

PERSONNALIZED APPROACH OF SUPERFICIAL VASCULAR MALFORMATIONS

From diagnostic to therapy, present and future...



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Centre de Compétence Malformations Vasculaires Superficielles (enfant/adulte)
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Mechanisms and therapeutic strategies in overgrowth and vascular anomalies

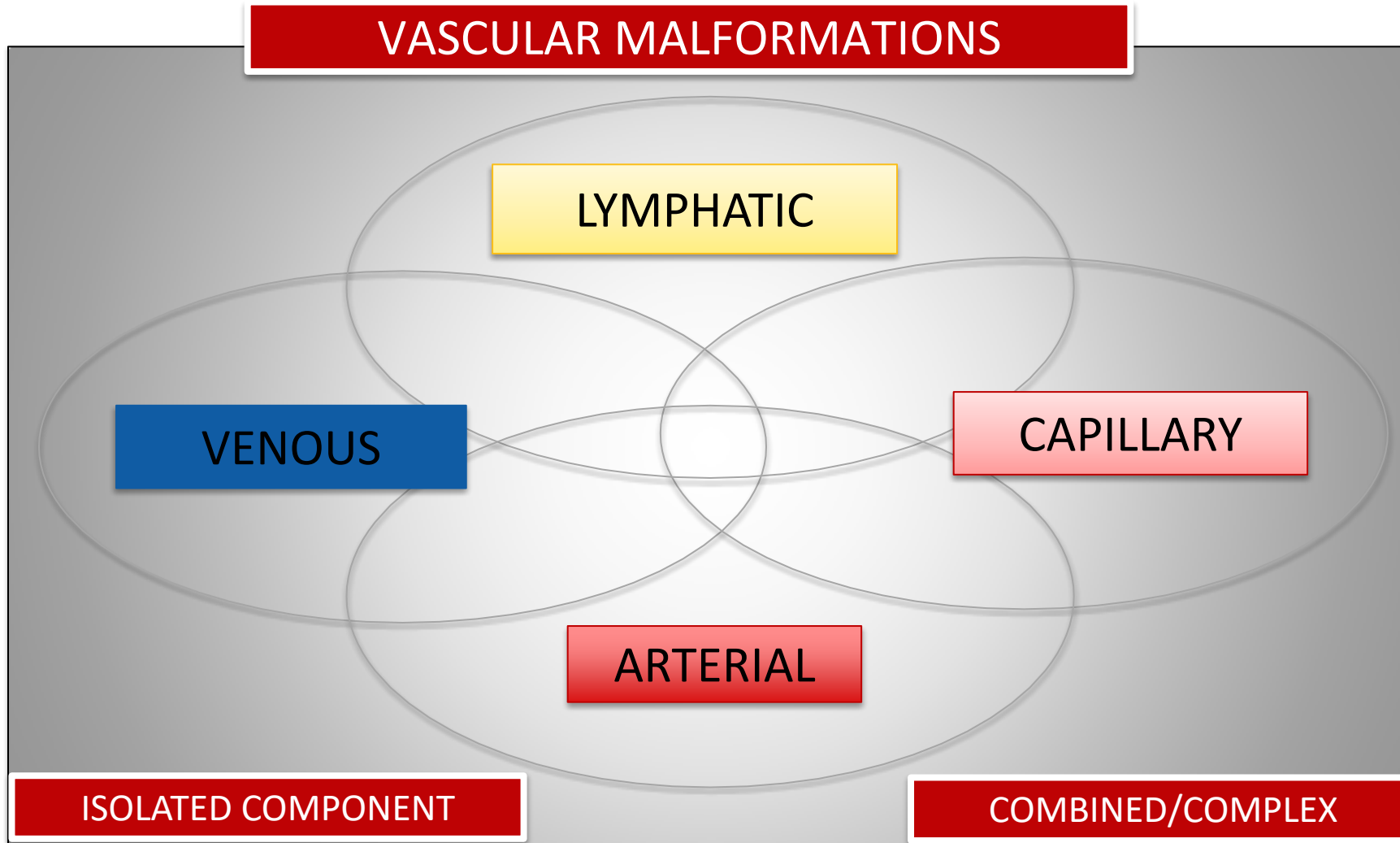


Congres of the European Society of Pediatric Radiology
Marseille, June 2022



SUPERFICIAL VASCULAR MALFORMATIONS

What are we talking about?



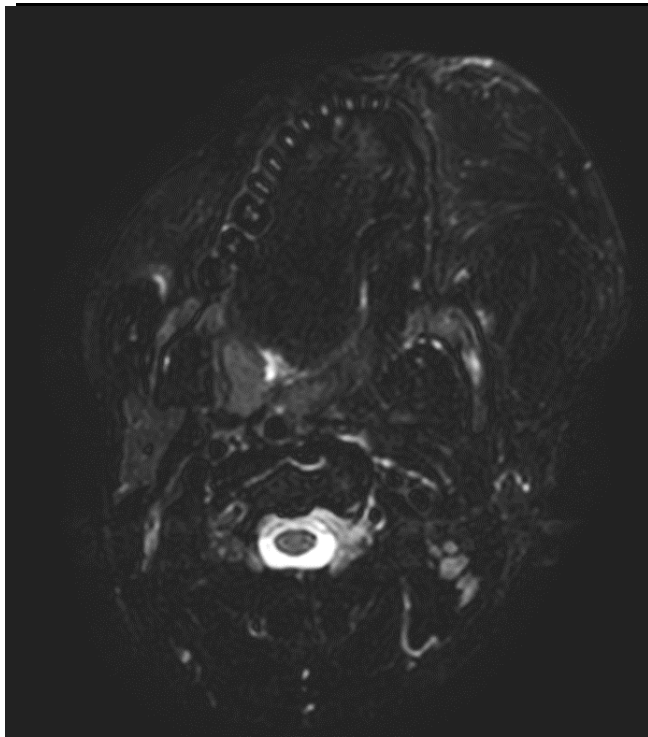


PERSONNALIZED APPROACH

What are we talking about ?

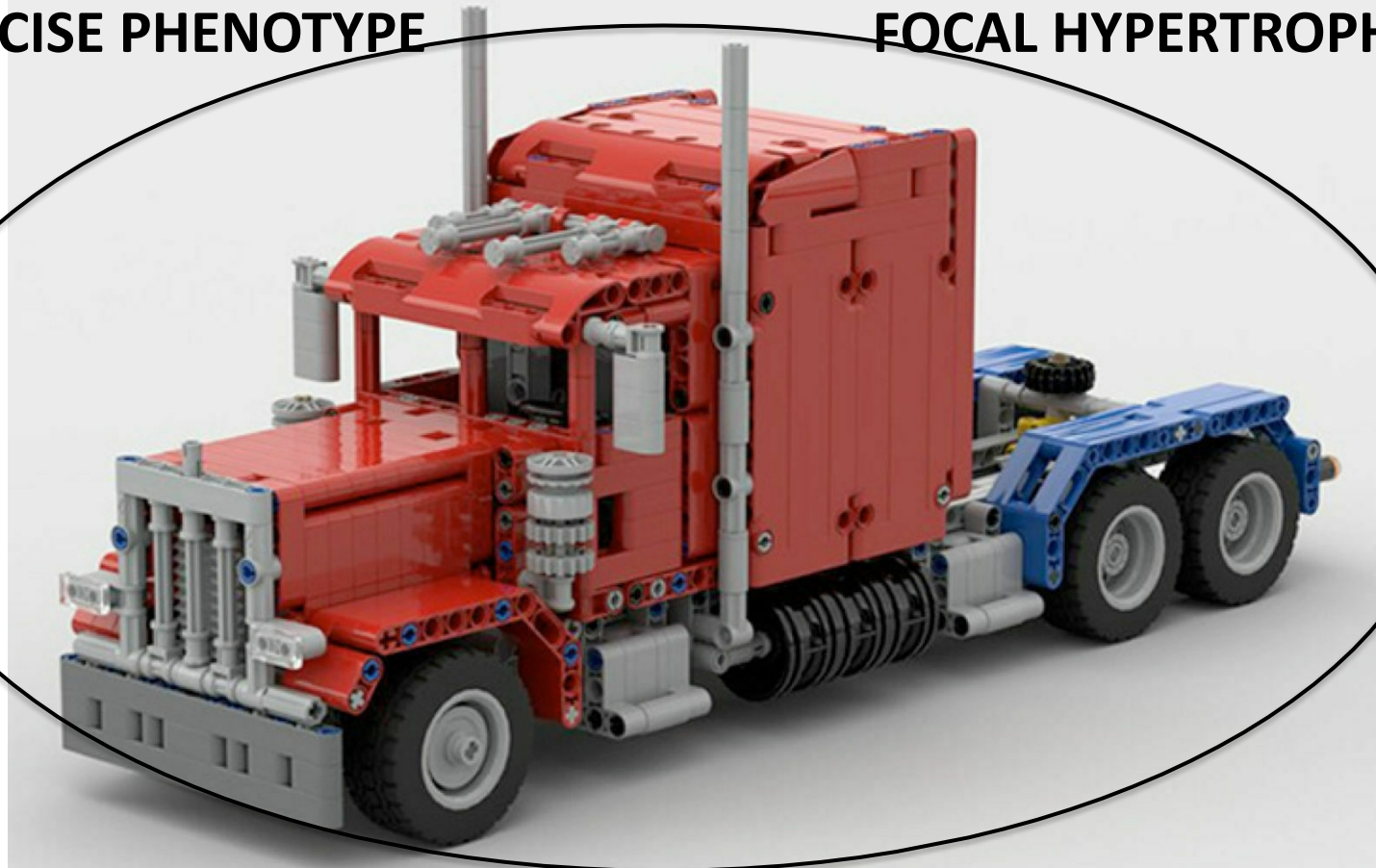
- Precise phenotyping +++
 - Vascular components
 - Low flow: LM (micro/macro/mixed), VM (cavernous/ectasia)
 - High flow: AVM/AVFs
 - CM (suggestive of syndromic/genetic entities)
 - CM-AVM : dominant mutation, importance of familial clinical examination
 - PROS : PIK3CA related overgrowth spectrum
 - Fatty component
 - Can participate more or less in segmental hypertrophy
 - May suggest a particular genotype (PTEN, PIK3CA variant...)



