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Actualización en Anomalías y Malformaciones Vasculares

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Jefe de Servicio de Cirugía Pediátrica

Hospital La Paz

Vascular birthmarks in infants: importance of treating the 10%

by **Thomas K. McInerny, M.D., FAAP**, **Bernard A. Cohen, M.D., FAAD, FAPD, FAAP**, and **Linda Rozell-Shannon, Ph.D., M.S.**

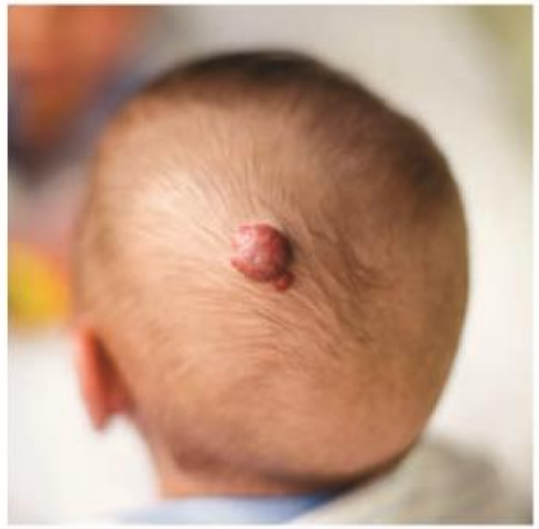
Since its inception in 1994, the Vascular Birthmarks Foundation (VBF) has focused on combating the old benign neglect philosophy of "leave it alone, it will go away" for treating, or not treating, an infant diagnosed with a vascular birthmark. The foundation, along with the Academy and pediatric dermatologists, is taking a more proactive role in early treatment education.

Annually, one in 10 infants is born with a vascular birthmark. These birthmarks include infantile hemangiomas, port wine stains, venous malformations, lymphatic malformations, arteriovenous malformations and associated syndromes such as PHACES, Klippel-Trenaunay and Sturge-Weber.

Based on the average of 4 million live births a year in the U.S., 400,000 babies will be born with a vascular birthmark. Ninety percent of these birthmarks will go away, requiring no intervention. The remaining 10%, or 40,000 vascular birthmarks, will be so significant that they will necessitate a referral to a vascular birthmarks expert for evaluation.

These 10% are the primary focus of the VBF, the Academy and pediatric dermatologists. These are the hemangiomas that can distort tissue, obstruct vision, impair eating, ulcerate and bleed profusely. They also include the port wine stains that can progress and thicken with a risk of pain, irritation, bleeding and infection as well as psychosocial scarring for the child and the family. Left untreated, these 10% can face a life of countless surgeries and psychotherapy sessions.

Prior to the 1980s, there were few options for treating a vascular birthmark. Couple this with the



new information has not yet trickled down to the decision-making insurance providers. Nearly 75% of the families seeking treatment will be denied on a first submission and will need to appeal.

In 2015, VBF worked with the Academy to send a letter to all insurance carriers strongly encouraging coverage of treatment, http://bit.ly/2n7OFlX.

Many physicians and families use this letter to appeal denials. Some are successful, and some are not. Many parents give up and pay cash for treatment. Surgeries can range from $4,000 to $40,000, and laser treatments can range from $500 to $1,500 each. This poses an unnecessary financial hardship on the families. VBF works with many to appeal denials and to urge insurers to cover treatment.

As we mark Vascular Awareness Birthmarks Month in May, the Vascular Birthmarks Foundation along with the Academy and pediatric dermatologists are calling on all primary care physicians to refer infants at the 4-week well-baby check-up to a vascular

present, does not appear to be resolving and has the potential to become disfiguring and/or problematic so that treatment can begin early. If birthmarks are growing quickly, it is important to send infants for consultation even earlier.

We also are calling on every insurance company to re-examine its policy on denying the treatment of the 10% affected by a vascular birthmark that will not resolve and who are at risk for serious complications.

Early diagnosis and early treatment will not only ward off psychosocial trauma to the family system and reduce the chances of a disfiguring lesion and pain to the infant, they also can reduce the number of treatments that eventually will be required for the untreated 10%.

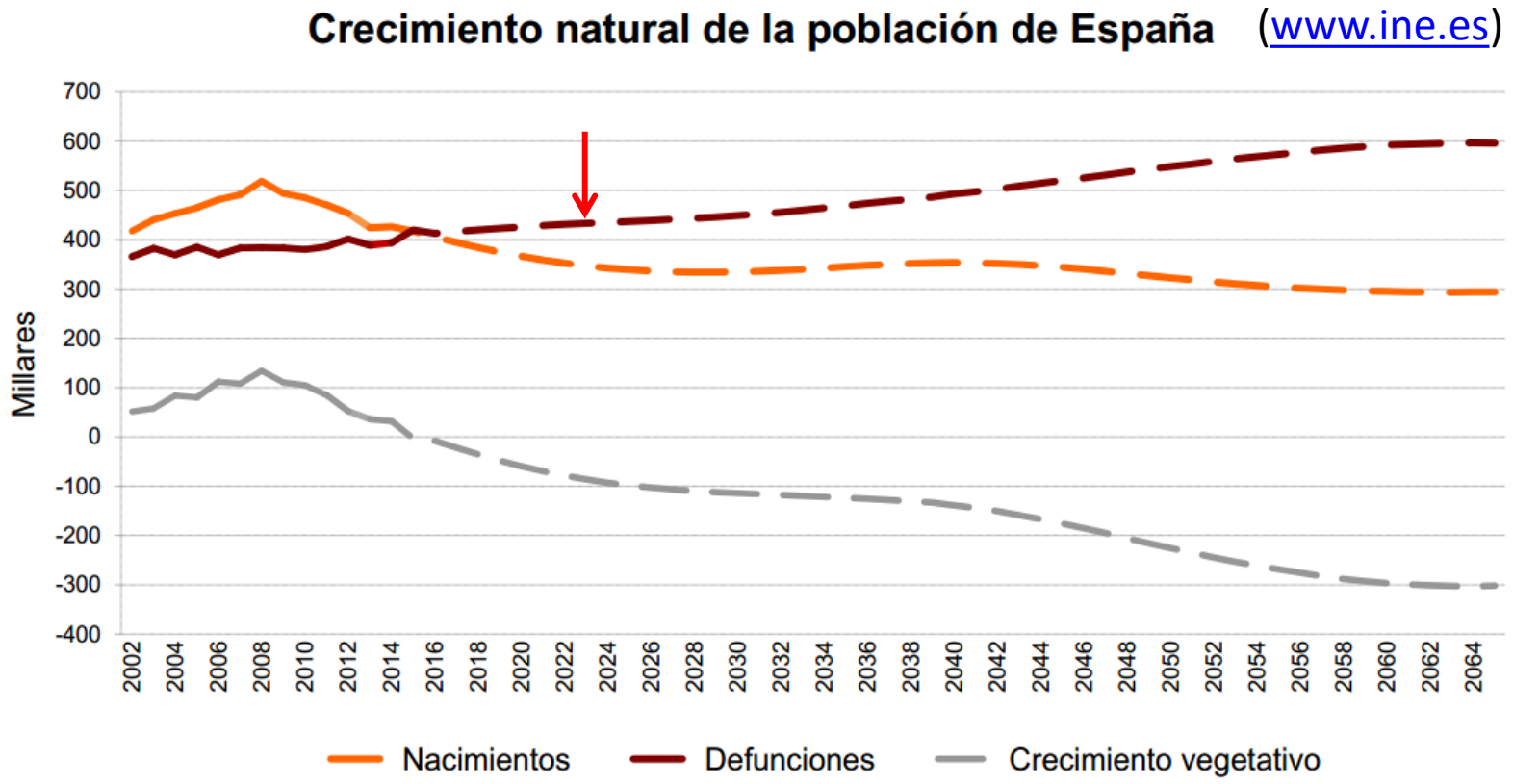
Early treatment for the 10% is win-win. The baby wins, the family system wins, the insurance company wins and the treating physicians wins. Though many would agree that 10% is a small number, it has large consequences for affected families. Early referral and treatment can prevent these consequences and provide the baby and family with the best possible outcome for a normal life.


Dr. McInerny


Dr. Cohen


Dr. Rozell-Shannon

__Dr. McInerny__ is AAP past president (2012-'13). __Dr. Cohen__ is past chair of the AAP Section on Dermatology Executive Committee and past president of the Society for Pediatric Dermatology. __Dr. Rozell-Shannon__ is president/founder of the Vascular Birthmarks Foundation.



En 2023 , nacerán 40.000 niños en España con una anomalía vascular

DÍA INTERNACIONAL

Cada año nacen en España casi 38.000 niños prematuros

En España se detectan al año más de 40.000 nuevos casos de cáncer de colon

Por DocNews el 03/04/2017

Sociedad

España registra 40.000 casos nuevos de Alzheimer cada año

OFTALMOLOGÍA

Casi 30.000 nuevos casos de DMAE cada año en España

http://www.issva.org/classification

INTERNATIONAL SOCIETY FOR THE STUDY OF VASCULAR ANOMALIES

Classification

Please click here to review the new classification. The classification was approved at the April 2014 General Assembly in Melbourne, Australia.

An abbreviate classification is available for your publication. Please click 2014 ISSVA Classification-Abbreviated to get this document.

For citations please use: ISSVA Classification of Vascular Anomalies ©2014 International Society for the Study of Vascular Anomalies Available at "issva.org/classification" Accessed [date]

ISSVA classification for vascular anomalies (issva.org)

Overview table

Vascular anomalies				
Vascular tumors	**Vascular malformations**			
	Simple	**Combined °**	**of major named vessels**	**associated with other anomalies**
Benign Locally aggressive or borderline Malignant	Capillary malformations Lymphatic malformations Venous malformations Arteriovenous malformations* Arteriovenous fistula*	CVM, CLM LVM, CLVM CAVM* CLAVM* others	See details	See list

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Ovarian Hemangiomas Do Not Harbor EWSR1 Rearrangements: Clinicopathologic Characterization of 10 Cases.

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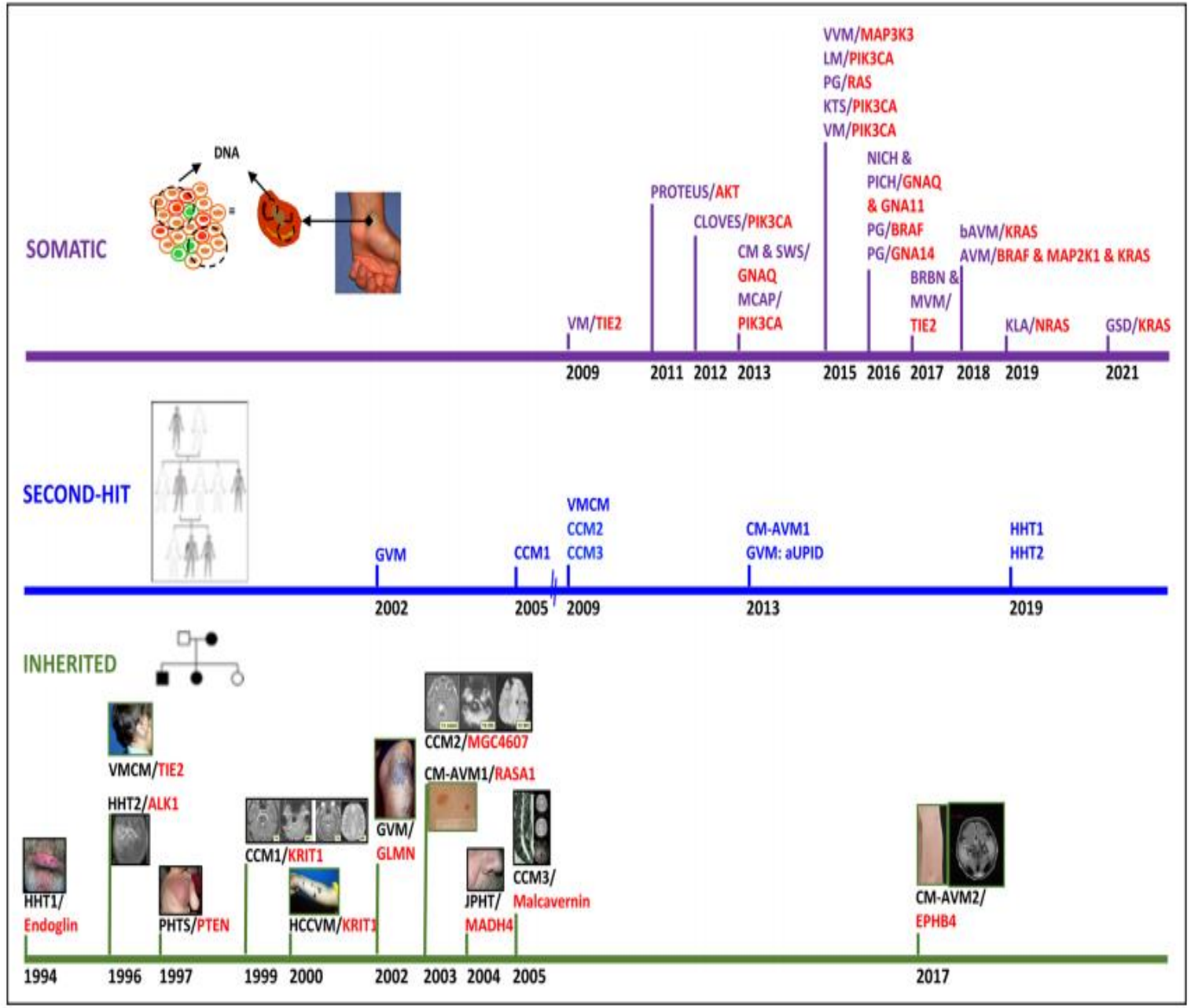
Abstract

Hemangiomas of the ovary are rare with a majority described as individual reports of unusual clinical presentations or morphologic findings. Both the expected and unexpected pathologic features of these tumors in the ovary are not well detailed. Therefore, we collected the largest series of ovarian hemangiomas to comprehensively define their clinicopathologic associations and examine the significance of hormone receptors in their pathogenesis. In addition, a novel EWSR1-NFATC1 fusion has recently been described in a case of hemangioma of bone. To our knowledge, EWSR1 rearrangement has not been evaluated in hemangiomas of other sites or in a case series. Accordingly, we used fluorescence in situ hybridization to investigate EWSR1 status in a majority of our cases. Clinical presentation was variable and dependent on tumor size. Patient age ranged 48 to 87 yr (median 63 yr). Tumors involved the right (n=6) and left (n=3) ovaries with laterality unknown in 1 case, and size ranged from 0.2 to 5.0 cm (median 1.0 cm). Three of 4 radiologic reports were either equivocal or could not exclude malignancy. Seven cases were of the cavernous type and 3 were mixed cavernous and capillary type. All lesions formed a single discrete, circumscribed mass that displaced the surrounding cortical stroma. The cavernous type showed dilated, thin-walled vessels and vascular thrombi, some of which were associated with dystrophic calcification. In addition to cavernous morphology, the mixed form exhibited features of capillary hemangioma such as lobulated growth of capillary-sized vascular spaces that lacked atypia or multilayering and were linked to a larger feeding vessel. Each tumor expressed CD31, CD34, FLI-1, ERG, but not D240. The hemangioma stromal cells, but not endothelium, expressed estrogen and progesterone receptors in every case. Stromal luteinization was seen in 2 cases. Follow-up ranged 1 to 139 mo and all patients were disease free. All cases were negative for EWSR1 rearrangement; however, 2 cases demonstrated additional intact copies of EWSR1 indicating aneusomy 22 or a structural abnormality of chromosome 22 resulting in apparent duplication of the EWSR1 gene region (at 22q12). Although an uncommon entity, awareness of ovarian hemangioma's unique and diverse clinical presentation as well as its potential to radiologically imitate malignant ovarian neoplasms are important.


SOMATIC
DNA
VM/TIE2
PROTEUS/AKT
CLOVES/PIK3CA
CM & SWS/
GNAQ
MCAP/
PIK3CA
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LM/PIK3CA
PG/RAS
KTS/PIK3CA
VM/PIK3CA
NICH &
PICH/GNAQ
& GNA11
PG/BRAF
PG/GNA14
BRBN &
MVM/
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HHT1/
Endoglin
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CCM1/KRIT1
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GVM/
GLMN
CCM2/MGC4607
CM-AVM1/RASA1
JPHT/
MADH4
CCM3/
Malcavernin
CM-AVM2/
EPHB4
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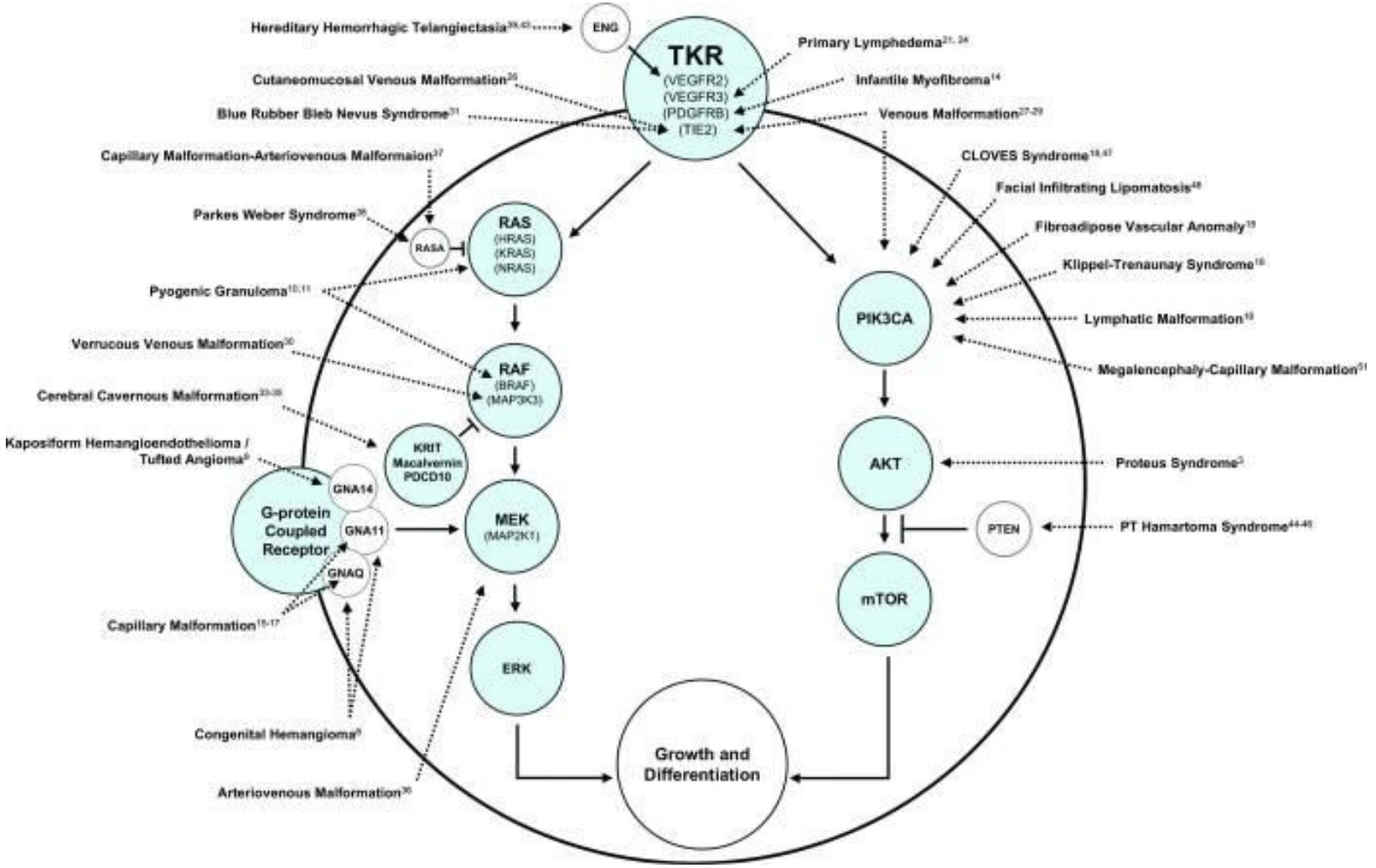
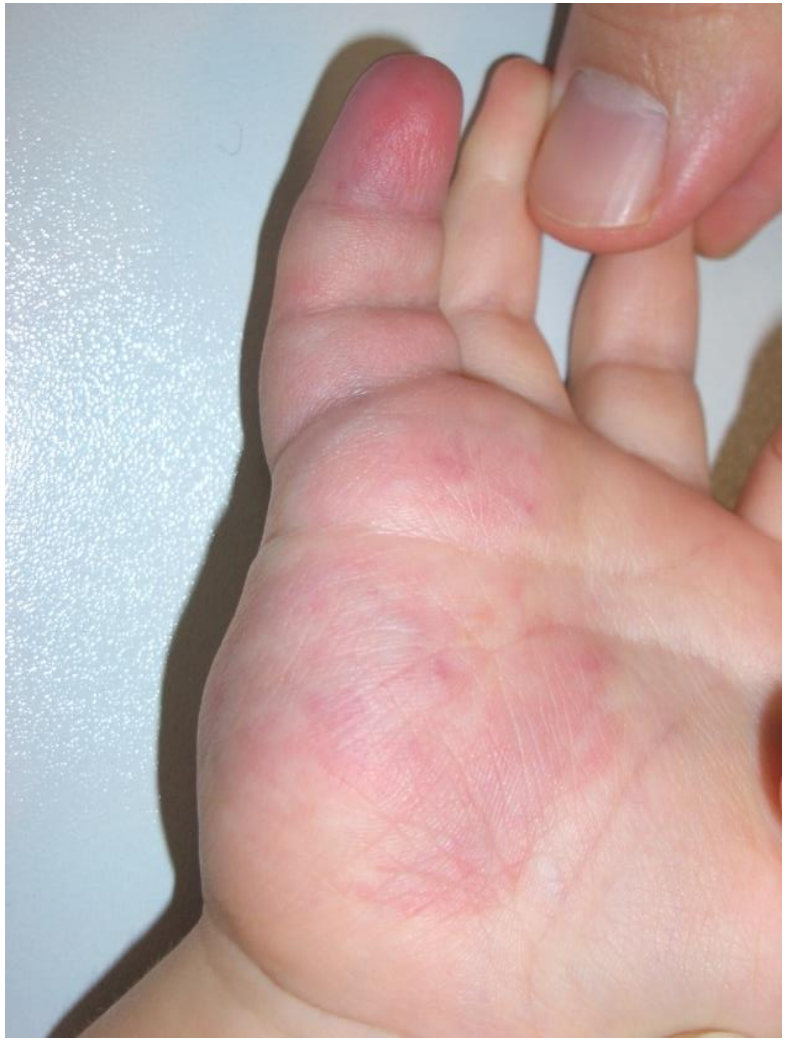
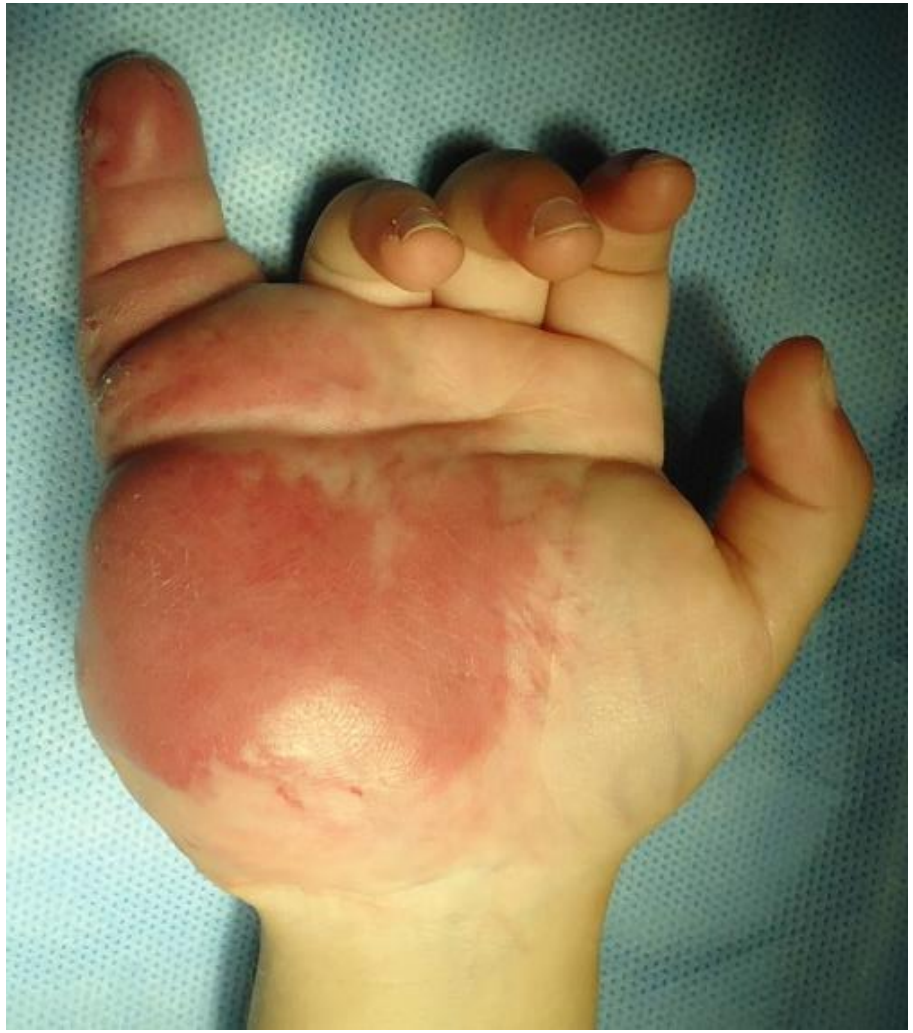
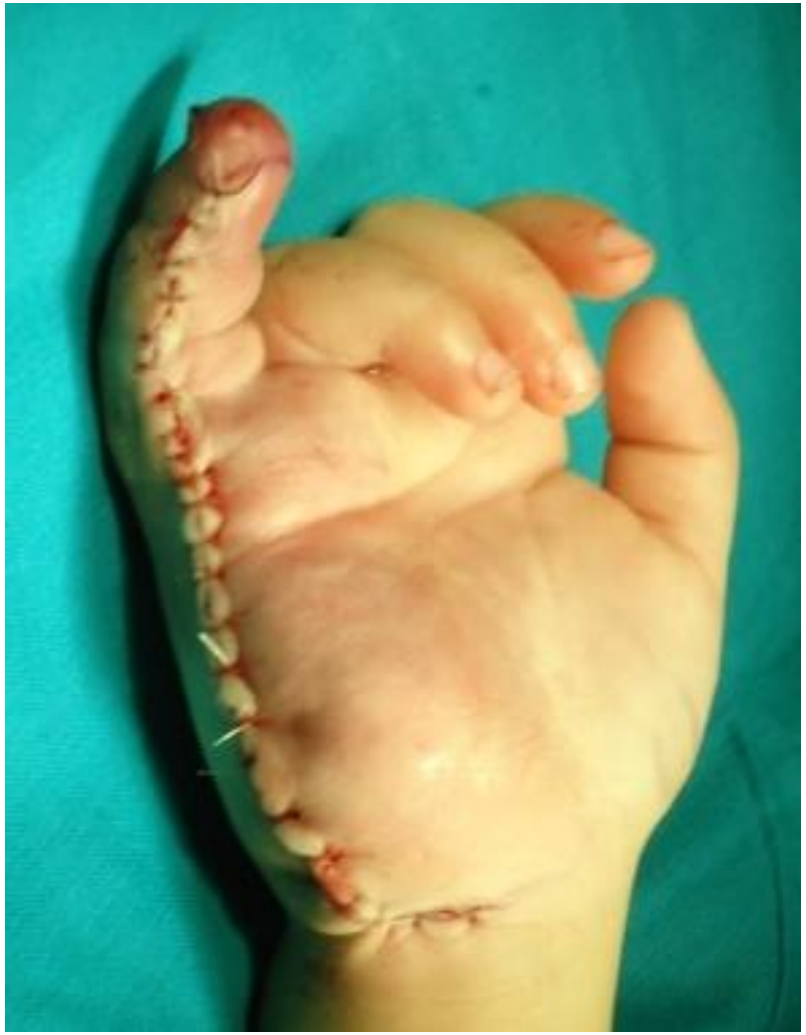
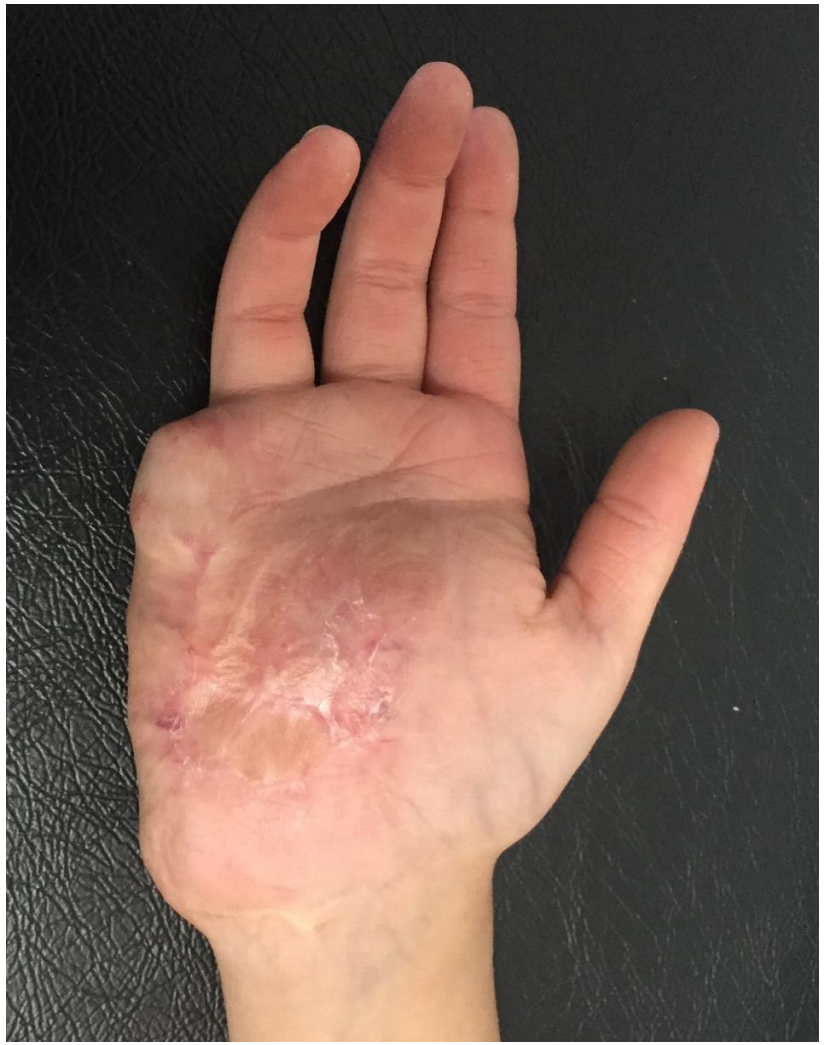
130 Anomalías Vasculares
57 MUTACIONES

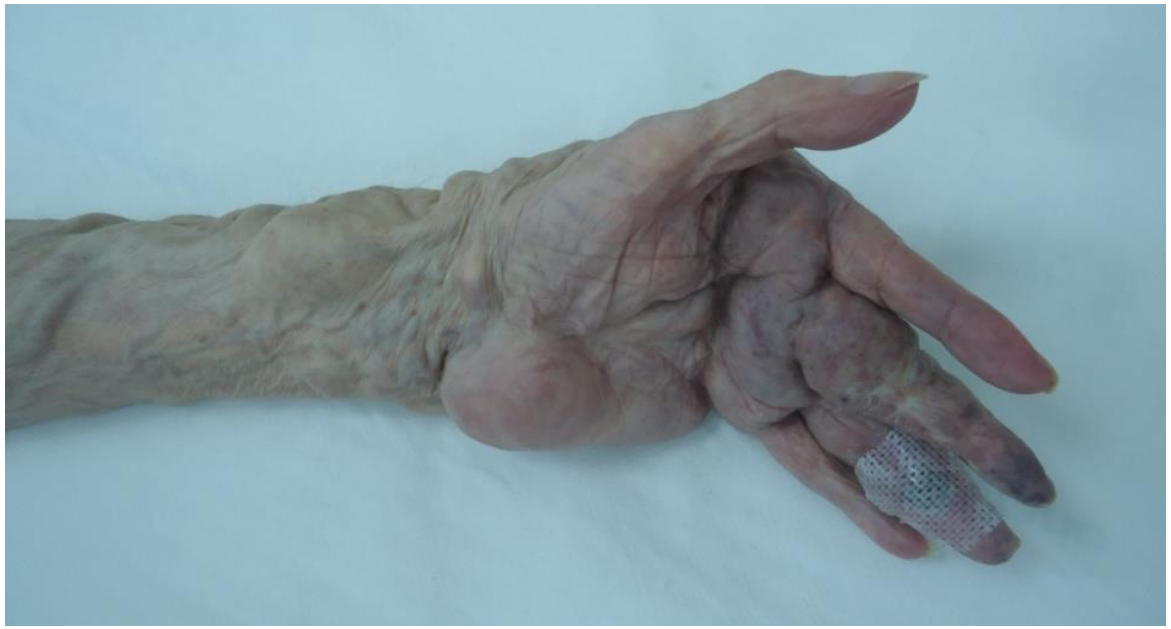


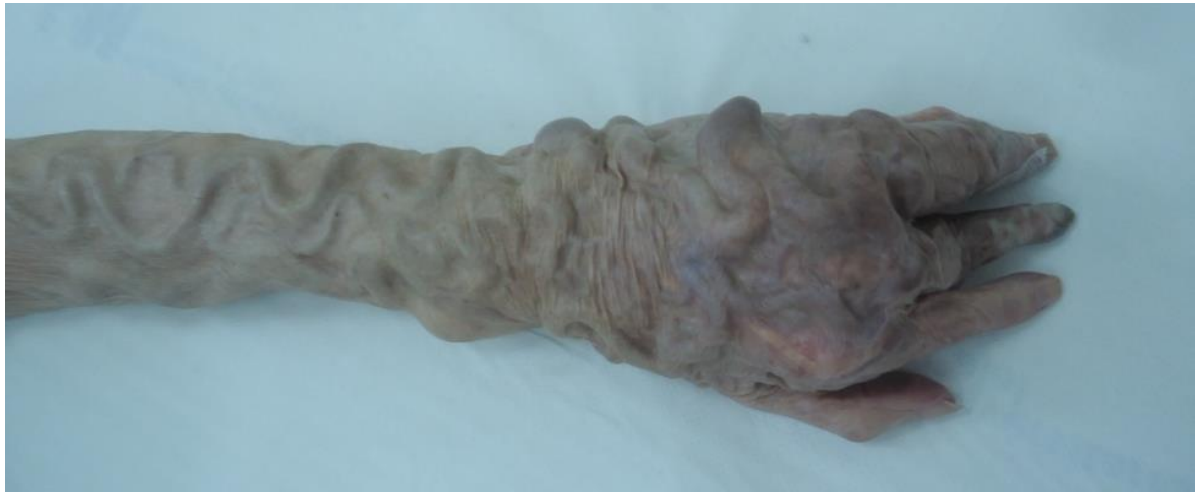


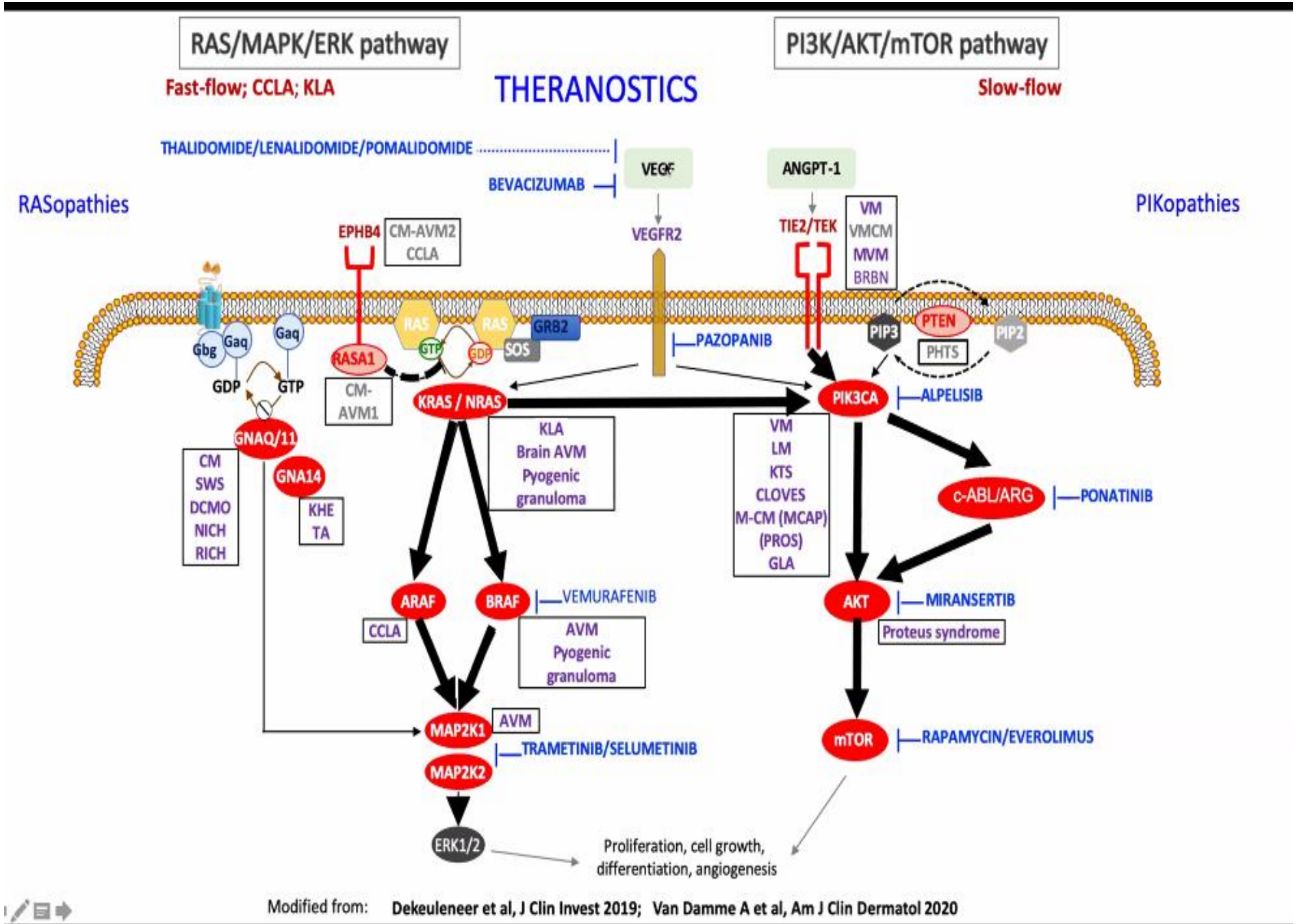












Modified from: **Dekeuleneer et al, J Clin Invest 2019; Van Damme A et al, Am J Clin Dermatol 2020**

