-chair

Pr. Leo SCHULTZE KOOL
Expertcenter for Hemangioma and Vascular Anomalies (Hecovan)
Radboud university medical center
Nijmegen, Netherlands

* 7 full centers
* 2 collaborative centers
* 14 applications for new full HCPs evaluated 2020

European Reference Network for rare or low prevalence complex diseases
Network Vascular Diseases (VASCERN)

VASCERN

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

Co-funded by the Health Programme of the European Union

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Objectives

- Define patient pathways
- Clarify coding (Orphanet, ICD)
- Set up a Virtual FAIR-based Registry
- Make Educational YouTube Videos
- Generate Pills of Knowledge (POK) to be distributed e.g. via ERN website
- Define clinical outcomes / outcome measures
- Elaborate Do's and Don'ts Factsheets
- Write Recommendations / Expert opinions
- Organize Training, Help new Centers to be established
- Set-up Clinical Trials & Research Projects
- Discuss difficult cases using CPMS (secured Clinical Patient Management System)

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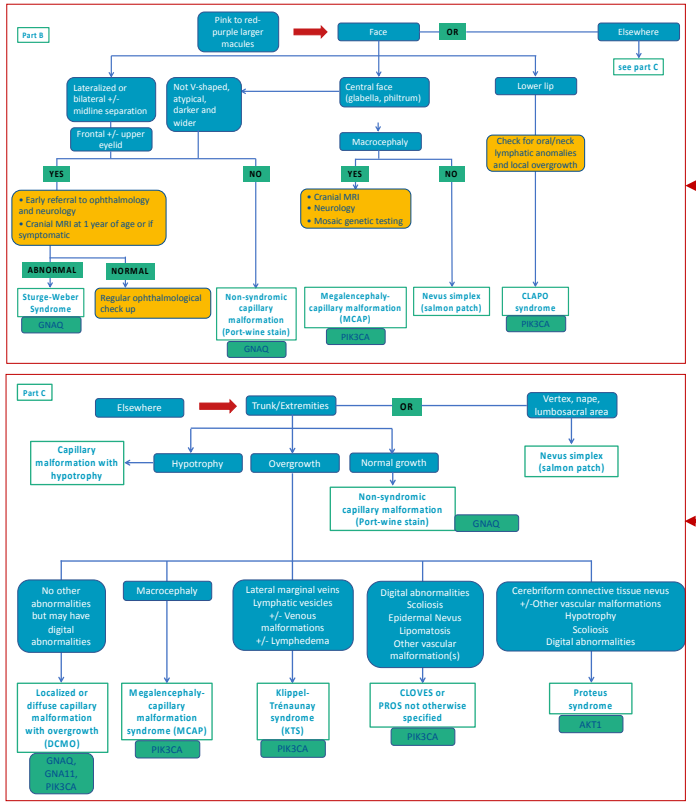
Results

https://vascern.eu/what-we-do/patient-pathways/#1472739978584-12bb752c-4524

The European Reference Network (ERN) for Rare Vascular Diseases (VASCERN): VASCA-Working Group – Capillary Malformation Patient Pathway

Baselga E, Boon L, Diociaiuti A, Dompmartin A, Dvorakova V, El Hachem M, Ghaffarpour N, Irvine A, Kapp F, Kyrklund K, Rößler J, Salminen P, van den Bosch C, van der Vleuten C, Schultze Kool L, Vikkula M



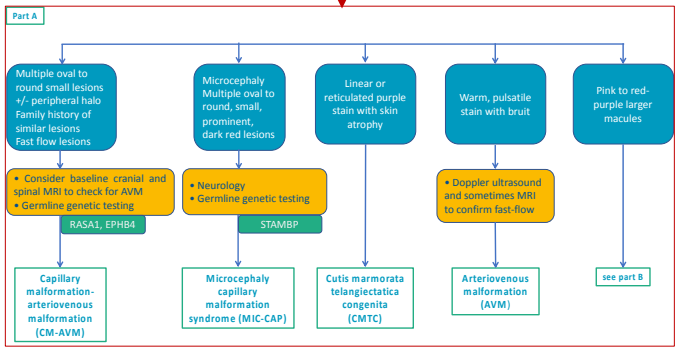
PURPOSE: Capillary malformations (CM) are a large group of vascular malformations with many clinical phenotypes and genotypes They may also be part of complex syndromes. Initial diagnostic workup for CM depend on recognition of the clinical phenotype. In order to guide patients and physicians in the evaluation of CM, the working group VASCA-WG within VASCERN (https://vascern.eu/) a European network for Rare Vascular Diseases has elaborated a CM patient pathway.

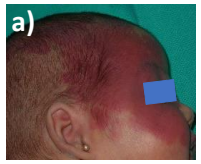
METHODS: A CM pathway was drafted by the Collaborating Center of Barcelona and discussed within the VASCA-WG monthly virtual meetings and finalized on a face-to-face meeting.

RESULTS: The pathway starts from the clinical suspicion of a capillary stain and recognition of patterns: 1) Multiple oval/round small lesions +/- white halo; 2) Multiple oval/round, small, prominent, dark red with microcephaly; 3) Linear/reticular with skin atrophy; 4) Warm/rapid-refill/pulsatile stains; 5) Pink to red-purple larger macules, distinguishing those affecting the face (forehead or other) and elsewhere. For CM on trunk/ extremities recognition of overgrowth or undergrowth further guides diagnosis and management.

CONCLUSIONS : The VASCA working group of VASCERN, a network of the 9 Expert Centers, has led to a consensus statement Patient Pathway for CMs. This Pathway should help clinicians and patients in the management of CM. This pathway is available on the VASCERN web-site (http://vascern.eu/).