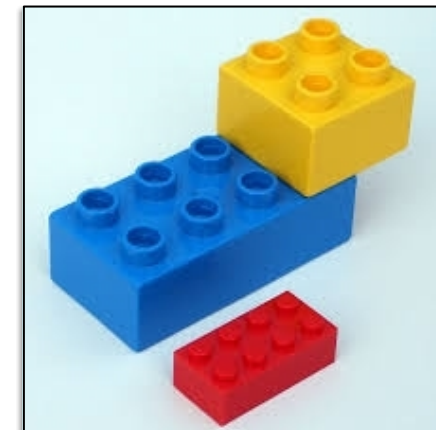
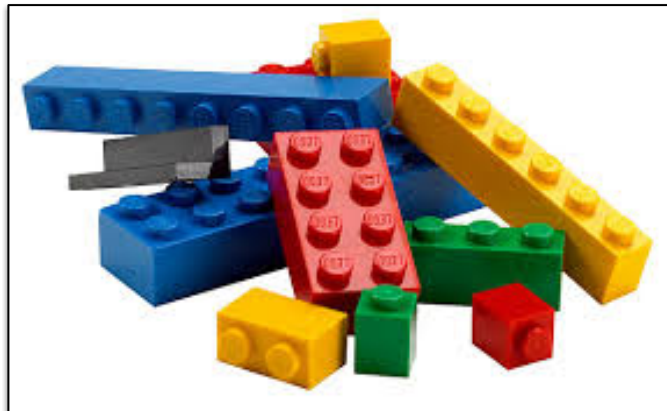


PRECISE PHENOTYPE

FOCAL HYPERTROPHY



**Ability to
discriminate
between**



FAT

VM & LM

CM

ARTERIAL

PERSONNALIZED DIAGNOSTIC AND THERAPEUTIC APPROACH

What are we talking about ?

➤ Precise phenotyping +++

➤ Vascular components

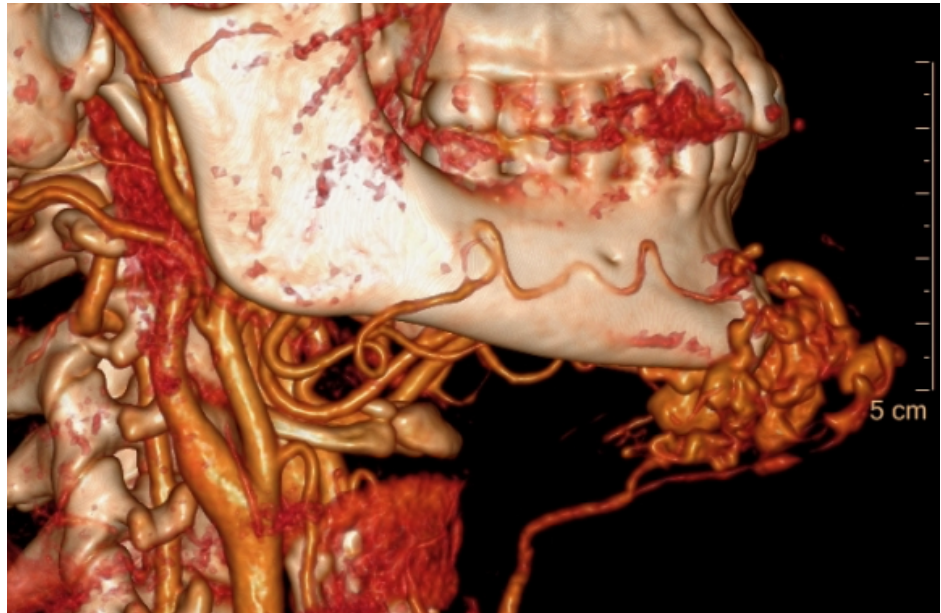
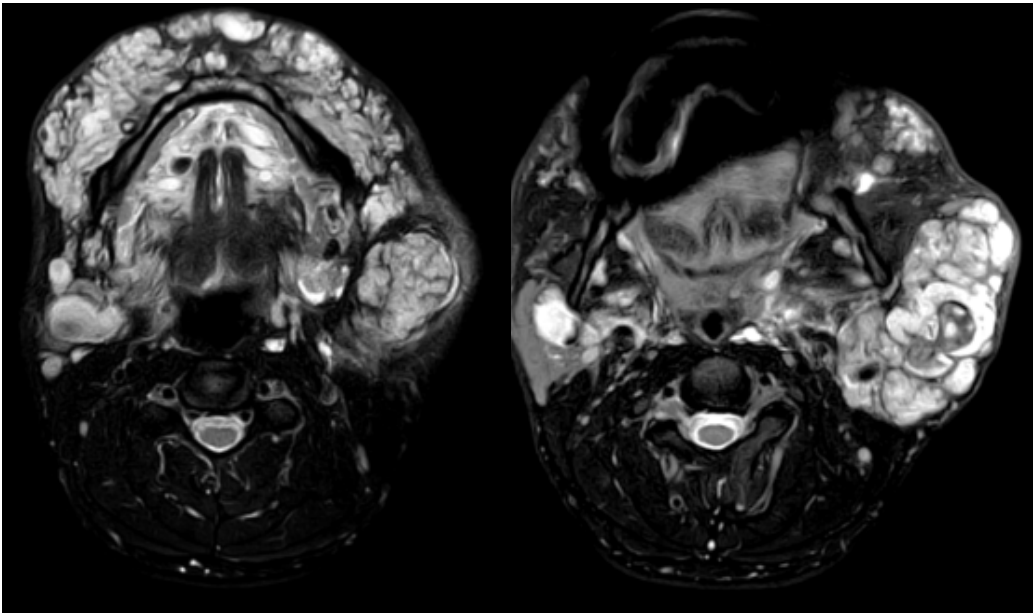
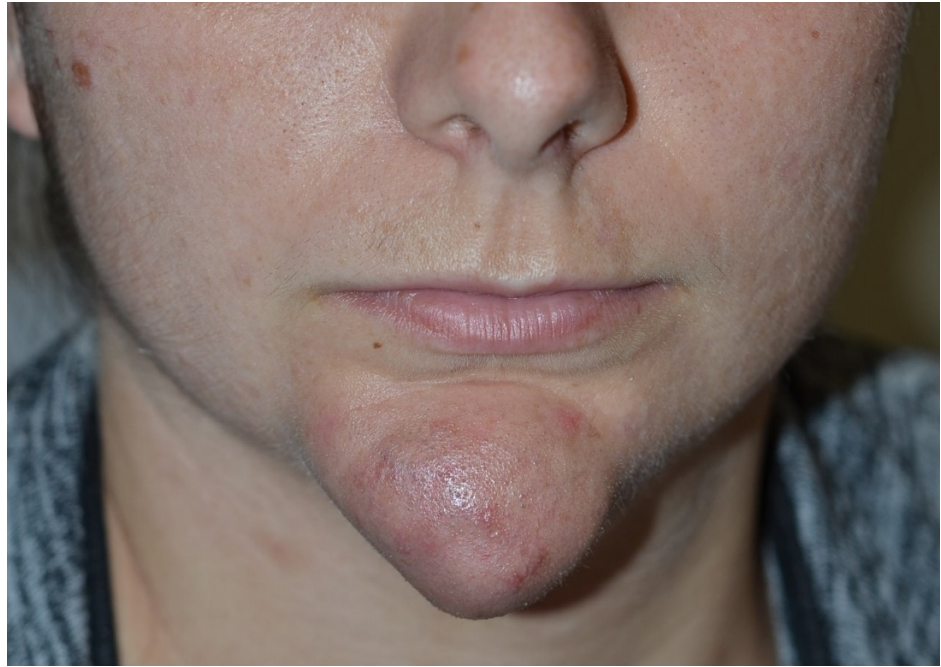
- Low flow: LF (micro/macro/mixed), VM (cavernous/ectasia)
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- CM (suggestive of syndromic/genetic entities)
 - CM-AVM : dominant mutation and interest of familial examination
 - PROS : PIK3CA related overgrowth spectrum

➤ Fatty component

- Can participate more or less in segmental hypertrophy
- May suggest a particular genotype (PTEN, PIK3CA variant...)