2007

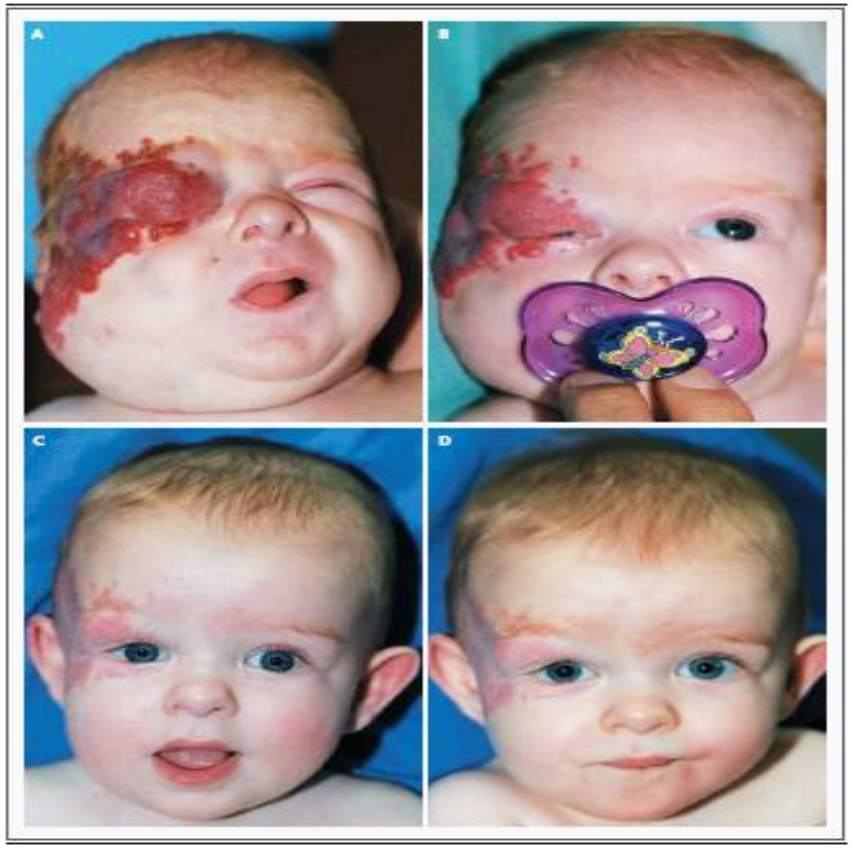
Event of **Interest**

Jan 9 Apple Inc CEO **Steve Jobs** announces the iPhone

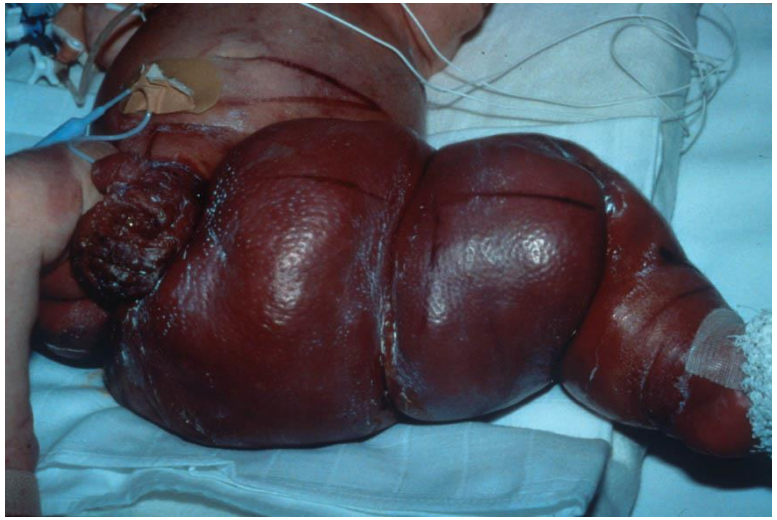
Apple Co-founder
Steve Jobs

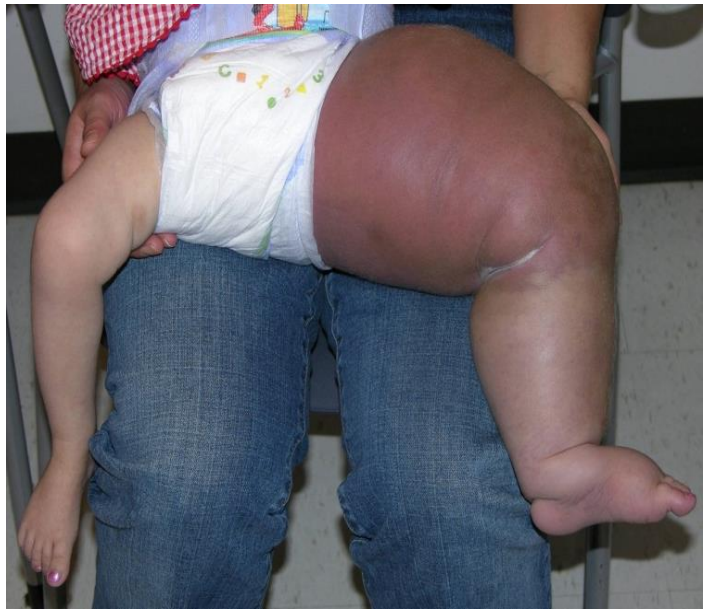
2007

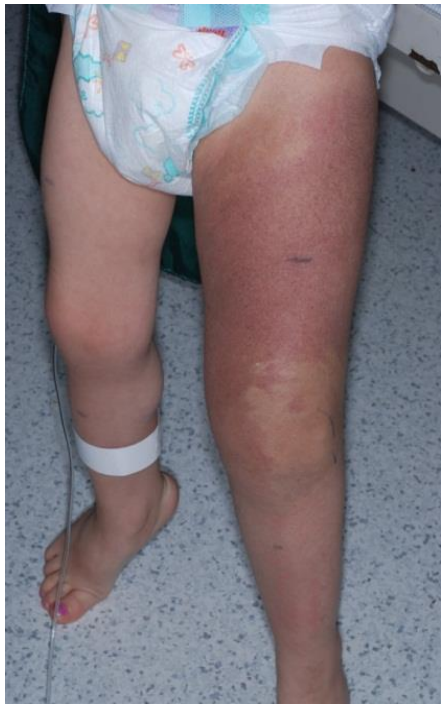
The NEW ENGLAND JOURNAL of MEDICINE

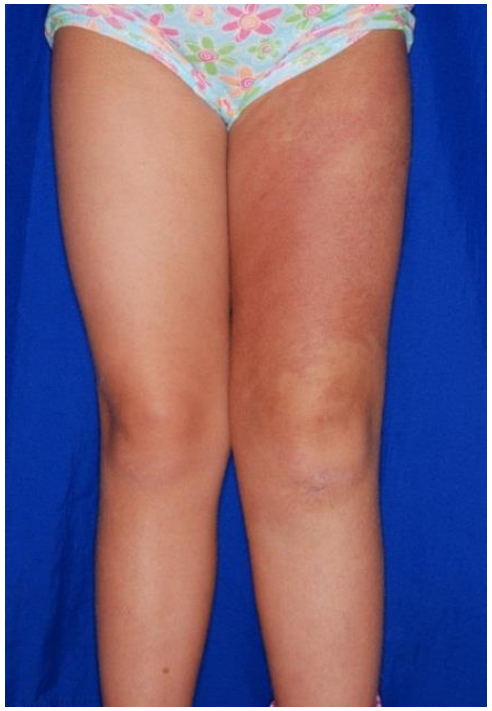


Infantile capillary hemangiomas are composed of a complex mixture of clonal endothelial cells associated with pericytes, dendritic cells, and mast cells.[1] Regulators of hemangioma growth and involution are poorly understood. During the growth phase, two major proangiogenic factors are involved: basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF)[1]; histologic studies have shown that both endothelial and interstitial cells are actively dividing in this phase. During the involution phase, apoptosis has been shown.[1] Potential explanations for









2007

Courtesy Dr D Adams

PEDIATRICS
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Pediatrics. 2016 Feb; 137(2): e20153257.
doi: 10.1542/peds.2015-3257

PMCID: PMC4732362
PMID: 26783326

Efficacy and Safety of Sirolimus in the Treatment of Complicated Vascular Anomalies

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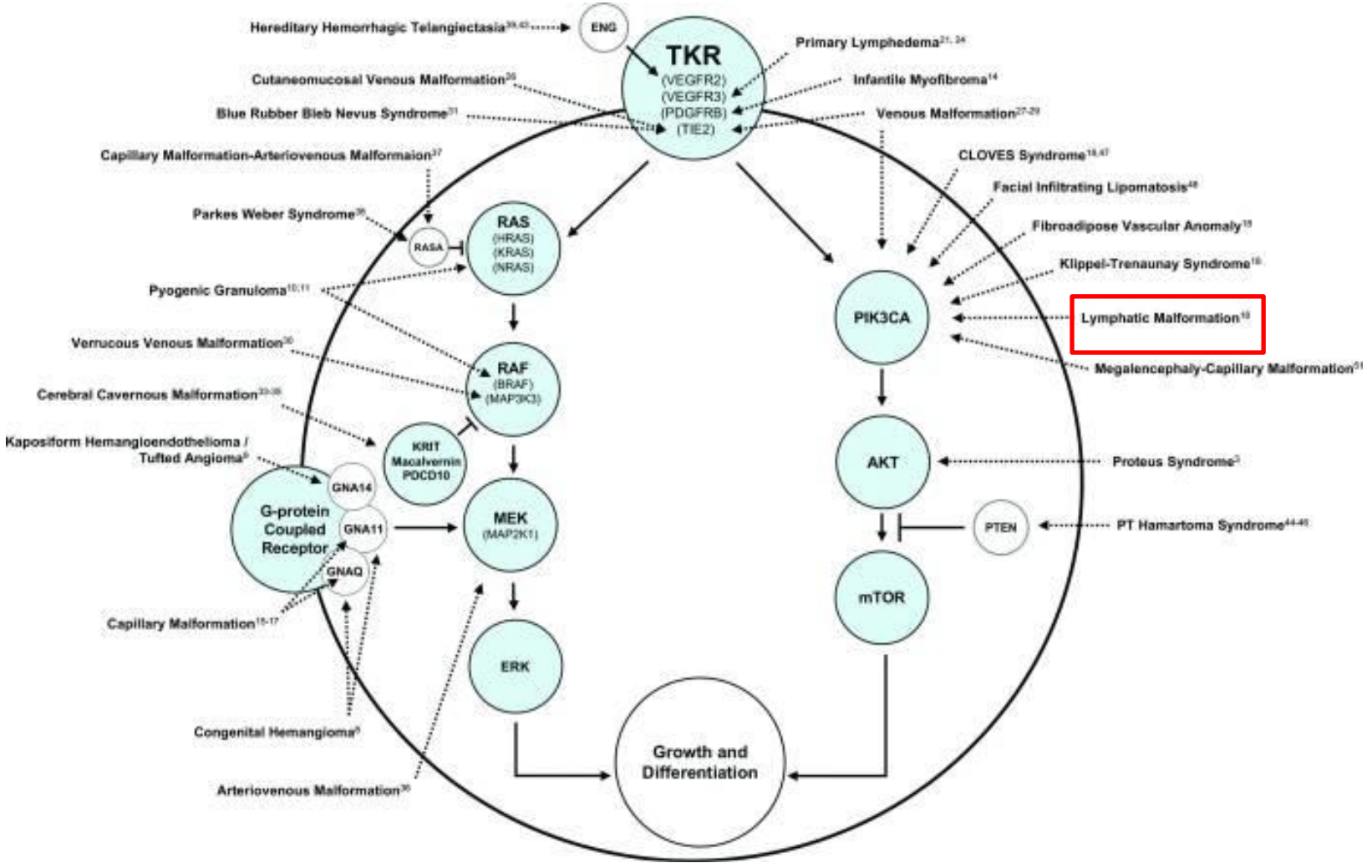
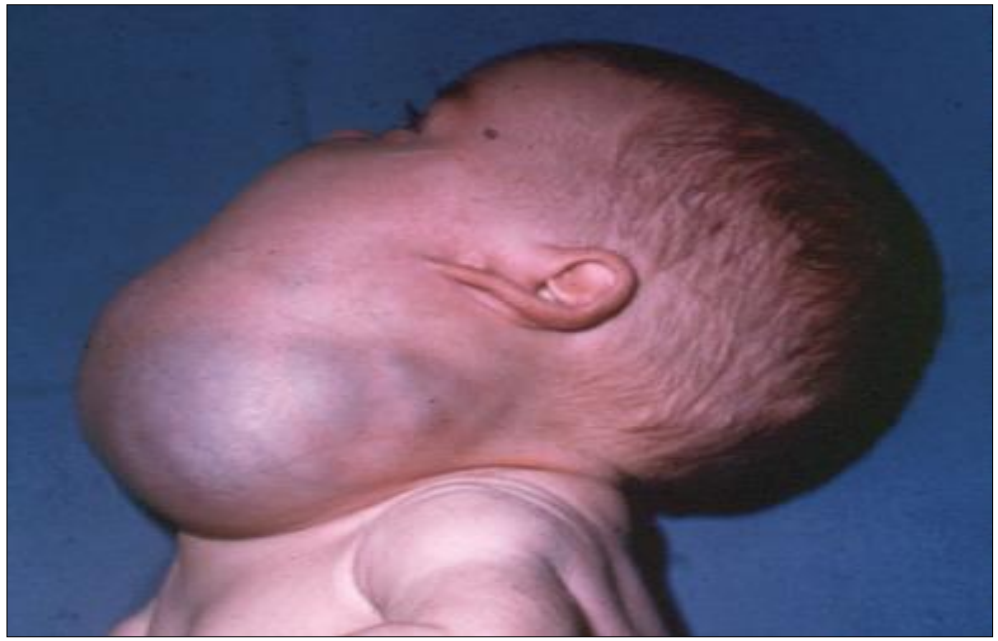
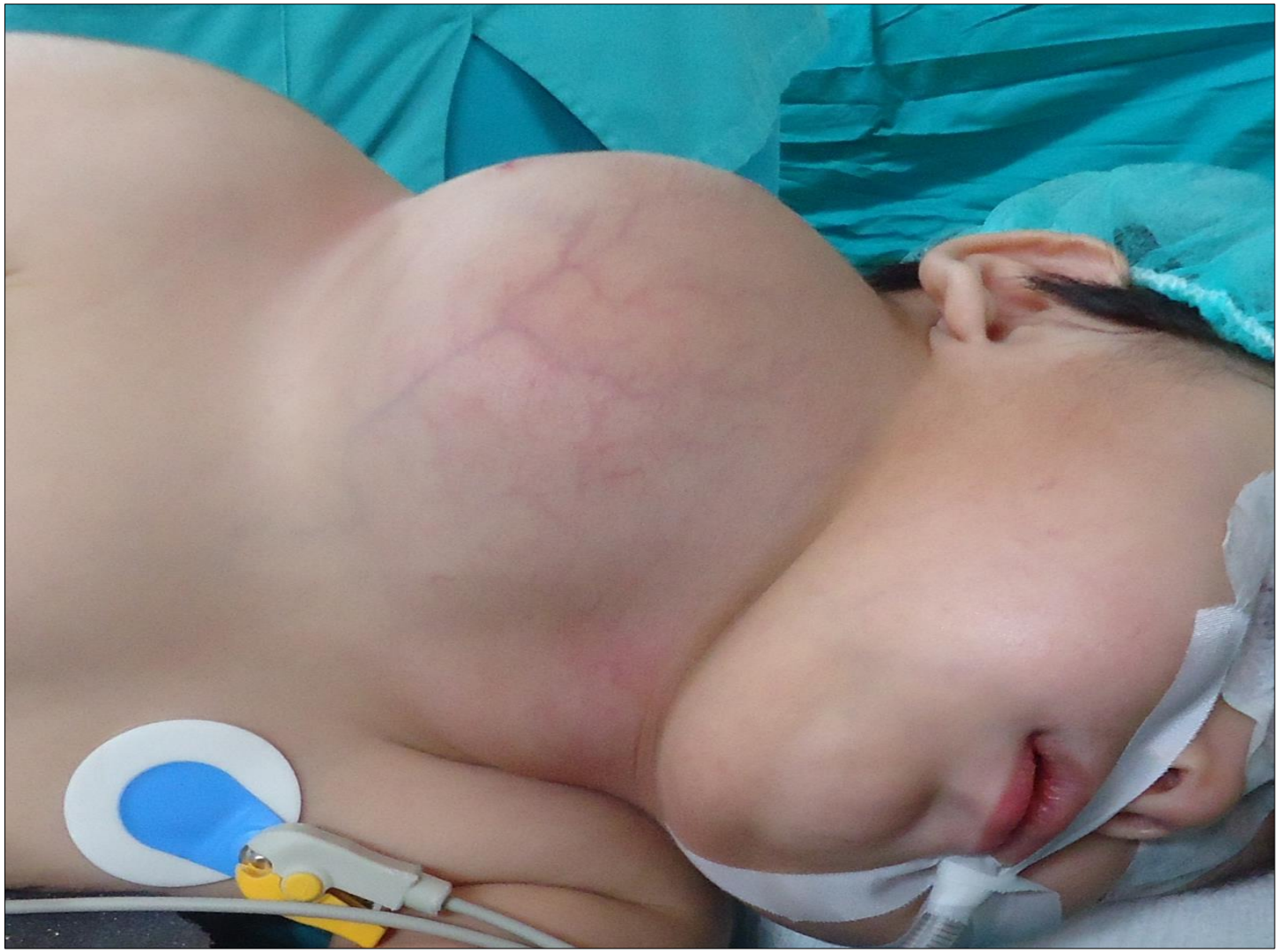
ISSVA classification of vascular tumors

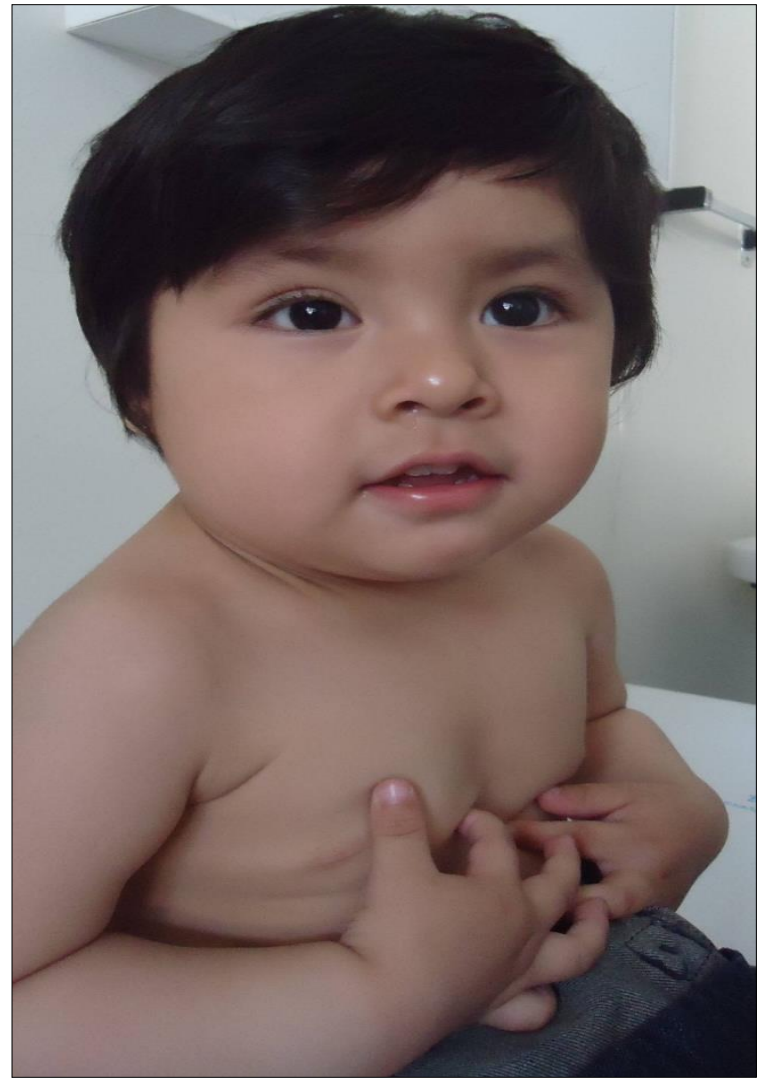
Benign vascular tumors	
Infantile hemangioma / Hemangioma of infancy	PROPRANOLOL
Congenital hemangioma	
Rapidly involuting (RICH) *	CONSERVATIVE
Non-involuting (NICH)	SURGERY
Partially involuting (PICH)	SURGERY
Tufted angioma * °	SIROLIMUS
Spindle-cell hemangioma	SURGERY
Epithelioid hemangioma	SURGERY
Pyogenic granuloma (aka lobular capillary hemangioma)	SURGERY
Others	
Locally aggressive or borderline vascular tumors	
Kaposiform hemangioendothelioma * °	SIROLIMUS
Retiform hemangioendothelioma	SIROLIMUS
Papillary intralymphatic angioendothelioma (PILA), Dabska tumor	SURGERY
Composite hemangioendothelioma	SIROLIMUS
Kaposi sarcoma	
Others	
Malignant vascular tumors	MULTIMODAL
Angiosarcoma	
Epithelioid hemangioendothelioma	
Others	