Capillary malformation (Vascular stain) Diagnostic Work-up





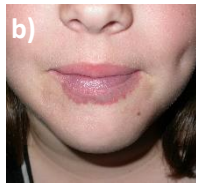


Figure 1 – CM on face.
a) Forehead, r/o SWS;
b) lower lip, r/o CLAPO

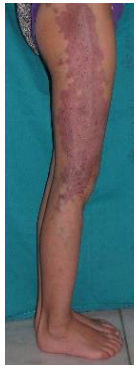
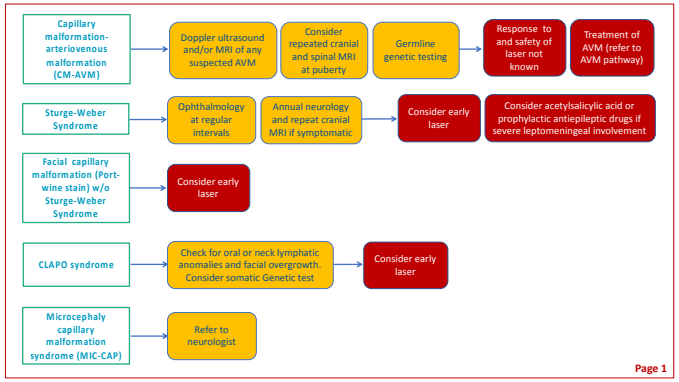
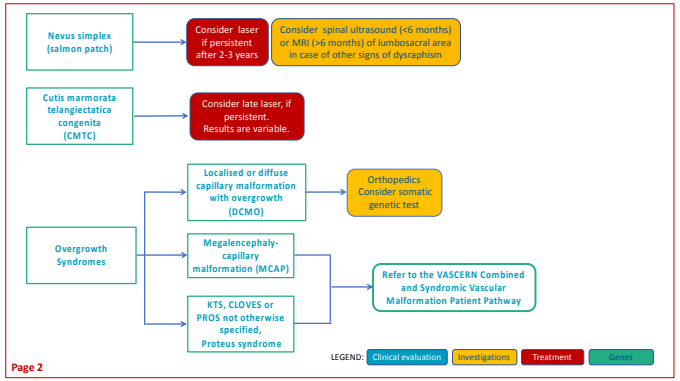


Figure 2 - CM on extremitis and Overgrowth + lateral vein + lymphatic vesicles r/o KTS

Management/Treatment of Capillary malformation (Vascular stain)





ACKNOWLEDGEMENTS: This project has been supported by the European Reference Network on Rare Multisystemic Vascular Diseases (VASCERN) - Project ID: 769036, which is partly co-funded by the European Union within the framework of the Third Health Program "ERN-2016 - Framework Partnership Agreement 2017-2021." More information available at: https://vascern.eu

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Results

https://vascern.eu/what-we-do/patient-pathways/#1472739978584-12bb752c-4524

Patient Pathway for the Management of Lymphatic Malformations (LMs): A European Reference Network (ERN) collaboration by the Vascular Anomalies (VASCA) Working Group of VASCERN

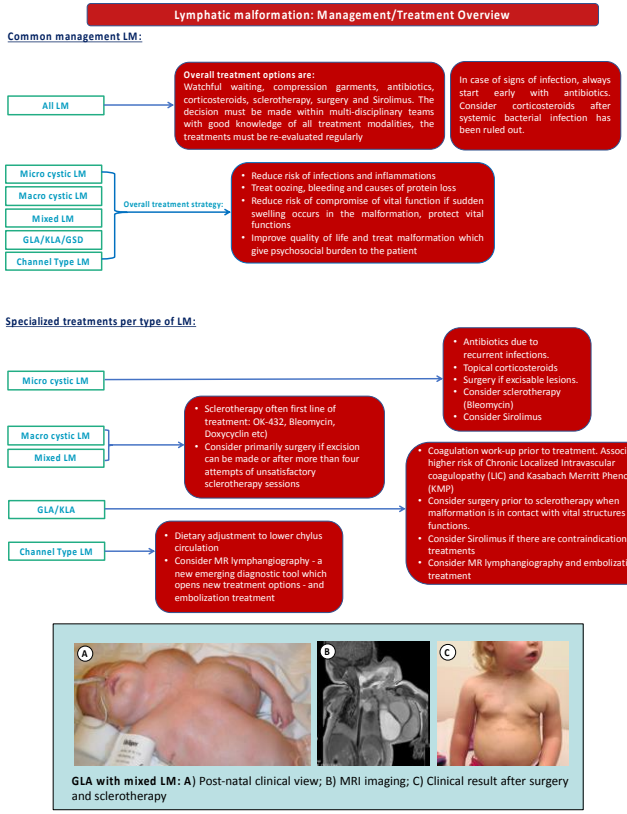
Ghaffarpour N, Baselga E, Boon L, Diociaiuti A, Dompmartin A, Dvorakova V, El Hachem M, Irvine A, Kapp F, Kyrklund K, Rößler J, Salminen P, van den Bosch C, van der Vleuten C, Schultze Kool L, Vikkula M

PURPOSE: Lymphatic malformations (LMs) are part of vascular anomalies. They are rare congenital malformations caused by an abnormal development of lymphatic vessels and classified according to the International Society for Study of Vascular Anomalies in macrocytic, microcystic and mixed lesions and also encompass the complex multisystemic LMs such as GLA, GSD, CCLA. The aim of this work was to draft a patient pathway for the management of LMs.

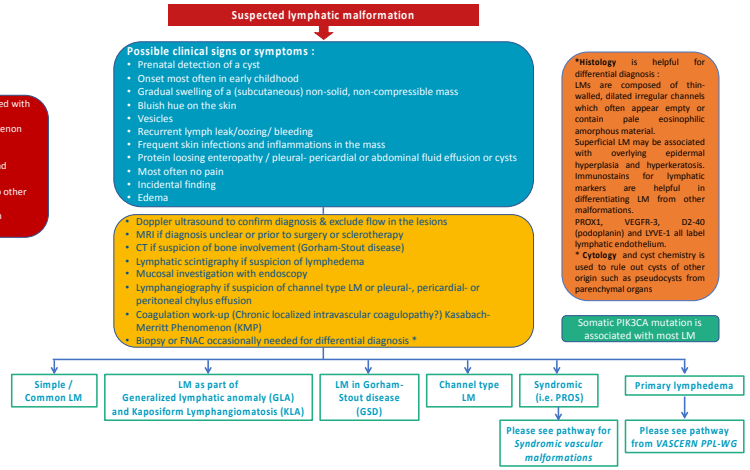
METHODS: By the initiative of the European Commission, European Reference Networks (ERNs) have been established. They are composed of experts and patient representatives in 24 fields of rare diseases. Rare vascular diseases have been identified as one of the fields requiringdedicated working groups (VASCERN). VASCA-WG is the working group for vascular anomalies. Establishing clinical pathways for patient management for several vascular anomalies including LMs, Venous Malformations, Arterio-Venous Malformations, Capillary Malformations and Rare Infantile Hemangiomas has been prioritized. Each patient pathway was presented as a draft by a chosen lead expert to the joined VASCA-WG on monthly video conferences and finalized during a bi-annual face-to-face meeting.