➤ Adequate imaging tools (segmentation for quantification/volumetry)

- Doppler-ultrasound as a first step for characterization +++ (well-circumscribed/infiltration, low/fast flow)
- MRI +++ for low-flow malf : : fat sat T2 W-sequences at least two planes +++, T1 fat/microshunts infiltration
- Angio-CT for high-flow malf +++ (except if previous embolization using ONYX !)



PERSONNALIZED DIAGNOSTIC AND THERAPEUTIC APPROACH

Today, such approach means genotyping +++

➤ Genotyping

- Based on a precise clinical and radiological phenotype (patient-familly)
- Orientation towards somatic /constitutional mutation (variant) (important for adequat sample : blood vs tissue)
- Double objective : diagnostic (cas-index/familial) and therapeutic (targeted therapy)

➤ Therapeutic management

- Conventional therapies : IR +++
 - Percutaneous approach for low flow vascular malformations +++
 - Choice of sclerosing agent related to personal experience (alcohol, polidocanol, bleomycin/ pure vs foam)
 - Under general anesthesia/ hypnosis
 - One day care /hospitalisation in ICU (ENT locations related to post-procedure oedema)

PERSONNALIZED DIAGNOSTIC AND THERAPEUTIC APPROACH

What are we talking about ?

➤ Genotype

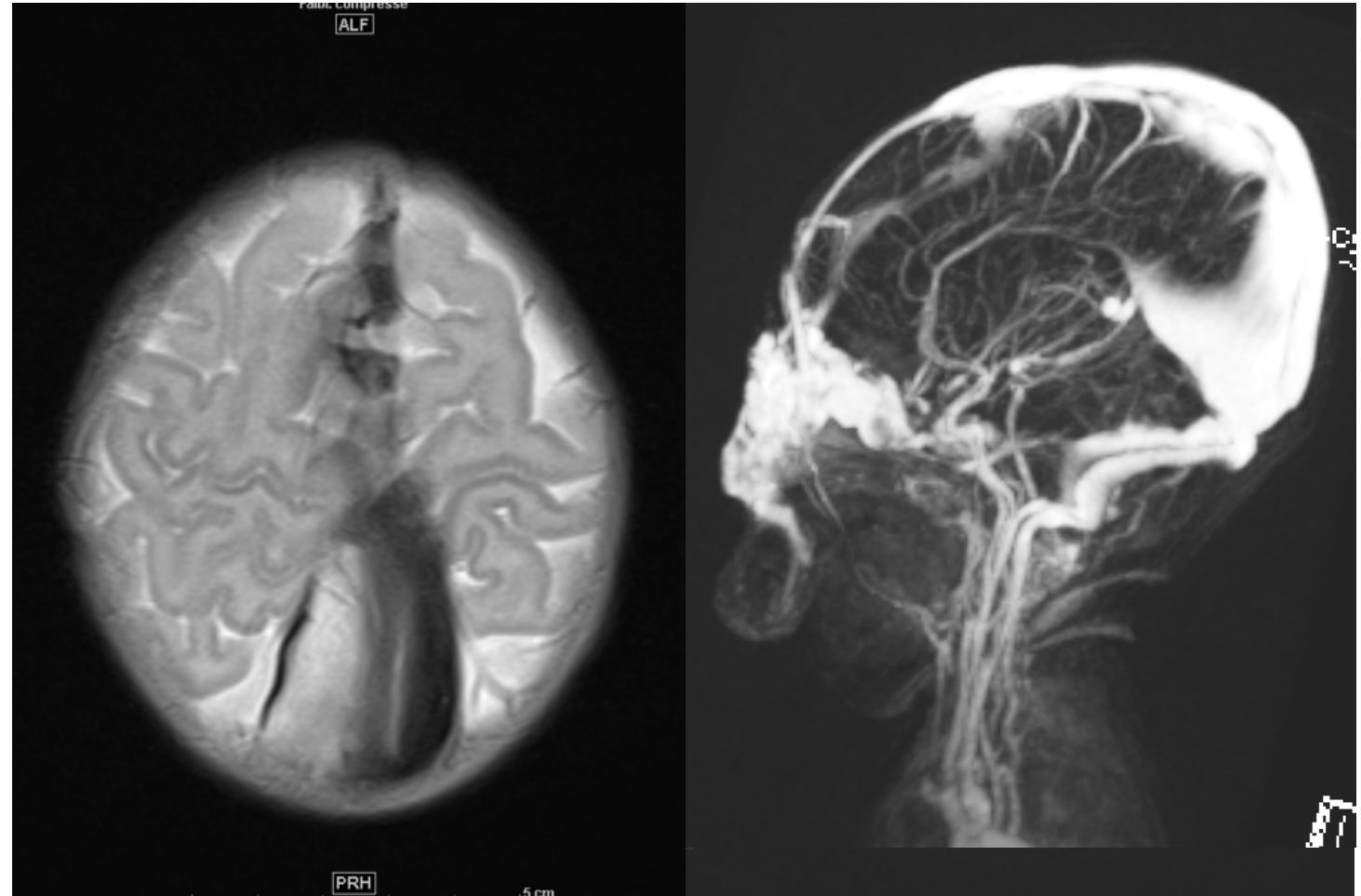
- Based on a precise clinical and radiological phenotype (patient-famililly)
- To look for somatic or constiturional mutation (variant) (adequat sample)
- Double objectif : diagnostic (familial) and therapeutic (targeted therapy)

➤ Therapeutic support

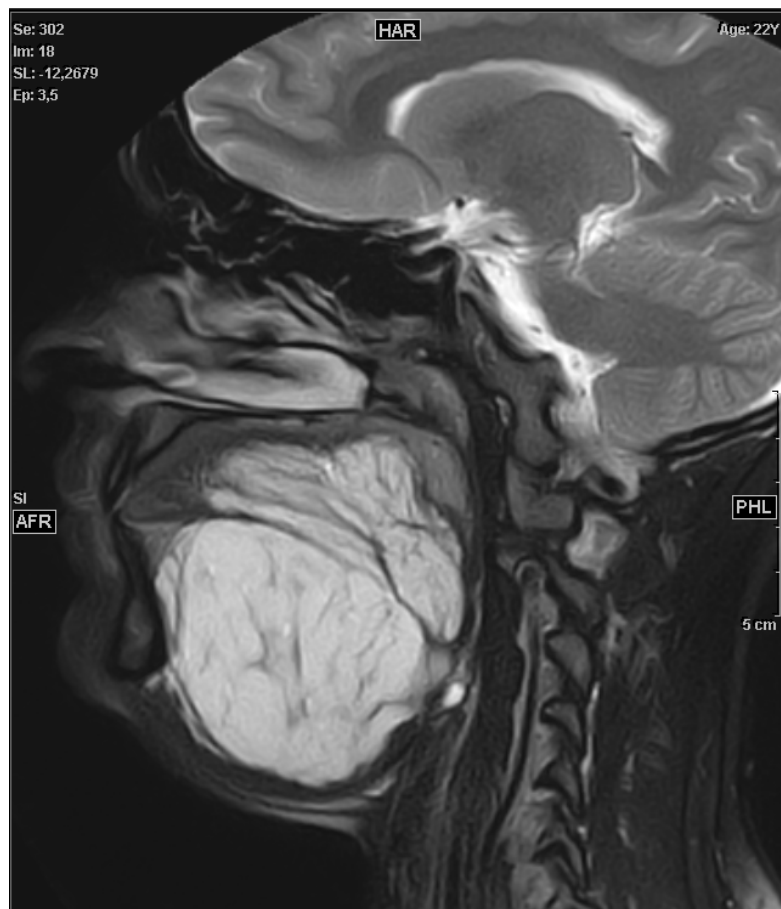
- Conventional therapies
 - IR +++/Surgery/Laser
- Medical therapy
 - Control of inflammatory episodes by analgesic drugs (ML microK / MV thromboses) +++
 - Steroids or NSAIDs, aspegic, low molecular weight heparin (LIVC+++)
 - Betablockers (high flow lesions)
 - Anti-angiogenic drugs +++
 - Targeted or not (Rapamycin : action on the end of PIK3CA-mTOR signaling pathway)
 - ON/OFF action on somatic activating variant -> long-term therapy
 - Dedicated to extensive/diffuse highly symptomatic vascular malformations