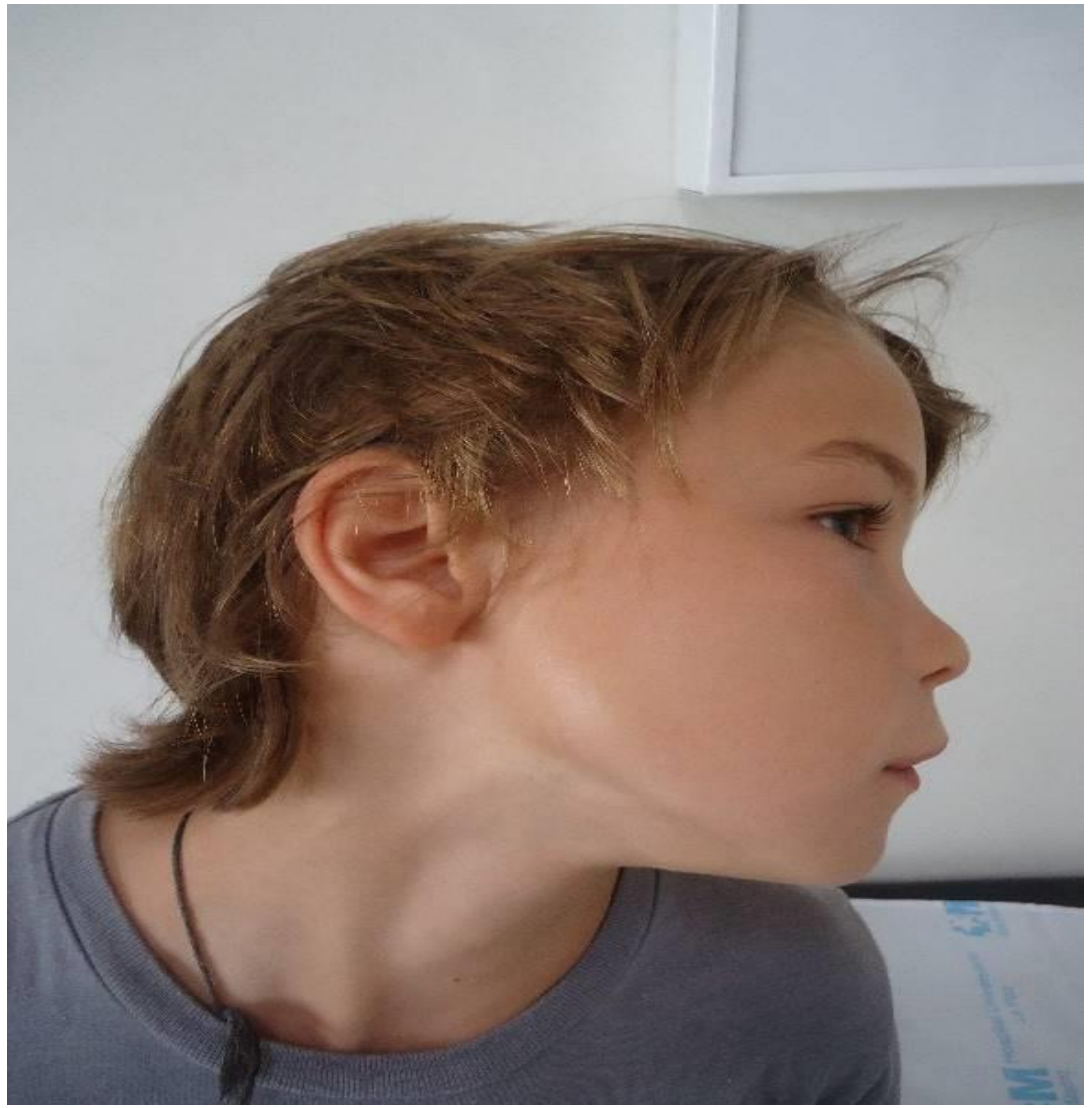
MALFORMACIONES LINFÁTICAS

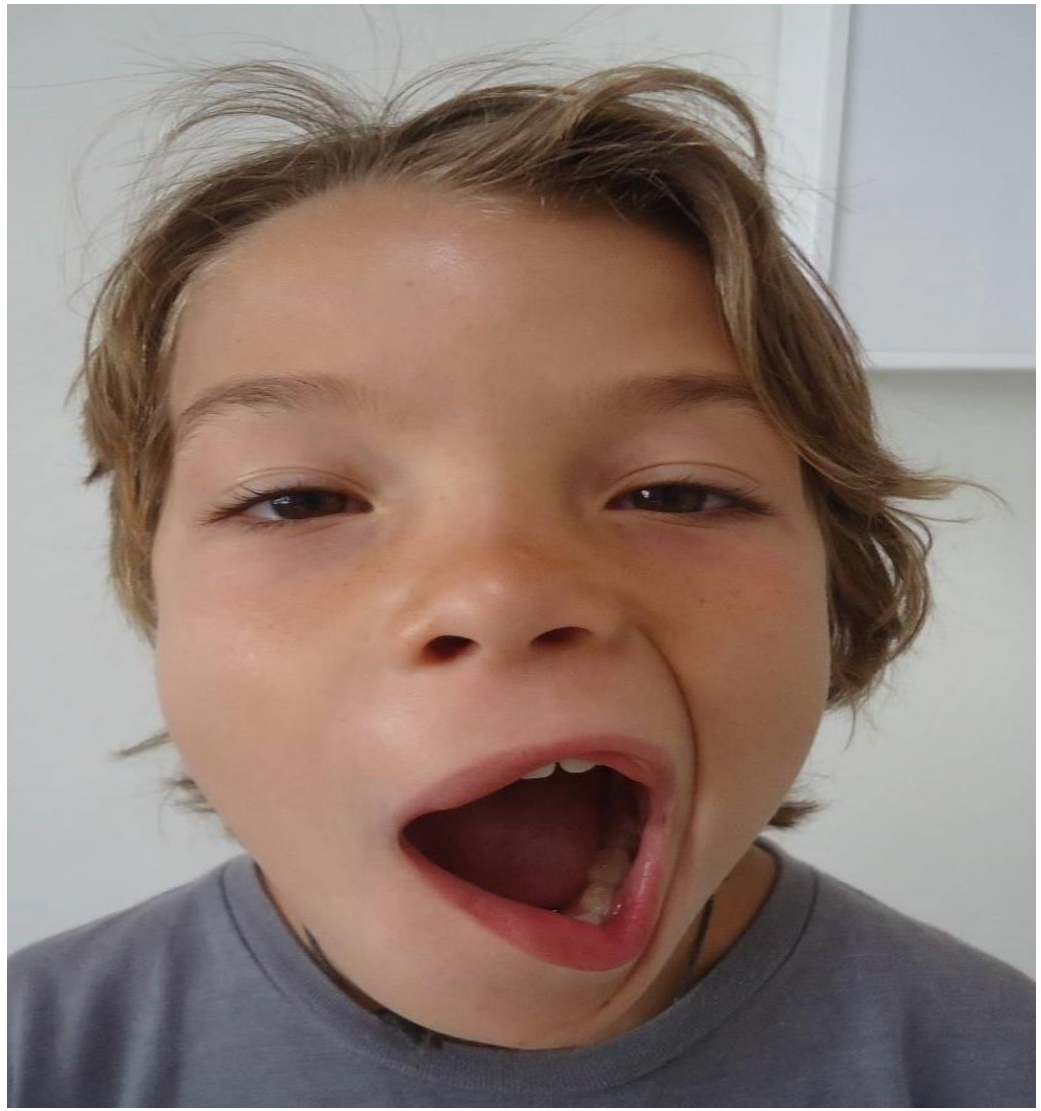


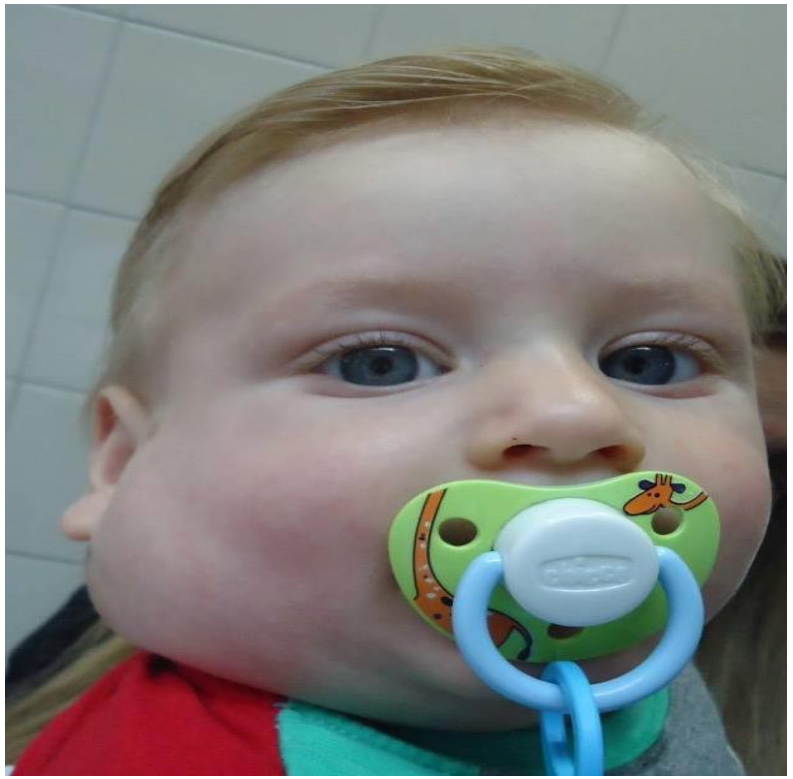


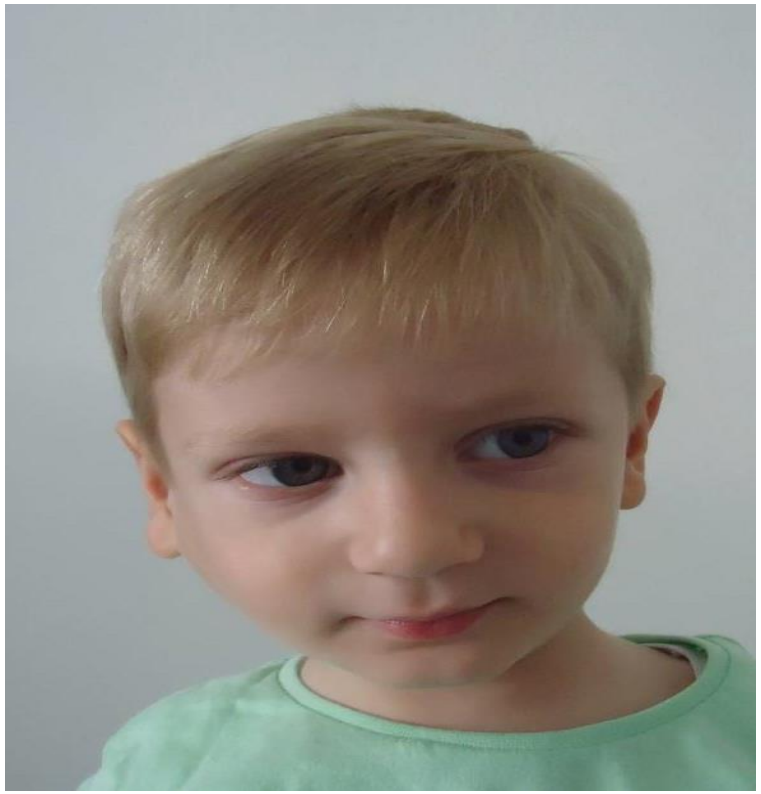


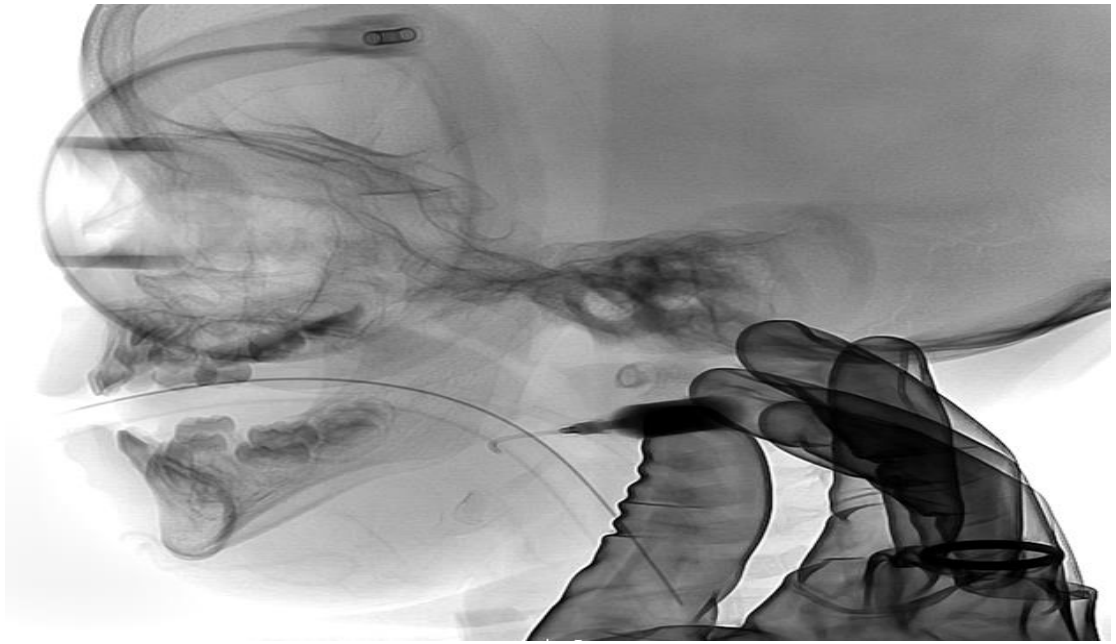


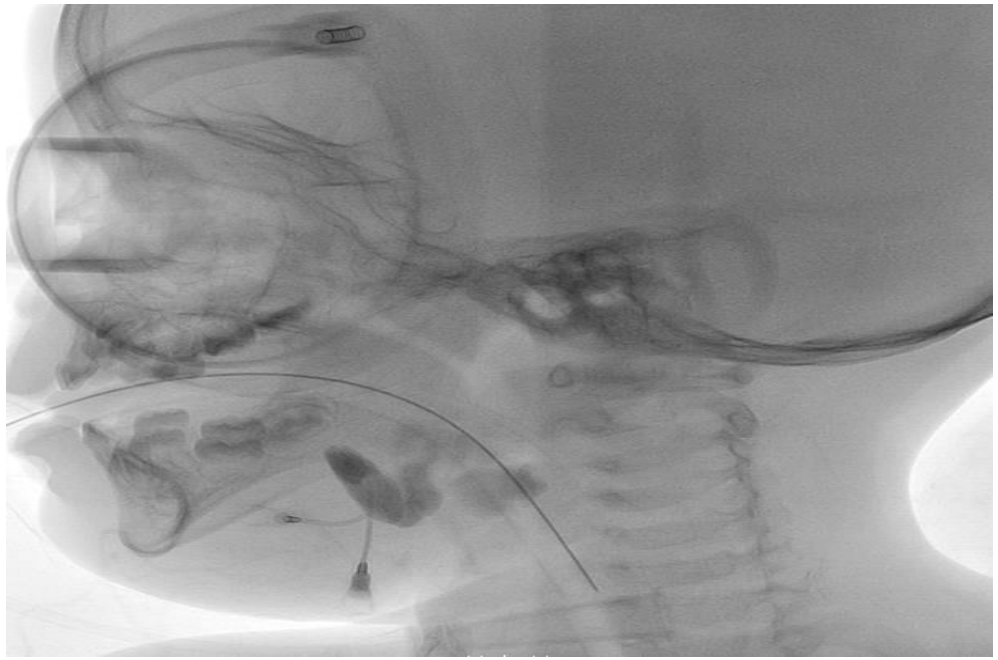


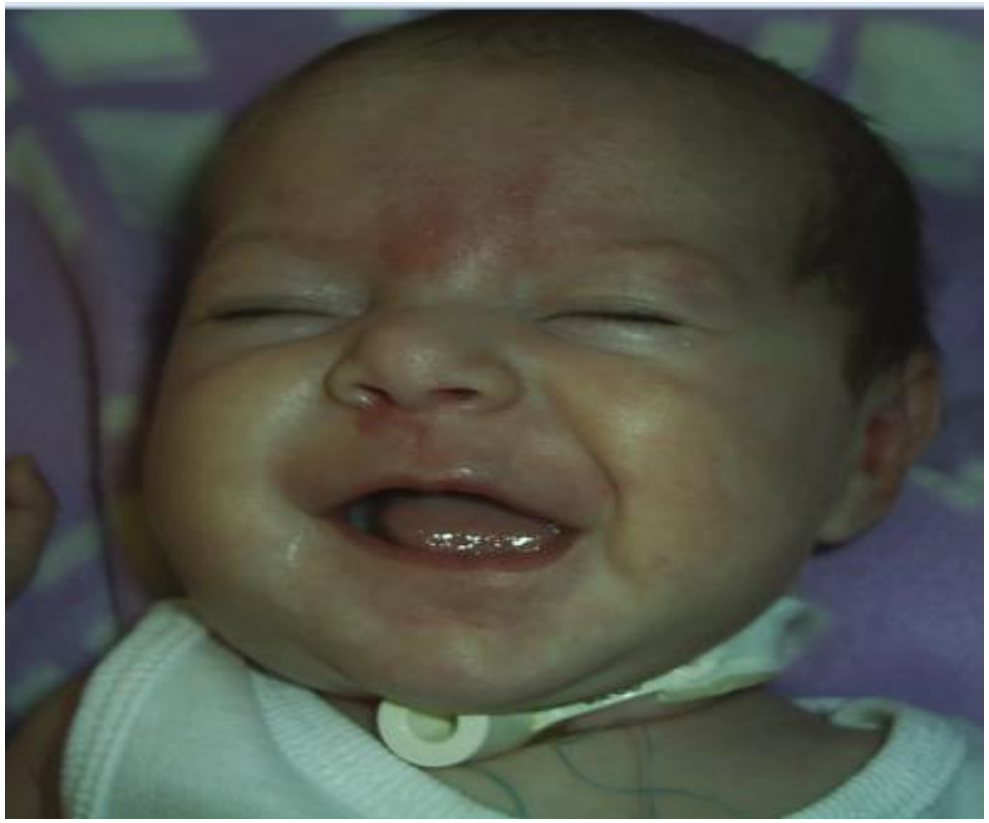


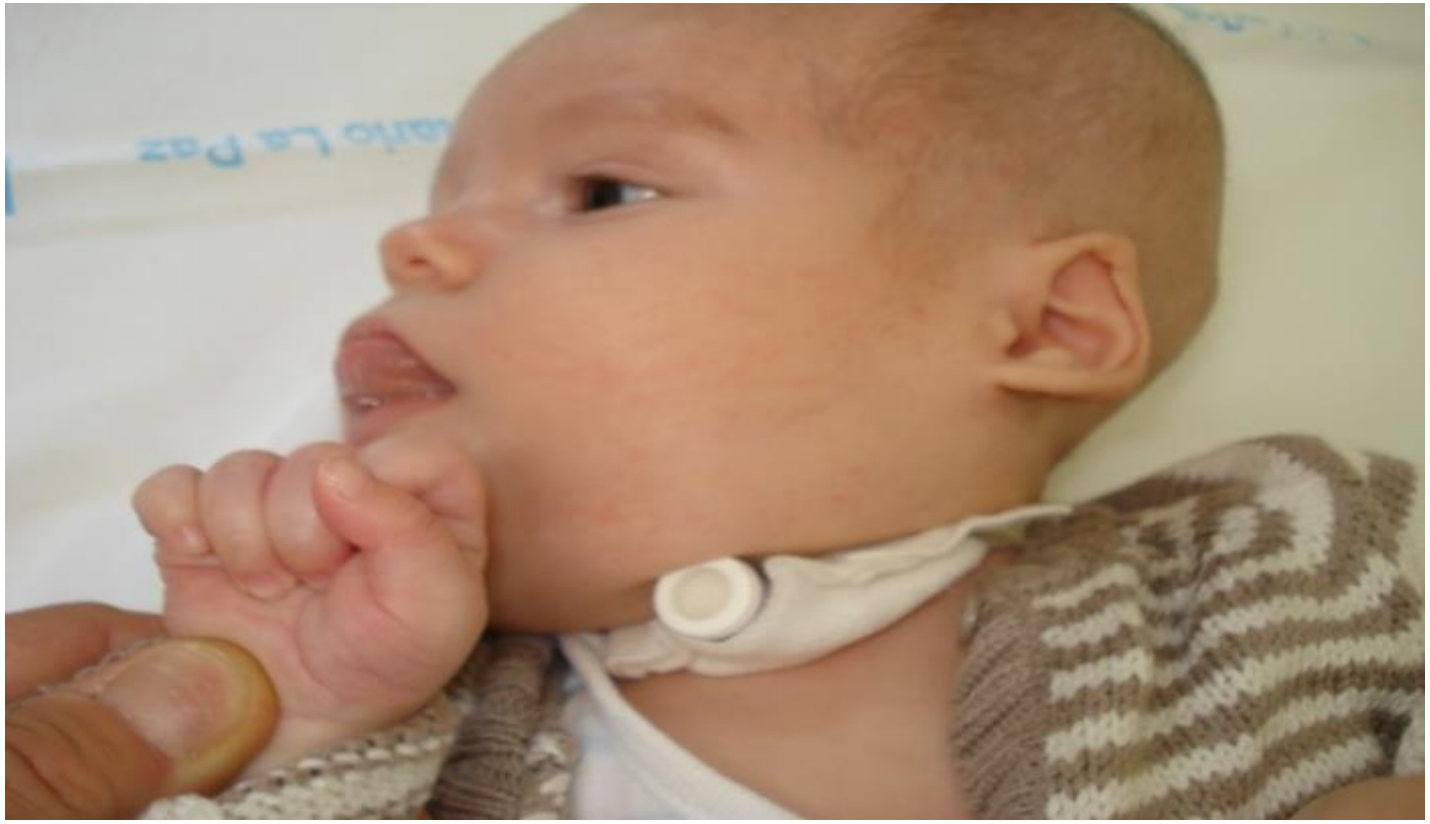


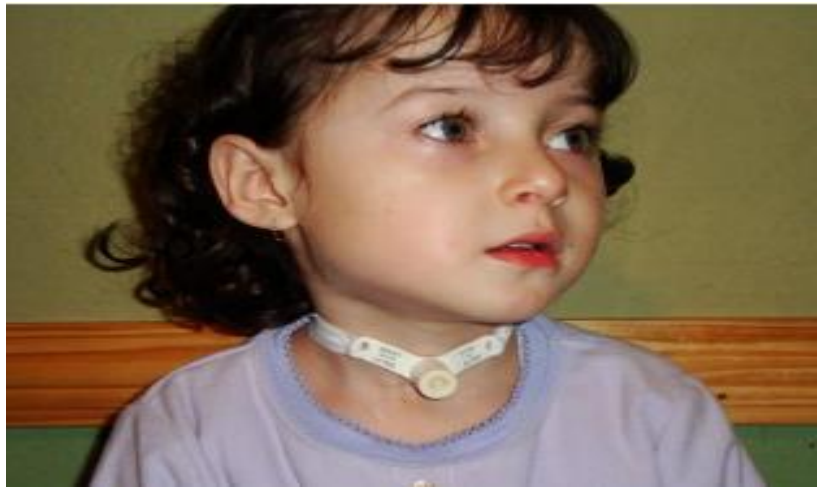


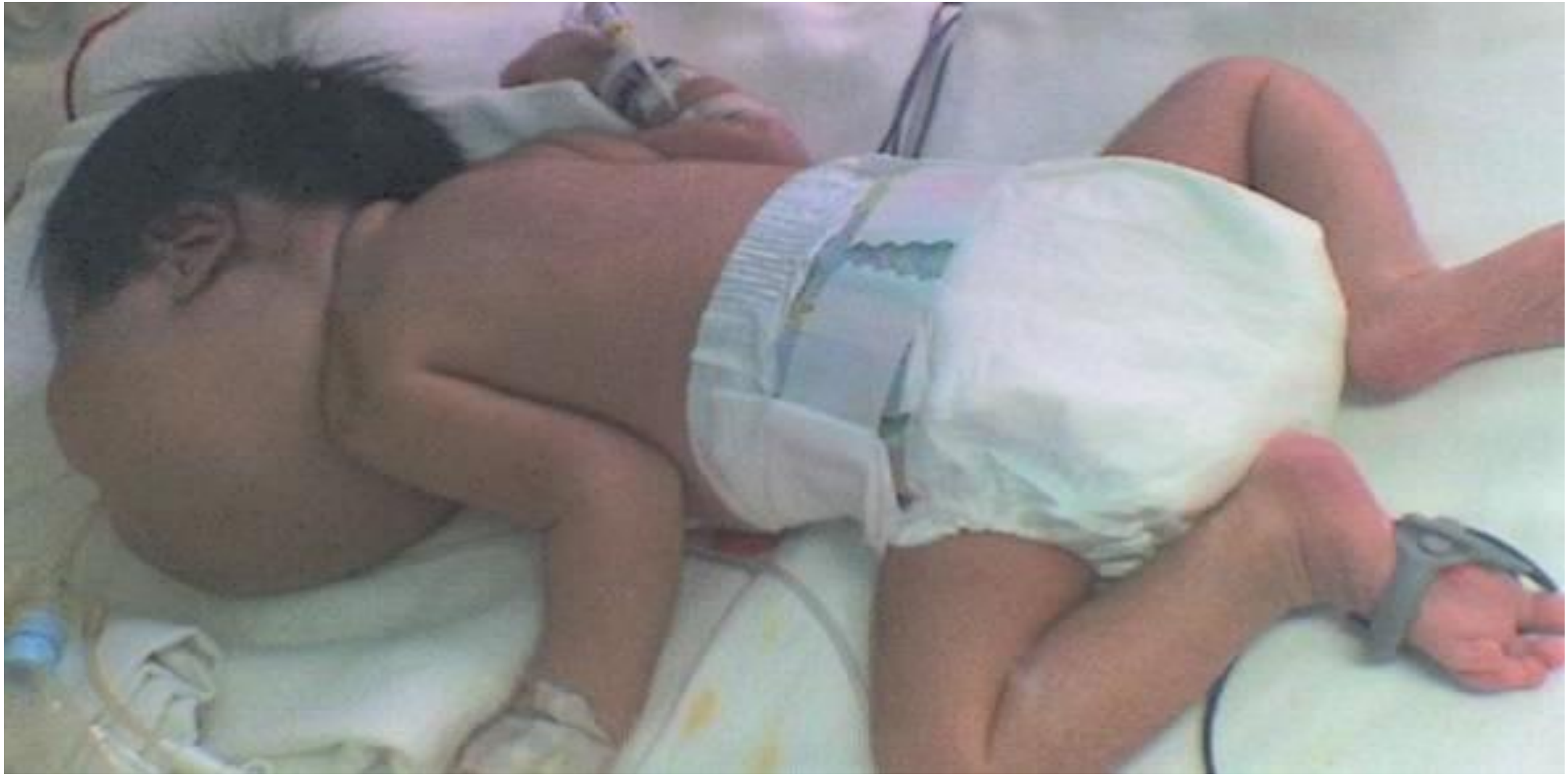


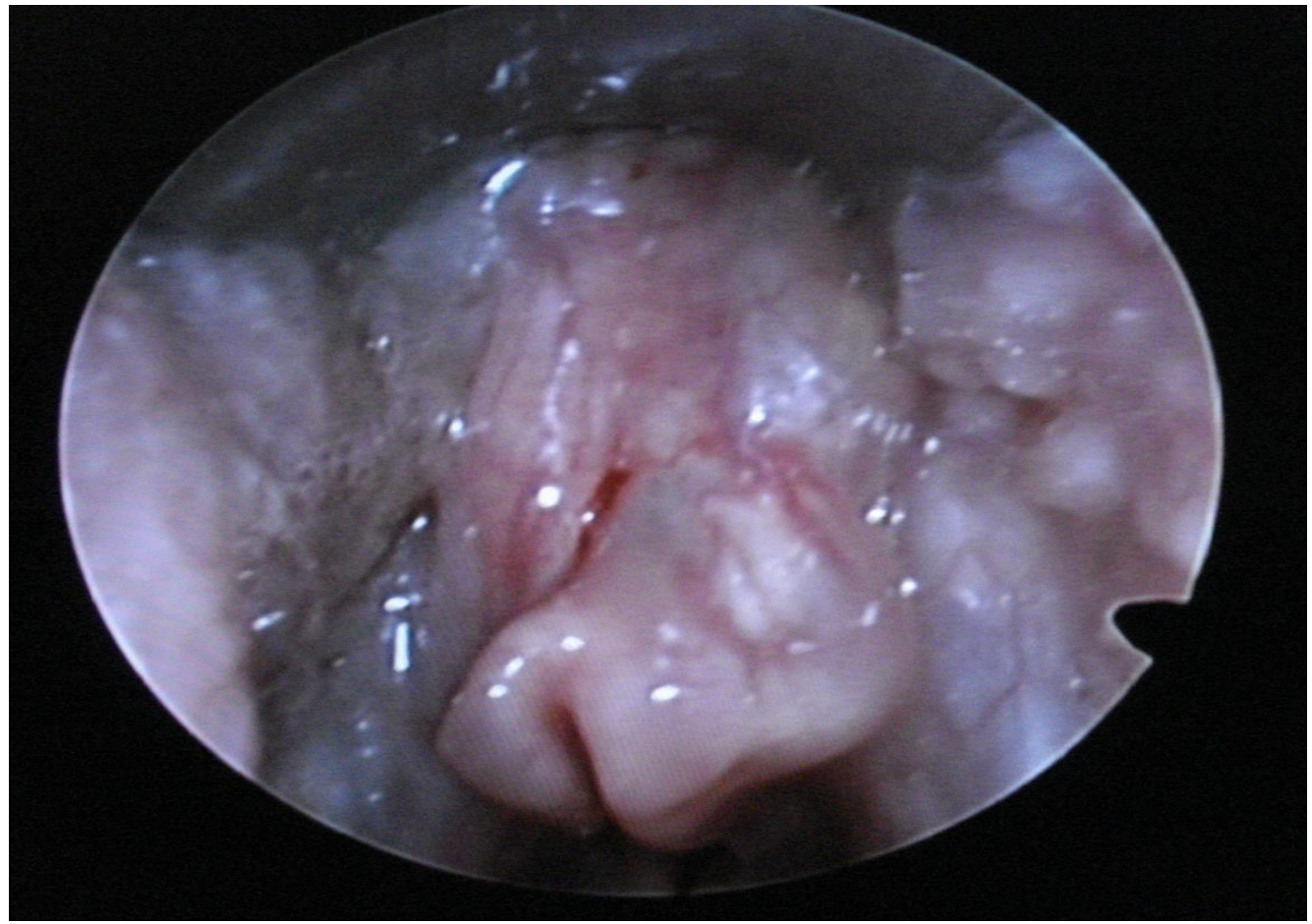












SIROLIMUS 3 SEMANAS
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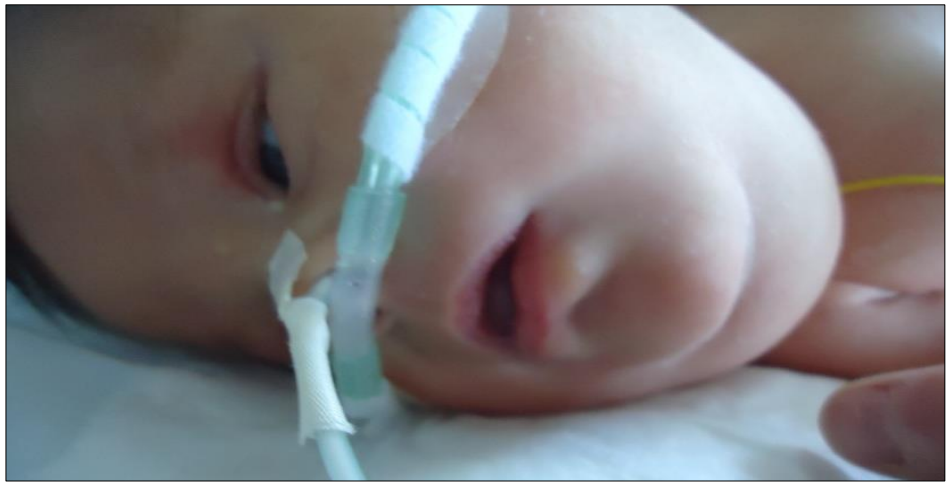
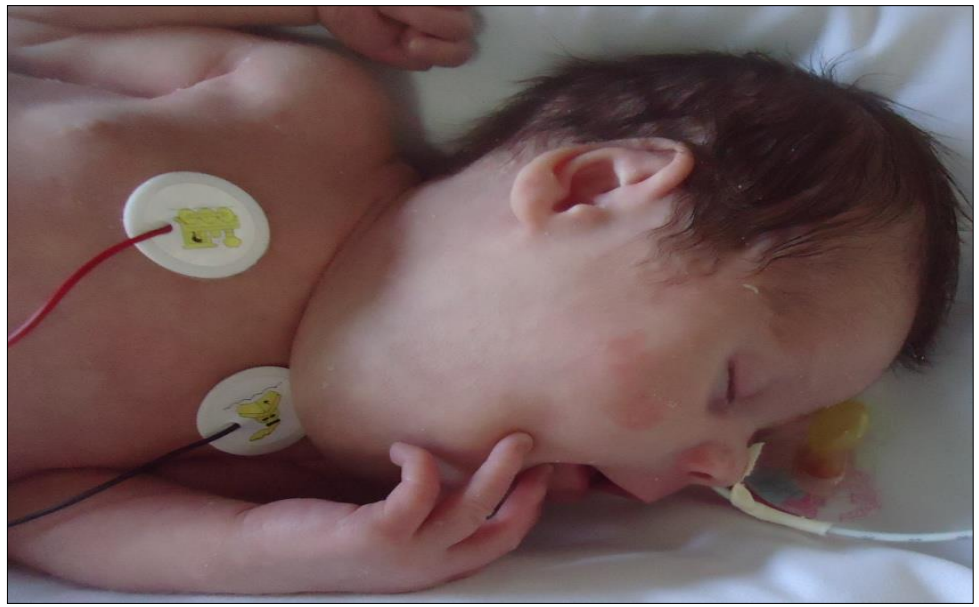
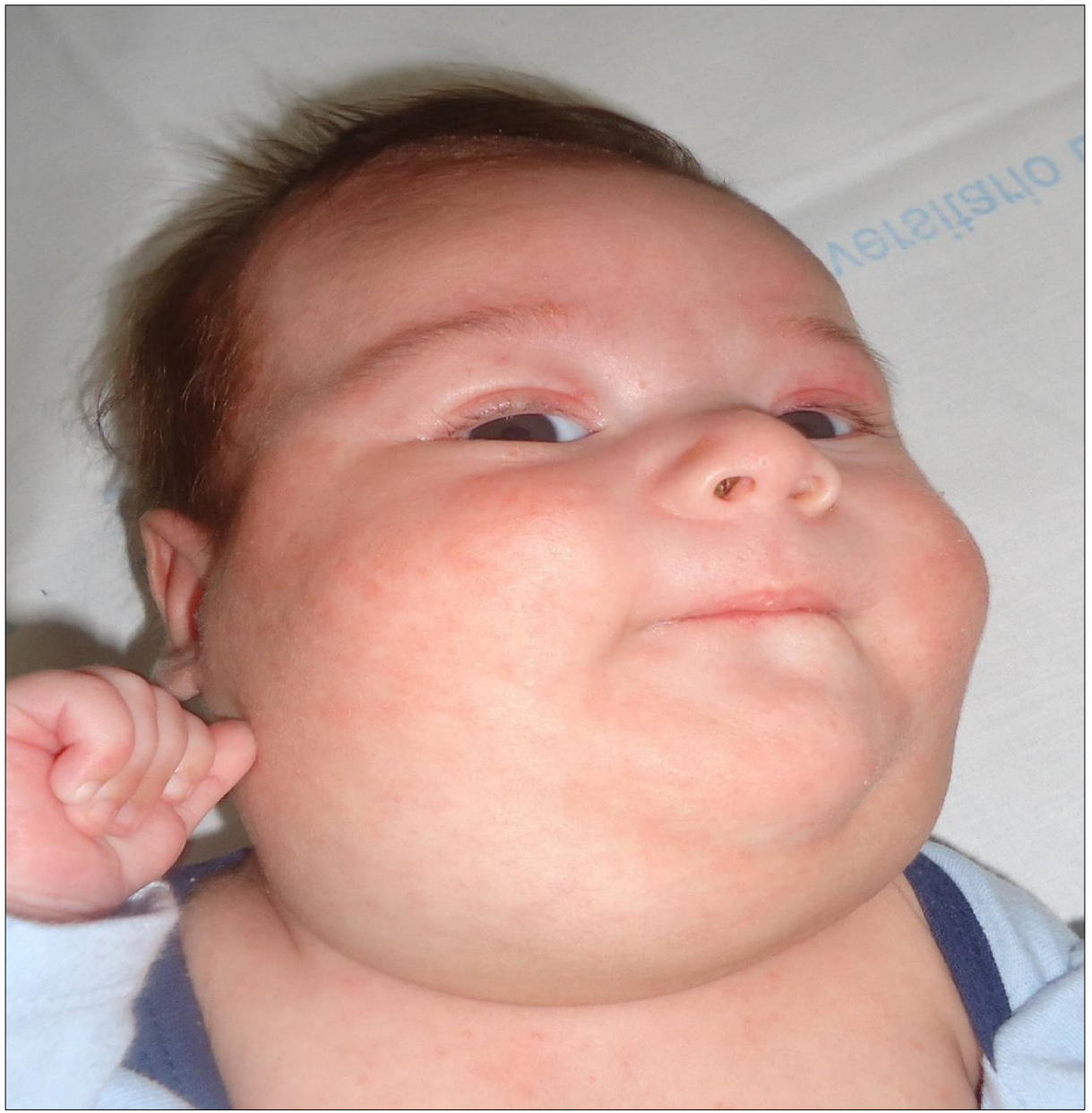


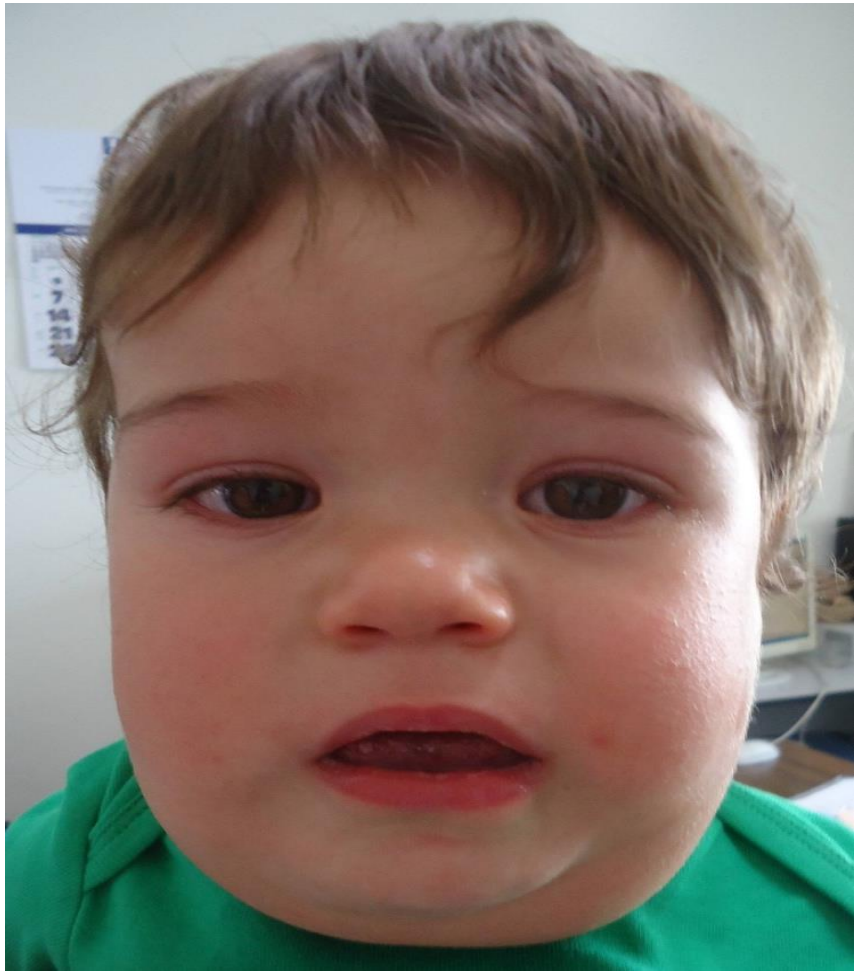


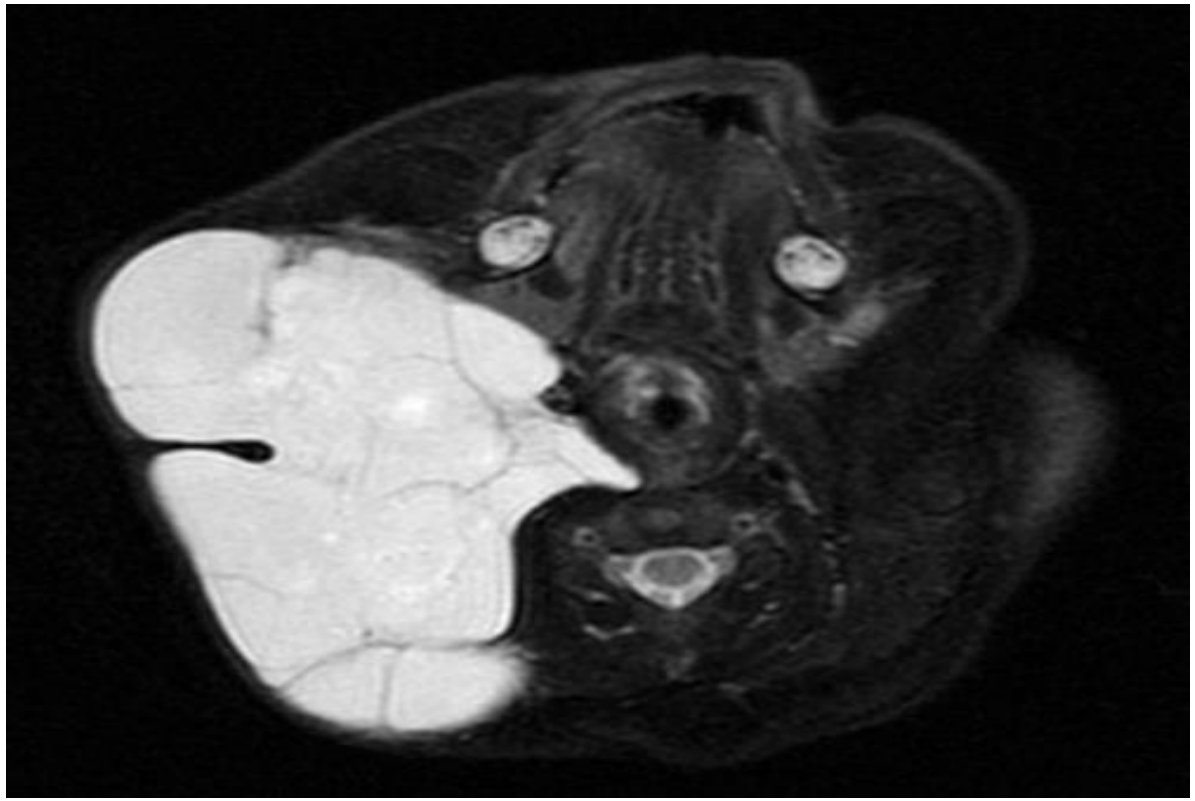


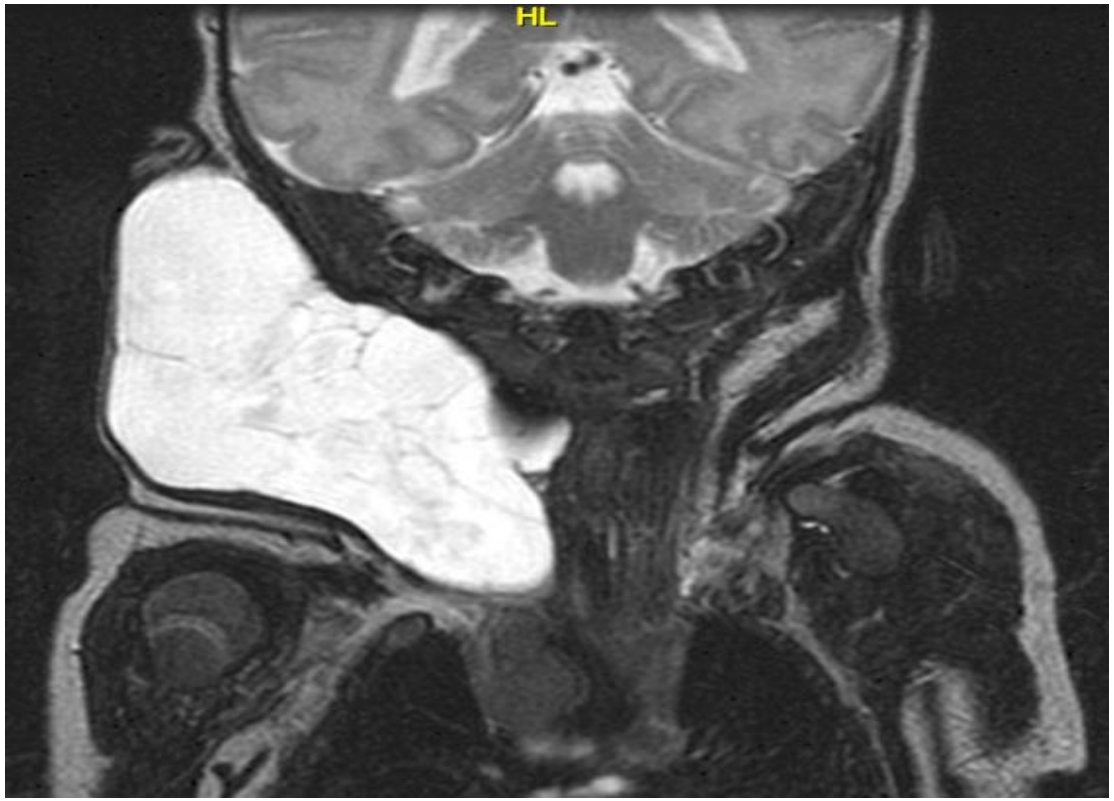
RAPAMUNE

6 MESES

1 AÑO



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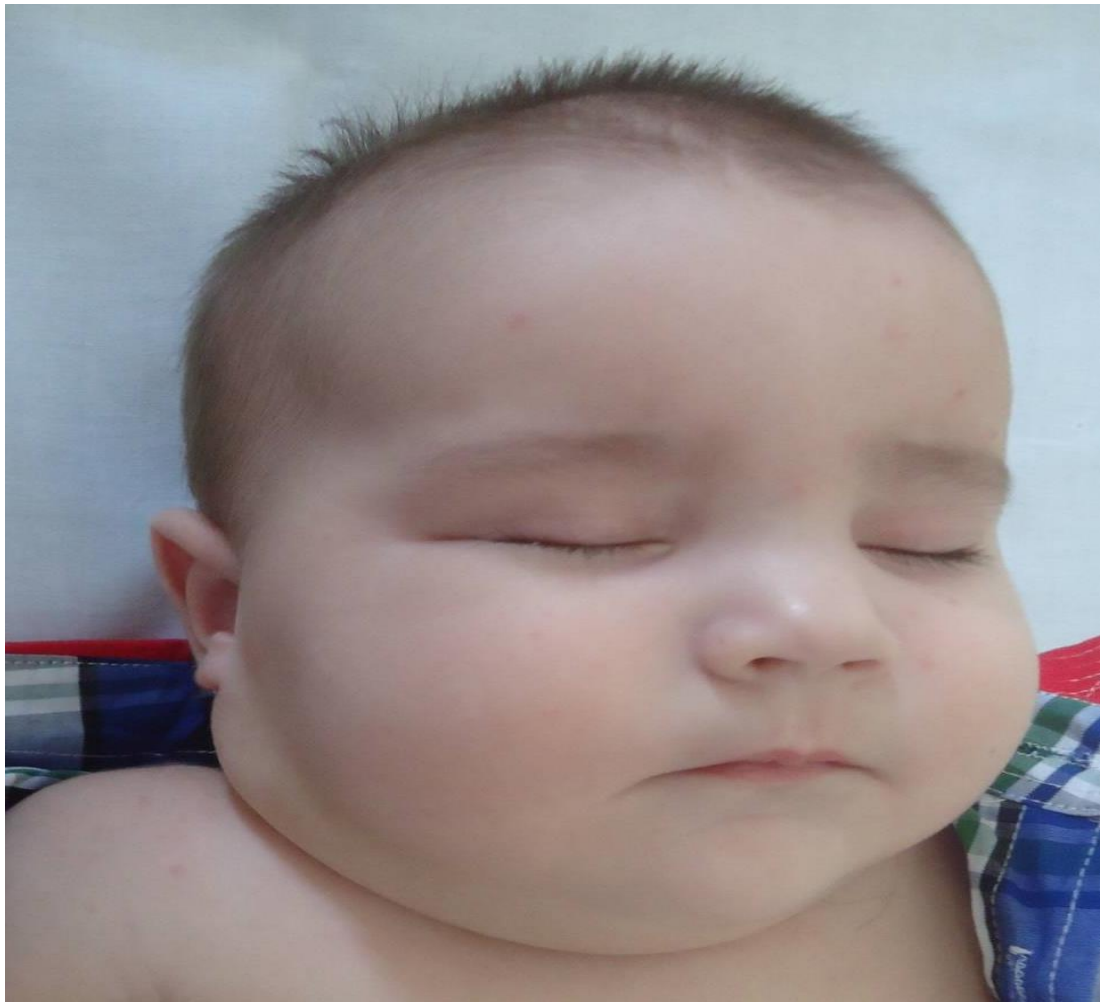