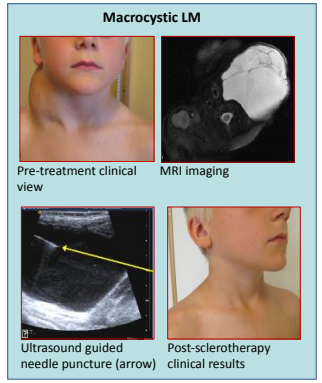
RESULTS: The layout of the LM patient pathway is in concordance with other patient pathways of the VASCA-WG with color-coded boxes (Clinical evaluation, suggested investigations, treatment options, associated genes and particularities). The LM pathway gives guidance on when to consider different subtypes of LMs, on appropriate diagnostic approaches, treatment options and on causative mutations.

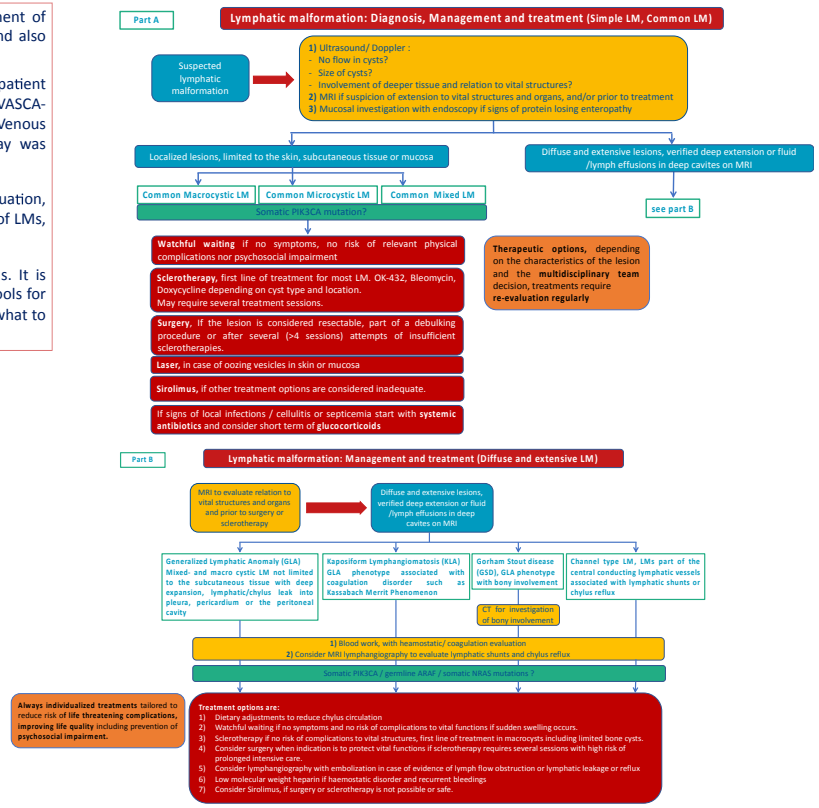
CONCLUSIONS : The patient pathway for LM is an expert opinion statement reflecting strategies and recommendations for the management of LMs. It is preferable that patients are evaluated, and re-evaluated post treatment within expert, multidisciplinary teams. Patient pathways are not only important tools for the referring physicians and the expert multidisciplinary teams dealing with the rare diseases, but also for patients having the diseases to be informed on what to expect from the healthcare system. The LM pathway is available on the VASCERN web-site (http://vascern.eu/)



GLA with mixed LM: A) Post-natal clinical view; B) MRI imaging; C) Clinical result after surgery and sclerotherapy







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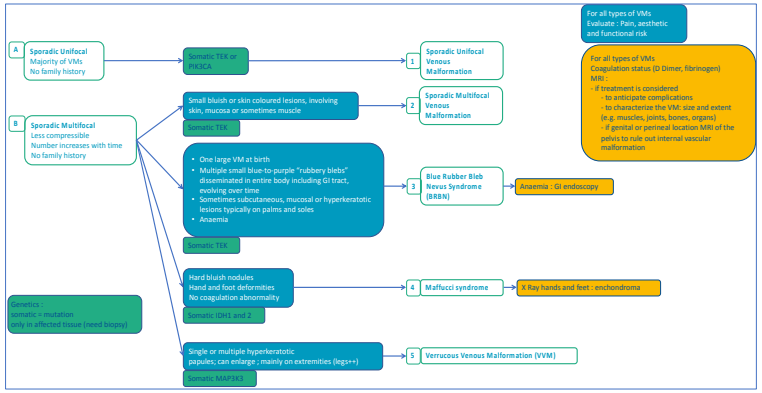
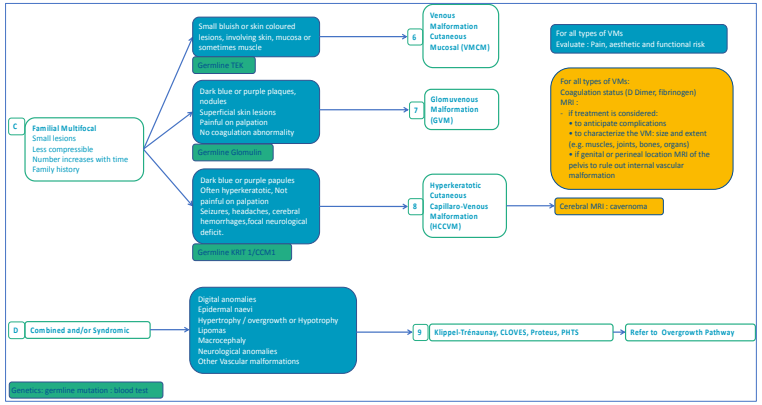
Results

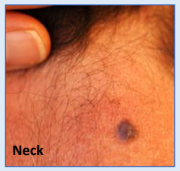
https://vascern.eu/what-we-do/patient-pathways/#1472739978584-12bb752c-4524

The European Reference Network for Rare Vascular Diseases (VASCERN): VASCA-Working Group – Venous Malformation Patient Pathway