PERSONNALIZED APPROACH

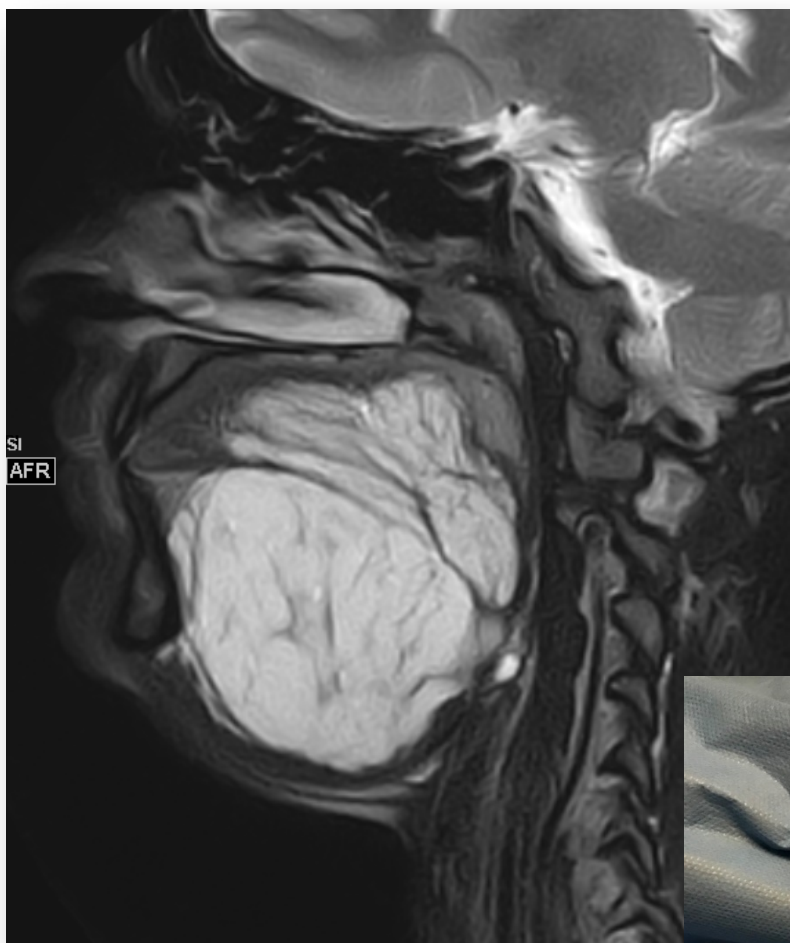
IN DAILY PRACTICE !



MAIN LIMITATION FOR PERCUTANEOUS PROCEDURES
DIRECT CONNECTION OF THIS EXTENSIVE VM WITH THE SUPERIOR LONGITUDINAL SINUS

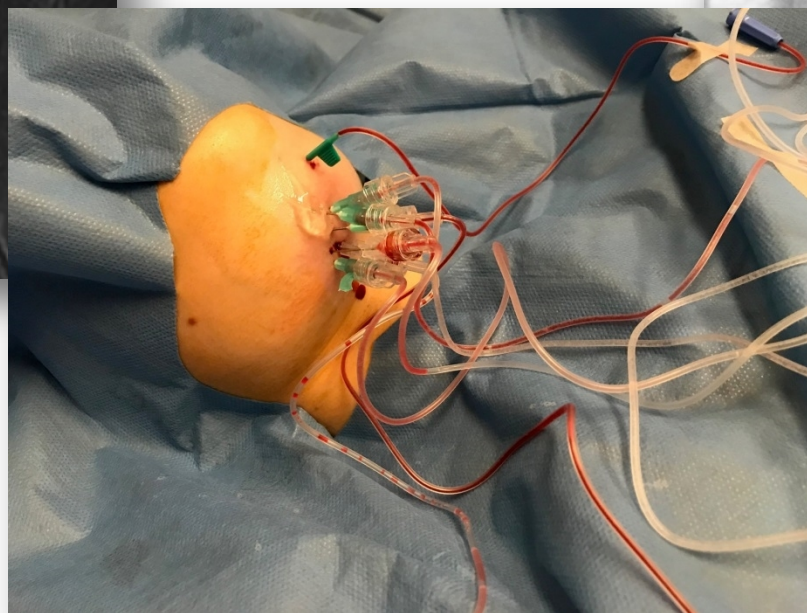
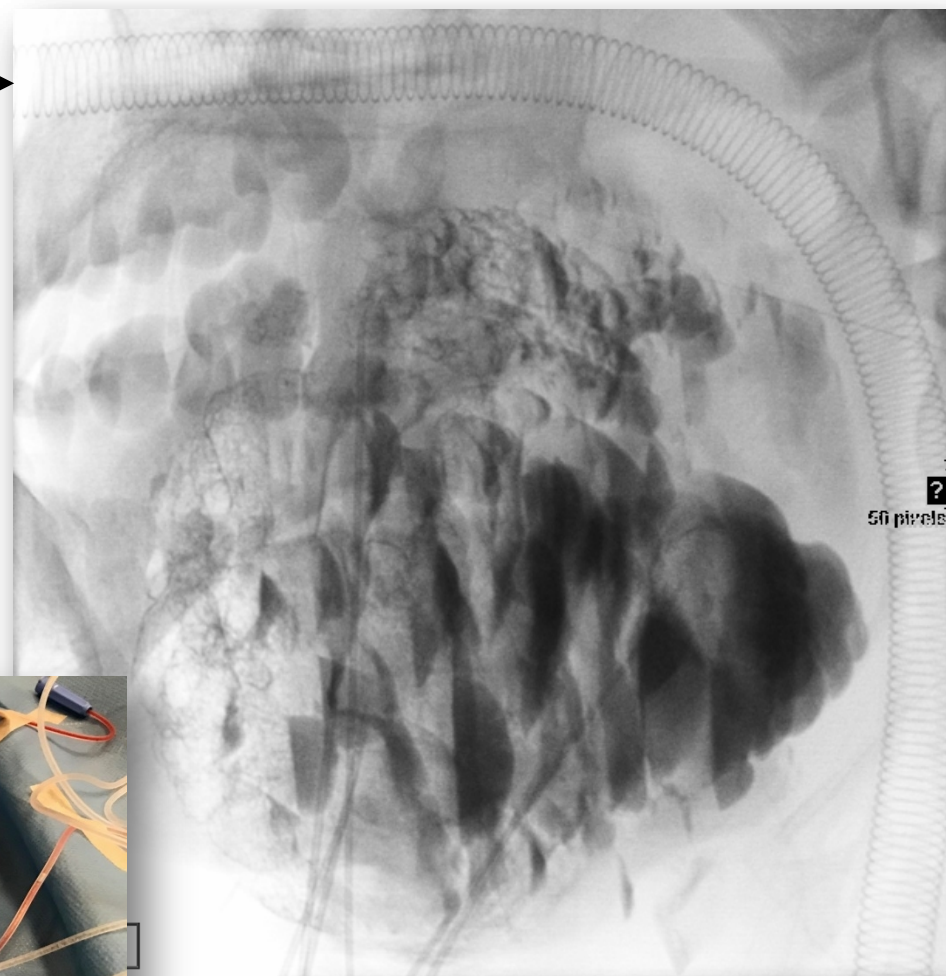


18 YO, referred for extensive ENT VM resistant to 7 prior percutaneous procedures
Severe elocution difficulties and esthetic impact on a markedly depressive patient

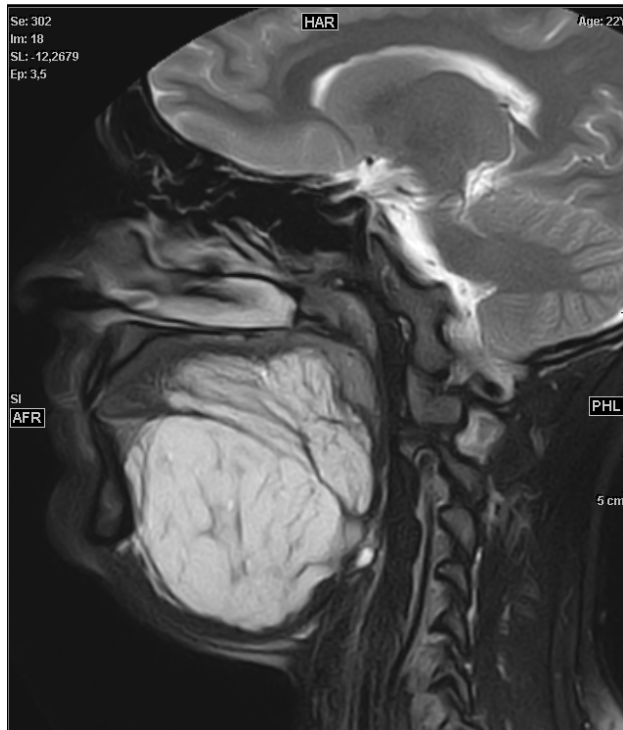


Naso-tracheal tube →

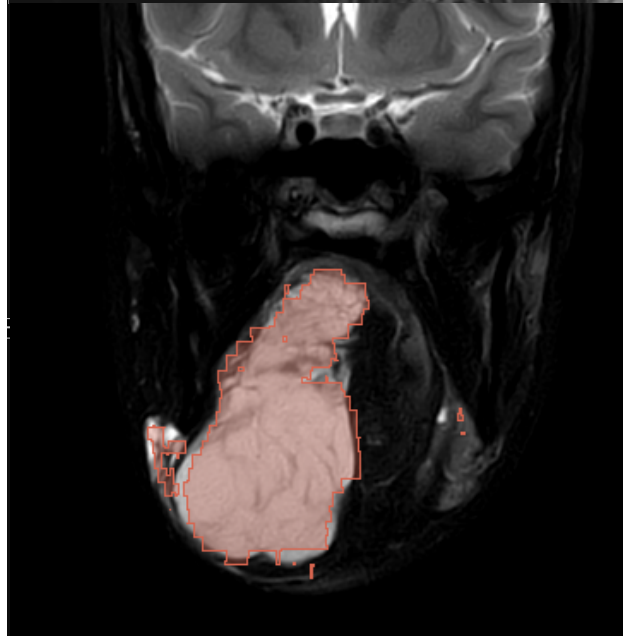
Transferred to ICU
for early post-operative
course due to
post procedure
oedema