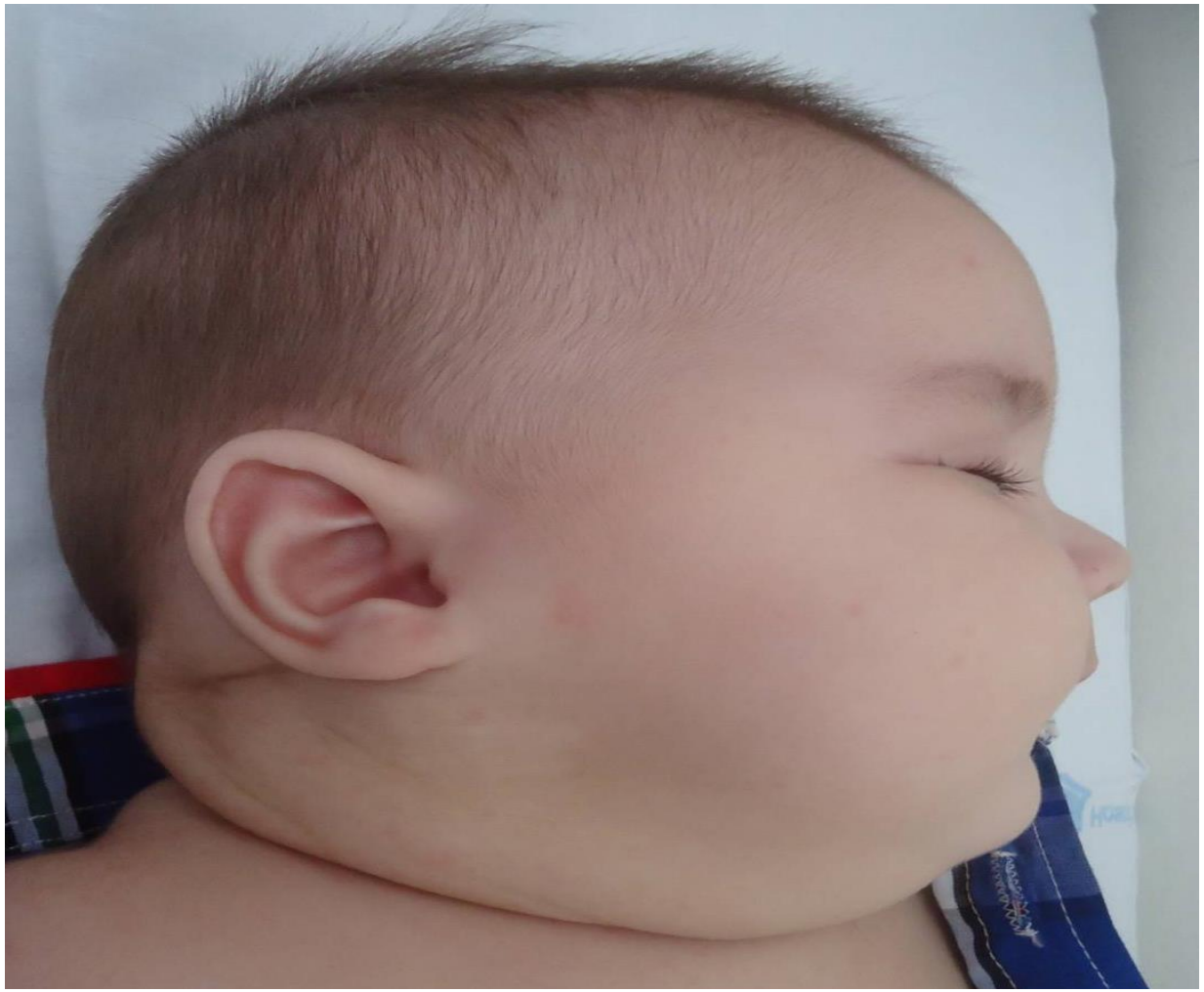

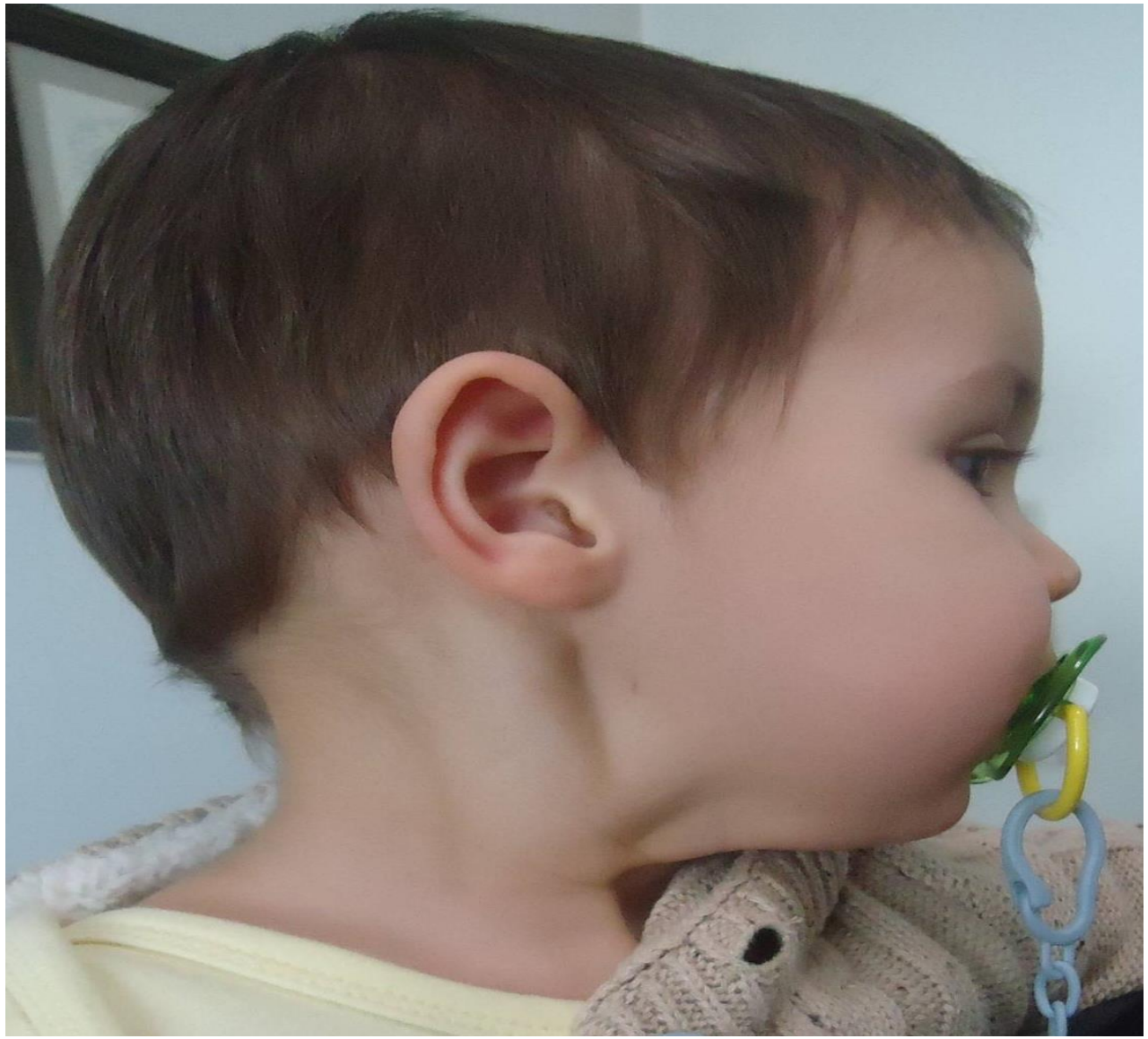

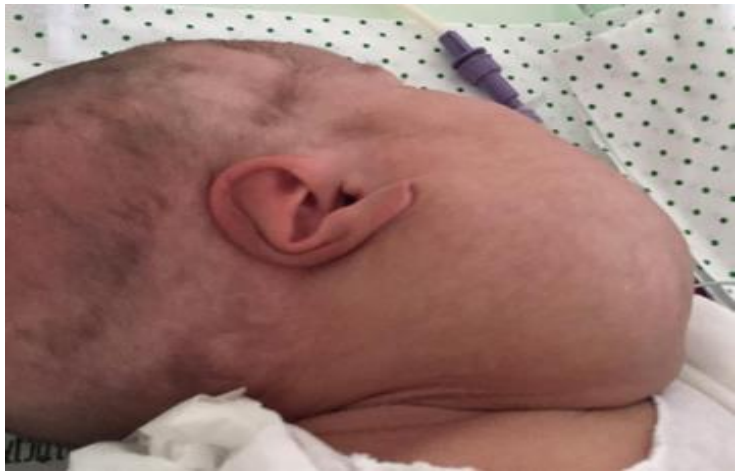

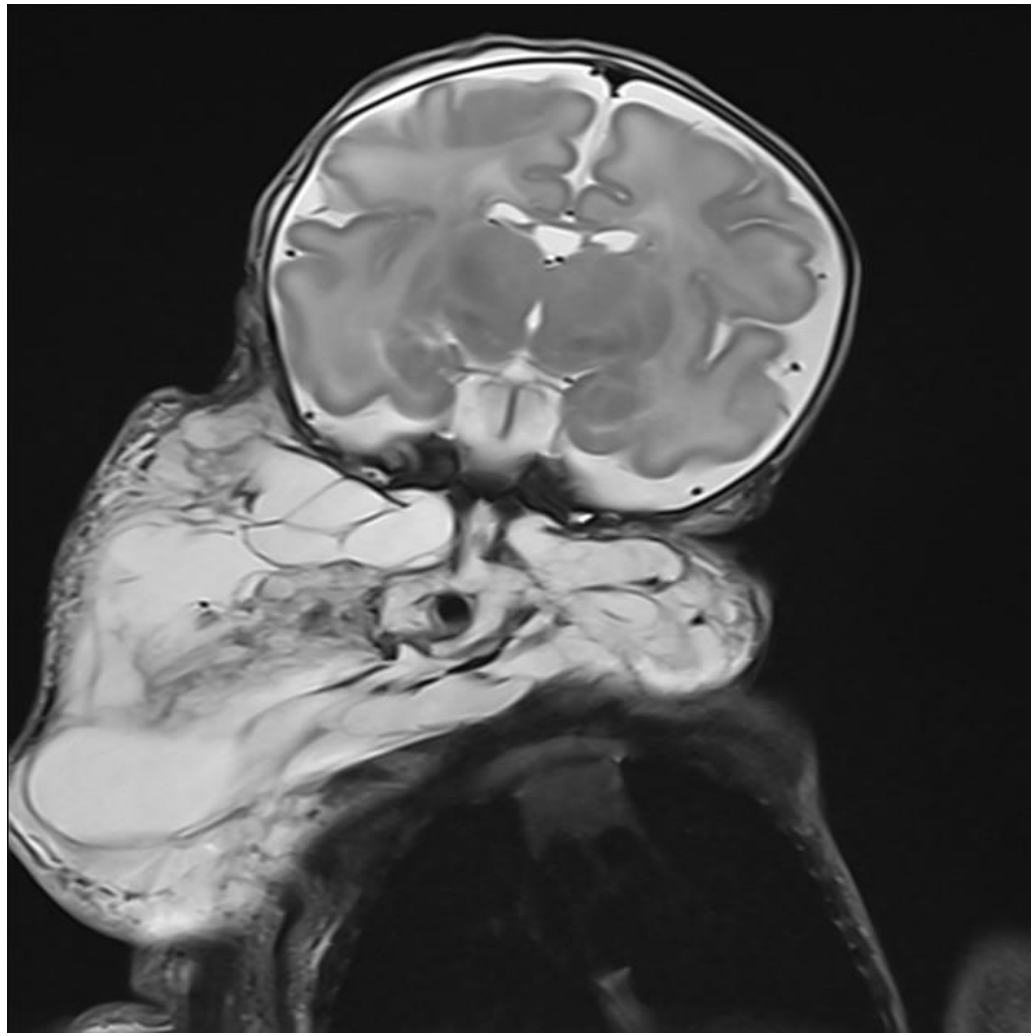

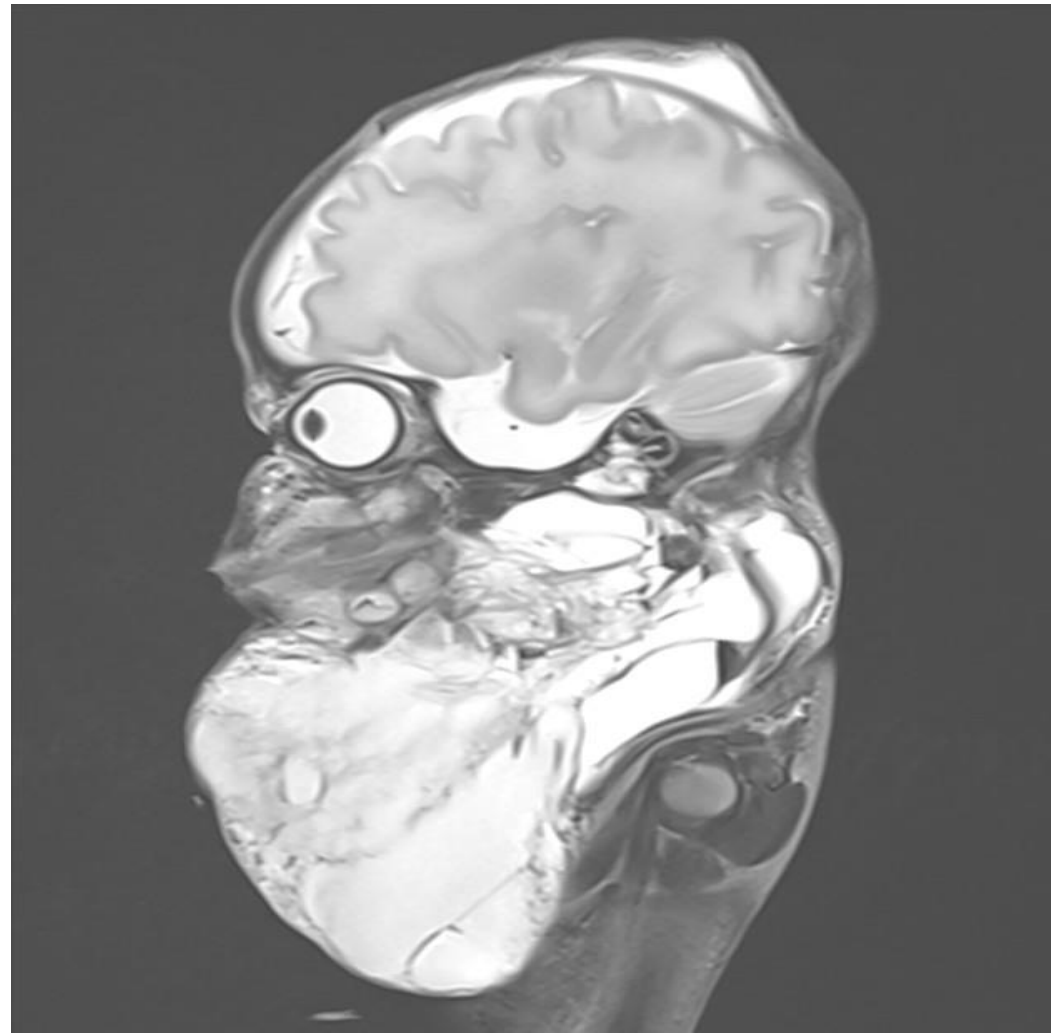

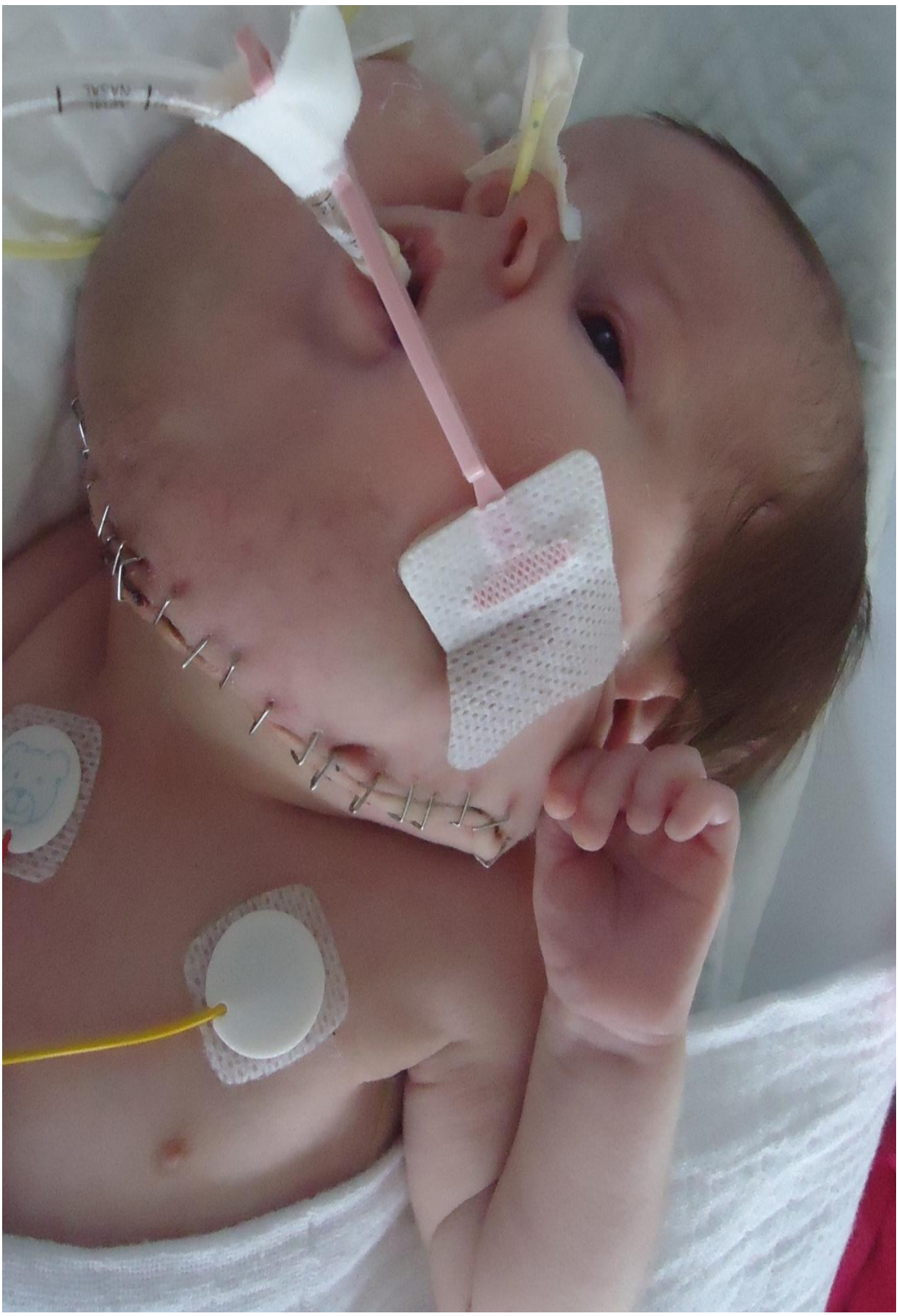
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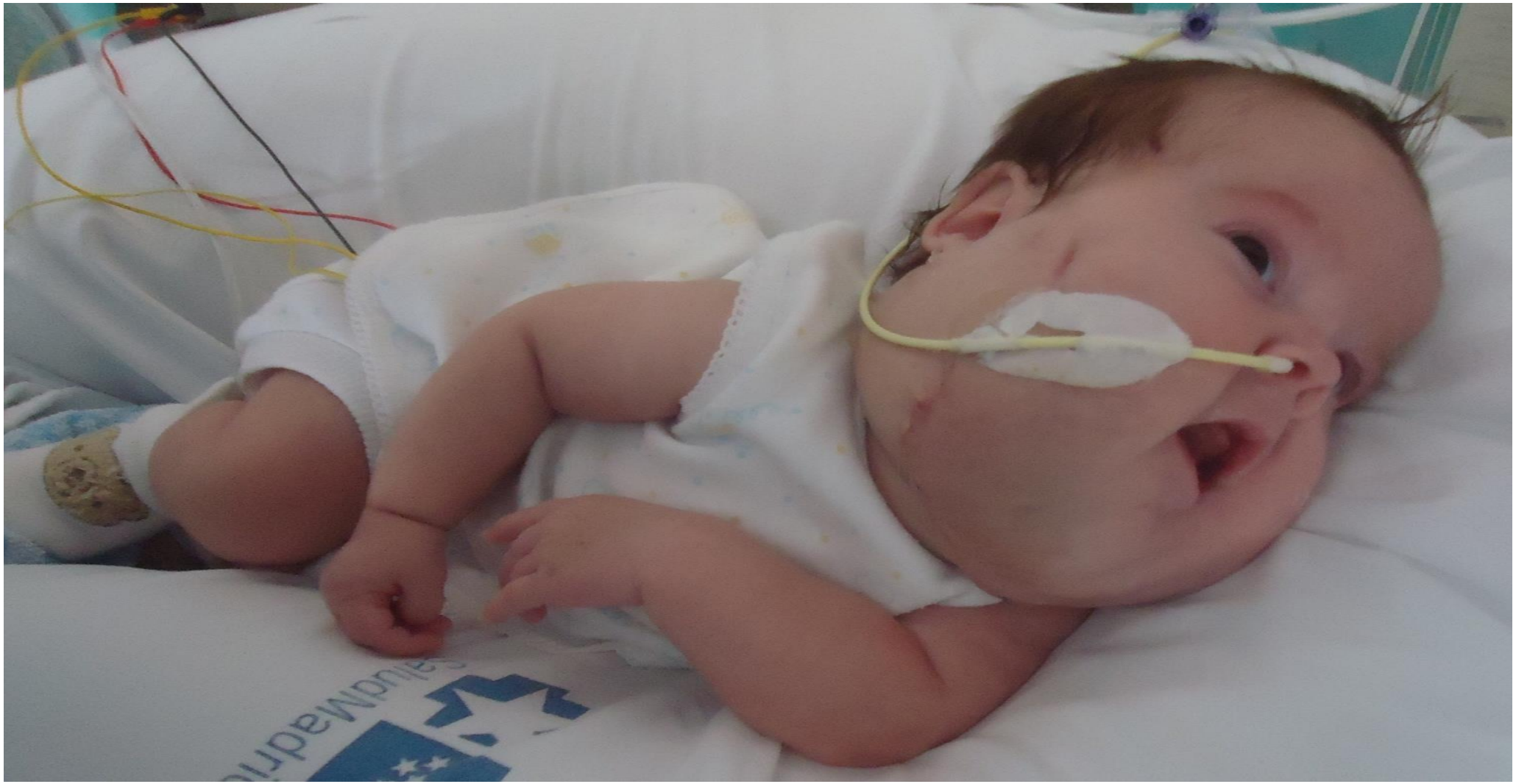
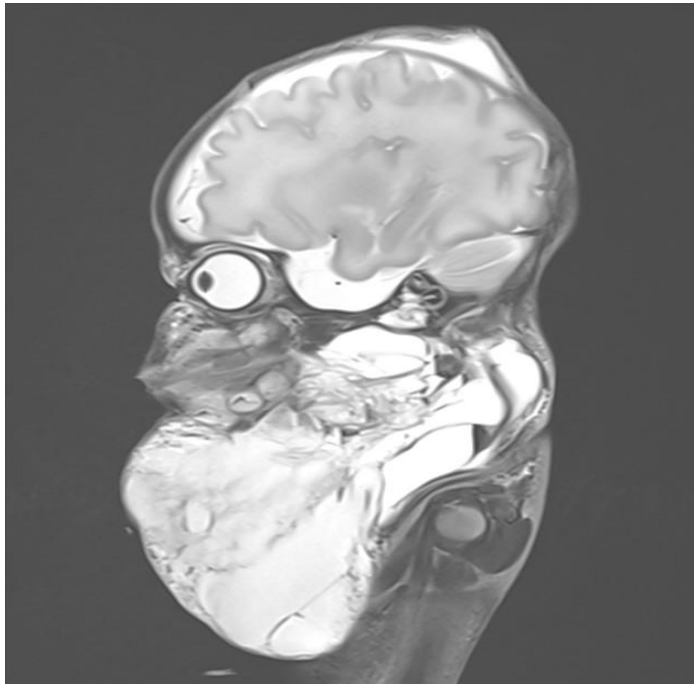
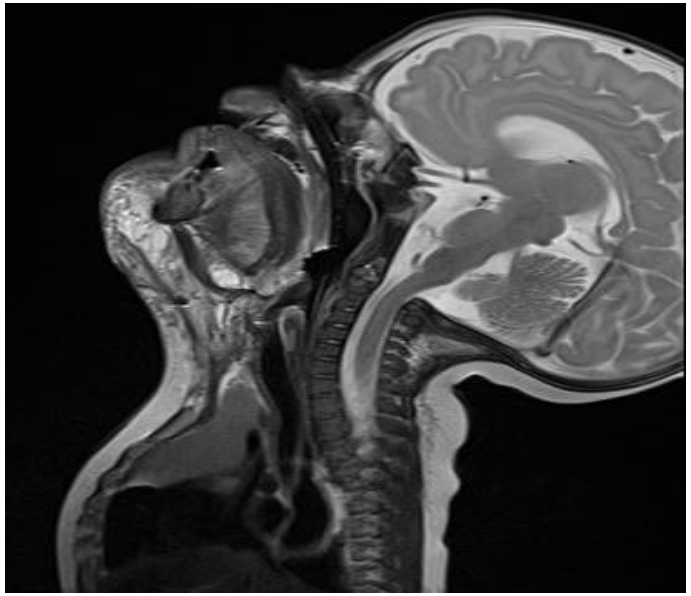
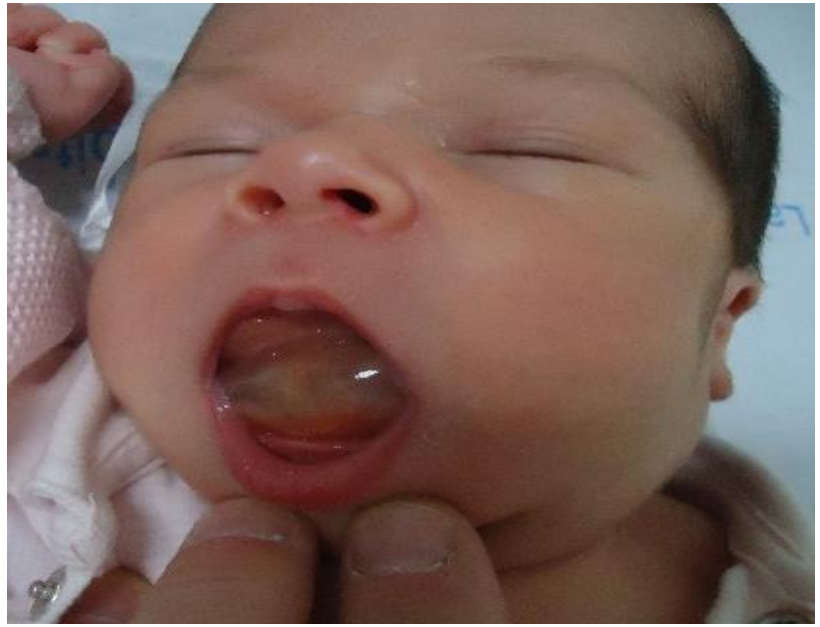
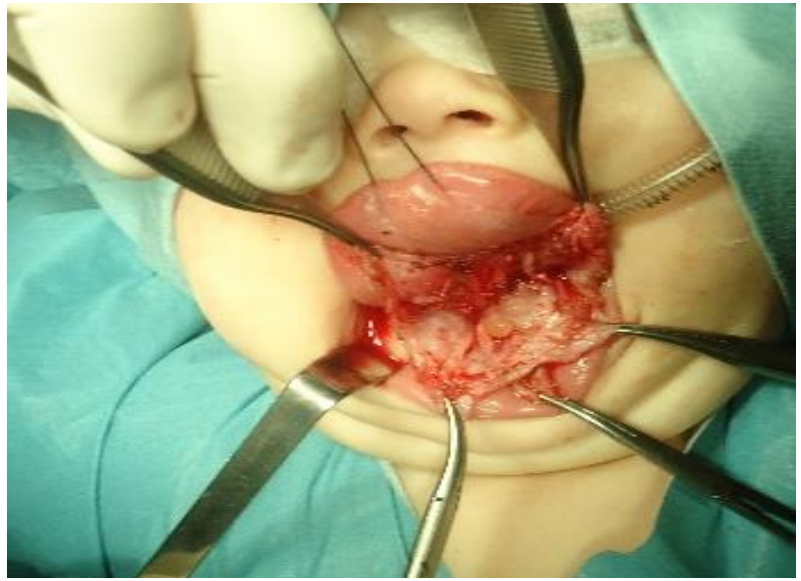
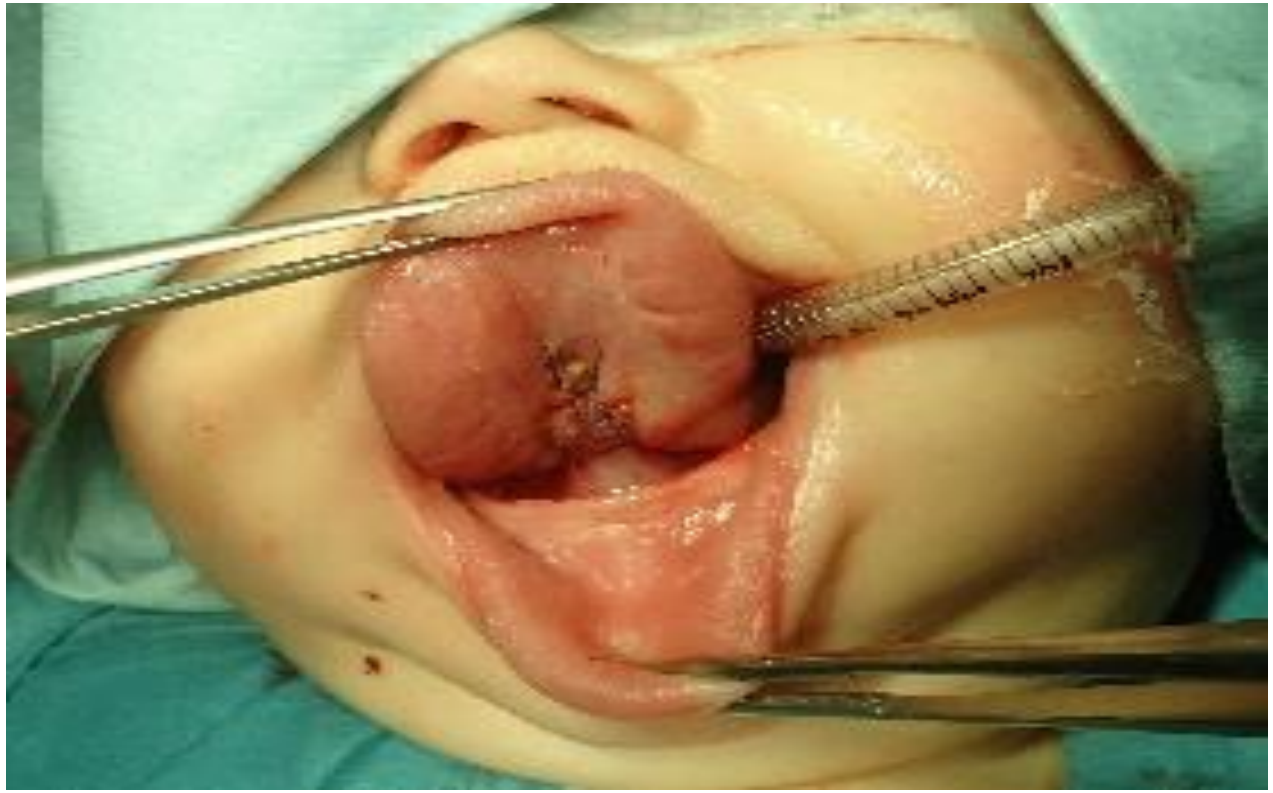


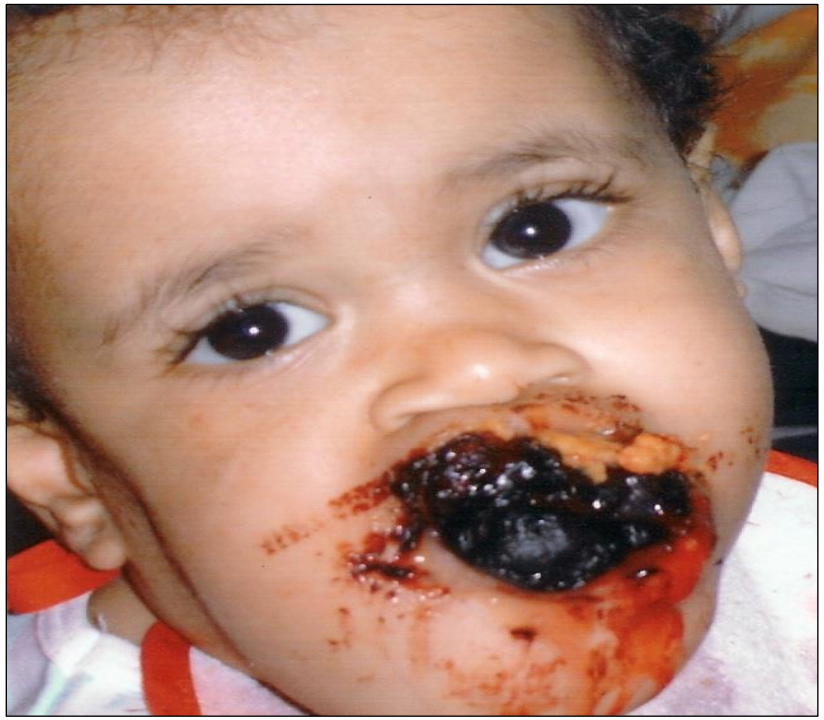


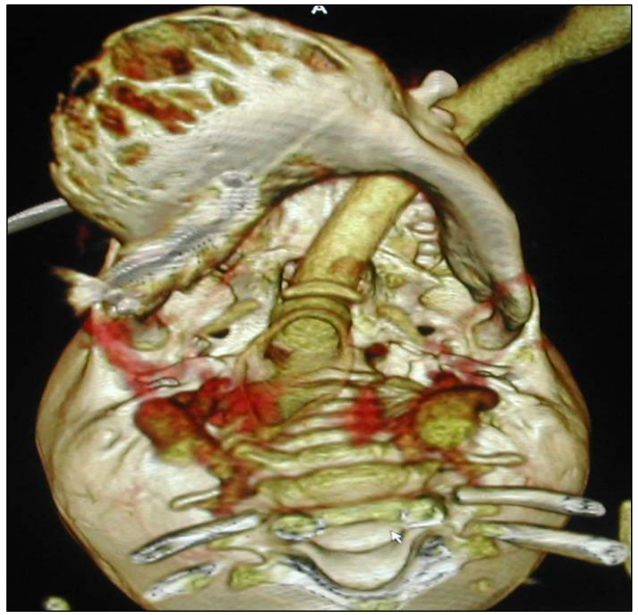


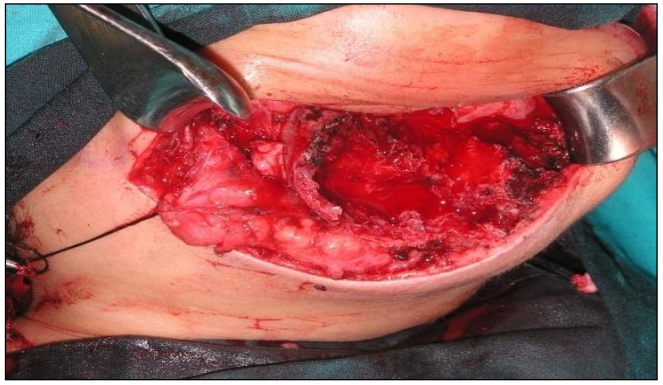


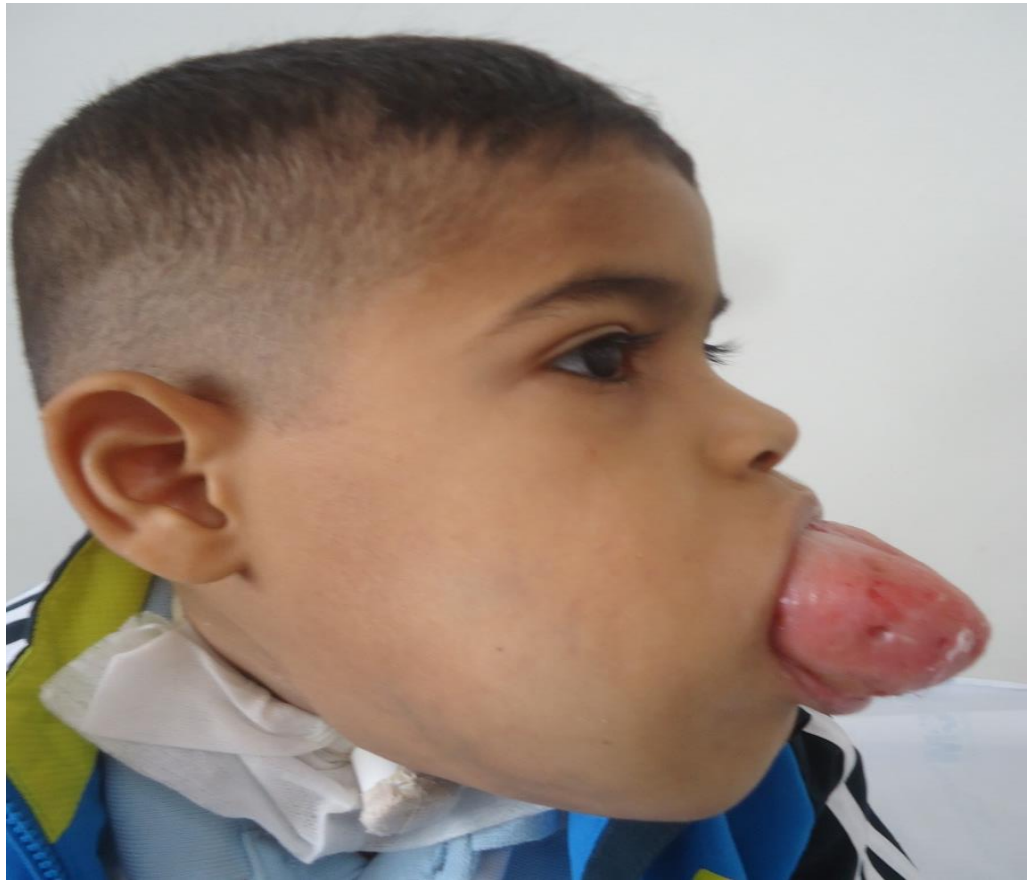


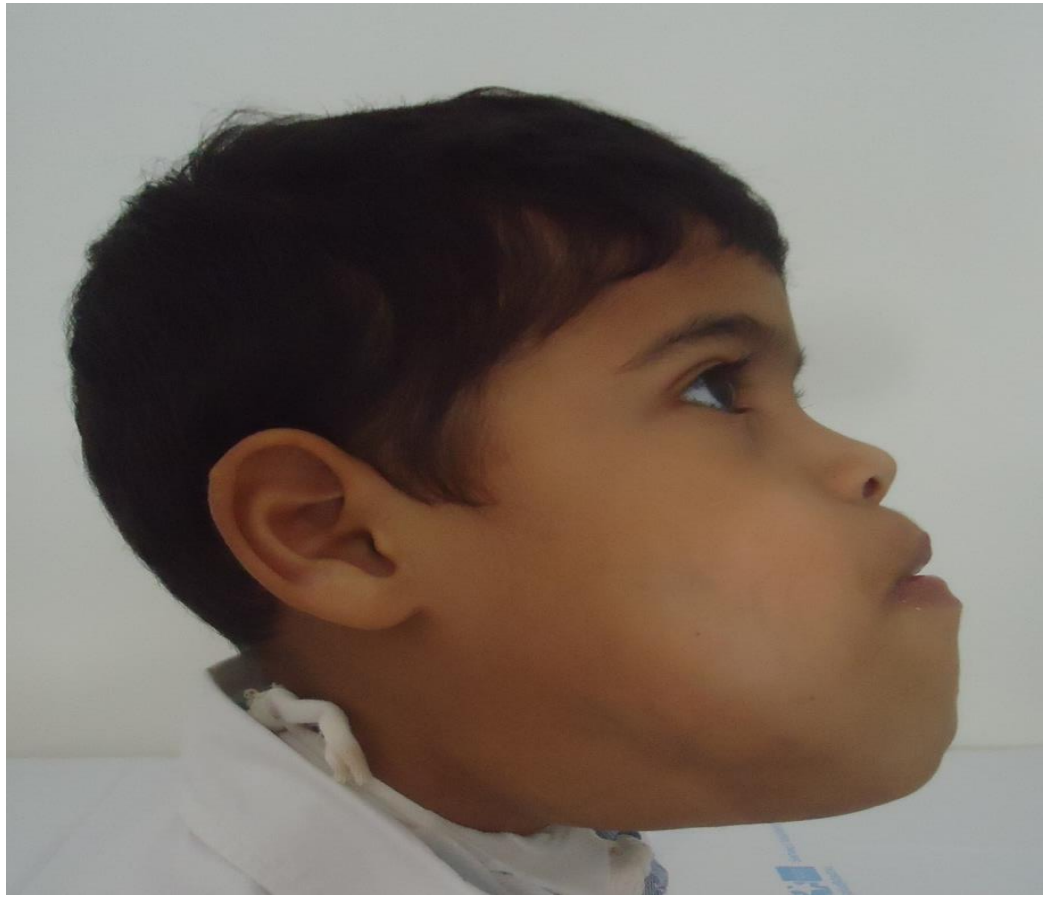


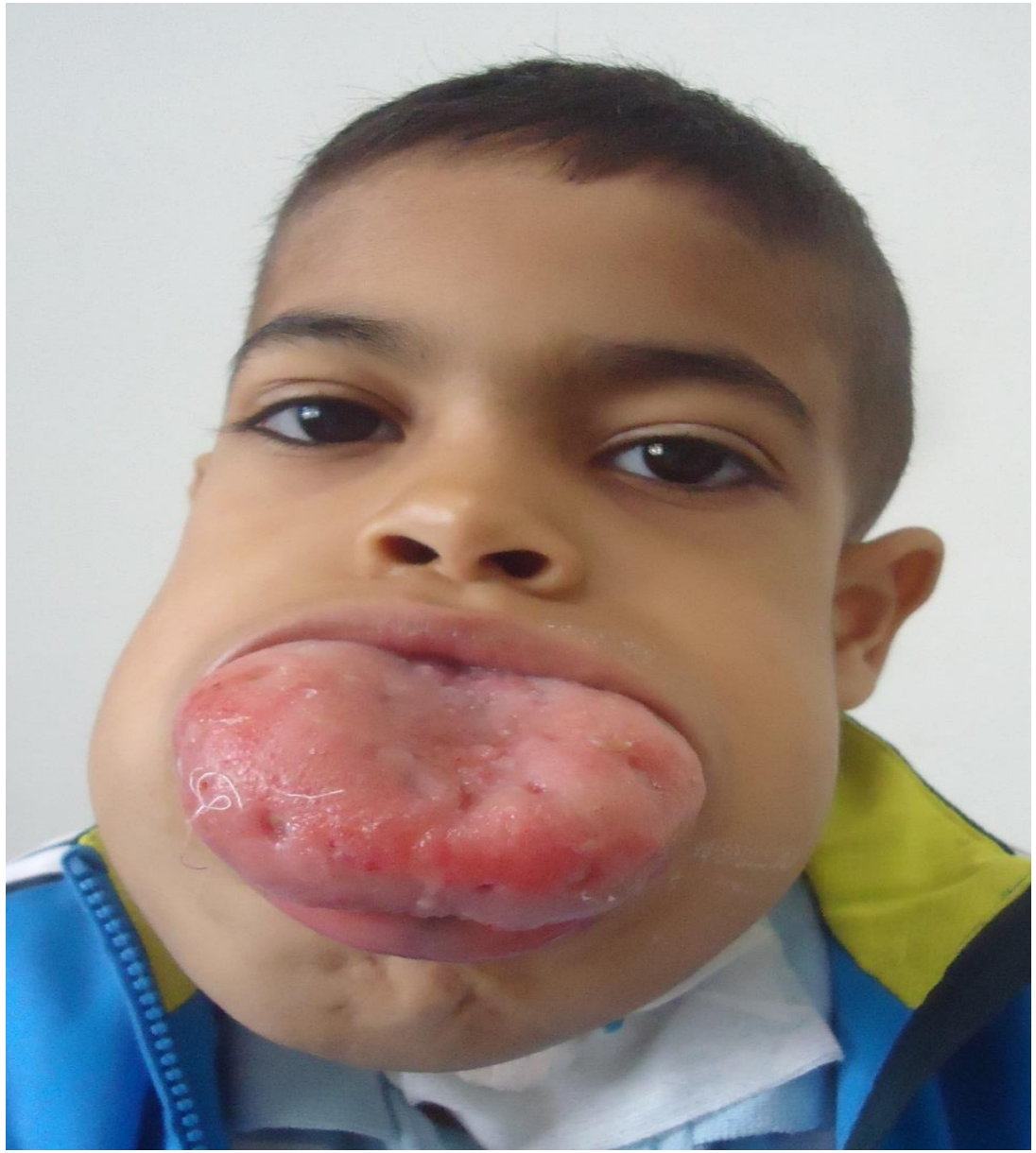


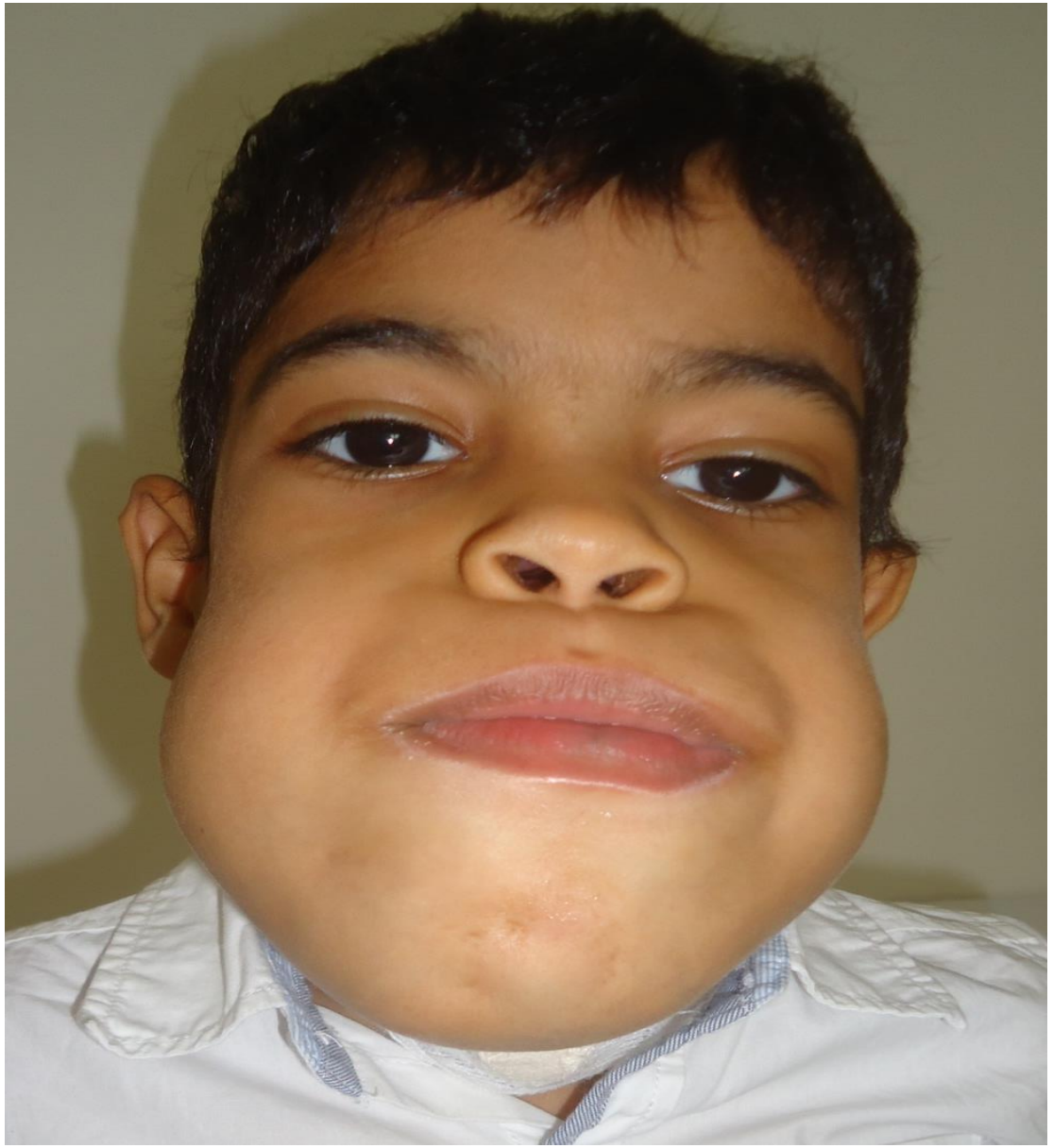












Sirolimus for refractory vascular anomalies

Cameron C Trenor 3rd [1]

Comment > Pediatr Blood Cancer. 2011 Dec 1;57(6):904-5.

Eur J Pediatr Surg. 2017 Feb;27(1):86-90. doi: 10.1055/s-0036-1593383. Epub 2016 Oct 10.

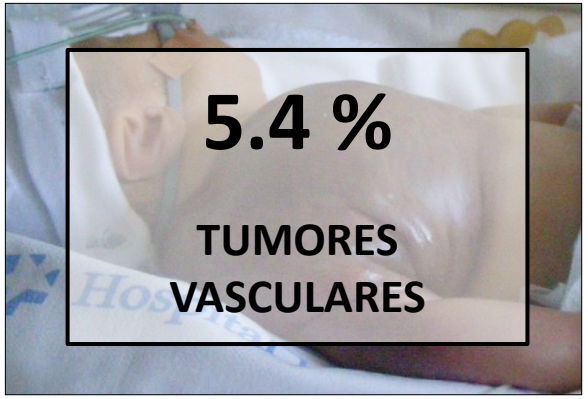
Sirolimus in the Treatment of Vascular Anomalies.

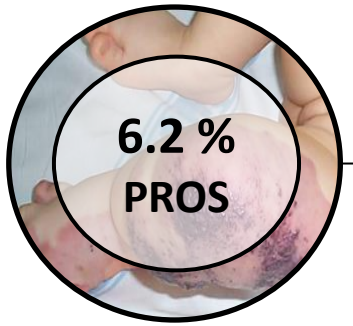
Triana P[1], Dore M[1], Cerezo VN[1], Cervantes M[1], Sánchez AV[1], Ferrero MM[2], González MD[2], Lopez-Gutierrez JC[2].