Dompmartin A, Baselga E, Boon L, Diociaiuti A, Dvorakova V, El Hachem M, Ghaffarpour N, Irvine A, Kapp F, Kyrklund K, Rößler J, Salminen P, van den Bosch C, van der Vleuten C, Schultze Kool L, Vikkula M







Venous Malformation

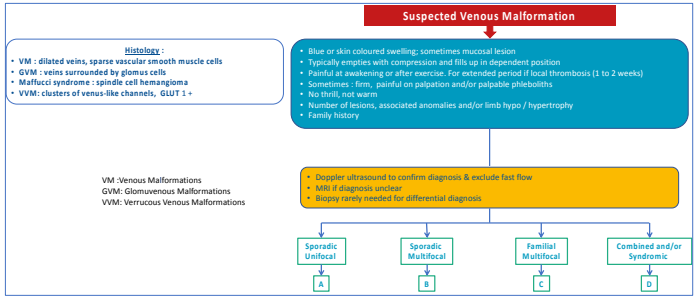
Glomangiomatosis

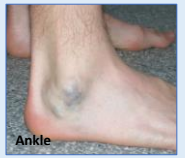
Purpose: VASCERN (https://vascern.eu/) is a European network for Rare Vascular Diseases. Its working group (VASCA-WG) focuses on Vascular Anomalies. The group elaborates patient pathways to guide patients and physicians towards efficient diagnostic and management measures.

Methods: A VM pathway was first drafted by the Collaborative Center of Caen and subsequently discussed within the VASCA-WG monthly virtual meetings and annual face-to-face meetings.

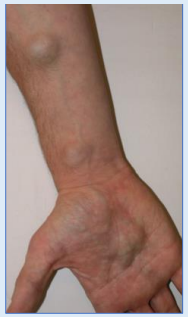
Results: The Pathway starts from the clinical suspicion of a venous type malformation and lists the clinical characteristics to look for to support this suspicion. Subsequent imaging and histopathology is suggested. These steps should enable to confirm/inferm the suspicion and to separate the patients into 4 subtypes: 1) sporadic uni or 2) multifocal, 3) familial, multifocal and 4) combined and/or syndromic. The management of each one of these is detailed in subsequent pages of the pathway. Colour is used to differentiate 1) clinical evaluations, 2) investigations, 3) treatments and 4) associated genes. Actions relevant to all types are marked in separate boxes, including e.g. MRI if treatment is considered. When definite diagnoses have been reached, the pathway also points towards disease specific additional investigations/follow up that is needed. In the last two pages, different options for management are detailed for each subtype, including conservative and invasive treatments, as well as novel molecular therapies.

Conclusion: The collaborative efforts of the VASCA working group of VASCERN, a network of the 9 Expert Centers, has led to a consensus Patient Pathway for VMs. This Pathway should help clinicians and patients. It also emphasizes the role of multidisciplinary expert centers in the management of VM patients. This pathway will become available on the VASCERN web-site (http://vascern.eu/).

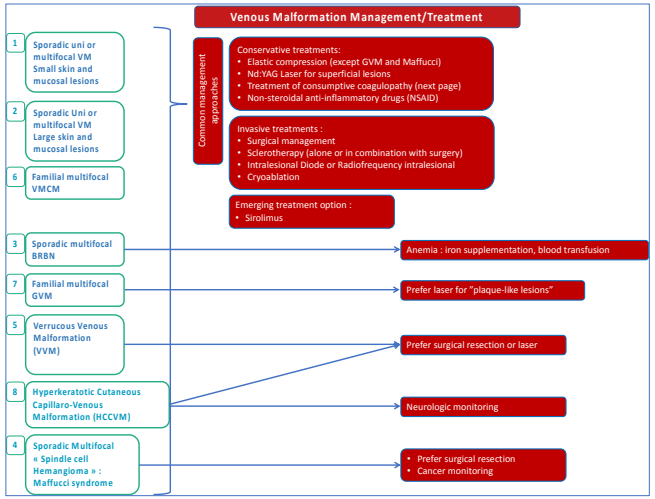


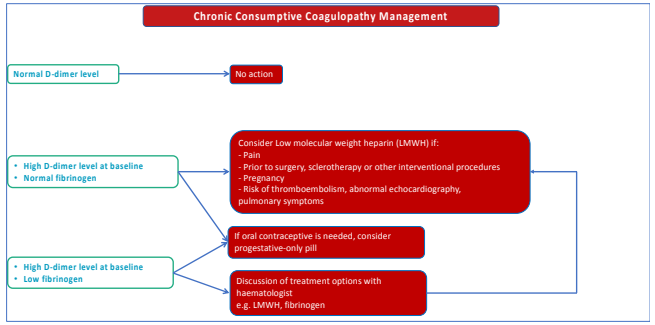


Unifocal sporadic VM



Multifocal sporadic VM





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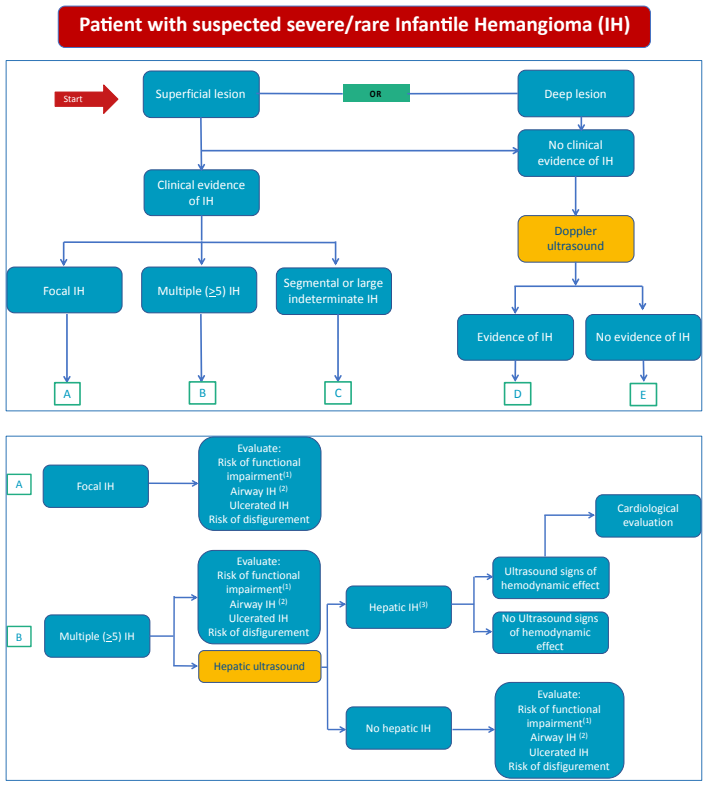
Results

https://vascern.eu/what-we-do/patient-pathways/#1472739978584-12bb752c-4524

Severe/rare infantile hemangioma patient pathway

by the Vascular Anomalies (VASCA) Working Group of VASCERN

Diociaiuti A, Baselga E, Boon L, Dompmartin A, Dvorakova V, El Hachem M, Ghaffarpour N, Irvine A, Kapp F, Kyrklund K, Rößler J, Salminen P, van den Bosch C, van der Vleuten C, Schultze Kool L, Vikkula M