JANUARY

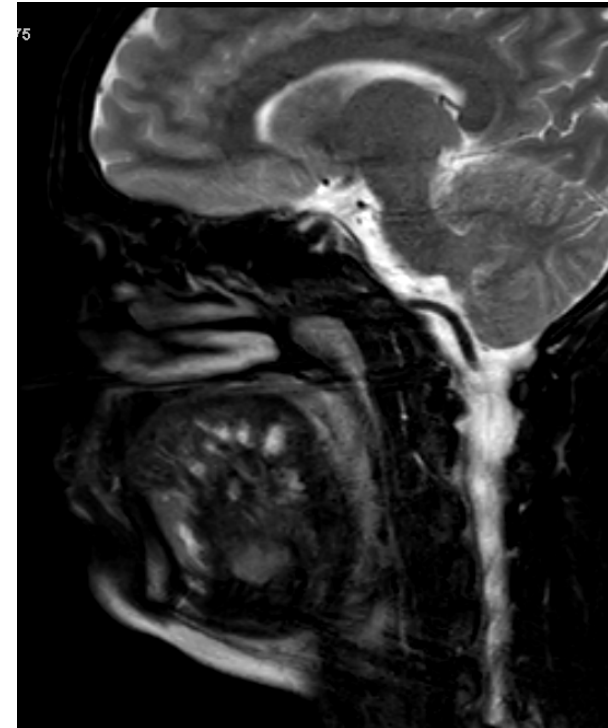


141 cc



→ 28 cc

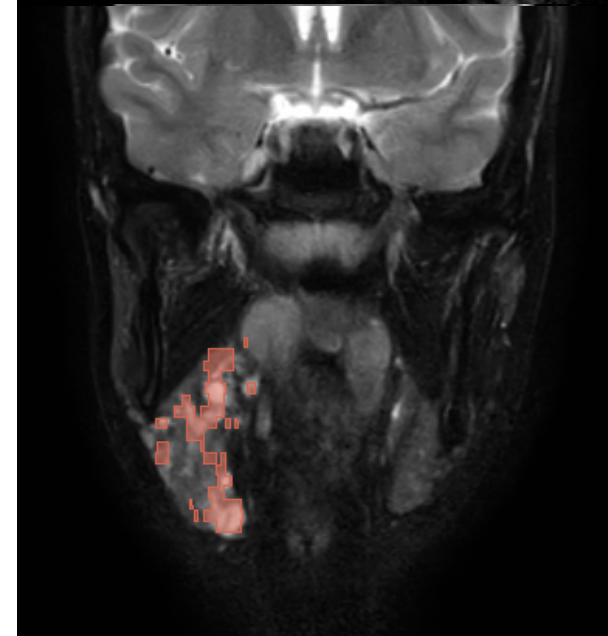
JULY



AFTER 1 PROCEDURE

RELATIVE REDUCTION 80 %

EXCELLENT RESPONSE



JANUARY

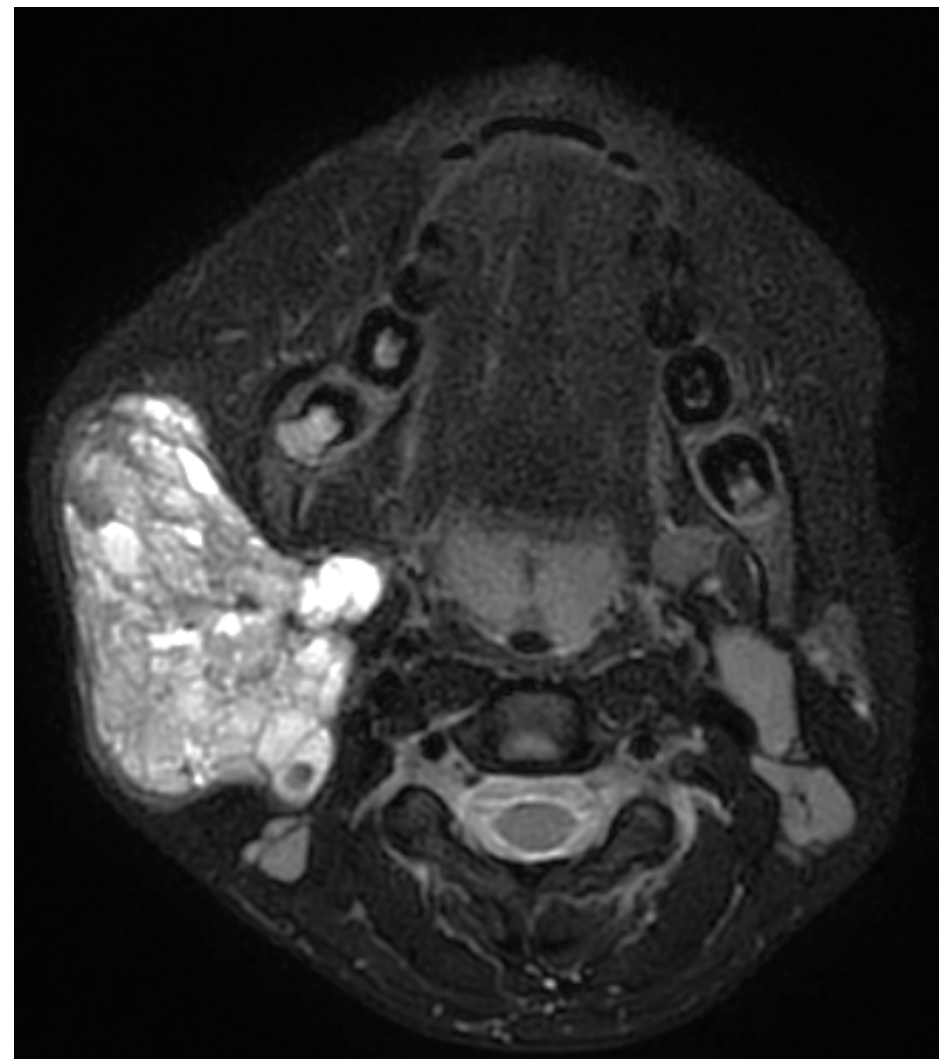


JULY



SUBJECTIVE CLINICAL ASSESSMENT

DRAMATICAL IMPROVEMENT ON THE QUALITY OF LIFE