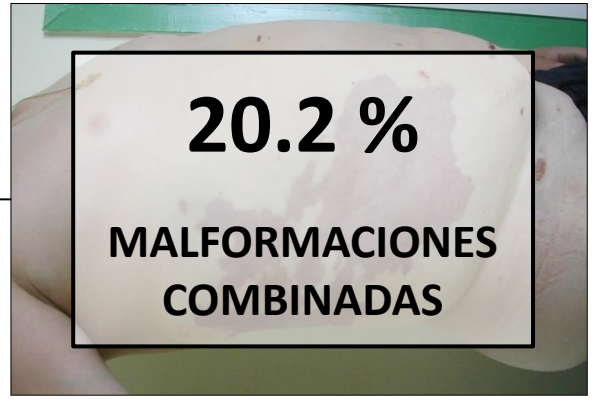
- *What phenotypes are best for treatment?*
- *Different dosing regimens?*
- *Risk stratifications?*
- *Do we need dual inhibition?*
- *Are there other methods of drug delivery?*
- *Need for improved response criteria?*
- *Need for adaptive study designs*
- *Need for collaborative studies with clinical, translational and basic science questions*

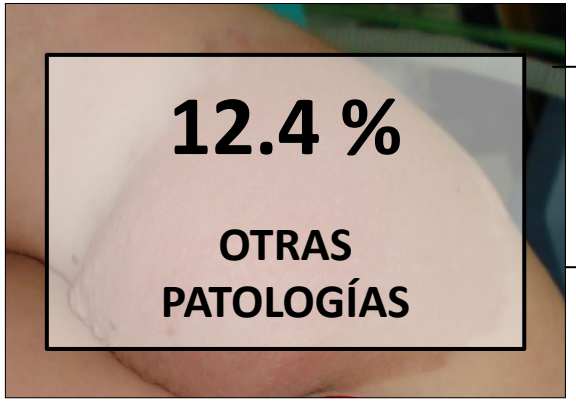
SIROLIMUS

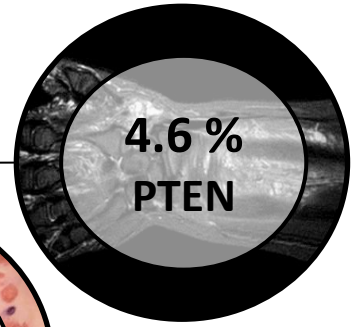
129 PACIENTES

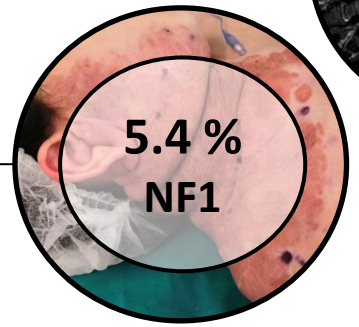






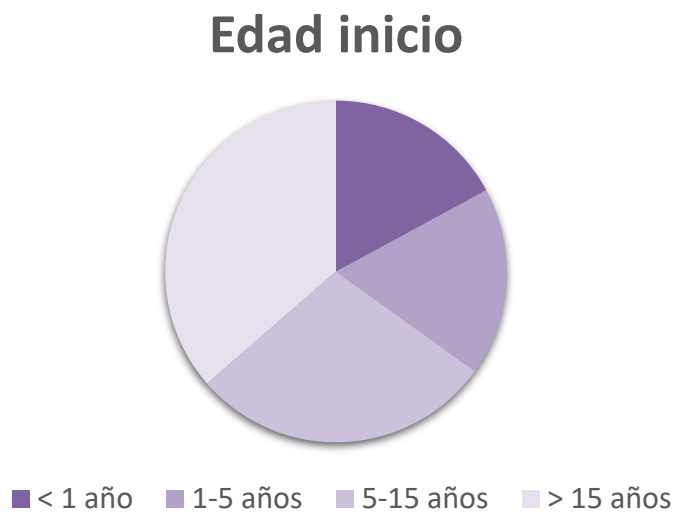


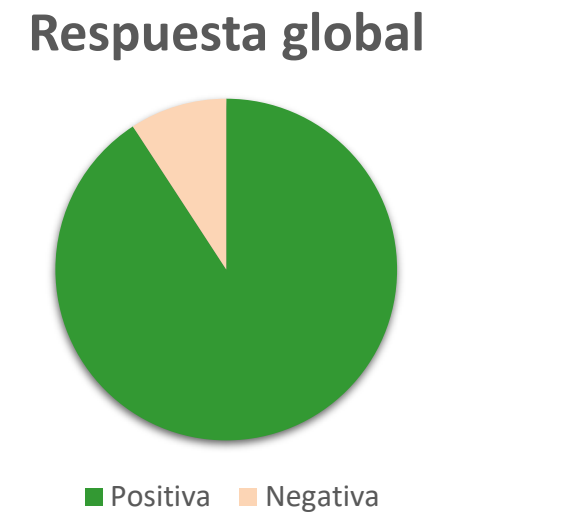




RESULTADOS

129 PACIENTES





Edad: 9,7 años

Respuesta positiva: 90,8%

RESULTADOS

129 PACIENTES

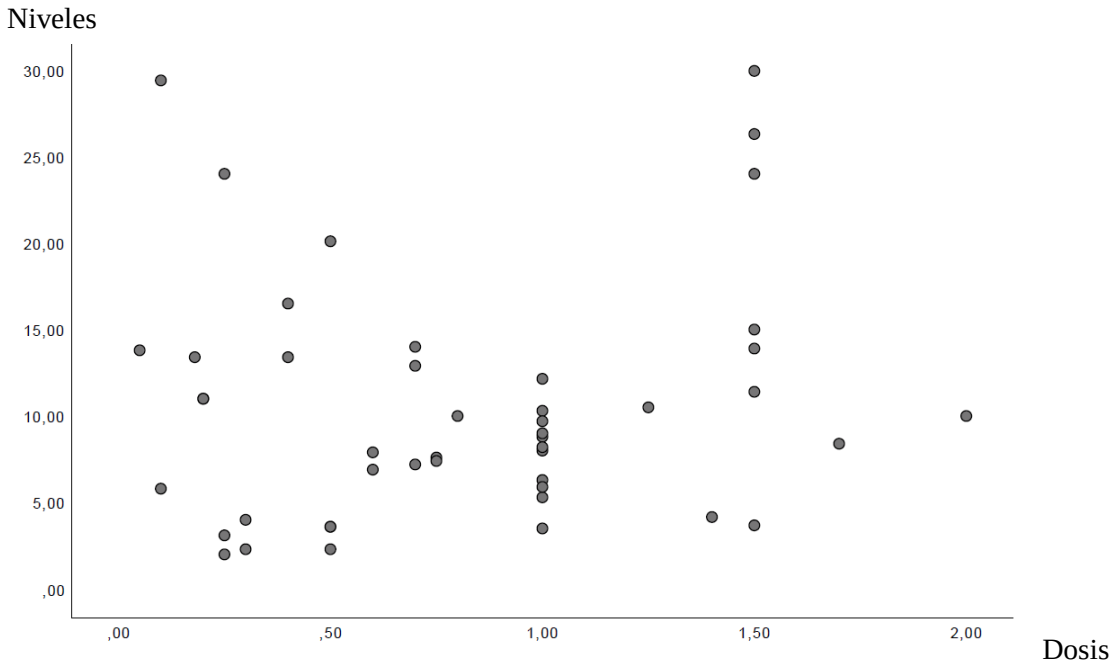
EFECTOS 2rios LEVES 33,3%	EFECTOS 2rios MODERADOS 1,6%	EFECTOS 2rios GRAVES 7,8%
Mucositis (38,4%)	Mareos (0,8%)	Neumonía (3,9%)
Dislipemia (21,5%)	Dolor articular (0,8%)	Insuficiencia renal (0,8%)
Rash o acné (9,2%)		
Metrorragias (9,2%)		
Vómitos o diarrea (7,7%)		
Leucopenia o linfopenia (4,6%)		

Triana P, López-Gutierrez JC. Menstrual disorders associated with sirolimus treatment. Pediatr Blood Cancer. 2021 Mar;68(3):e28867

RESULTADOS

¿Las dosis de sirolimus están relacionadas con los niveles en sangre?

NO



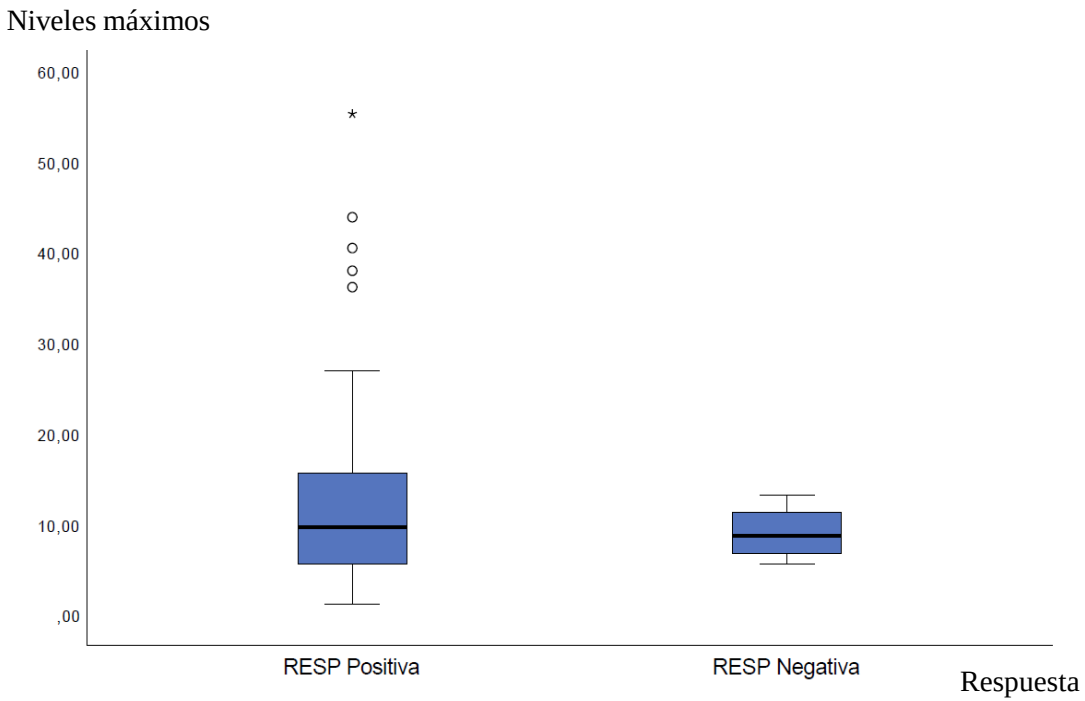
Gran variabilidad farmacodinámica

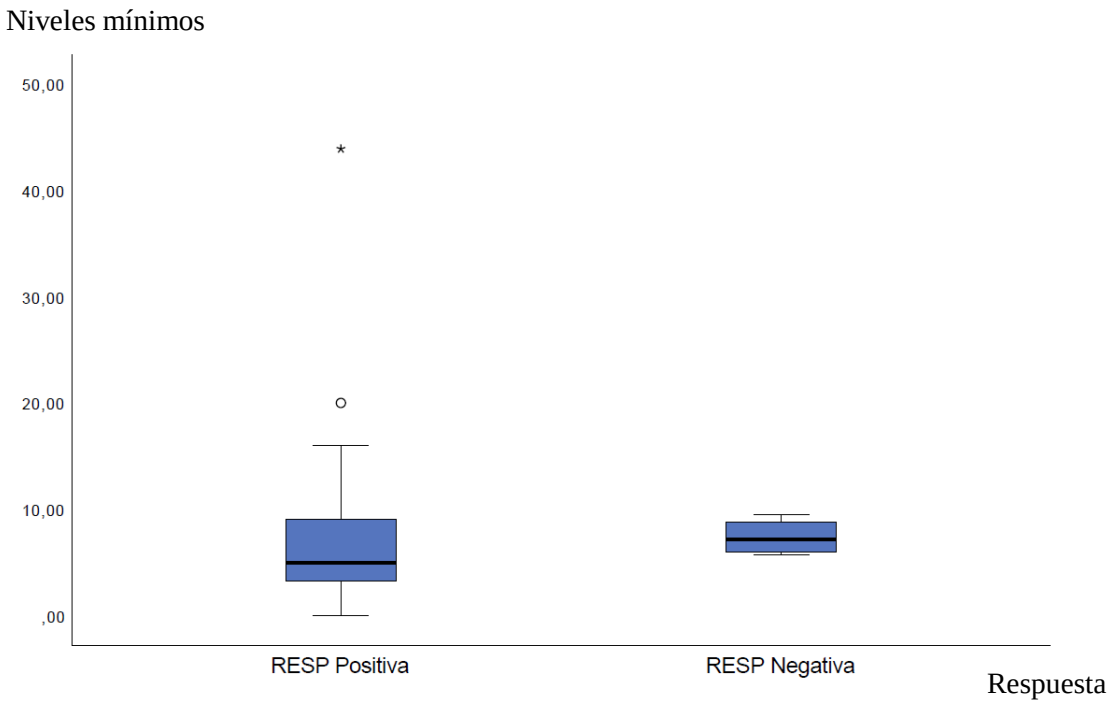
Triana P, Miguel M, Díaz M, López-Gutierrez JC. Clinical Monitoring Challenges in the Pharmacological Treatment and Management of Lymphatic Anomalies With Mammalian Target of Rapamycin Inhibition. Ther Drug Monit. 2019 Aug;41(4):547-548

RESULTADOS

¿La respuesta está relacionada con los niveles en sangre?

NO





RESULTADOS

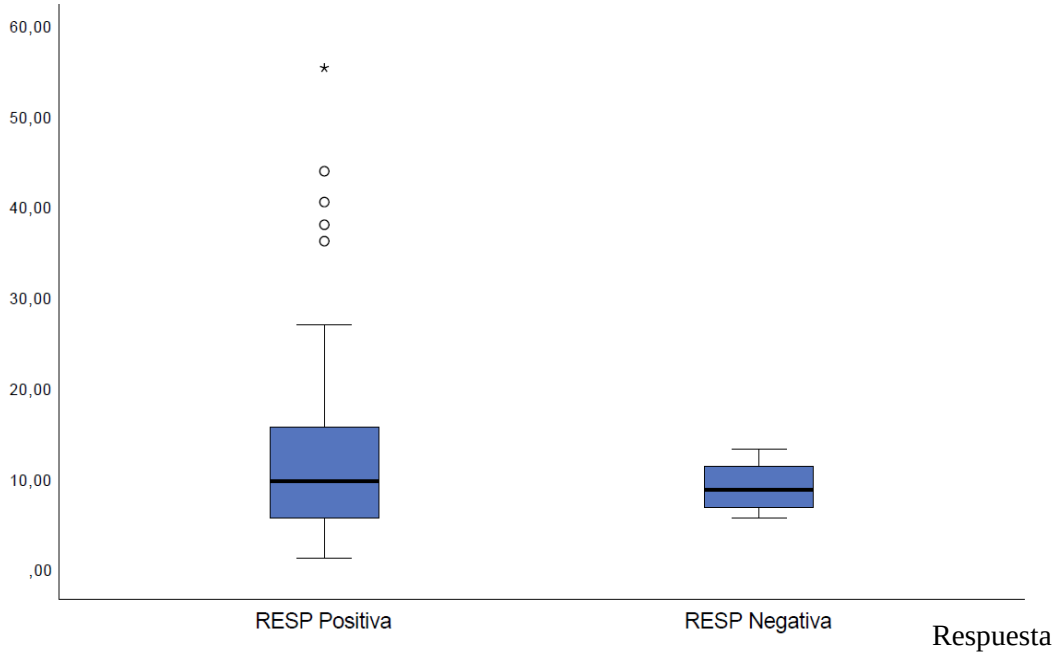
¿La respuesta está relacionada con los niveles en sangre?

NO

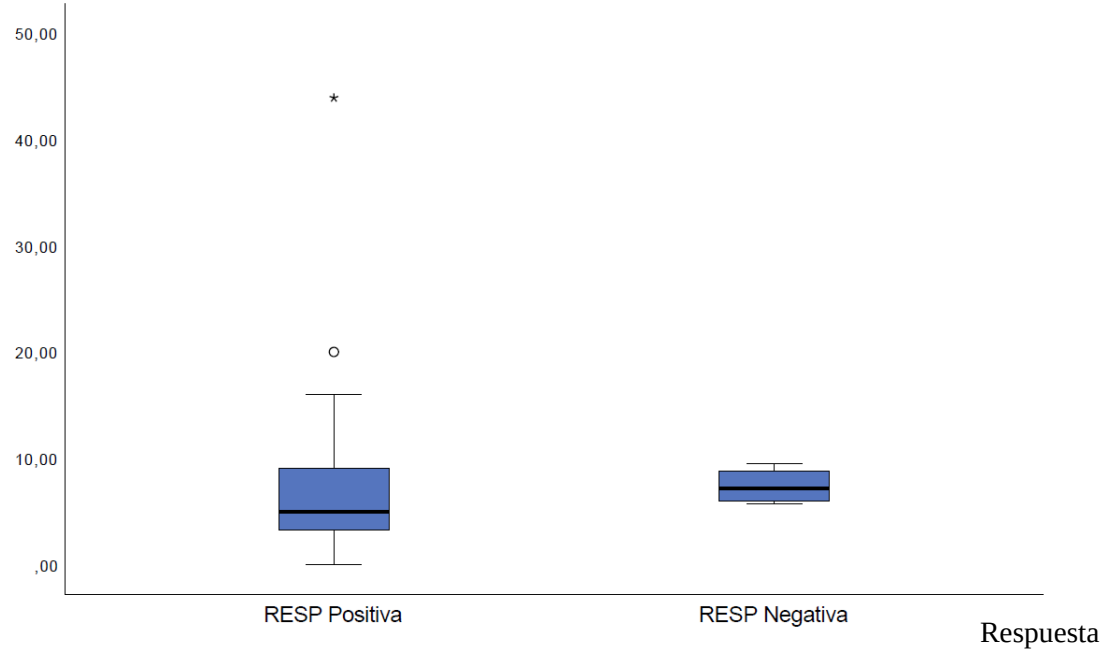
Recomendación estándar: niveles entre 5-15 ng/mL

Recomendación: ajustar dosis a síntomas, no a niveles

Niveles máximos



Niveles mínimos



RESULTADOS

¿Qué pacientes responden mejor?

No hay diferencias

CATEGORÍAS	p
Sexo	0,540
Tipo de anomalía vascular	0,601
Subtipo de anomalía vascular	0,265
Localización	0,747
Extensión	0,302
Síntomas	0,446
Genética	0,490
Tratamientos previos	0,687

RESULTADOS

¿Qué pacientes responden mejor?

CATEGORÍAS	p
Sexo	0,540
Tipo de anomalía vascular	0,601
Subtipo de anomalía vascular	0,265
Localización	0,747
Extensión	0,302
Síntomas	0,446
Genética	0,490
Tratamientos previos	0,687

Correlación NEGATIVA con la dismetría

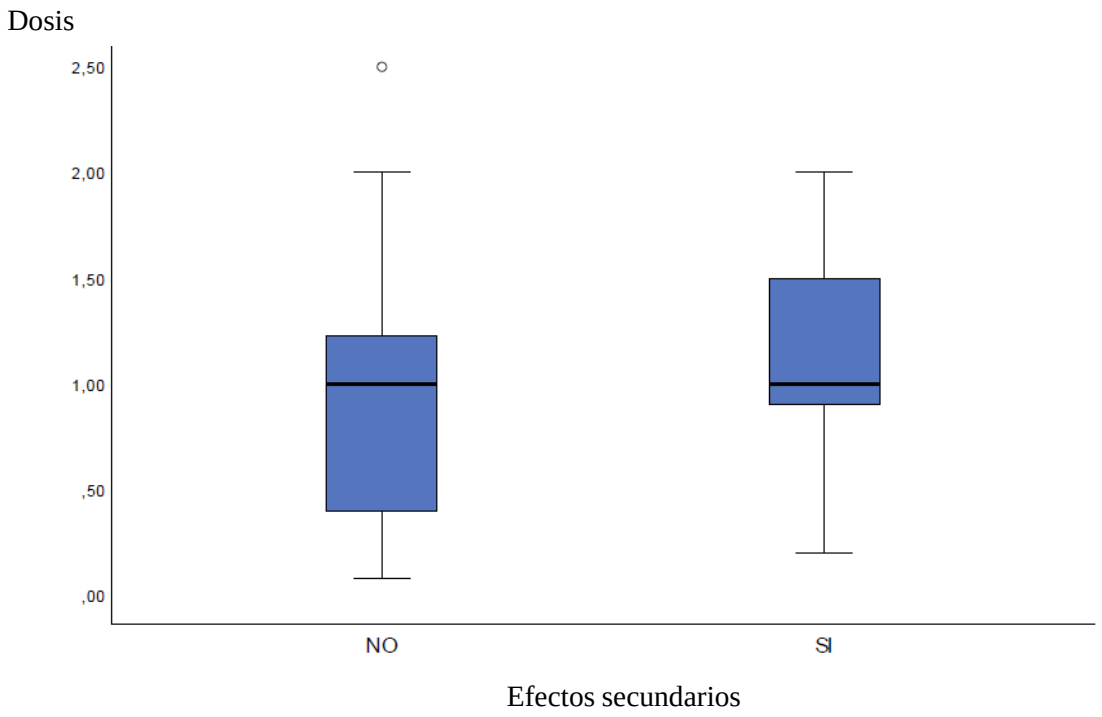
Dismetría | p = 0,036

	Resp POSITIVA	Resp NEGATIVA
SIN dismetría	103	8
CON dismetría	6	3

RESULTADOS

¿Los efectos 2rios están relacionados con las dosis y los niveles en sangre?

SÍ



	p
Dosis	0,04
Niveles	0,2

No relación entre leves, moderados o graves

RESULTADOS

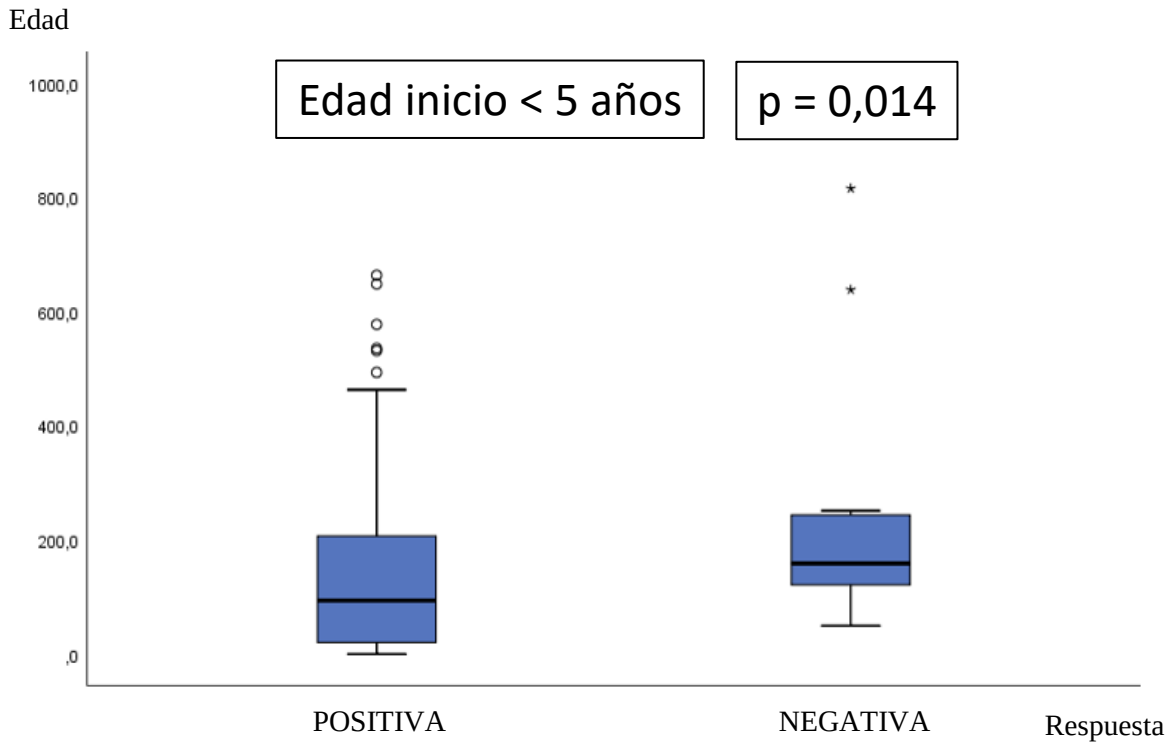
¿Cuándo empezar el tratamiento?

Primera línea

Riesgo de complicaciones

Riesgo de secuelas

Mejor cuanto antes



Edad inicio < 5 años

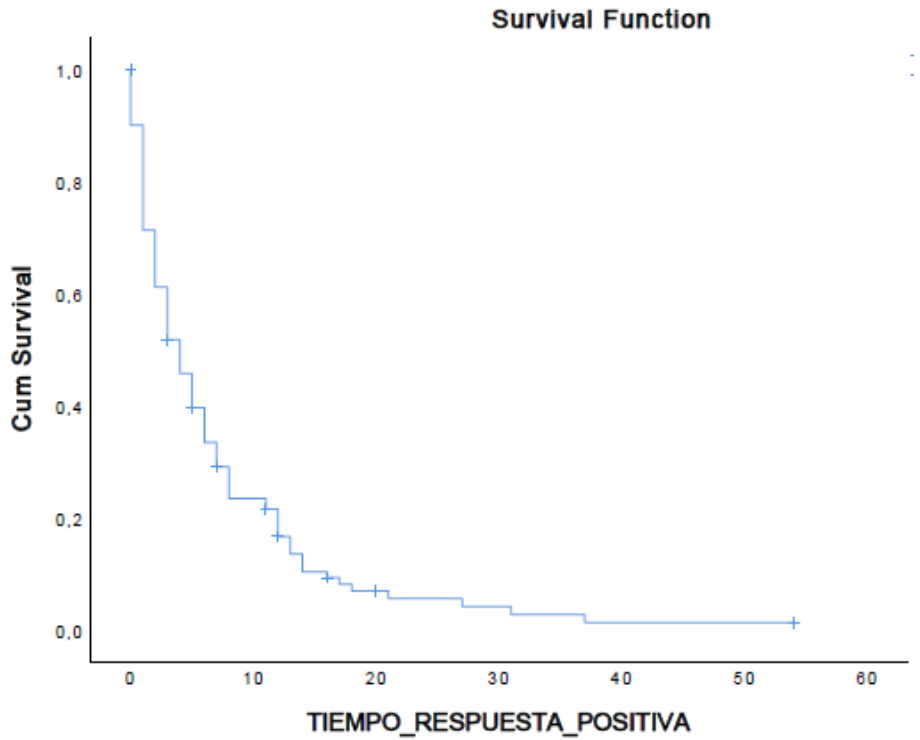
p = 0,014

RESULTADOS

¿Cuánto esperar para confirmar la respuesta?

12 meses

DURACIÓN	Respuesta POSITIVA
4 meses	51%
6 meses	67%
12 meses	84%
14 meses	90%



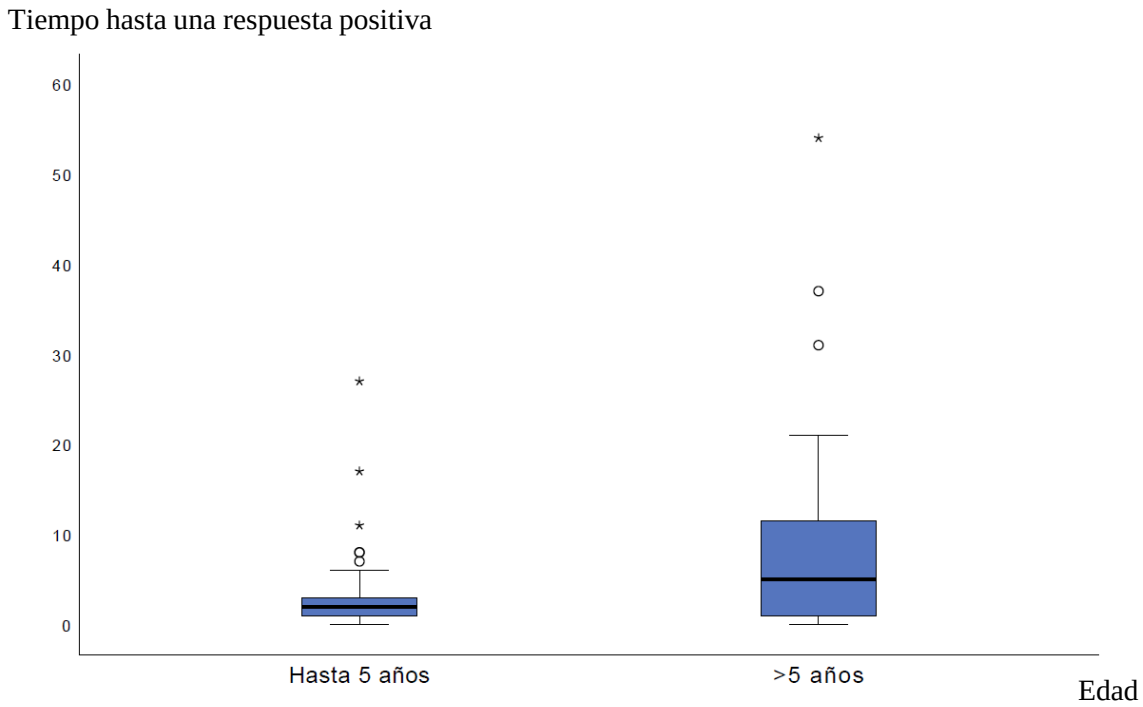
RESULTADOS

¿Qué pacientes responden antes?

EDAD INICIO	Respuesta POSITIVA
< 5 años	2 meses
> 5 años	6 meses

p = 0,004

Menores de 5 años

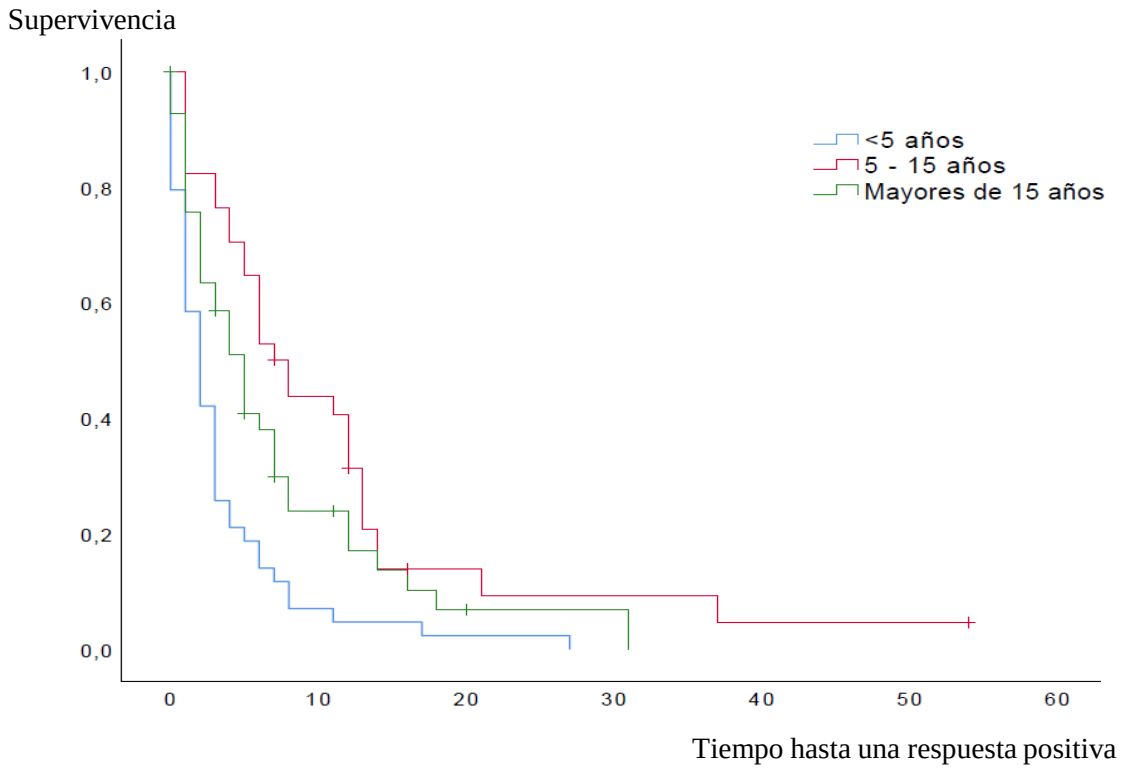


RESULTADOS

¿Qué pacientes responden antes?

EDAD INICIO	Respuesta POSITIVA
< 5 años	2 meses
5-15 años	7 meses
> 15 años	5 meses

Menores de 5 años



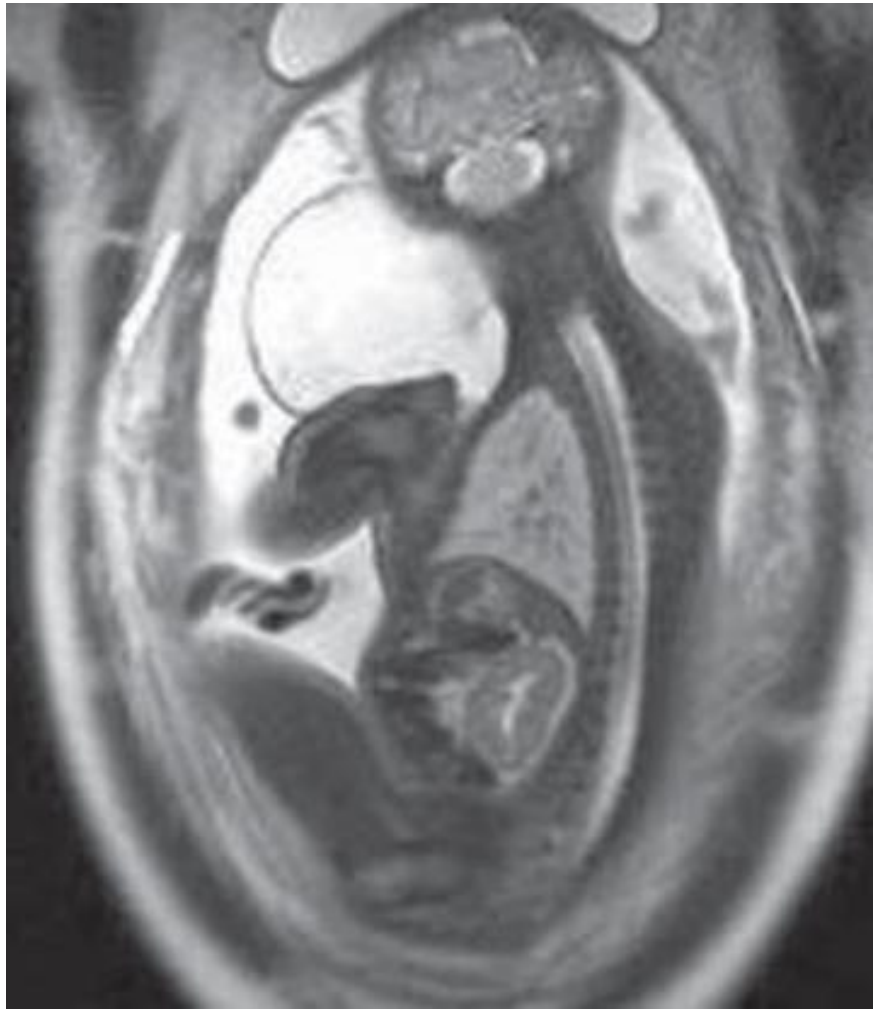
RESULTADOS

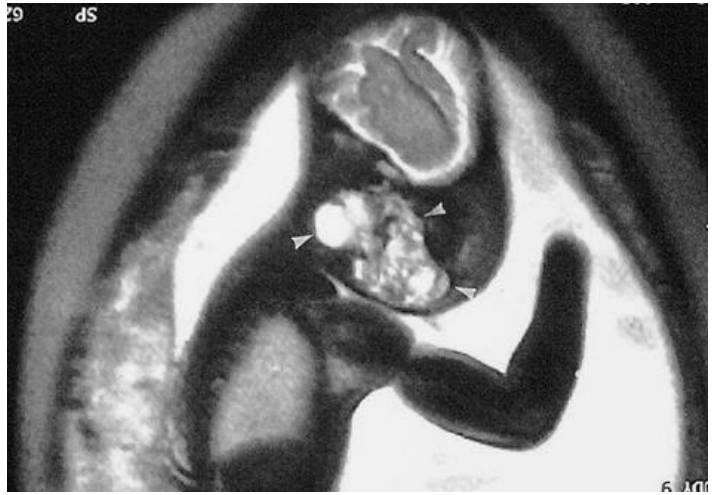
¿Qué pacientes responden antes?