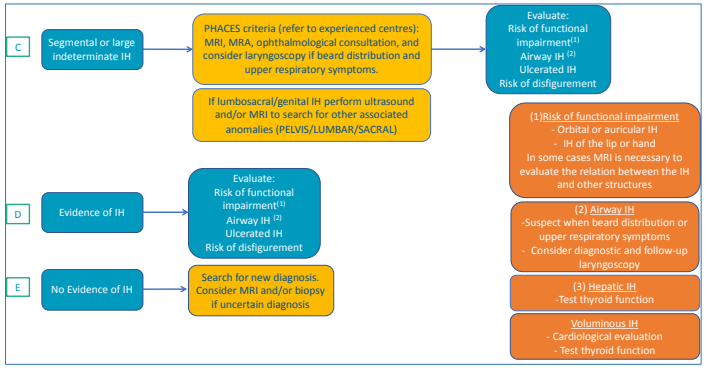


PURPOSE: Infantile hemangiomas (IHs) are common vascular tumors, but a rare subgroup of them is particularly sever. Risk of functional impairment, airway obstruction, ulceration and risk of disfigurement are possible. Syndromic conditions and cardiac failure may be associated with segmental IH or hepatic IH respectively. The VASCA working group within the VASCERN (https://vascern.eu/), a European network for Rare Vascular Diseases, has elaborated an IH patient pathway as a guide for physicians for an appropriate management of severe/rare cases.

METHODS: The severe/rare IH pathway was first drafted by Bambino Gesù Children's Hospital and then discussed within the VASCA-WG monthly virtual meetings and finalized on a face-to-face meeting.

RESULTS: The pathway starts from the clinical suspicion of an IH that may be focal, multiple, segmental or large/indeterminate. Segmental or large indeterminate IHs may be part of syndromic conditions such as PHACE, PELVIS/LUMBAR/SACRAL. Five or more cutaneous IHs may be associated with hepatic hemangiomas that can have a hemodynamic effect. Moreover, the beard distribution may be associated with life-threatening laryngeal IH. Orbital or auricular IH and localization on the lip or hand may result in functional impairment. In the pathway clinical evaluations, investigations to rule out associated malformations or comorbidities, and treatments are discussed.

CONCLUSIONS : The VASCA working group of VASCERN, a network of 9 European Expert Centers, has generated a Patient Pathway for IHs. This Pathway should help physicians to manage severe/rare IHs. This pathway is available on the VASCERN web-site (http://vascern.eu/)



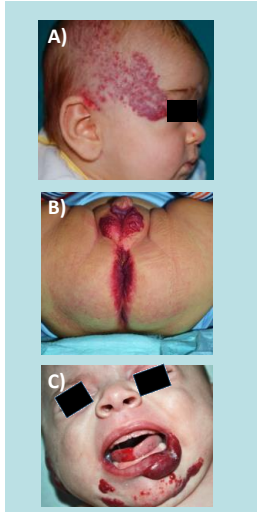
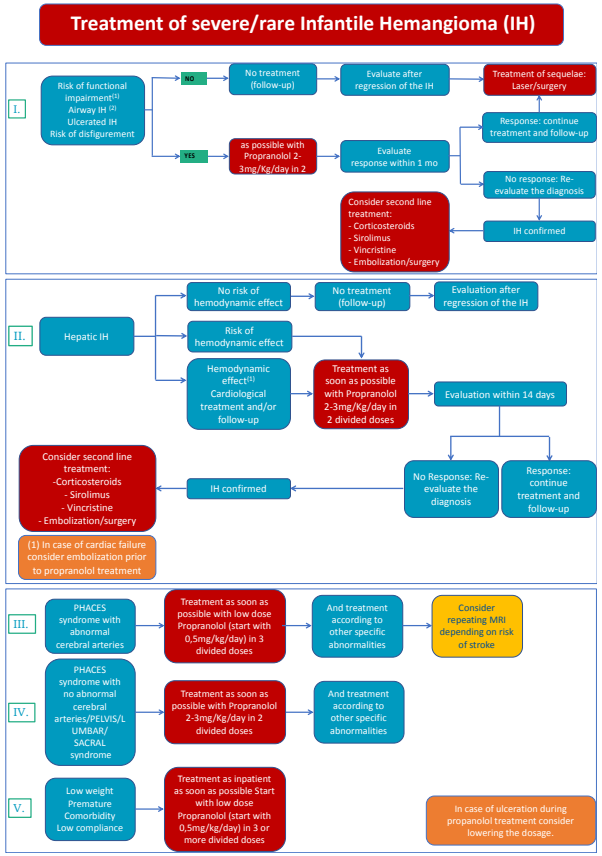


Figure1 – IH phenotypes description A); B) ; C)



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Results

Orphanet codes for vascular anomalies & lymphedemas (lead Prof Paivi Salminen, Helsinki, Finland)

This work was finalised for lymphedemas with the PPL WG of VASCERN > update on the Orphanet web site ?