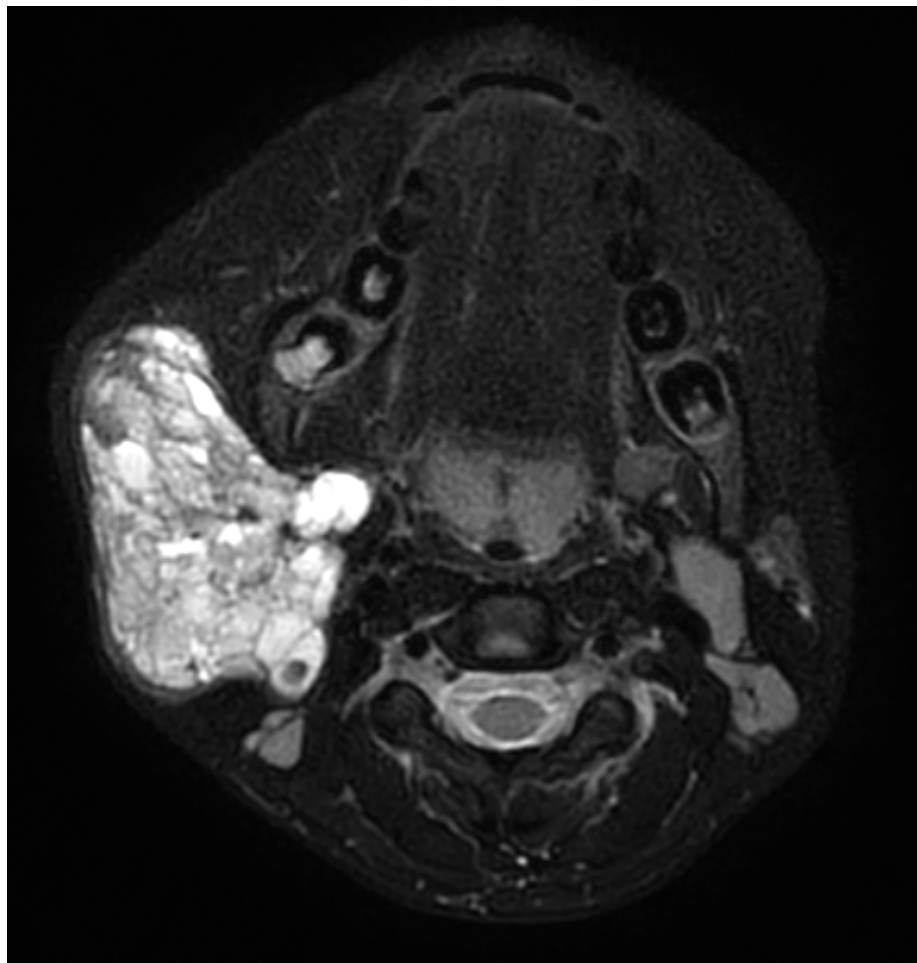


JUNE 2017

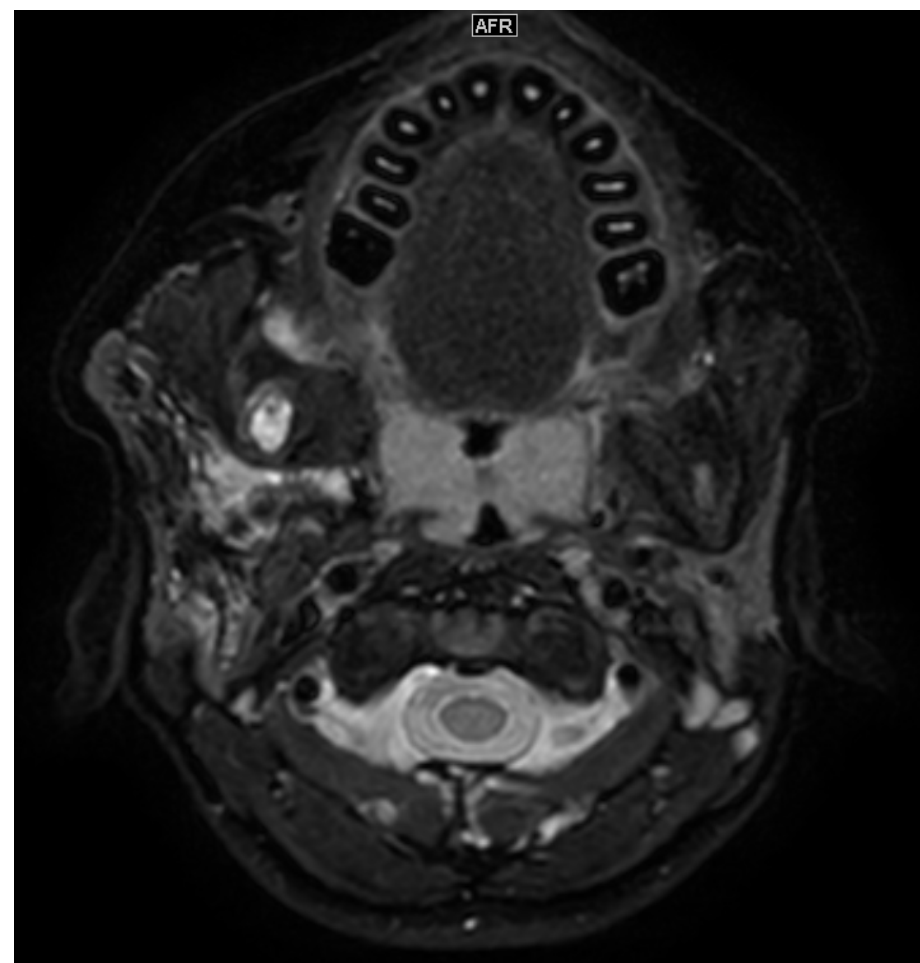


THREE PERCUTANEOUS PROCEDURES
ON A ONE YEAR PERIOD USING BLEOMYCINE
(/3 months)





JUNE 2017



JUNE 2018

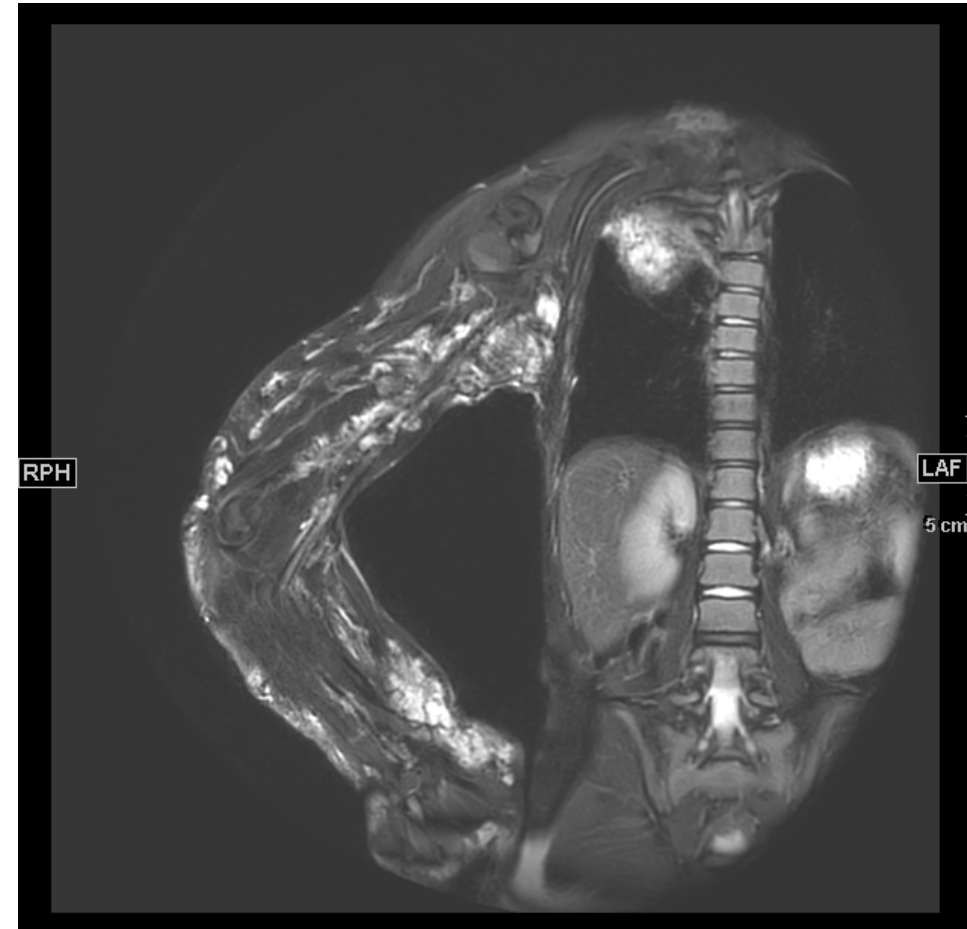
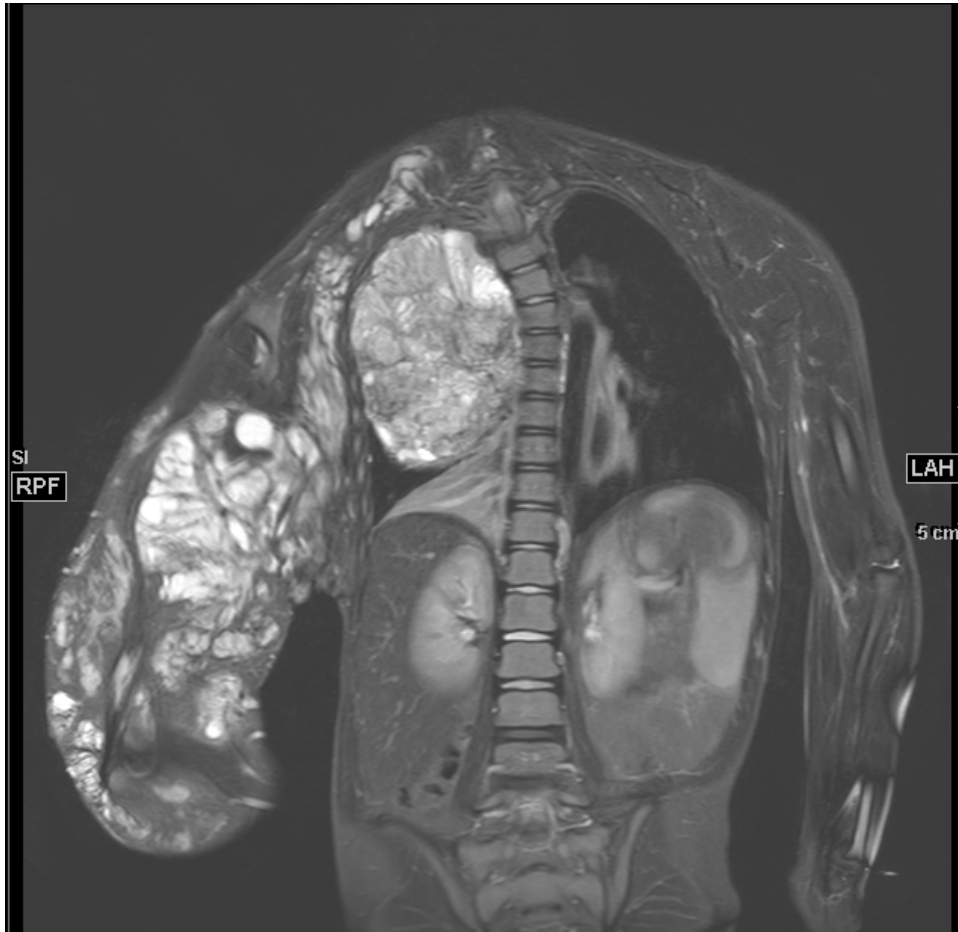