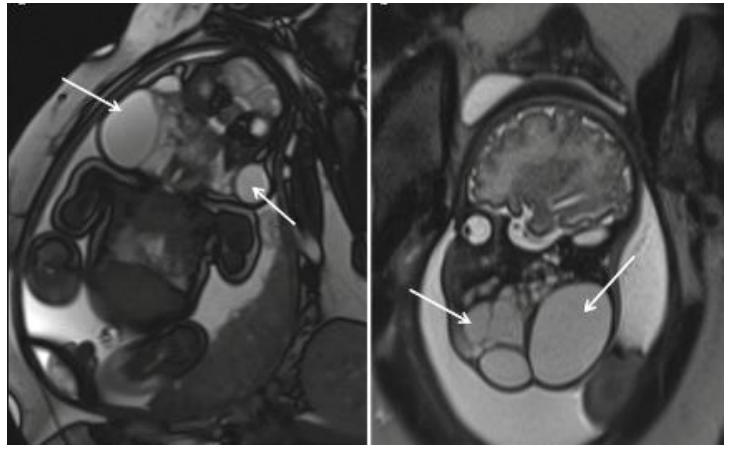
No hay diferencias

CATEGORÍAS	p
Tipo de anomalía vascular	NS
Subtipo de anomalía vascular	NS
Localización	NS
Extensión	NS
Síntomas	NS
Genética	NS
Gravedad	NS

Fetal diagnosis of LM and managements options







Fetal exposure to Sirolimus has been demostrated as safe

Pregnancy Outcomes in Solid Organ Transplant Recipients with Exposure to Sirolimus *Am J Transplant.* 2013

S. Constantinescu, L. Coscia, M. Moritz, C. McGrory, C. Ramirez, V. Armenti

Medicine, Temple University School of Medicine, Philadelphia
Surgery, Thomas Jefferson University, Philadelphia
Surgery, Lehigh Valley Health Network, Allentown, PA
National Transplantation Pregnancy Registry, Philadelphia

TRANSPLANTATION PROCEEDINGS

< Previous Article **December 2004** Volume 36, Issue 10, Pages 3232–3233 Next Article >

Absence of teratogenicity of sirolimus used during early pregnancy in a liver transplant recipient

I. Jankowska, U. Oldakowska-Jedynak, Z. Jabiry-Zieniewicz, A. Cyganek, J. Pawlowska, M. Teisseyre, P. Kalicinski, M. Markiewicz, L. Paczek, J. Socha

CORRESPONDENCE

Maternal Sirolimus Therapy for Fetal Cardiac Rhabdomyomas

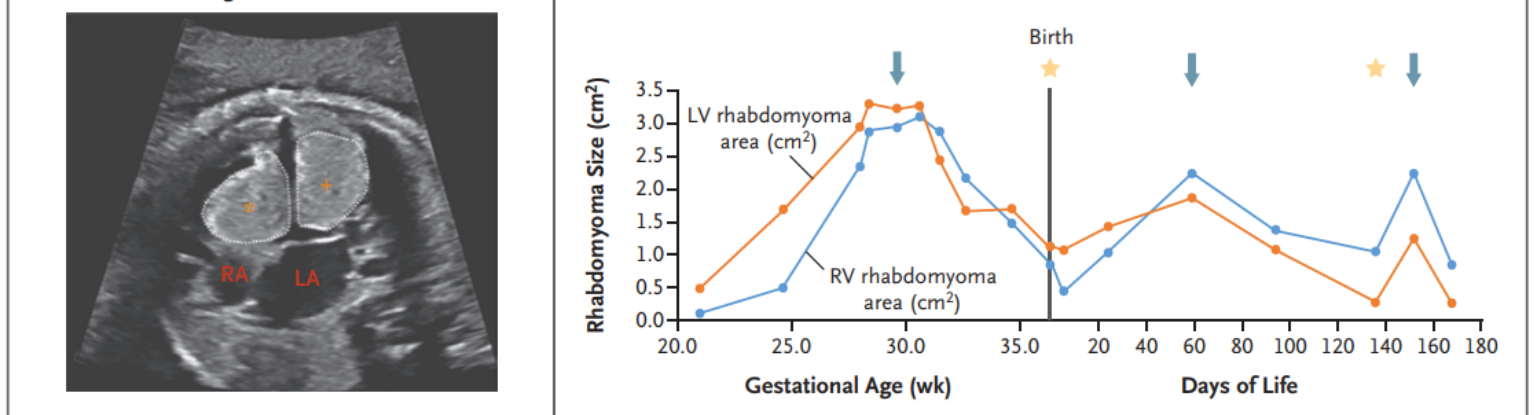
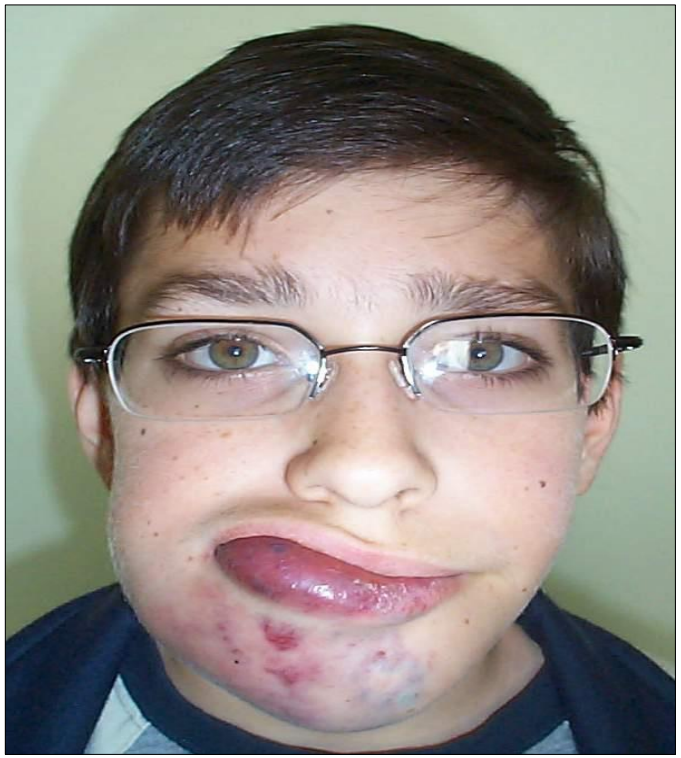
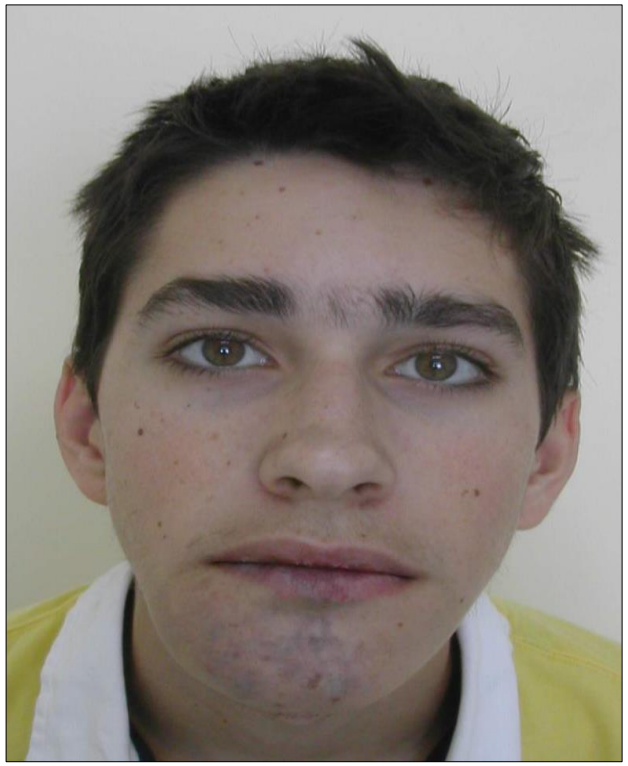


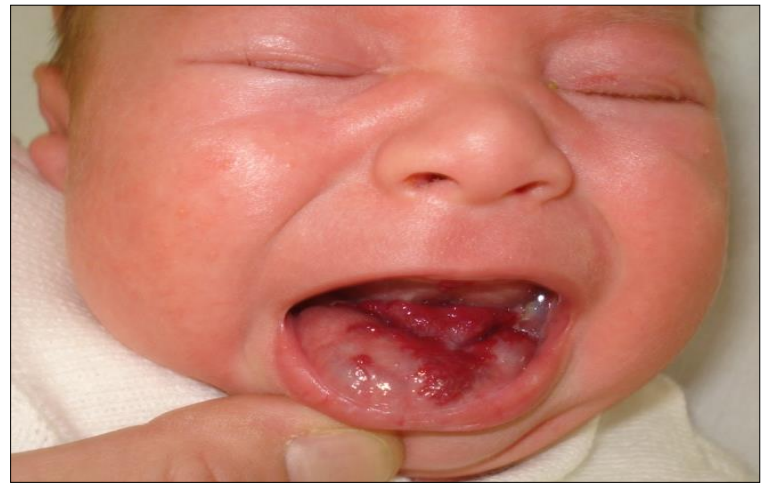
Figure 1. Findings on Echocardiography before and after Birth.

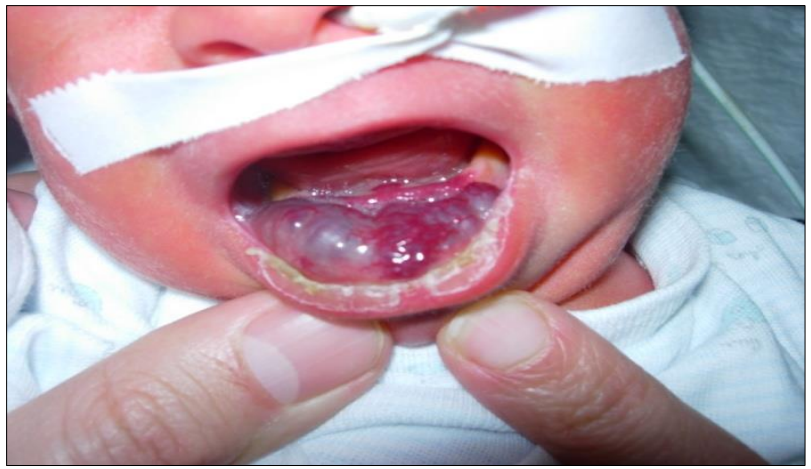
Panel A shows a fetal echocardiogram in the apical four-chamber view at 30 weeks of gestation. Two large echogenic intracardiac masses are shown: one in the right ventricle (RV) (star) and one in the left ventricle (LV) (cross). The dotted lines indicate the areas measured. RA denotes right atrium, and LA left atrium. Panel B shows changes over time in the area of the masses in the RV and the LV on the same echocardiographic view in serial studies. The points on each line denote individual echocardiographic measurements of the area of each mass, arrows the initiation of sirolimus, and stars discontinuation of sirolimus.

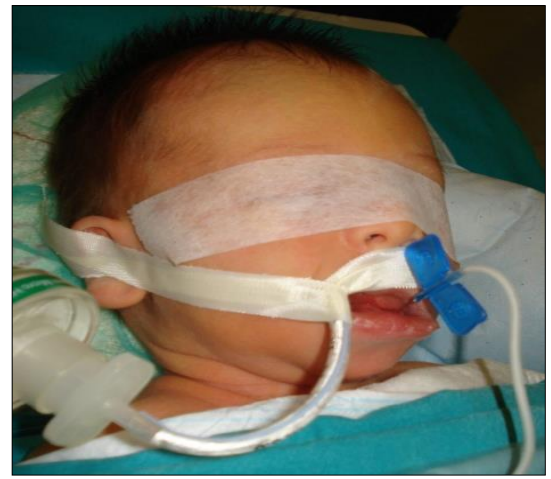
MALFORMACIONES VENOSAS

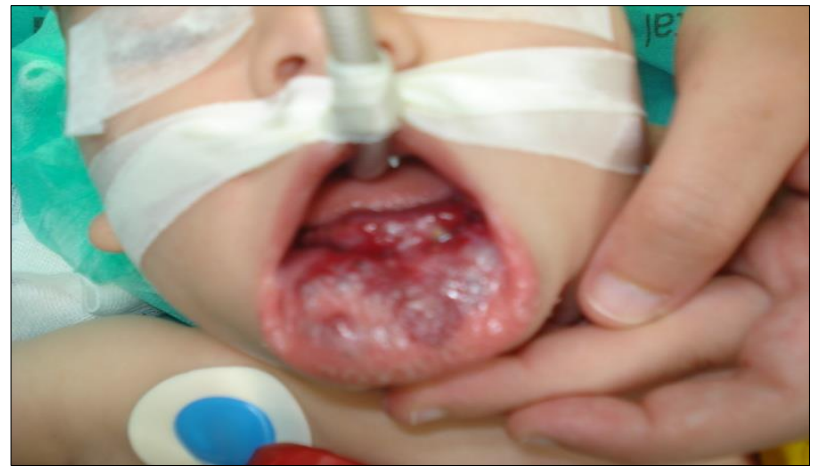


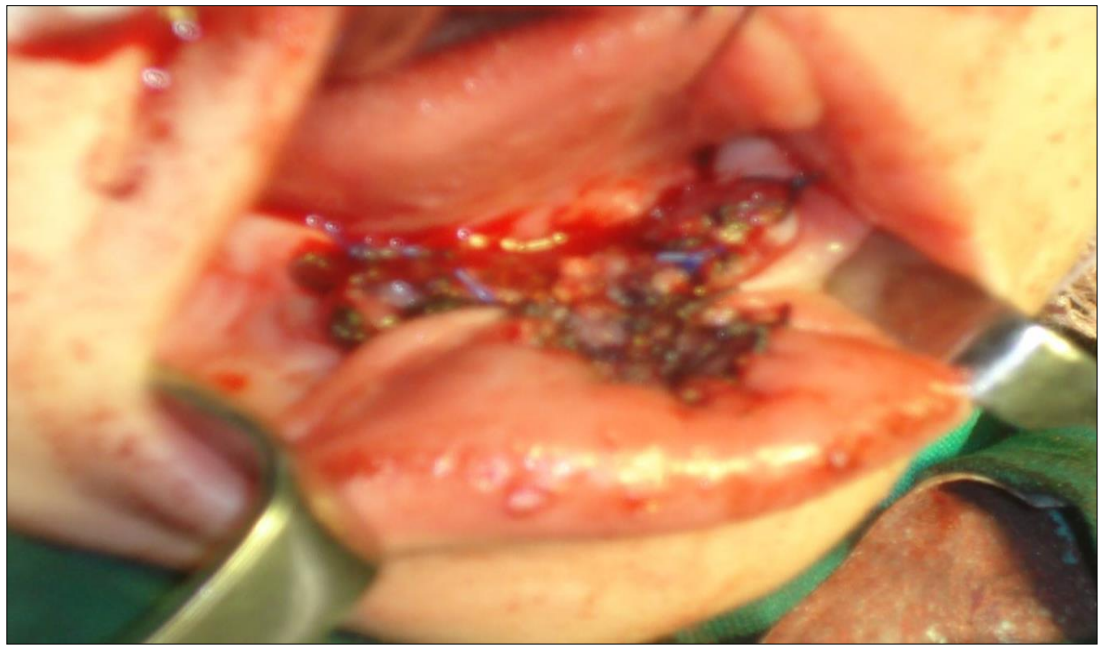


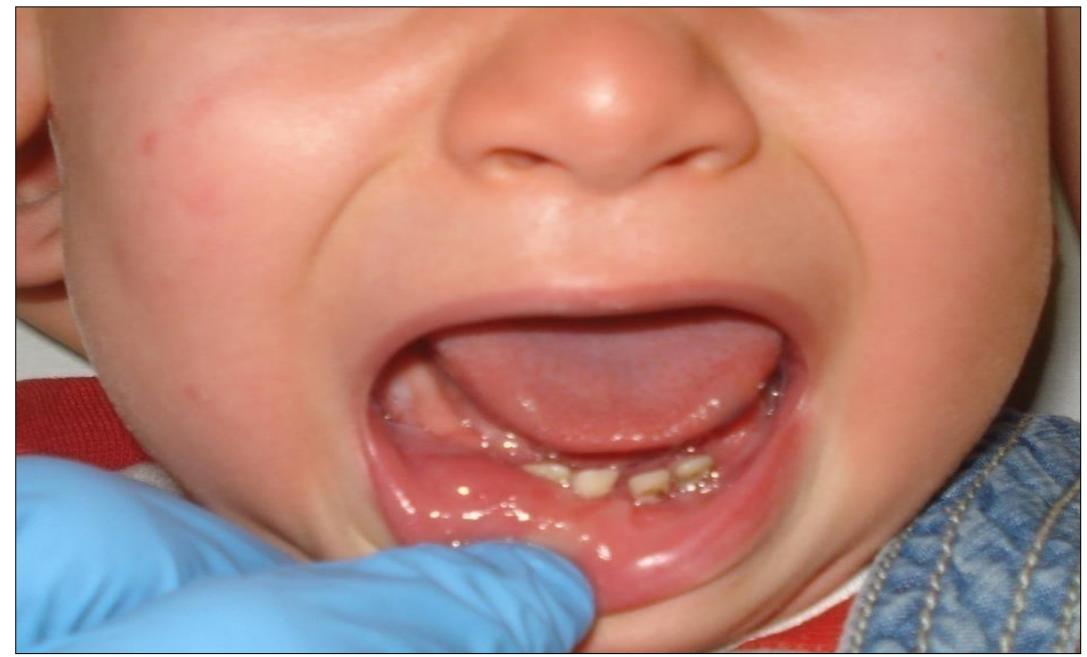












Somatic Activating *PIK3CA* Mutations Cause Venous Malformation

Nisha Limaye,[1] Jaakko Kangas,[2,6] Antonella Mendola,[1,6] Catherine Godfraind,[3,4] Matthieu J. Schlögel,[1] Raphael Helaers,[1] Lauri Eklund,[2] Laurence M. Boon,[1,5] and Miikka Vikkula[1,*]

A Somatic *MAP3K3* Mutation Is Associated with Verrucous Venous Malformation

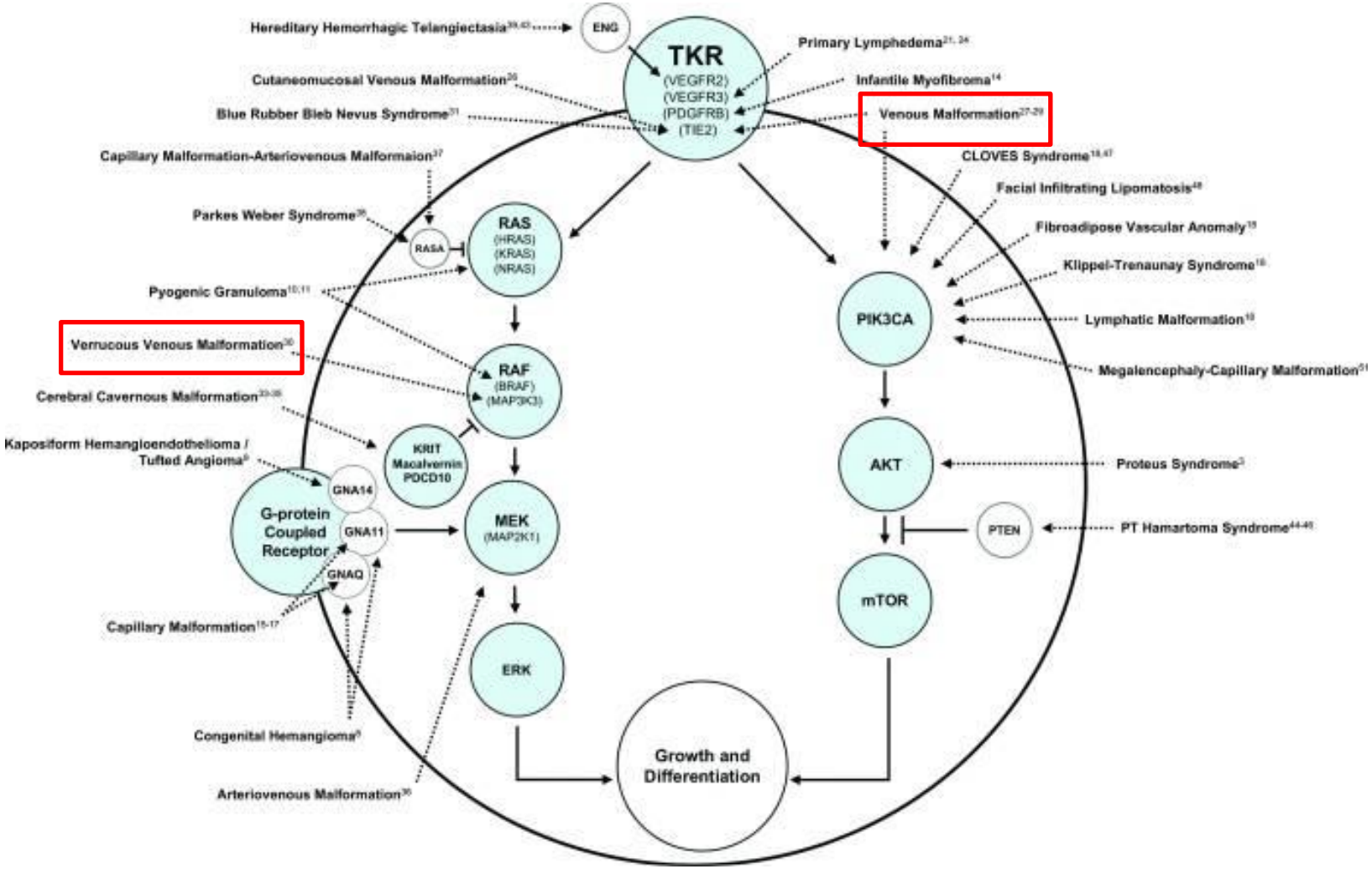
Javier A. Couto,[1] Matthew P. Vivero,[1] Harry P.W. Kozakewich,[2,3] Amir H. Taghinia,[1,2] John B. Mulliken,[1,2] Matthew L. Warman,[2,4,5,6] and Arin K. Greene[1,2,*]

Blue Rubber Bleb Nevus (BRBN) Syndrome is caused by Somatic *TEK* (TIE2) Mutations

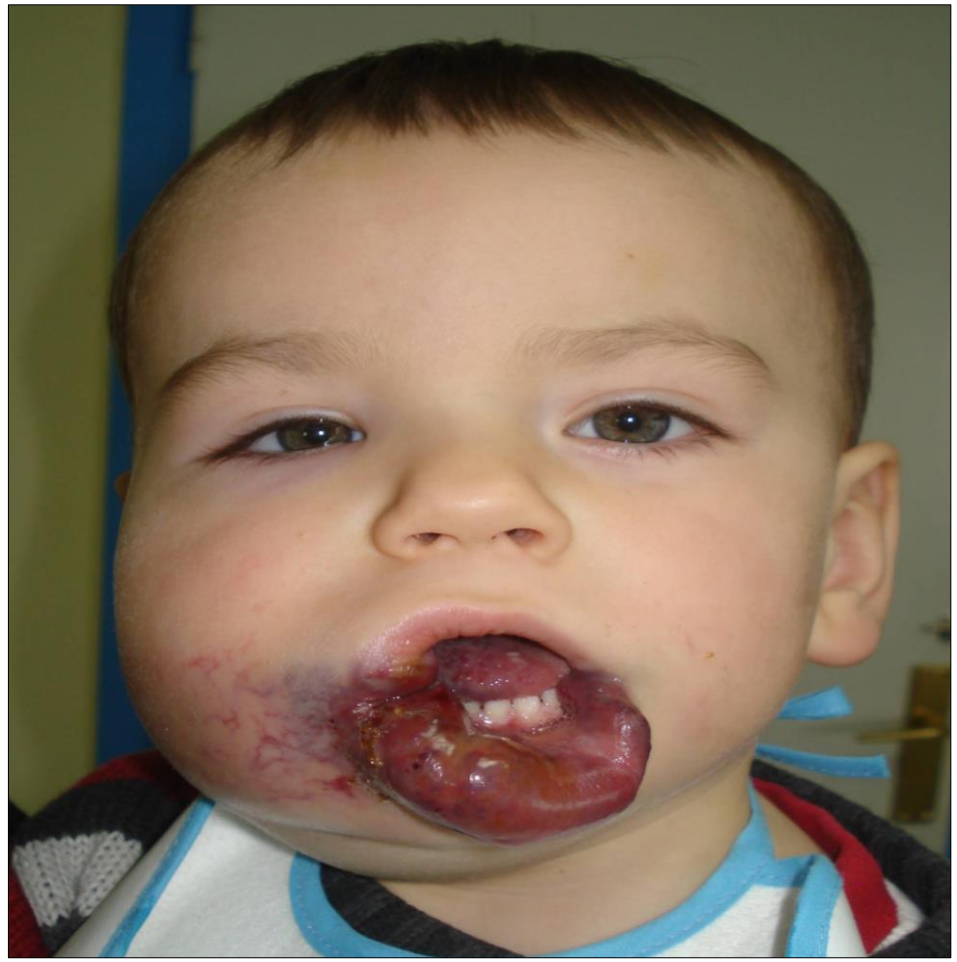
Julie Soblet, Jaakko Kangas, Marjut Nätynki, Antonella Mendola, Raphaël Helaers, Melanie Uebelhoer, Mika Kaakinen, Maria Cordisco*, Anne Dompmartin, Odile Enjolras**, Simon Holden***, Alan D. Irvine, Loshan Kangesu, Christine Léauté-Labrèze, Agustina Lanoel, Zerina Lokmic, Saskia Maas, Maeve A. McAleer,

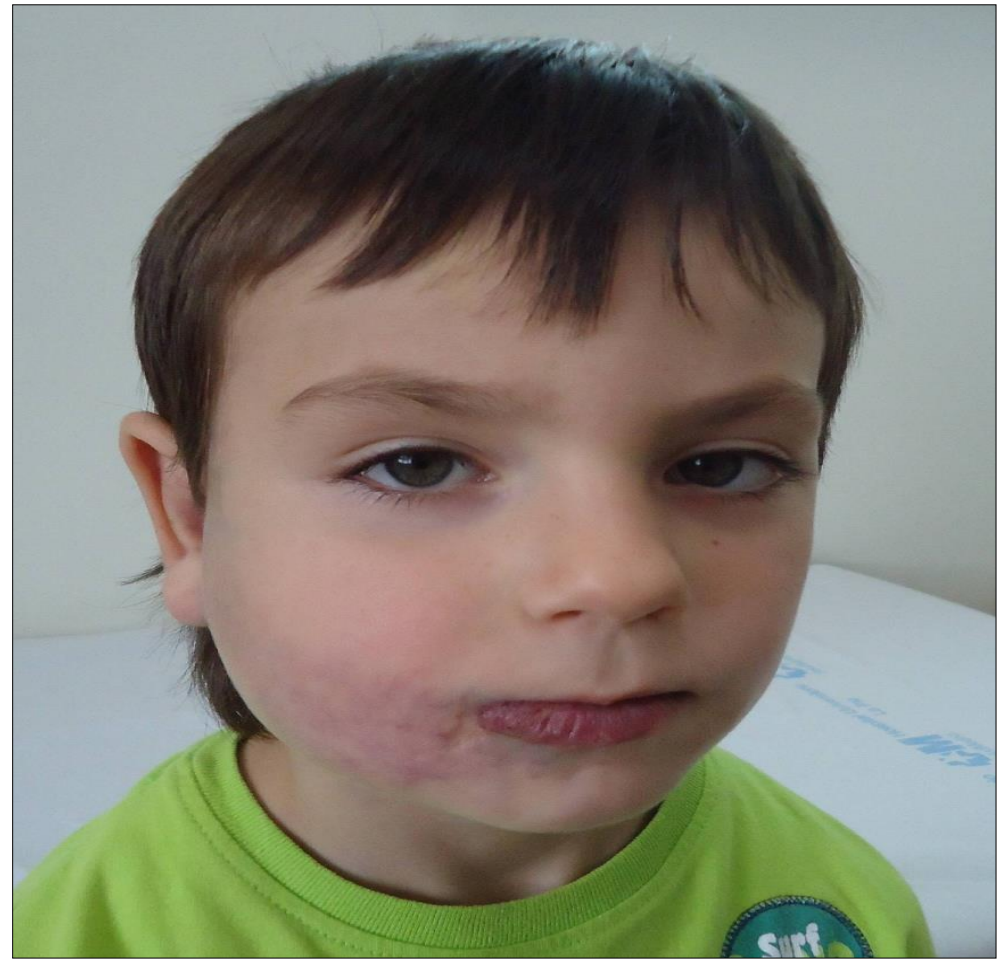
Four common glomulin mutations cause two thirds of glomuvenous malformations ("familial glomangiomas"): evidence for a founder effect

P Brouillard, M Ghassibe, A Penington, L Boon, A Dompmartin, I Temple, M Cordisco, D Adams, F Piette, J Harper, S Syed, F Boralevi, A Taieb, S Danda, E Baselga, O Enjolras, J Mulliken, and M Vikkula

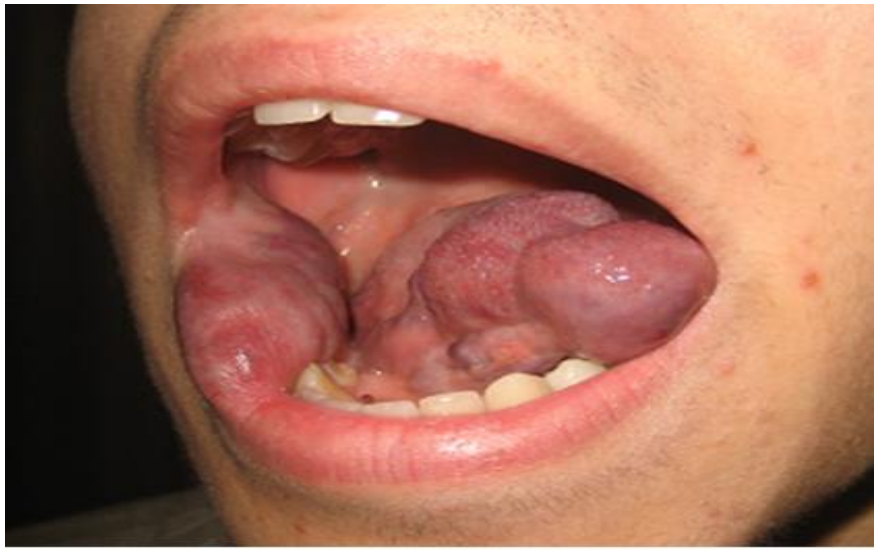


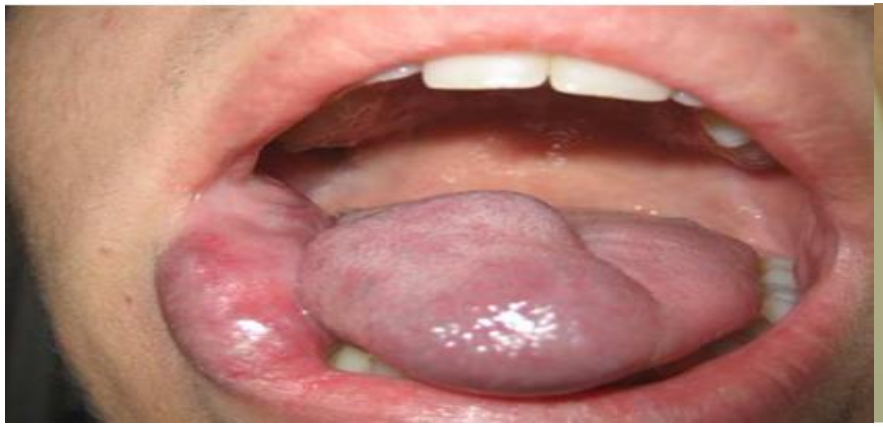
Greene A.K. Goss J.A. Vascular anomalies: From a clinicohistologic to a genetic framework. *Plast ReconstrSurg.* 2018; 141: 709e