Work is ongoing for the vascular anomalies with Orphanet

https://www.orpha.net/

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Results

Registry for Vascular Anomalies (lead Prof Leo Schultze Kool, Nijmegen, the Netherlands)

1) KEY ITEMS to register defined

2) FAIR principal
and thus independent of registry software being used allowing linking to biodatabanks etc

3) VIRTUAL registry; each center owns its data, only accessible by request and permission

4) Definition of DISEASE-SPECIFIC ITEMS for 4 research projects ongoing in VASCA

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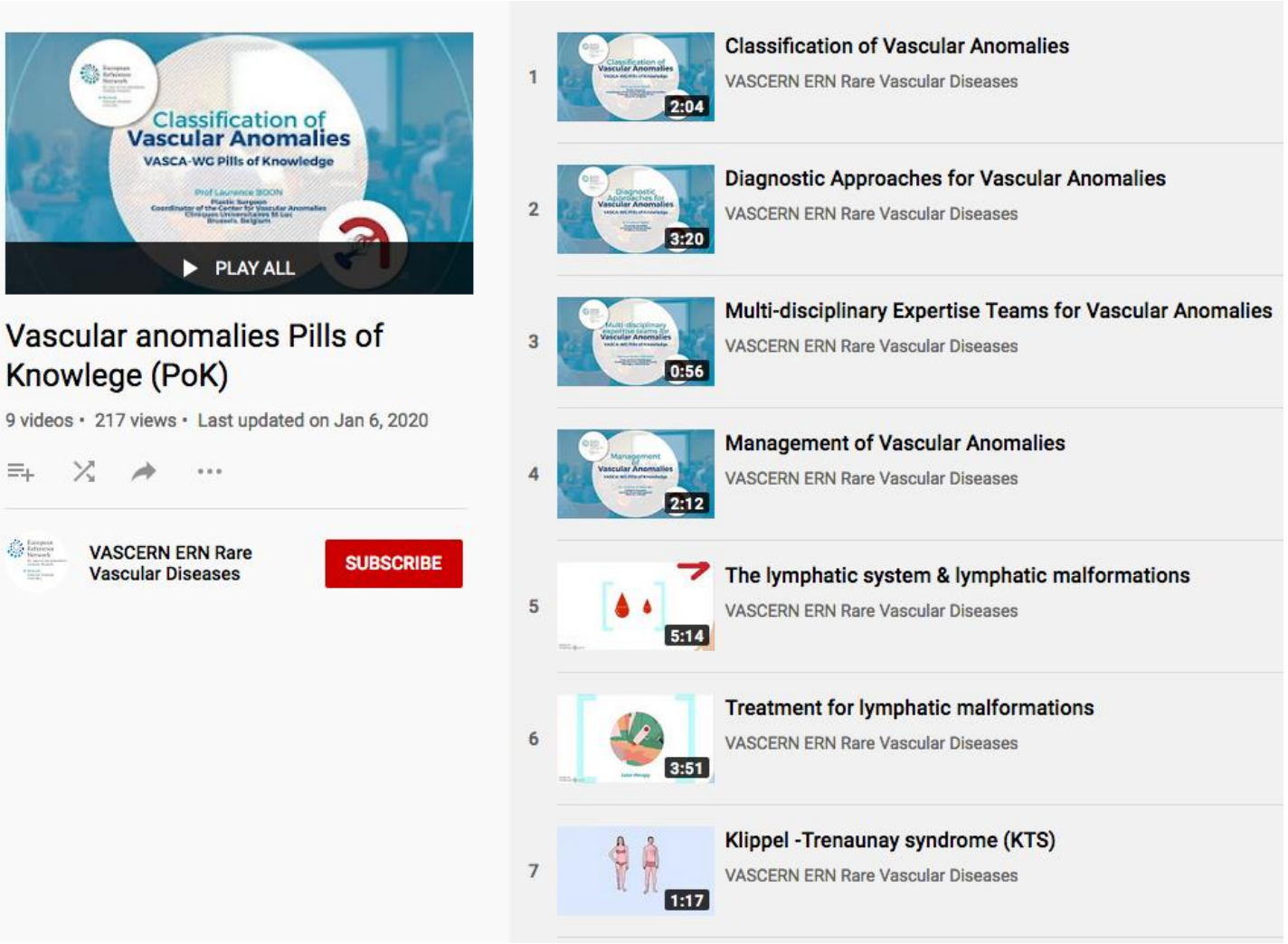
Results

https://www.youtube.com/playlist?list=PLynYSx6bbQwSvt7QbrZnEGsEBl1MlHyUp

Educational YouTube videos :



New:
PIK3CA related video

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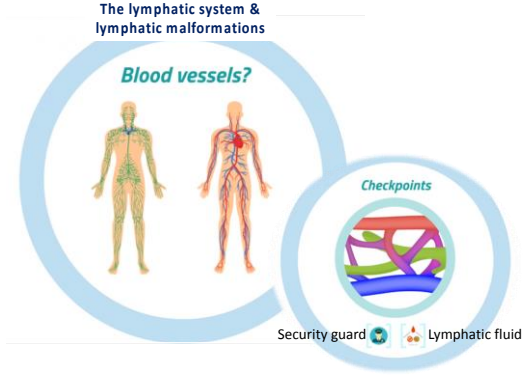
Results

https://www.youtube.com/playlist?list=PLynYSx6bbQwSvt7QbrZnEGsEBl1MlHyUp

Pills of Knowledge (POKs): Poster @ ISSVA 2020

The European Reference Network (ERN) for Rare Vascular Diseases (VASCERN): Results from 2 years collaboration of Patient Advocates with the Vascular Anomalies (VASCA) Workgroup

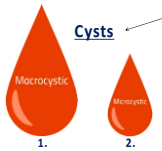
van den Bosch C, Barea M, Baselga E, Boon L, Borgards P, Diociaiuti A, Dompmartin A, Dvorakova V, El Hachem M, Ghaffarpour N, Irvine A, Kapp F, Kyrklund K, van Oord A, Rößler J, Salminen P, Schultze Kool L, van der Heijden L, van der Vleuten C, Vikkula M



The lymphatic malformations > lymphatic vessel developed in a abnormal way

The lymphatic fluid in the effective vessels tends to accumulate in cavities and Cysts. These abnormalities appear at the particular locations in the body: head, neck, armpit.

Cysts

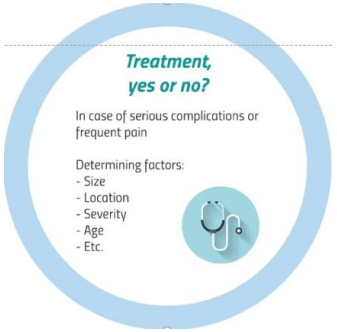


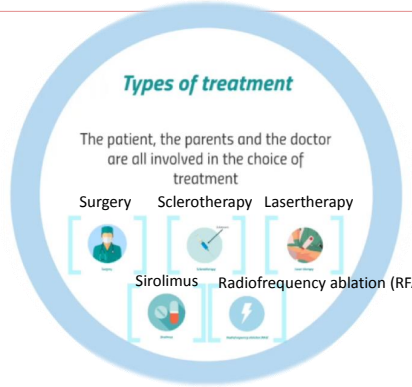
1. Large cavities filled with lymphatic fluid; 2. Small cavities filled with lymphatic fluid

The LM doesn't cause any major problem at all. The seriousness of the condition varies with patients. It depends on the location, size and severity of the LMs.