JUNE 2017



JUNE 2018

DIFFUSE LYMPHATIC MALFORMATION NON ACCESSIBLE TO CONVENTIONAL THERAPIES
GENOTYPE : PIK3CA VARIANT allowing TARGETED THERAPY



ZOE AFTER 18 MONTHS OF ALPELISIB THERAPY

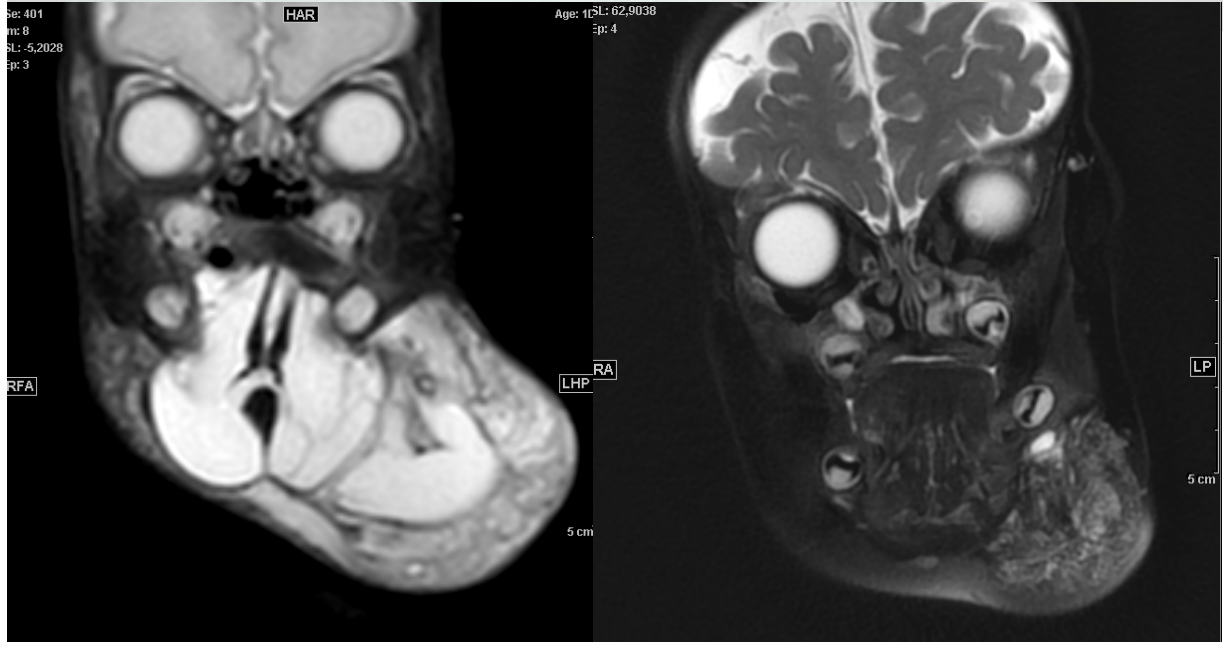
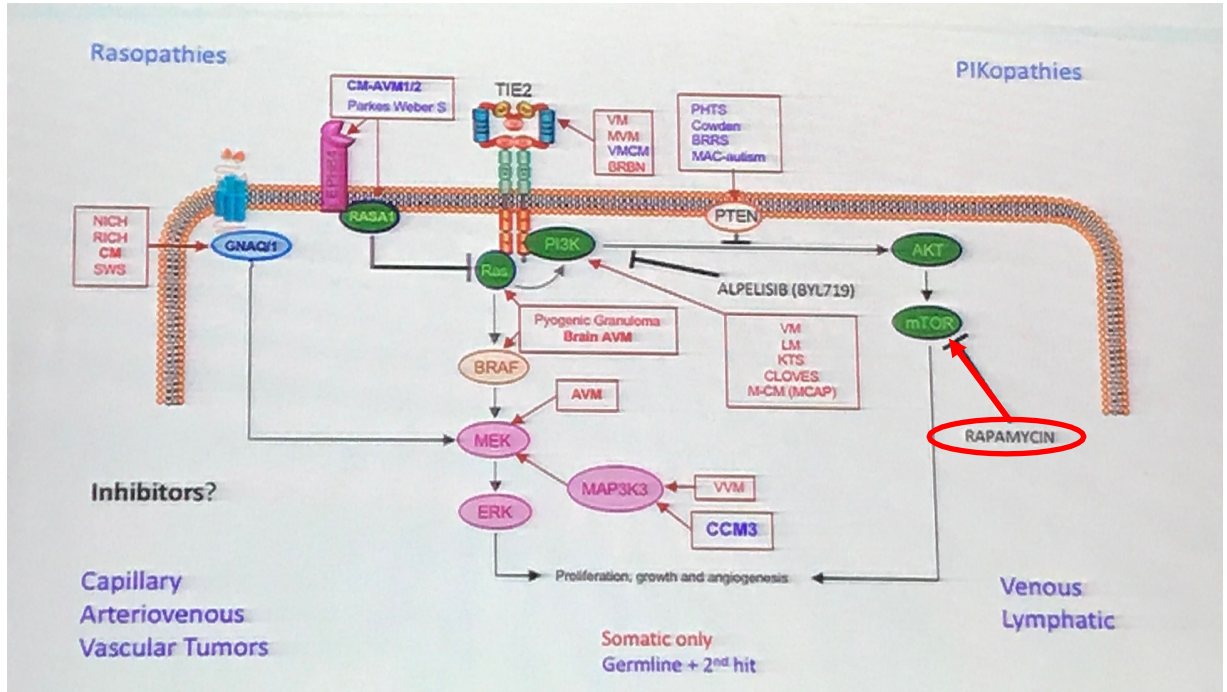
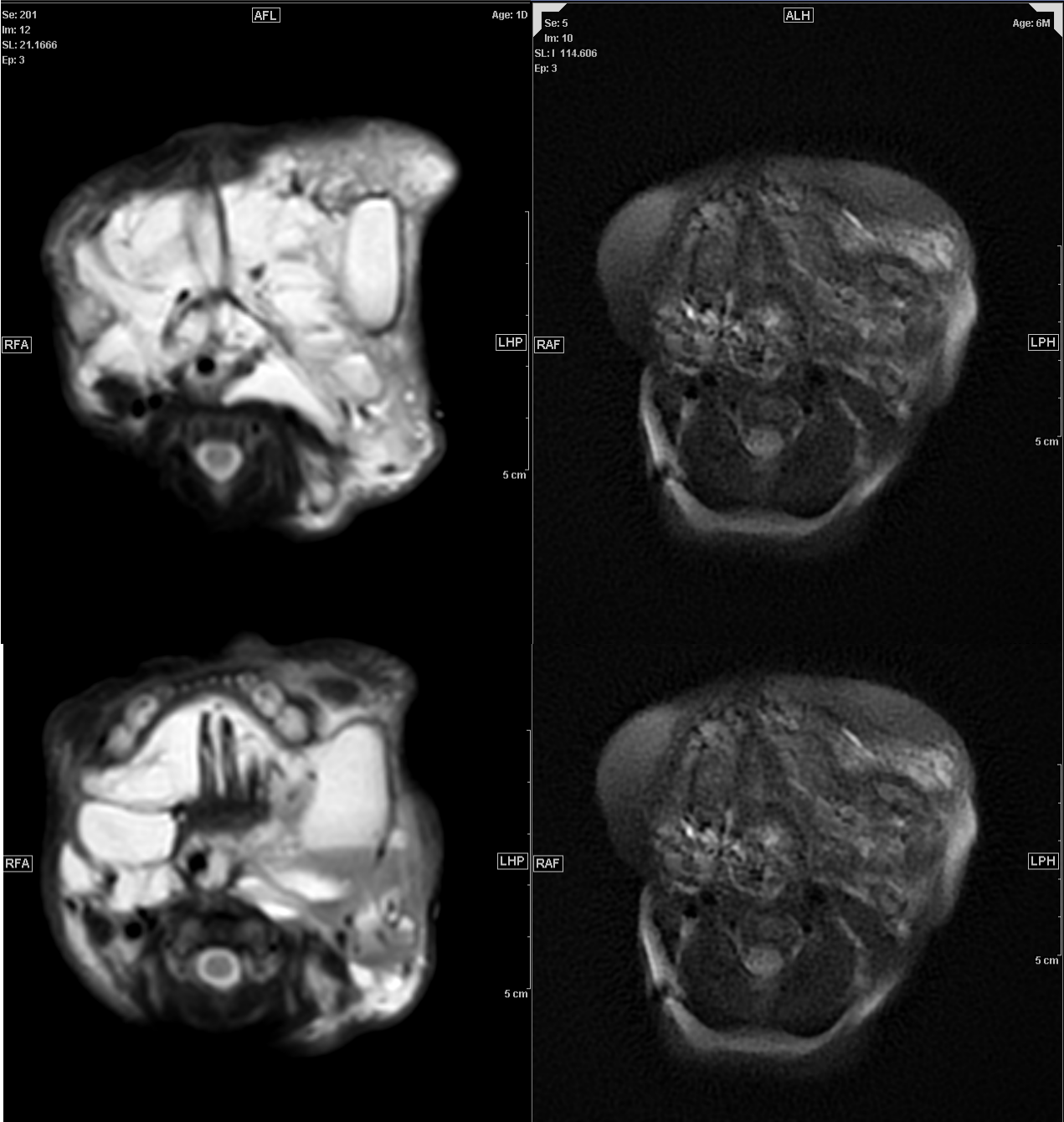
Targeted therapy in patients with PIK3CA-related overgrowth syndrome