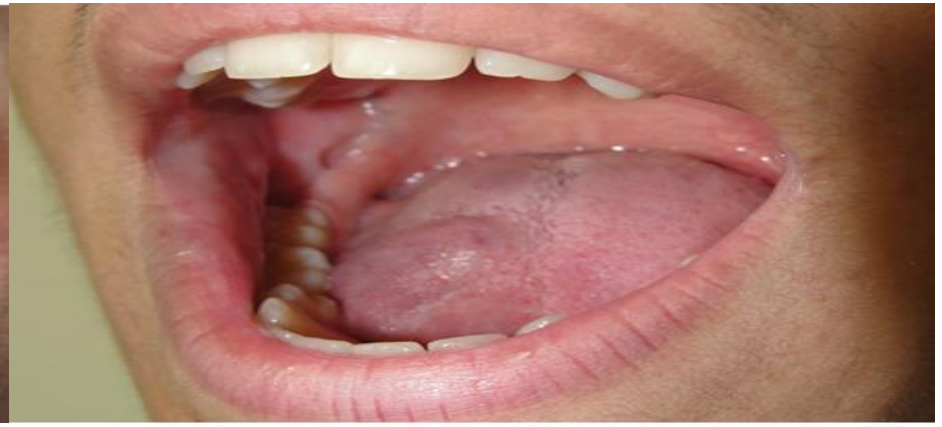


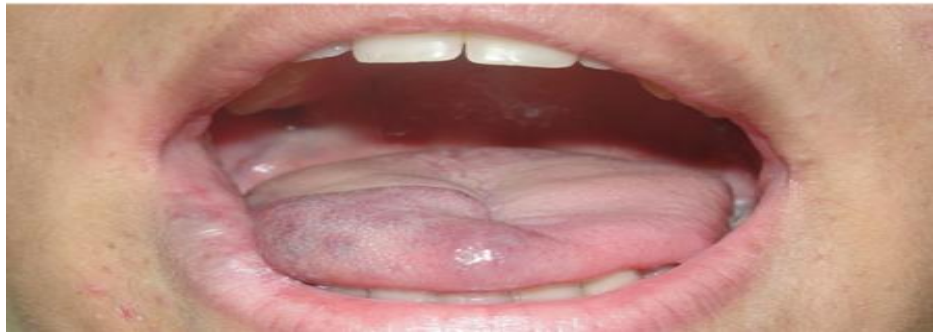


LASER NdYag



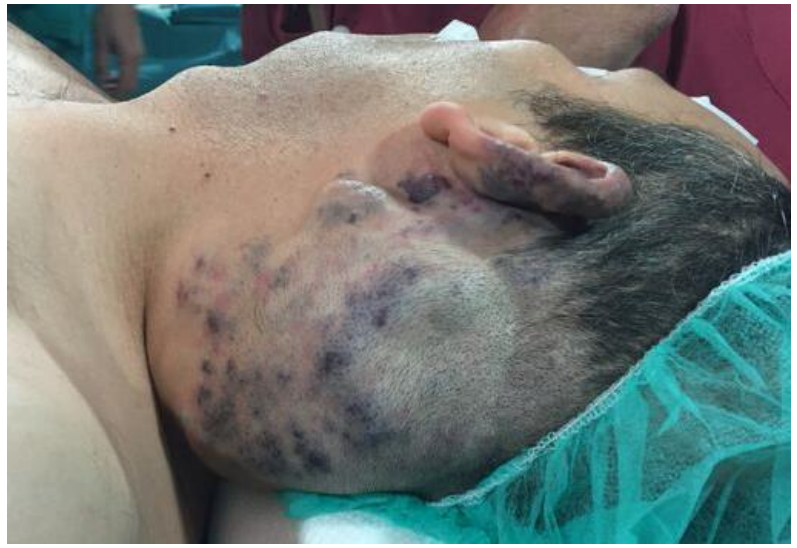


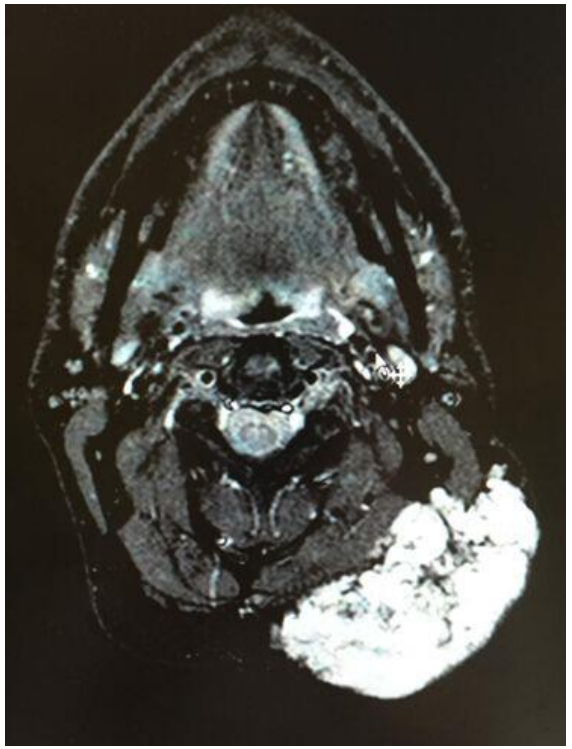


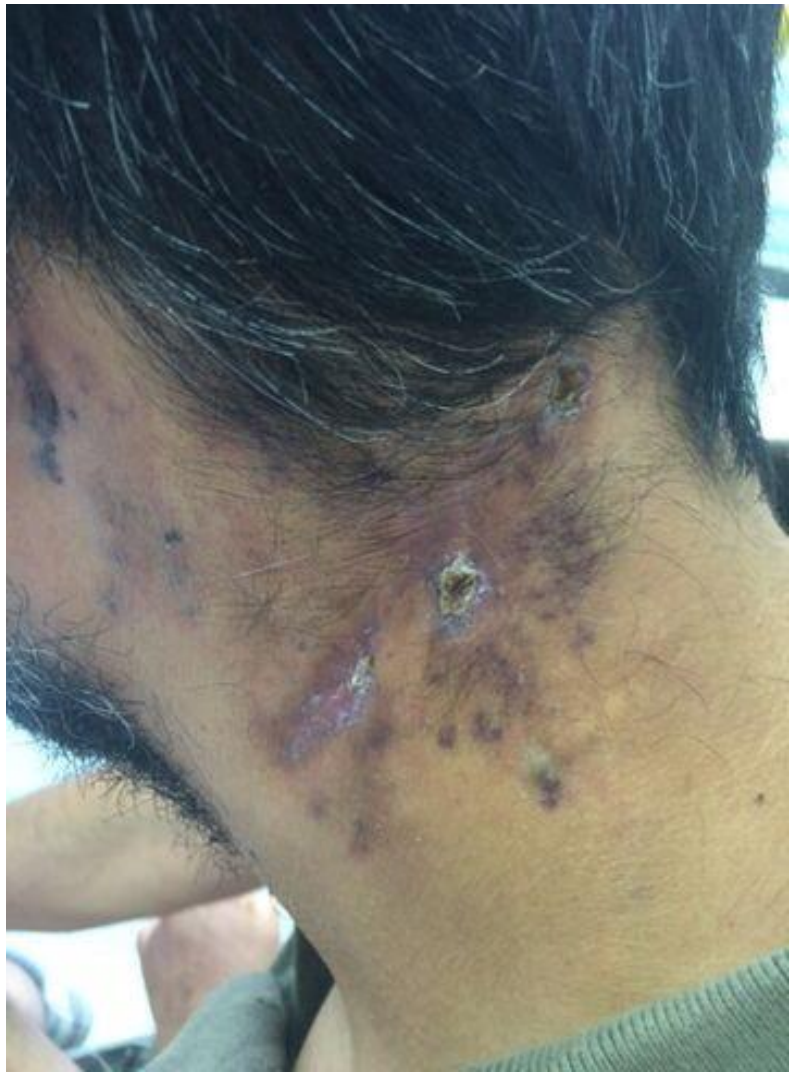


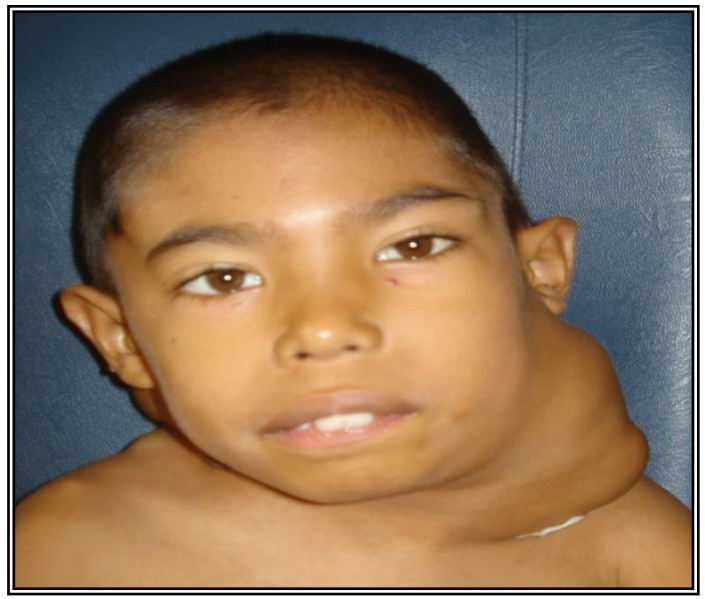
Dr P Boixeda

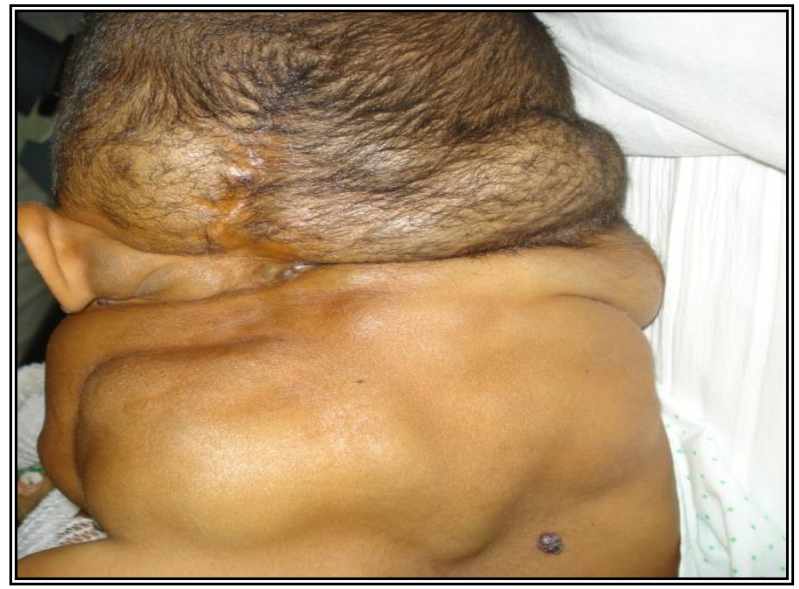
LASER DIODO

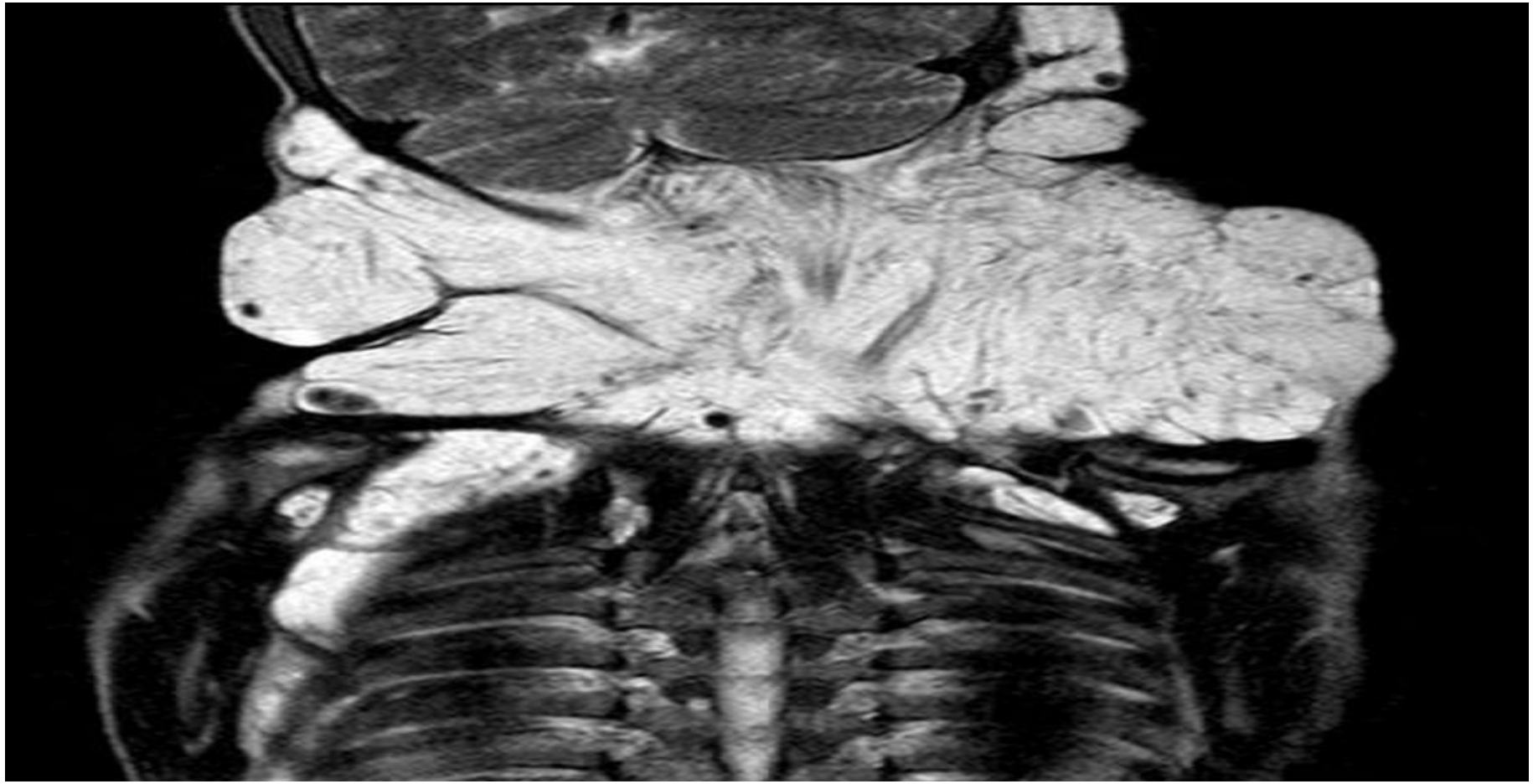


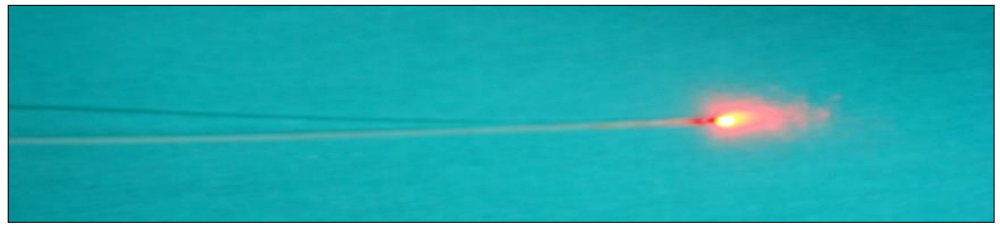


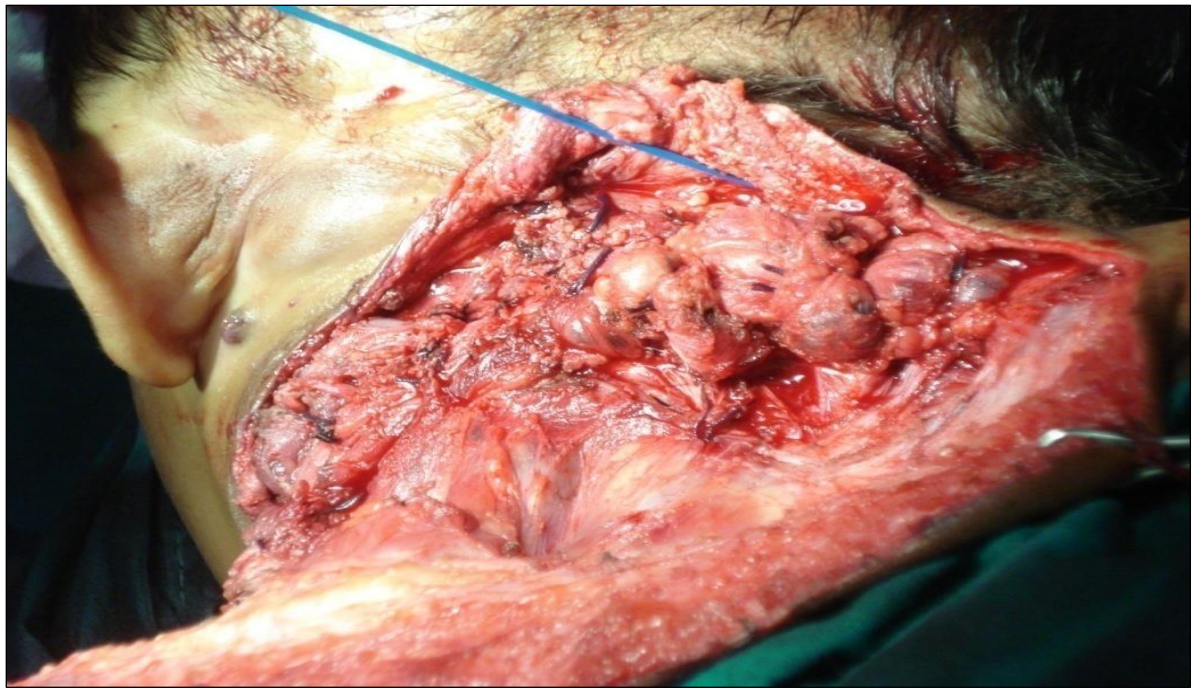


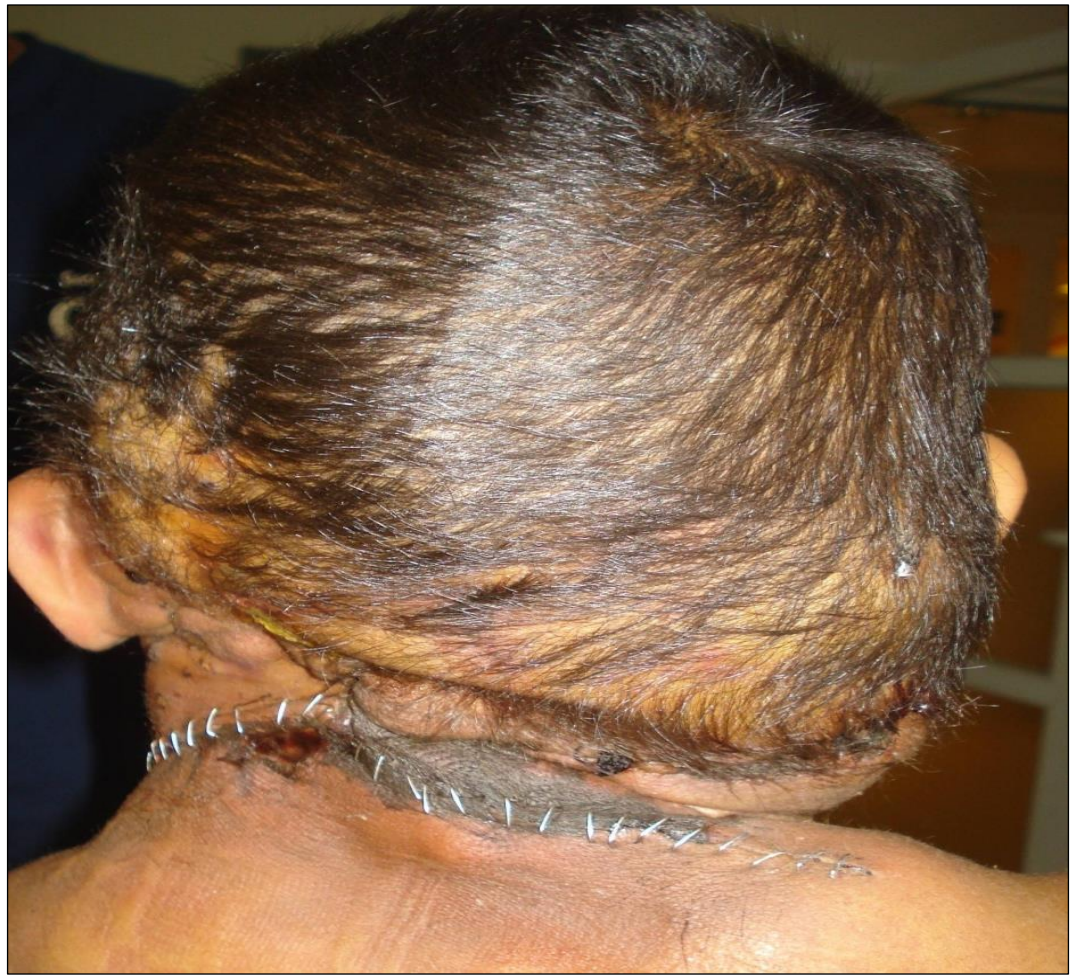




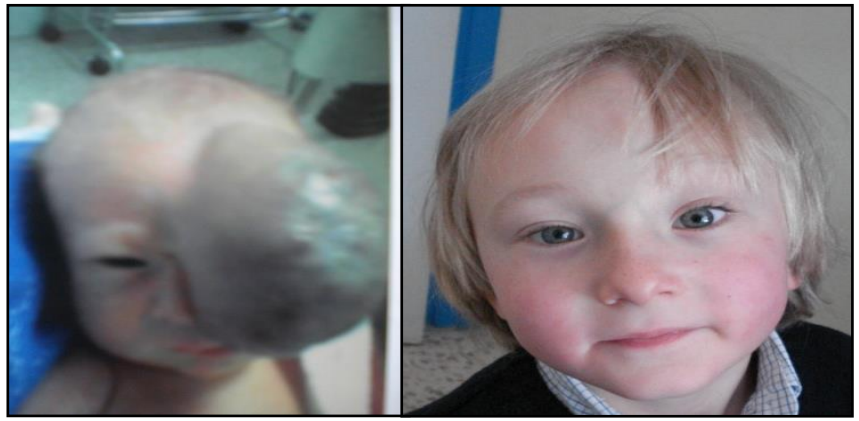


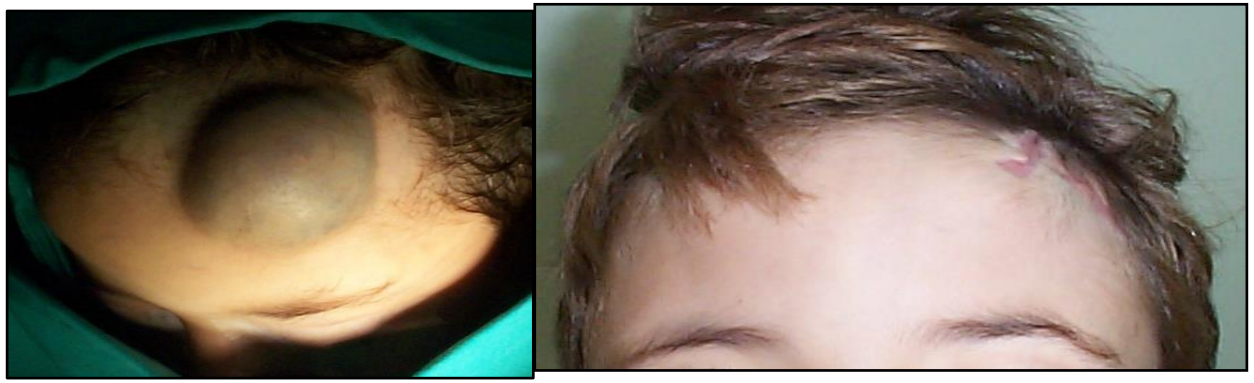


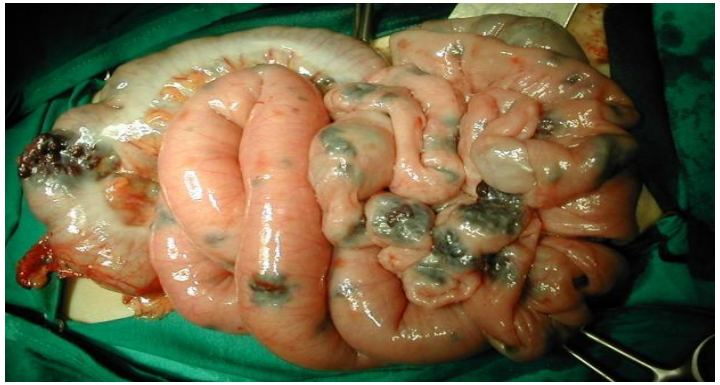


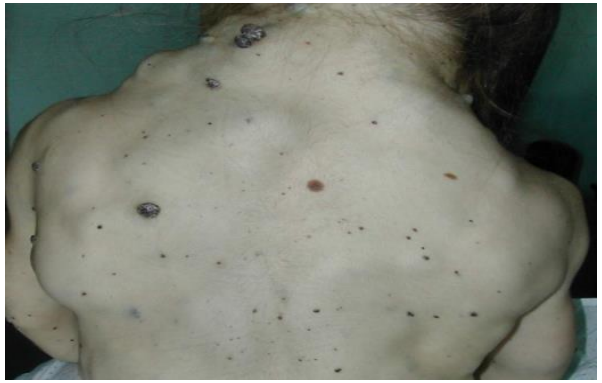


Blue Rubber Bleb Nevus Syndrome

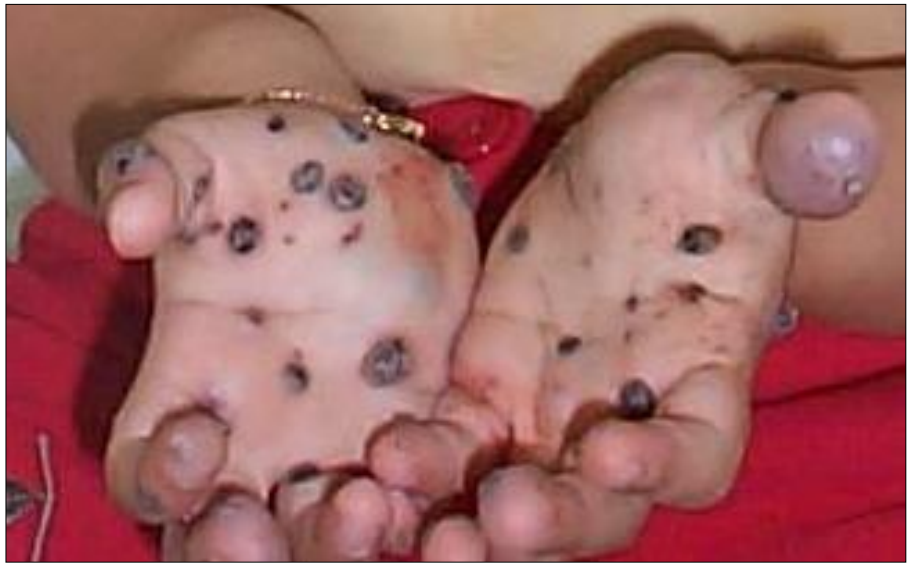


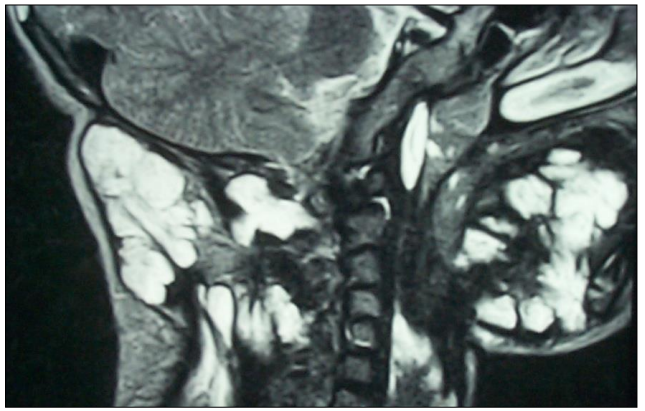


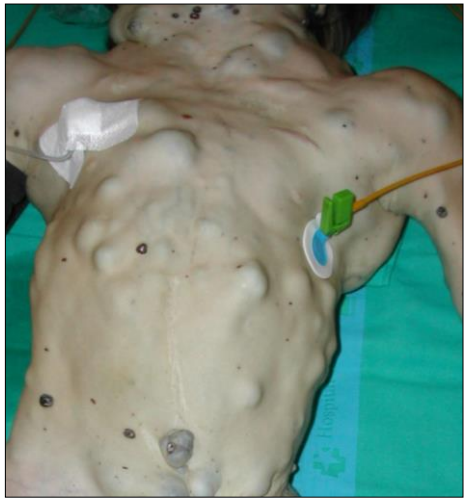




Blue Rubber Bleb Nevus Syndrome







Zhang B. ***Efficacy and safety of sirolimus in the treatment of blue rubber bleb naevus syndrome in paediatric patients****.Clin Exp Dermatol. 2019 May 10*.

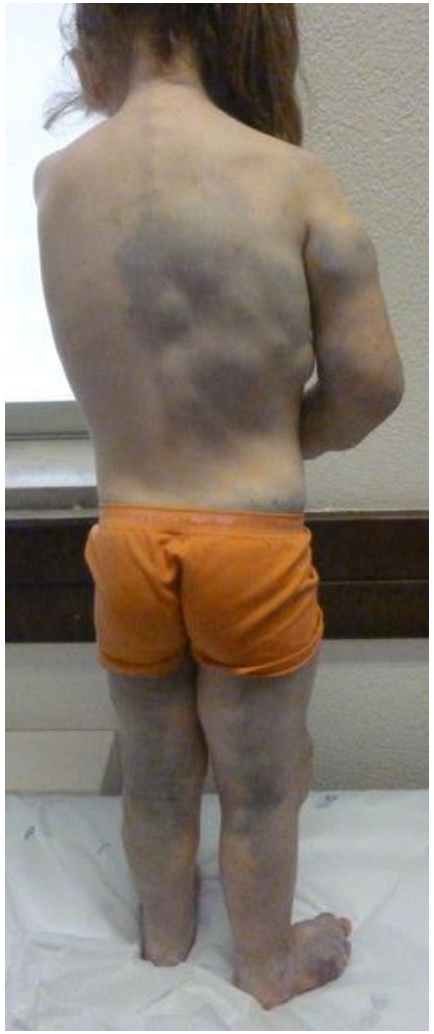
REBASTINIB

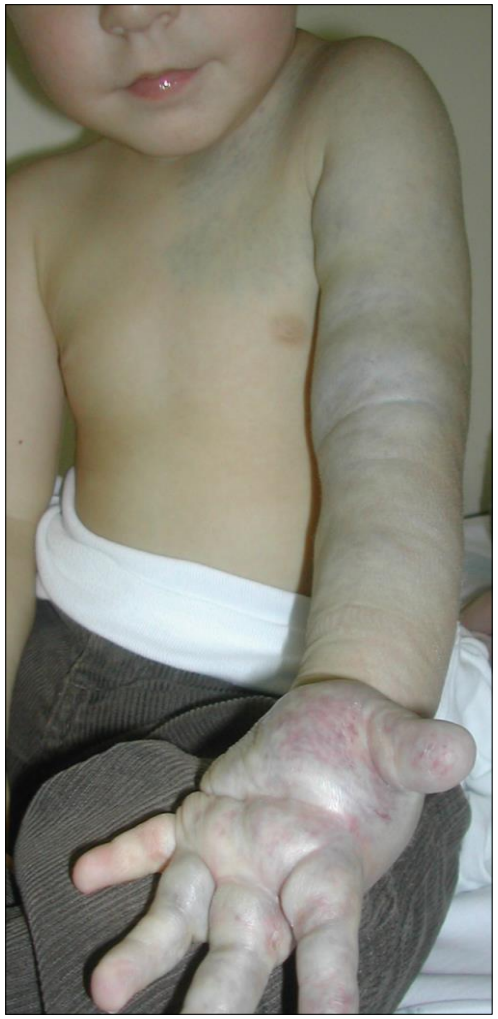
- A potent and selective inhibitor of the TIE2 kinase
- In a Phase 1 clinical study, biomarker data have demonstrated rebastinib-induced increases in the TIE2 ligand angiopoietin 2, providing evidence of TIE2 inhibition
- Rebastinib is currently being evaluated in a Phase 1b/2 clinical study in combination with paclitaxel (NCT03601897) and in a Phase 1b/2 clinical study in combination with carboplatin (NCT03717415) for ovarian cancer

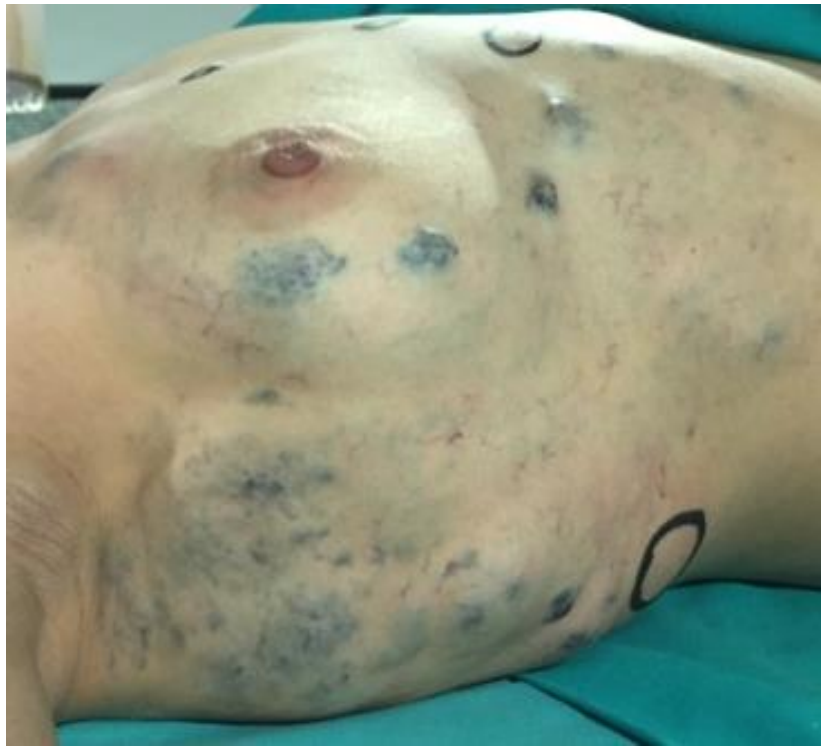
Rebastinib no está comercializado en España.

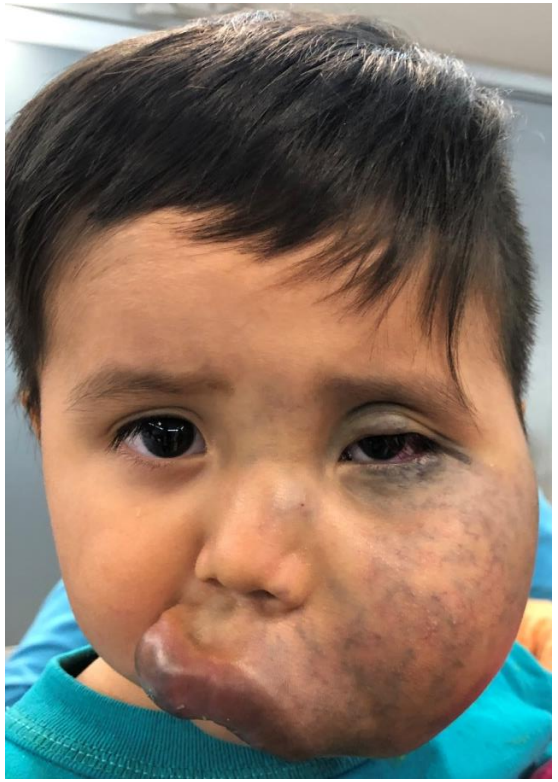
Rebastinib in the management of difusse venous malformations

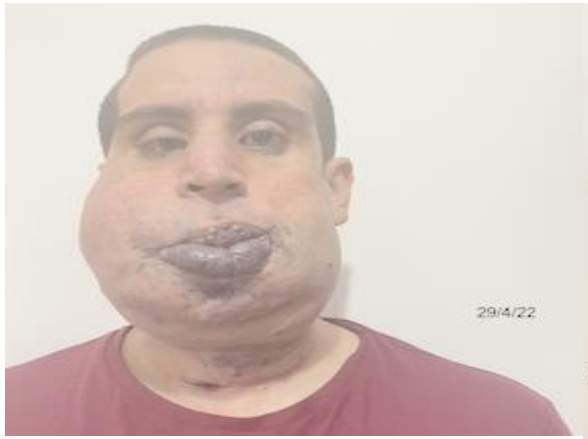
DECIPHERA PHARMACEUTICALS - LA PAZ CHILDREN´S HOSPITAL







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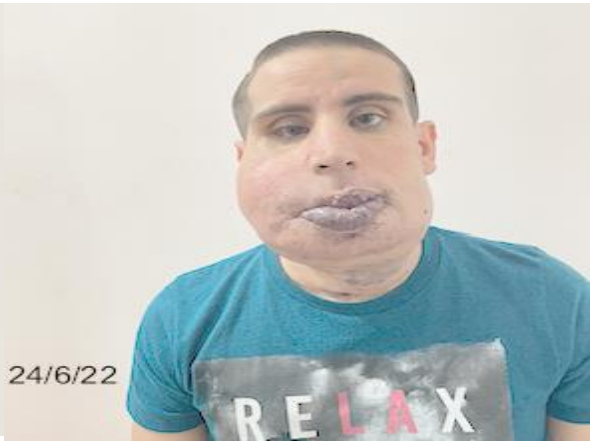
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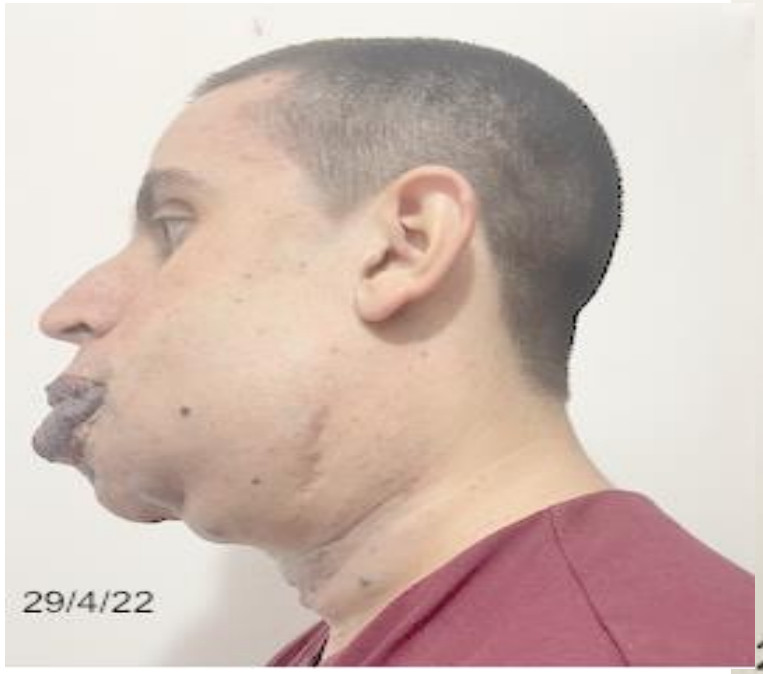
RELAX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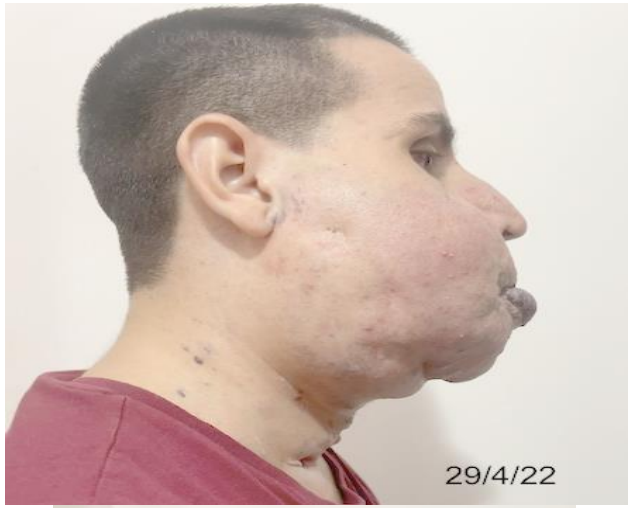
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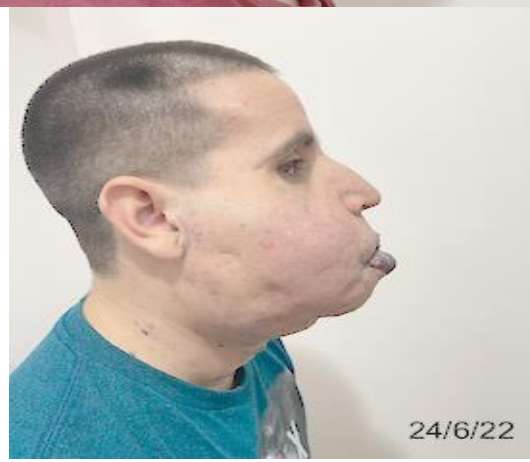
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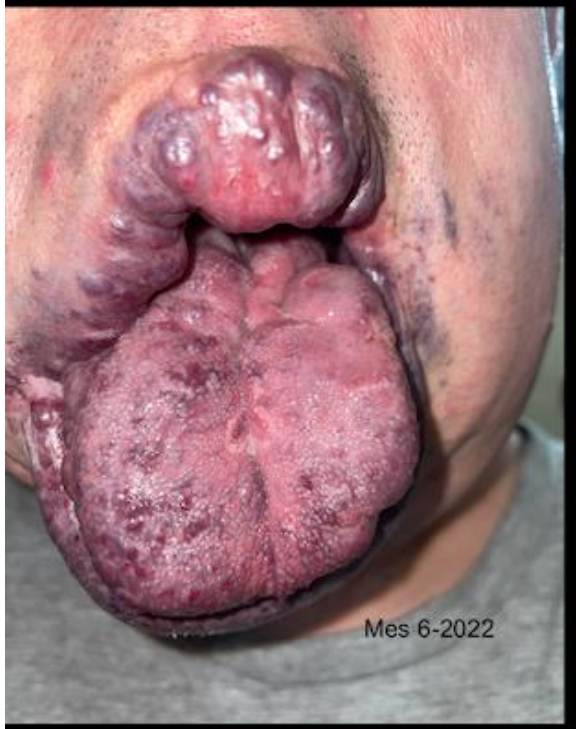
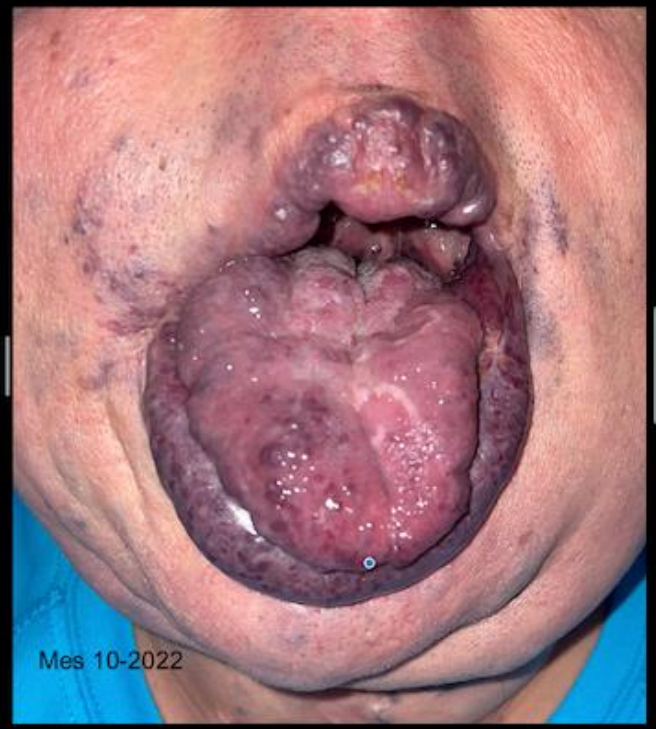

Mes 6-2022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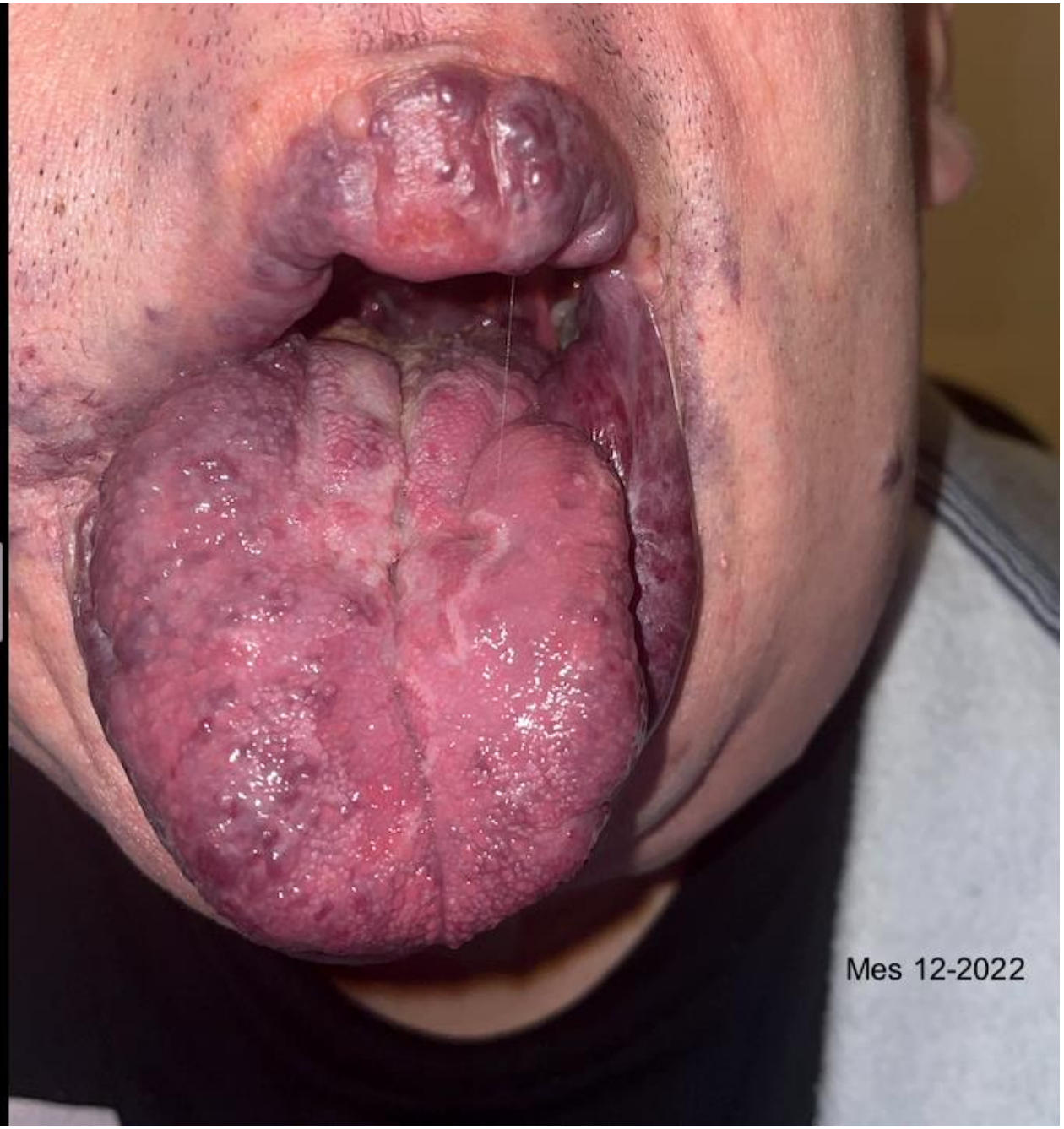
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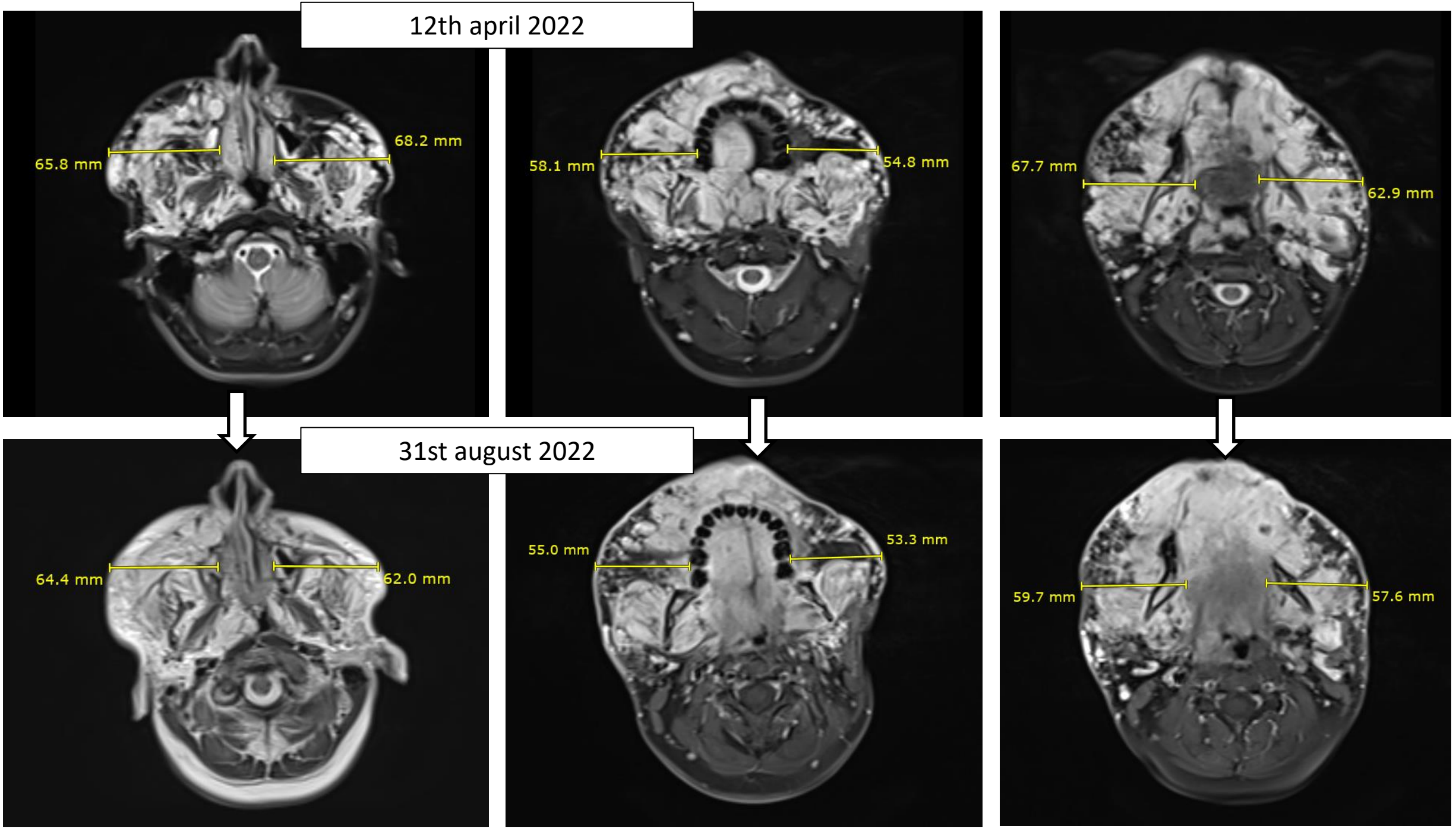

12th april 2022
65.8 mm
68.2 mm
58.1 mm
54.8 mm
67.7 mm
62.9 mm
31st august 2022
64.4 mm
62.0 mm
55.0 mm
53.3 mm
59.7 mm
57.6 mm