COMPLICATIONS
- Infections
- Bleeding
- Swelling (with increase redness, firmness and pain)
- Shrinking
- Leakage of lymphatic fluid

Social Insecurity



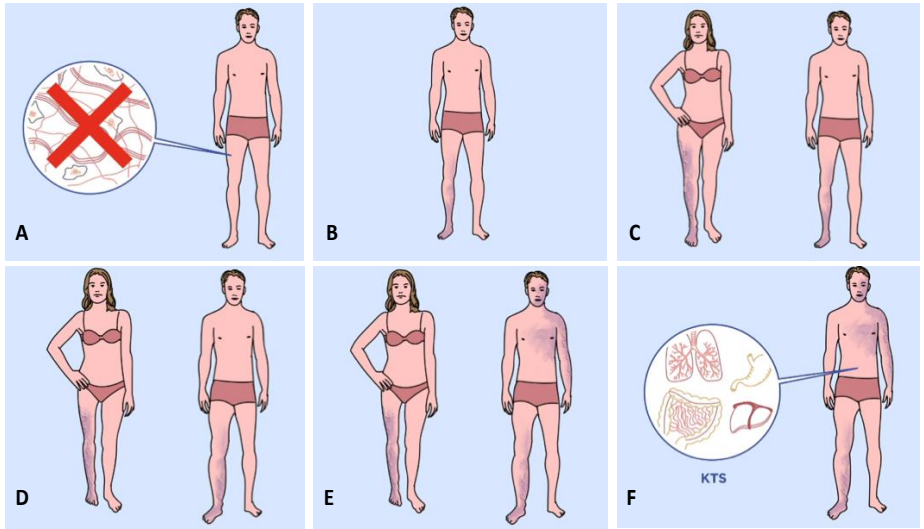


PURPOSE: European Reference Networks (ERNs) for Rare Diseases were established on the founding principle of patient empowerment, participation and patient-centricity. The object is to improve access, safety and quality of diagnosis, care and treatment for people living with a rare or complex condition. European Patient Advocacy Groups (ePAGs) are recognized as integral to the strategic and operational delivery of ERNs, and play an active role in network decisions, opinion-making structures and delivery of results.

METHODS: In the VASCA WG 5 Patient Organizations (POs) are active. They participate in the monthly virtual meetings and in the 2 annual face-face meetings. Producing Pills of Knowledge (PoK) is an ongoing deliverable for the VASCERN WG, made by the clinicians and the ePAG. A PoK can be for example a short single video lesson in which an expert talks about a specific topic that has been selected and validated by the VASCA WG.

RESULTS: The ePAG produced 3 videos which were validated by VASCA WG, and translated to English:
1) The lymphatic system & lymphatic malformations
2) Treatments for lymphatic malformations
3) Description of the Klippel-Trenaunay Syndrome
These videos describe the disease and treatments currently available in a clear and understandable manner to educate patients and non specialized clinicians.
All videos will have subtitles in several European languages.

CONCLUSIONS : The cooperation of the ePag with the VASCA WG have tangible results for VA patients worldwide. More PoKs will be produced by other POs on other VAs (e.g. one on PIK3CA is almost finalized).



Description of the Klippel-Trenaunay Syndrome (KTS) - A) In parts of the body, cells are not properly formed; B) KTS > a combination of one or more port-wine stains: CMs; C) KTS > abnormal veins or small lymphatic blisters are visible; D) KTS > bone and/or soft tissue overgrowth. Sometimes undergrowth can occur and the leg - or body part affected - is smaller or thinner; E) Usually, KTS is limited to one limb. Sometimes it can be located in several limbs and/or extended to parts of the torso; F) KTS can also affect internal organs.

ACKNOWLEDGEMENTS: This project has been supported by the European Reference Network on Rare Multisystemic Vascular Diseases (VASCERN) - Project ID: 769036, which is partly co-funded by the European Union within the framework of the Third Health Program "ERN-2016 - Framework Partnership Agreement 2017-2021." More information available at: https://vascern.eu

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Objectives

- ✔ Define patient pathways
- ✔ Clarify coding (Orphanet, ICD)
- Set up a Virtual FAIR-based Registry
- Make Educational YouTube Videos
- Generate Pills of Knowledge (POK) to be distributed e.g. via ERN website
- Define clinical outcomes / outcome measures
- Elaborate Do's and Don'ts Factsheets
- Write Recommendations / Expert opinions
- Organize Training, Help new Centers to be established
- Set-up Clinical Trials & Research Projects
- ✔ Discuss difficult cases using CPMS (secured Clinical Patient Management System)

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European Reference Network | VASCERN | Gathering the best expertise in Europe to provide accessible cross-border healthcare to patients with rare vascular diseases