Quitterie Venot¹, Thomas Blanc^{1,2,3,21}, Smail Hadj Rabia^{2,4,5,21}, Laureline Berteloot^{5,6}, Sophia Ladraa¹, Jean-Paul Duong^{2,7}, Estelle Blanc⁸, Simon C. Johnson⁹, Clément Huguin¹, Olivia Boccara⁴, Sabine Sarnacki^{2,3}, Nathalie Boddaert^{2,5,6}, Stephanie Pannier^{2,10}, Frank Martinez¹¹, Sato Magassa¹, Junna Yamaguchi¹, Bertrand Knebelmann^{1,2,11}, Pierre Merville^{12,13}, Nicolas Grenier¹⁴, Dominique Joly^{1,2,11}, Valérie Cormier-Daire^{2,5,15}, Caroline Michot^{2,5,15}, Christine Bole-Feysot⁵, Arnaud Picard^{2,16}, Véronique Soupre¹⁶, Stanislas Lyonnet^{2,5,15}, Jeremy Sadoine¹⁷, Lotfi Slimani¹⁷, Catherine Chaussain^{2,17}, Cécile Laroche-Raynaud¹⁸, Laurent Guibaud¹⁹, Christine Broissand²⁰, Jeanne Amiel^{2,5,15}, Christophe Legendre^{1,2,11}, Fabiola Terzi^{1,2} & Guillaume Canaud^{1,2,11*}



ASSOCIATION OF ANTI-ANGIOGENIC DRUGS AND SCLEROTHERAPIES



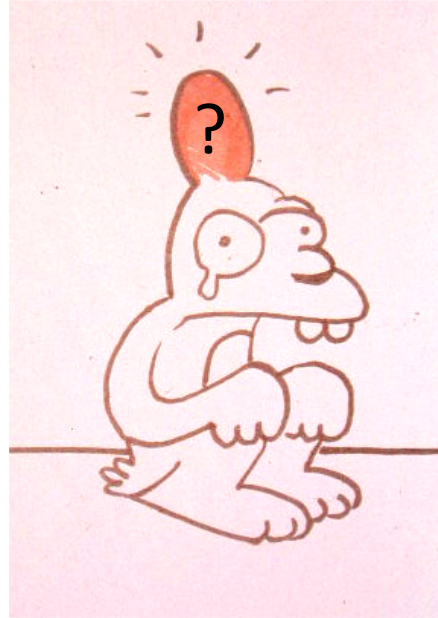




PERSONNALIZED APPROACH OF SUPERFICIAL VASCULAR MALFORMATIONS

From diagnostic to therapy, present and future...

- Precise phenotype
 - Based on clinical and imaging features
 - ✓ Adequate imaging tools after initial work-up based on Doppler ultrasound
- Genotype
 - ✓ Based on clinical and imaging phenotype
- Therapeutic management
 - IR +++ (bleomycine), surgery, laser
 - Medical therapy
 - ✓ Gene therapy, a new paradigm
 - ✓ It is now and in a near future for vascular malformations !

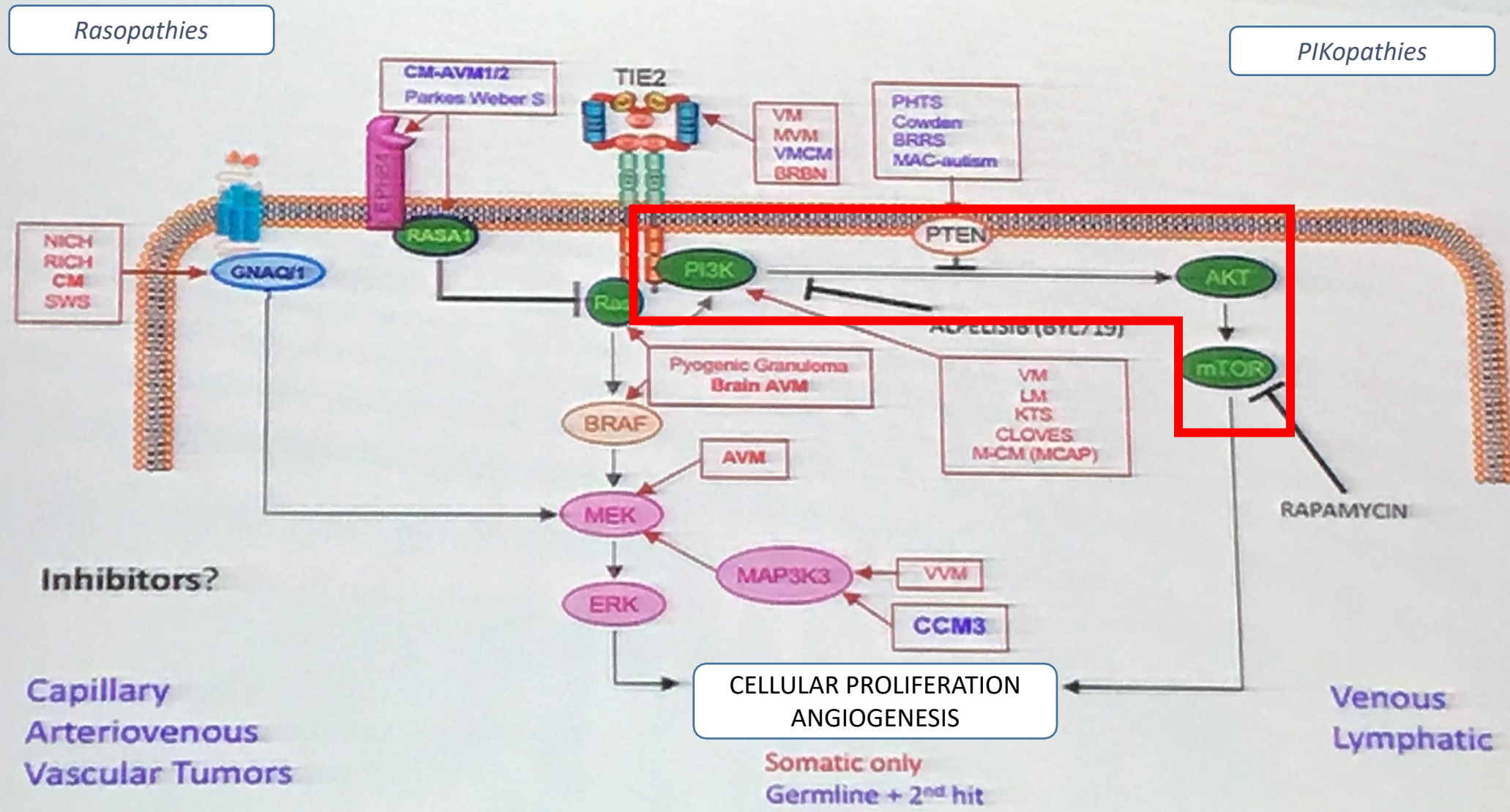


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SIGNALING PATHWAYS IN VASCULAR MALFORMATIONS



SIGNALING PATHWAYS IN VASCULAR MALFORMATIONS