VASCA sub-WGs: projects

	Group	VASCERN activity	VASCERN lead	Inter-ERN activity	Inter-ERN lead	Project	HCP / ePAG lead liaison	Organiser
1		VASCA PROJECTS - CONFIDENTIAL						
2								
3								
5								
7	VASCA-Anesthesia	yes	Ignatio Malagon	yes	Ignatio Malagon	Pediatric anesthesia	Leo Schultze Kool	Leo Schultze Kool
8								
9	VASCA-CPMS	yes		yes		Case discussion	Leo Schultze Kool	Leo Schultze Kool
10								
11	VASCA-Drug Therapies	no	no	no	no	VASE (Vascular Anomaly-Sirolimus-Europe), mTOR	Laurence Boon	Laurence Boon
18								
19	VASCA-Funding	yes	Marine?	no	no		Leo Schultze Kool	Friedrich Kapp
20								
21	VASCA-Guidelines/expert opinions	yes	no	no	no	Specific, rather than all incompassing. Status as of today	Miikka Vikkula	Miikka Vikkula
26								
27	VASCA-Genetics	no	no	no	no	Diagnostic genetic testing (harmonization and guidelines)	Miikka Vikkula	Nicole Revencu
30								
31	VASCA-Genotype/phenotype	no	no	no	no	VVM/HCCVM/"angiokeratoma"	Alan Irvine	Veronika Dvorakova
32								
33	VASCA-National networks	yes	no	yes	no	Establishment of expert networks	Leo Schultze Kool	Leo Schultze Kool
34								
35	VASCA-Orphanet	no	no	no	no	Orphanet and ICD10/11	Paivi Salminen	Paivi Salminen
37								
38	VASCA-Outcomes	no	no	no	no	Outcome measures for VAs	Laurence Boon	Laurence Boon
41								
42	VASCA-Pathology	no	no	no	no	VA pathology course	Miikka Vikkula	Michel Wassef
43								
44	VASCA-Patient passport	????	????	????	????	Electronic passport ?	Caroline van den Bosch	Caroline van den Bosch
45								
46	VASCA-PHTS	no	no	????	no	PHTS Vas	Miikka Vikkula	Miikka Vikkula
51								
52	VASCA-Pregnancy	yes	Julie de Backer	yes	????		Laurence Boon	???
53								
54	VASCA-Publications	no	no	no	no	Patient pathways to special VASCERN issue @ Eur J Med Genet 2021	Miikka Vikkula	Miikka Vikkula
60								
61	VASCA-Radiology	no	no	no	no	MR intranodal lymphangiography	Leo Schultze Kool	Willemijn Klein
63								
64	VASCA-Registry	yes	Leo Schultze Kool	yes	????	VASCA FAIR-based Registry	Leo Schultze Kool	Leo Schultze Kool
70								
71	VASCA-Seminars	yes	Marine?	no	no	WEBinars on VASCERN web-site	Miikka Vikkula	Miikka Vikkula
74								
75	VASCA-Surgery	no	no	no	no	Sirolimus and interventions	Laurence Boon	Laurence Boon
78								

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All outputs are on the website https://vascern.eu/what-we-do/

Q&A,

sharing best practices & inter-RDWGs projects

Webinars

- Each RDWG will select during VASCERN days topics & speakers for the new Webinar programme which we will launch in the upcoming weeks

- Zoom as a webinar platform: any comments?

Format

- timing? length?
- Questions and answers?
- With online chat?
- Questions for a posteriori answers ?

RDWG	Number of Panels	Panel Leads	Total Number of Panels (2018, 2019 & 2020)	Number of Closed Panels
HHT	1	Sophie DUPUIS-GIROD	2	0
	1	Anette KJELDSEN		
HTAD	1	Julie De BACKER	12	1
	3	Guillaume JONDEAU		
	1	Kalman BENKE		
	1	Janneke TIMMERMANS		
	1	Ingrid van DE LAAR		
	1	Leema ROBERT		
	1	Eloisa ARBUSTINI		
	1	Guglielmina PEPE		
	2	Erik BJORCK		
MSA	1	Julie De BACKER	10	2
	2	Leema ROBERT		
	3	Michael FRANK		
	1	Ingrid van DE LAAR		
	2	Bart LOEYS		
	1	Fransiska MALFAIT		
PPL	3	Robert DAMSTRA	**23**	7
	3	Kirsten van DUINEN		
	10	Sarah THOMIS		
	1	Vaughan KEELEY		
	1	Stéphane VIGNES		
	1	Michael OBERLIN		
	1	Sahar MANSOUR		
	3	Janine DICKINSON-BLOK		
VASCA	1	Miikka VIKKULA	7	3
	4	Leo SCHULTZE KOOL		
	1	Päivi SALMINEN		
	1	Andrea DIOCIAIUTI		

WP4 Sharing of experience: discussion of complex clinical cases on a secured Clinical Patient Management System - KPIs

https://vascern.eu/what-we-do/cpms-discussion-complex-clinical-cases/

Clinical cases panel leads:
please upload your case on CPMS

OR

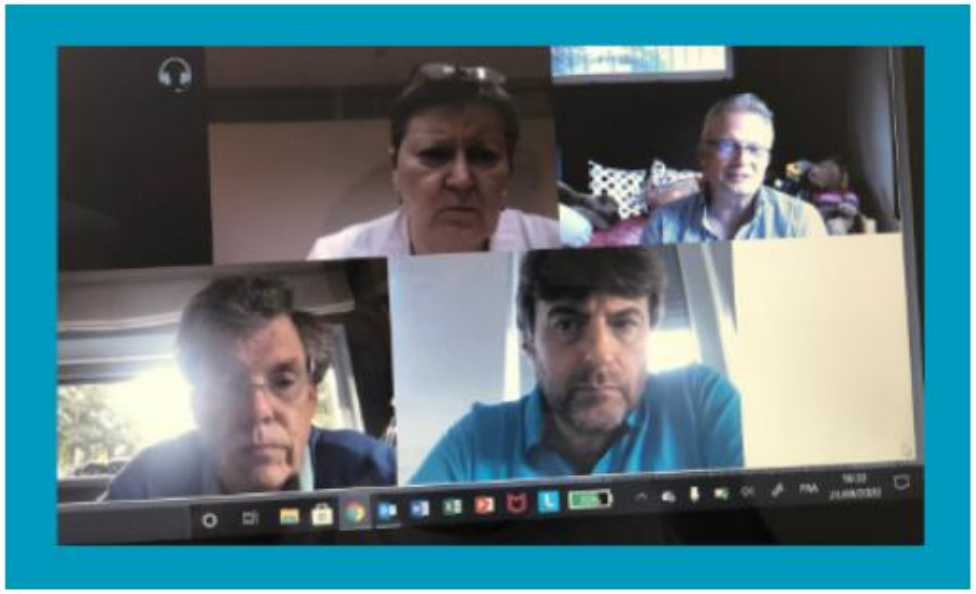
If you struggle, contact Ibrahim for him to upload

Sharing good practices: setting up VASCA CPMS monthly virtual meetings

CPMS virtual meetings this month

September 29, 2020

This month, members of the **Vascular Anomalies Working Group** (VASCA WG) held a virtual meeting using the Clinical Patient Management System (CPMS) in order to discuss two new patients cases.



VASCA WG held several CPMS case discussions on the CPMS.

Plan to have a bi-monthly or monthly meeting on the CPMS

Q&A on the Terms of References, Projects & Developments

Approval

- Questions, comments on the current functionning, structure, organisation, governance

- approval