25th april 2022

COAGULACIÓN

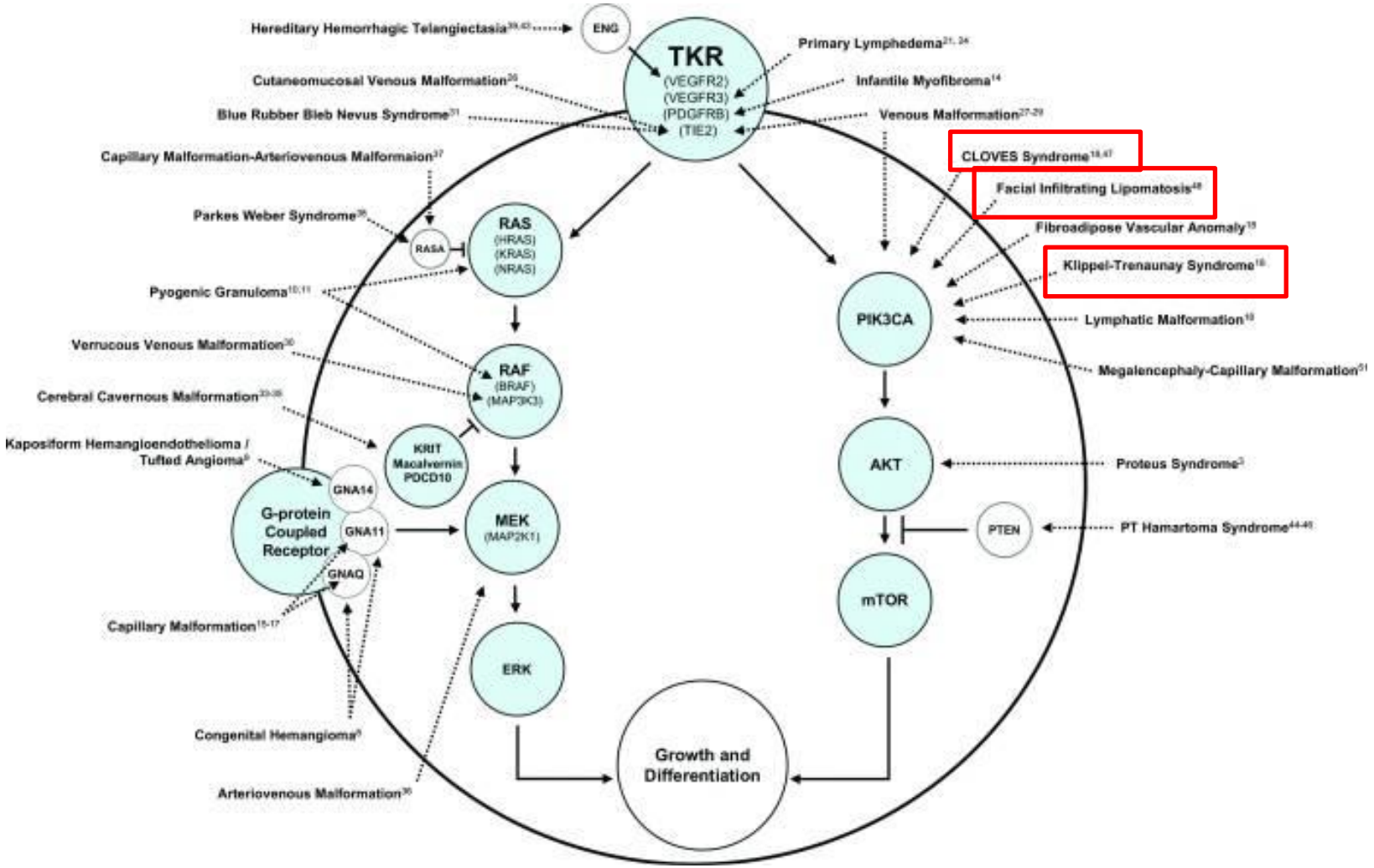
TIEMPO DE PROTROMBINA	10,7	seg	
ACTIVIDAD DE PROTROMBINA	105	%	(70-120)
INR	1,0		(0,8-1,2)
FIBRINOGENO DERIVADO	485 *	mg/dL	(150-450)
TIEMPO DE CEFALINA	26,4	seg	
RATIO DEL TIEMPO DE CEFALINA	0,98		(0,80-1,20)
D DÍMERO	4760 *	ng/mL	(0-500)

5th october 2022

COAGULACIÓN

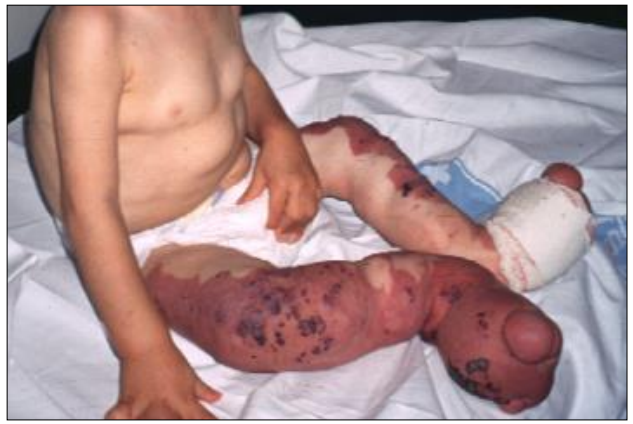
TIEMPO DE PROTROMBINA	10,5	seg	
ACTIVIDAD DE PROTROMBINA	109	%	(70-120)
INR	1,0		(0,8-1,2)
FIBRINOGENO DERIVADO	545 *	mg/dL	(150-450)
TIEMPO DE CEFALINA	25,9	seg	
RATIO DEL TIEMPO DE CEFALINA	0,96		(0,80-1,20)
D DÍMERO	2630 *	ng/mL	(0-500)

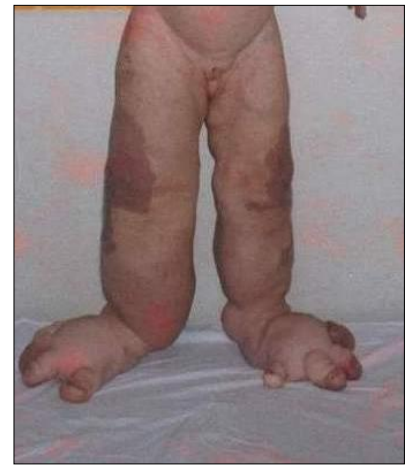
Descenso de dímero-D

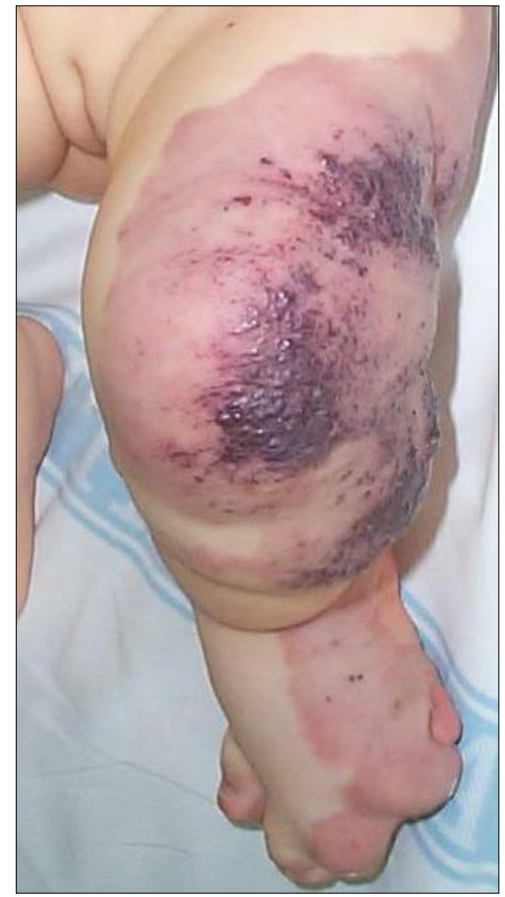


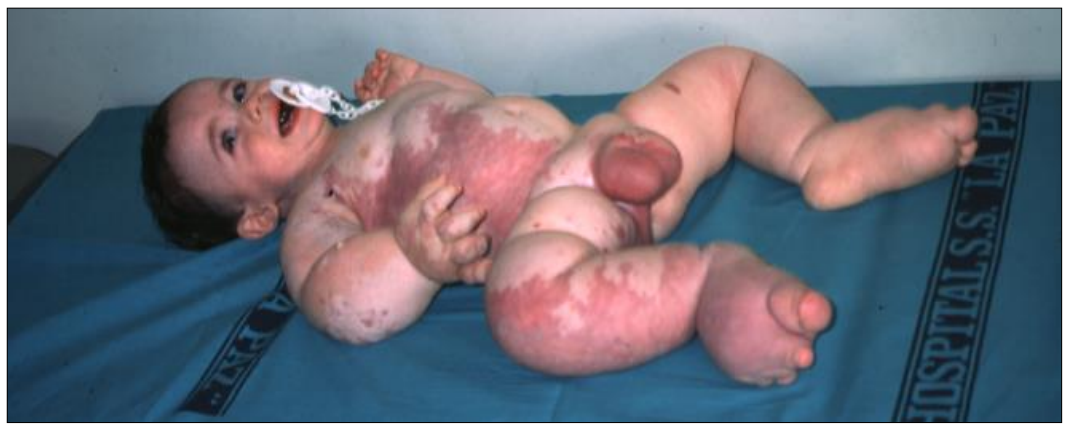
Greene A.K. Goss J.A. Vascular anomalies: From a clinicohistologic to a genetic framework. *Plast ReconstrSurg.* 2018; 141: 709e

POOR RESPONSE TO SIROLIMUS









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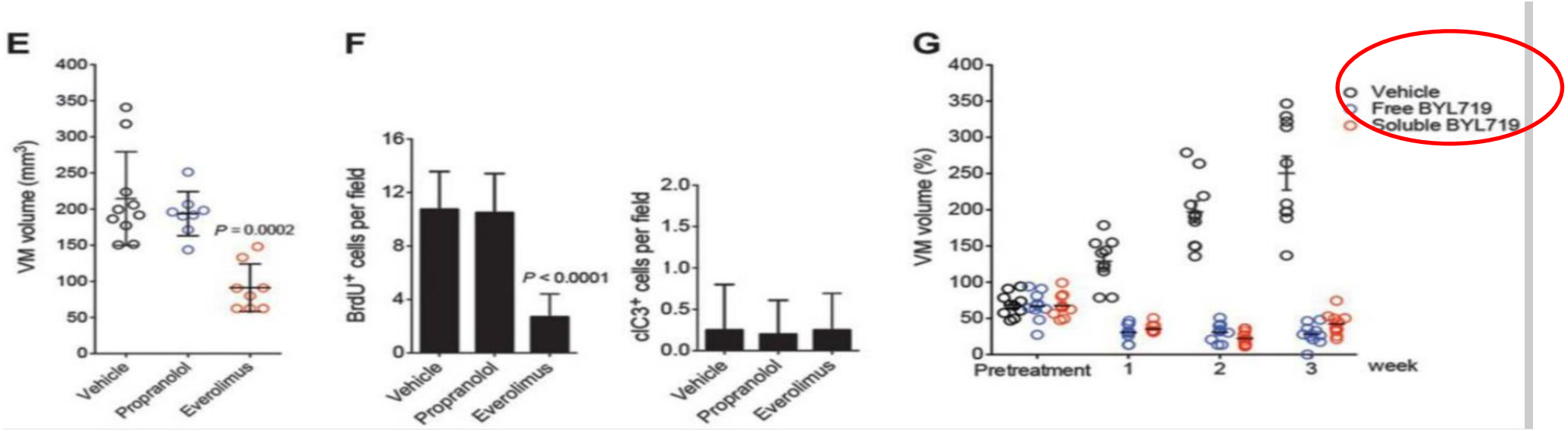
NIHMSID: NIHMS802641
PMID: 27030594

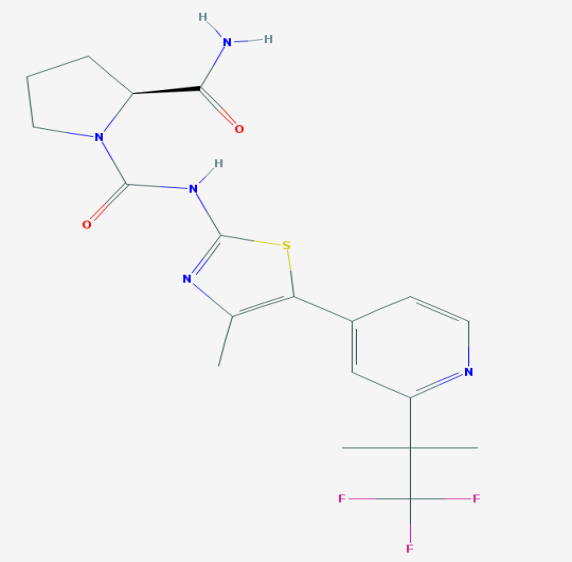
Somatic *PIK3CA* mutations as a driver of sporadic venous malformations

Pau Castel,[1] F. Javier Carmona,[1] Joaquim Grego-Bessa,[2] Michael F. Berger,[1,3] Agnès Viale,[4] Kathryn V. Anderson,[2] Silvia Bague,[5] Maurizio Scaltriti,[1,3] Cristina R. Antonescu,[3] Eulàlia Baselga,[6] and José Baselga[1,7,*]



▼Este medicamento está sujeto a seguimiento adicional, es prioritaria la notificación de sospechas de reacciones adversas asociadas a este medicamento.

Nature (2018)



ALPELISIB

2018

Targeted therapy in patients with PIK3CA–related overgrowth syndrome

Quitterie Venot[1], Thomas Blanc[1,2,3,21], Smail Hadj Rabia[2,4,5,21], Laureline Berteloot[5,6], Sophia Ladraa[1], Jean-Paul Duong[2,7], Estelle Blanc[8], Simon C. Johnson[9], Clément Hoguin[1], Olivia Boccara[4], Sabine Sarnacki[2,3], Nathalie Boddaert[2,5,6], Stephanie Pannier[2,10], Frank Martinez[11], Sato Magassa[1], Junna Yamaguchi[1], Bertrand Knebelmann[1,2,11], Pierre Merville[12,13], Nicolas Grenier[14], Dominique Joly[1,2,11], Valérie Cormier-Daire[2,5,15], Caroline Michot[2,5,15], Christine Bole-Feysot[5], Arnaud Picard[2,16], Véronique Soupre[16], Stanislas Lyonnet[2,5,15], Jeremy Sadoine[17], Lotfi Slimani[17], Catherine Chaussain[2,17], Cécile Laroche-Raynaud[18], Laurent Guibaud[19], Christine Broissand[20], Jeanne Amiel[2,5,15], Christophe Legendre[1,2,11], Fabiola Terzi[1,2] & Guillaume Canaud[1,2,11]*

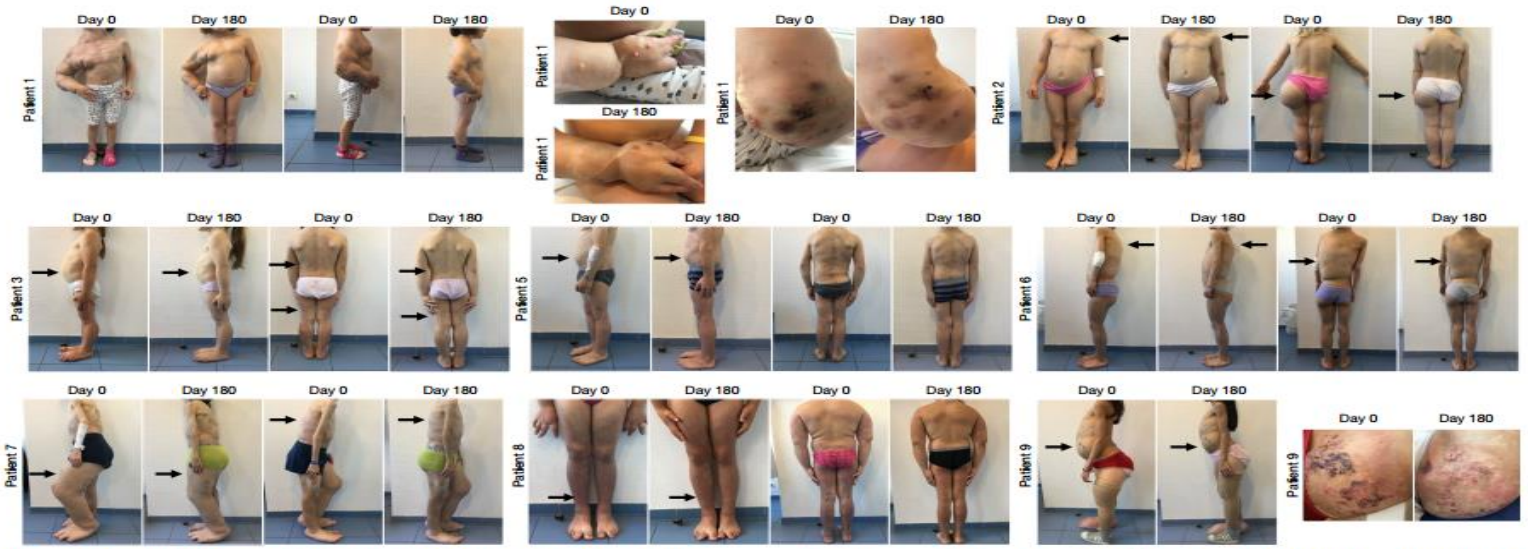
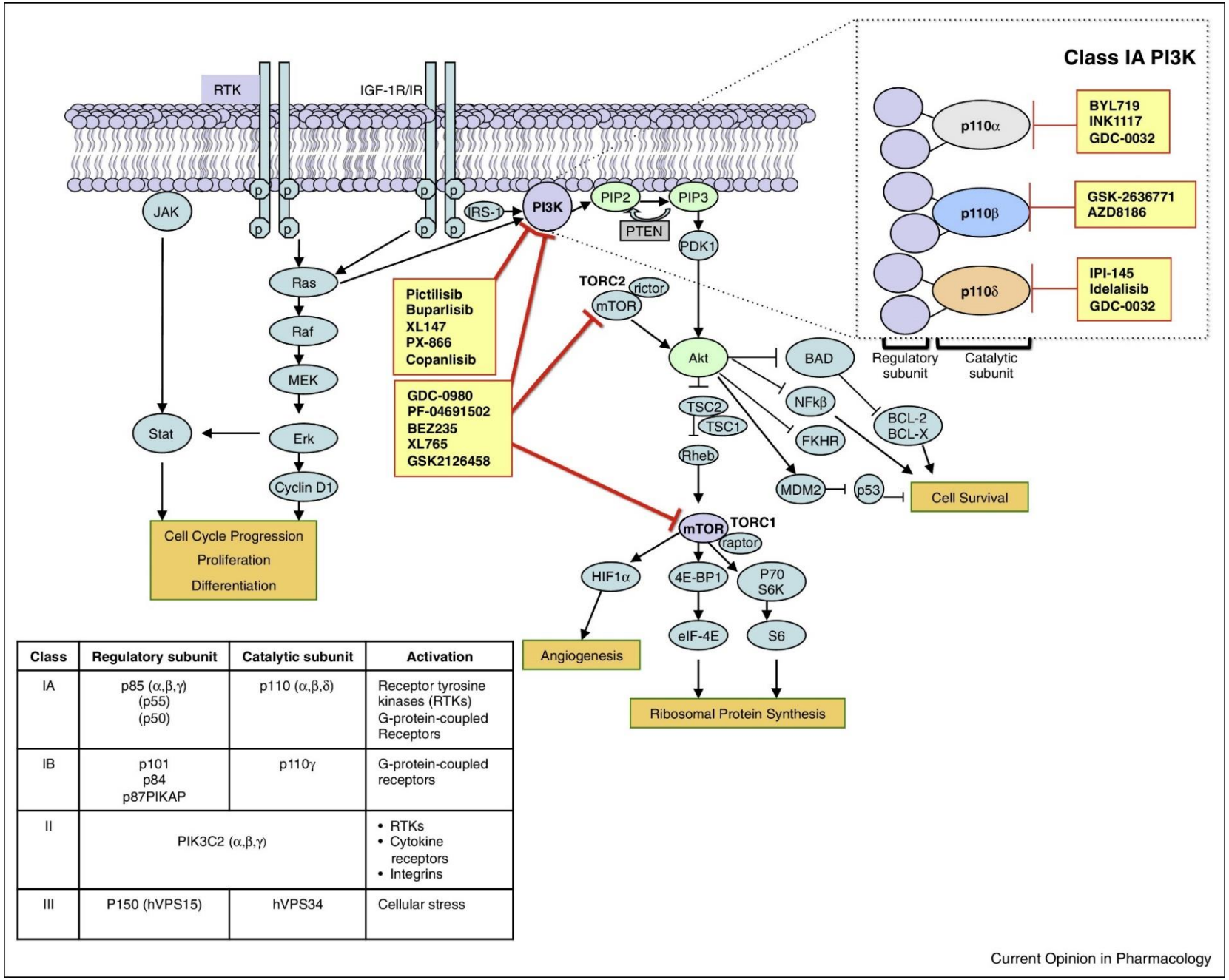


Fig. 5 | Efficacy of BYL719 treatment in patients with PROS. Images of patients 1–9 before and after six months of BYL719 treatment. Patient 1 is a four-year-old girl suffering from severe vascular malformations involving the right arm and chest with permanent pain. After six months of treatment we saw a marked improvement in all vascular malformations as well as the scoliosis. Patient 2 is a 4-year-old girl with scoliosis and hypertrophic left buttock who had already undergone left foot partial amputation. After six months of treatment we saw an improvement in the scoliosis and reduction of the hypertrophic lesion. Patient 3 is a 5-year-old girl with CLOVES syndrome and chronic gastrointestinal bleeding. After six months of treatment, chronic bleeding stopped. Patient 4 is a 5-year-old girl with left hemifacial hyperplasia that was progressing despite multiple surgeries. After six months of treatment we saw for the first time an improvement in the hypertrophy (not shown for reasons of confidentiality). Patient 5 is a 6-year-old boy with CLOVES syndrome. The treatment led to a reduction in lipomatous tumours and scoliosis. Patient 6 is a 10-year-old girl with CLOVES syndrome and a severe lipomatous tumour on her back. BYL719 led to a marked improvement in the scoliosis and shrinkage of the tumour. Patient 7 is an 11-year-old boy with CLOVES syndrome, chronic gastrointestinal bleeding and severe dyspnea. Treatment improved all symptoms and the bleeding stopped. Patient 8 is an 11-year-old girl with CLOVES syndrome and severe dyspnea. Treatment improved the subcutaneous lipoma as well as dyspnea. Patient 9 is a 13-year-old girl with CLOVES syndrome, splenomegaly and severe vascular malformations involving the left kidney and limbs. Vascular malformations were markedly improved and the size of the spleen reduced after treatment.



Class	Regulatory subunit	Catalytic subunit	Activation
IA	p85 (α,β,γ) (p55) (p50)	p110 (α,β,δ)	Receptor tyrosine kinases (RTKs) G-protein-coupled Receptors
IB	p101 p84 p87PIKAP	p110γ	G-protein-coupled receptors
II	PIK3C2 (α,β,γ)		• RTKs • Cytokine receptors • Integrins
III	P150 (hVPS15)	hVPS34	Cellular stress

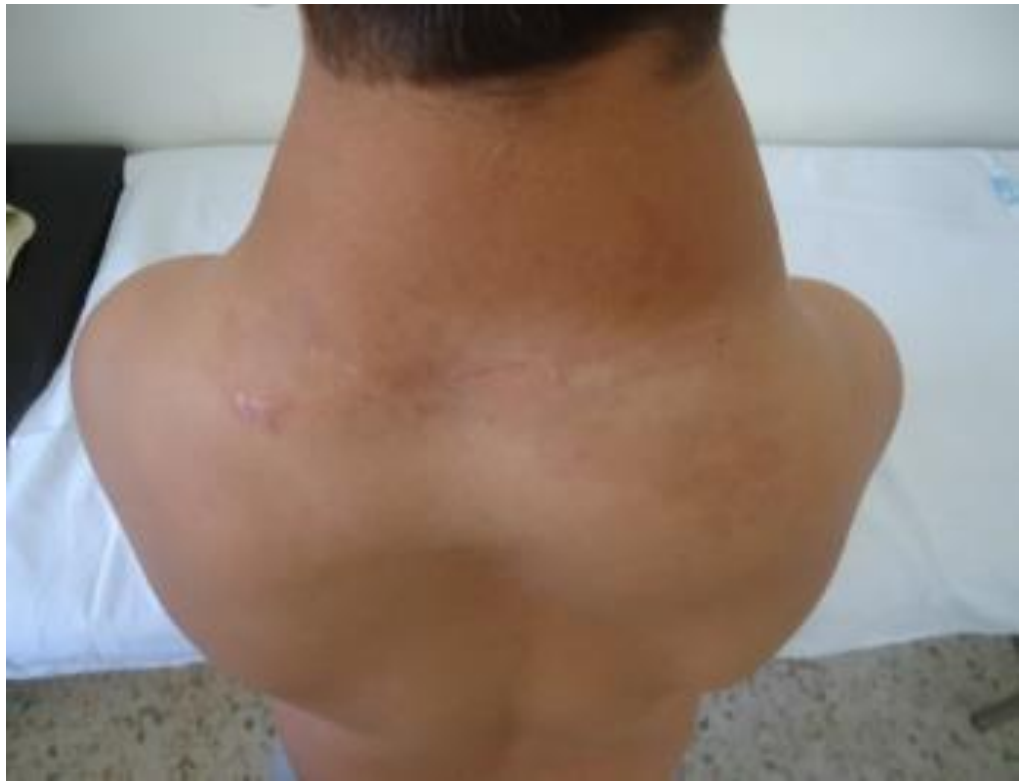
ALPELISIB

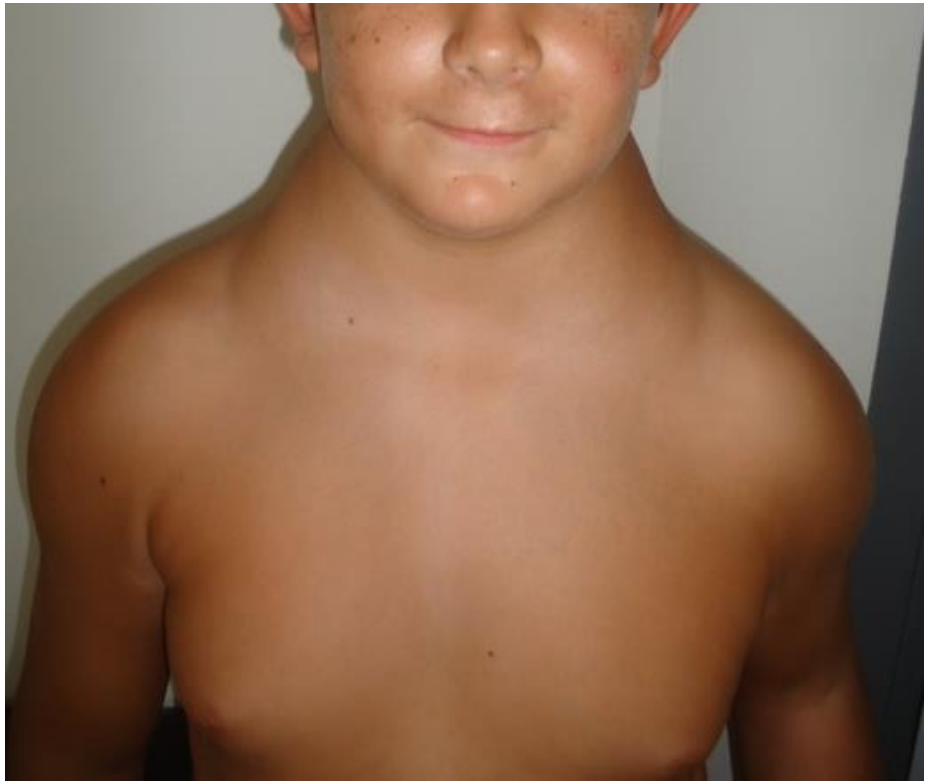
SERASELISIB

TASELISIB

Yap TA . Drugging PI3K in cancer:
refining targets and therapeutic strategies.
Current Opinion in Pharmacology, 2015 . Vol.8.(98-107)

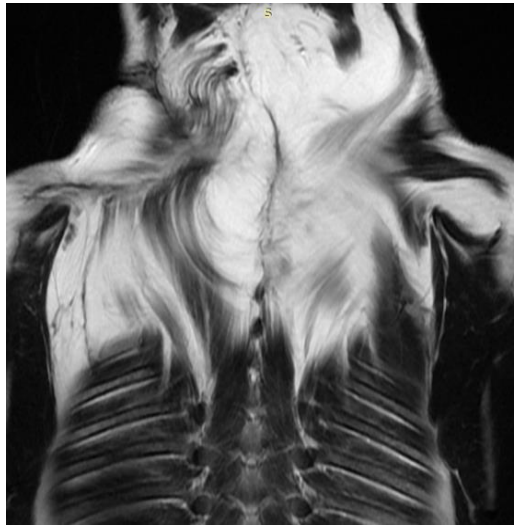
Seraselisib, taselisib, pictilisib, buparlisib, copanlisib no están comercializados en España.

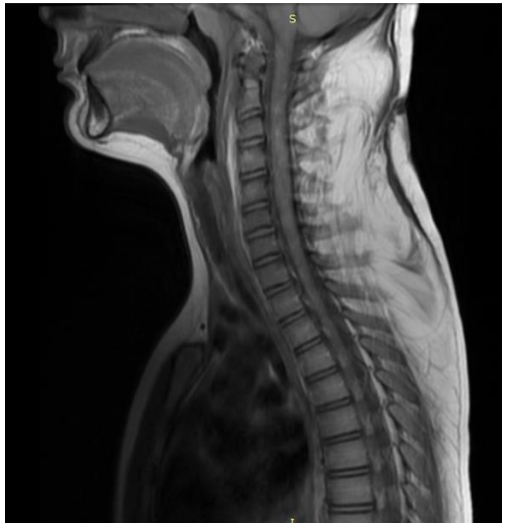




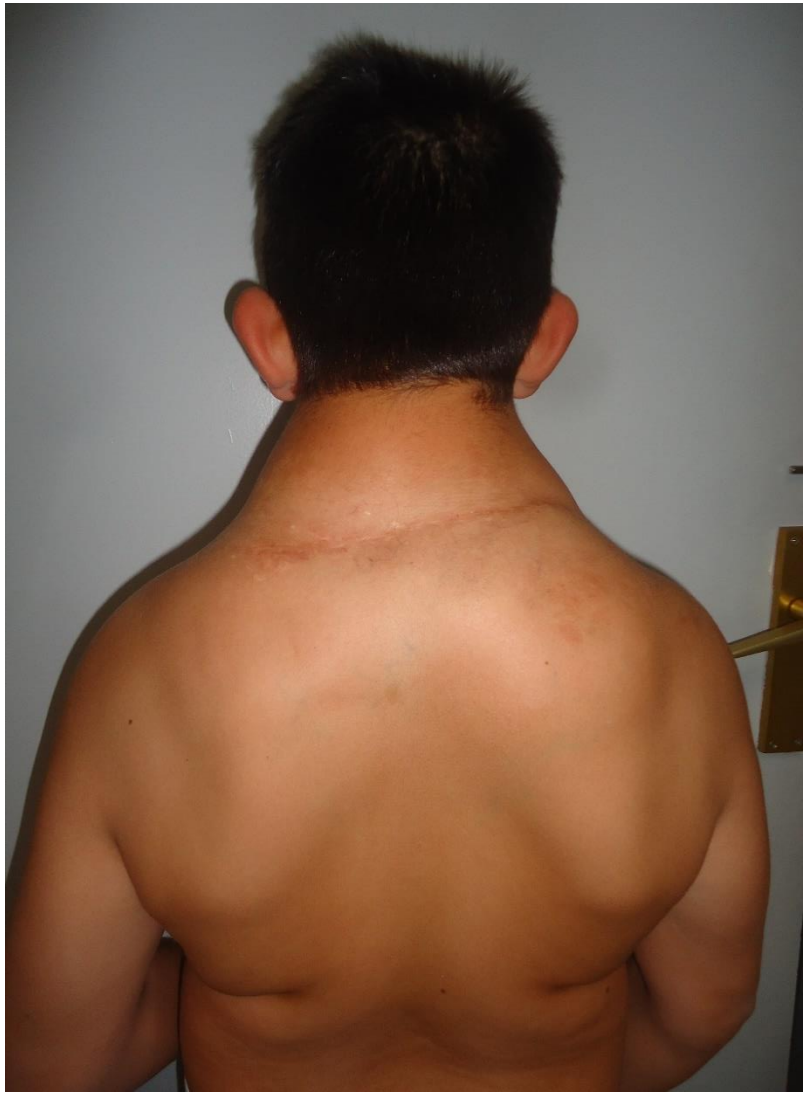
PIK3CA

c.3140A>G	p.His1047Arg

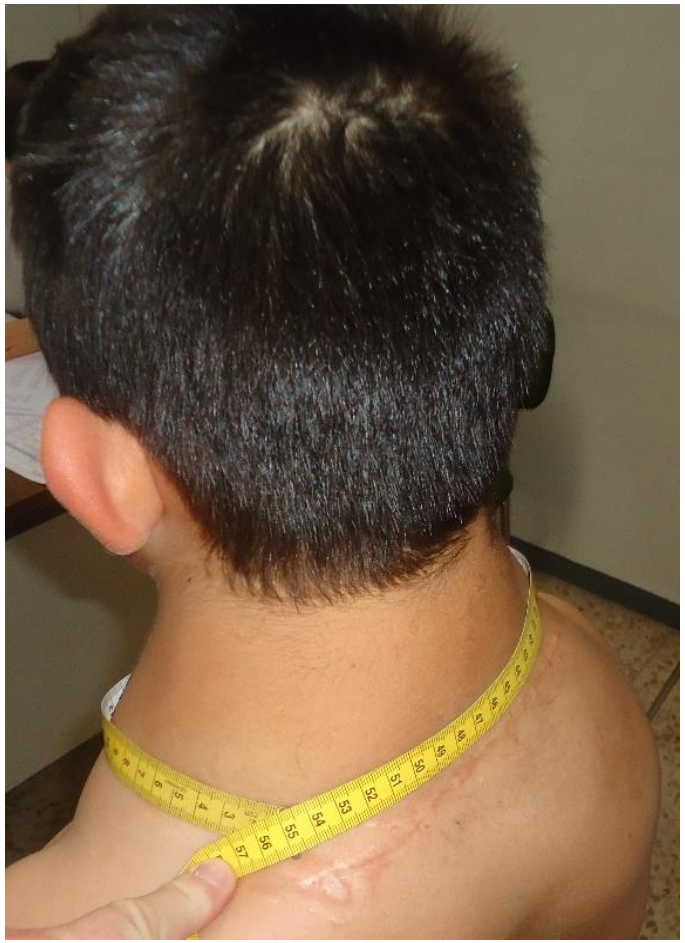


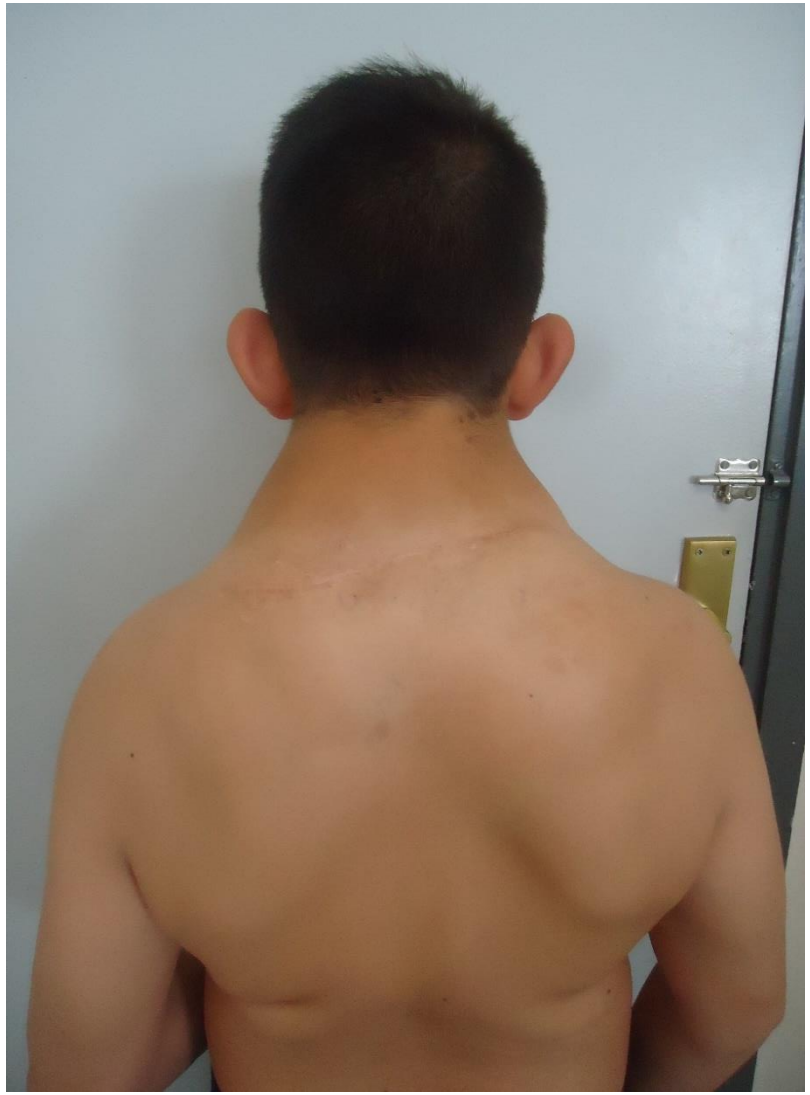


7 meses con ALPELISIB



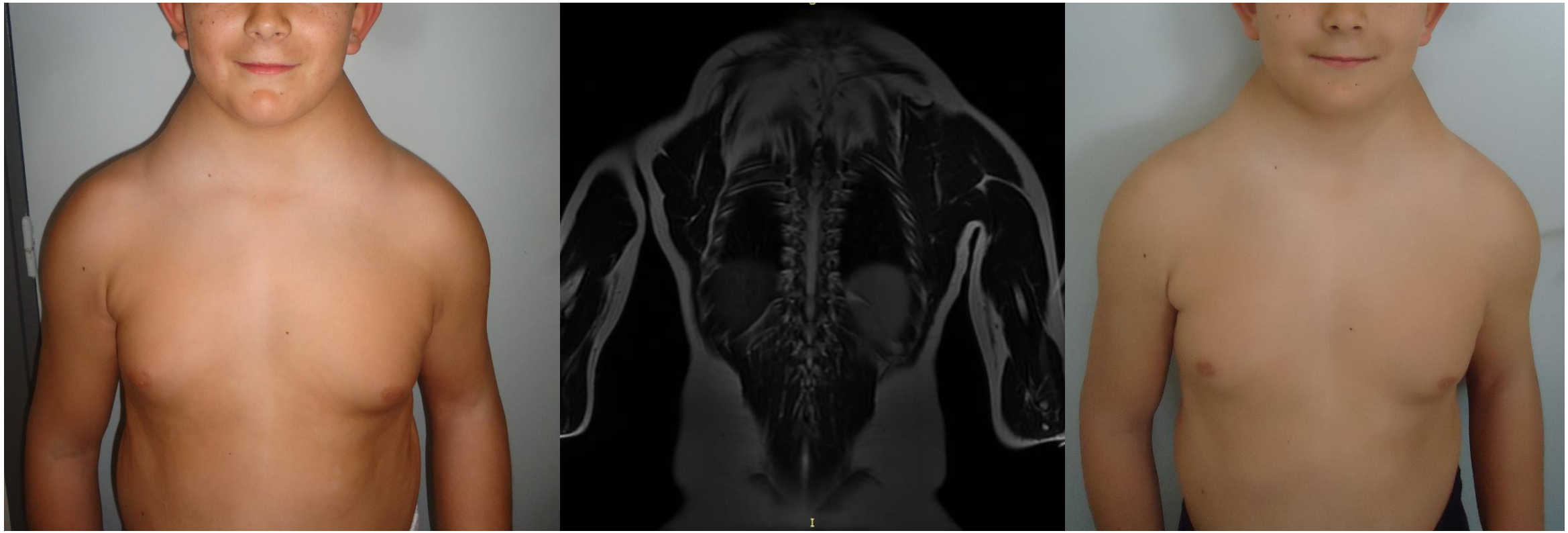
54 cms



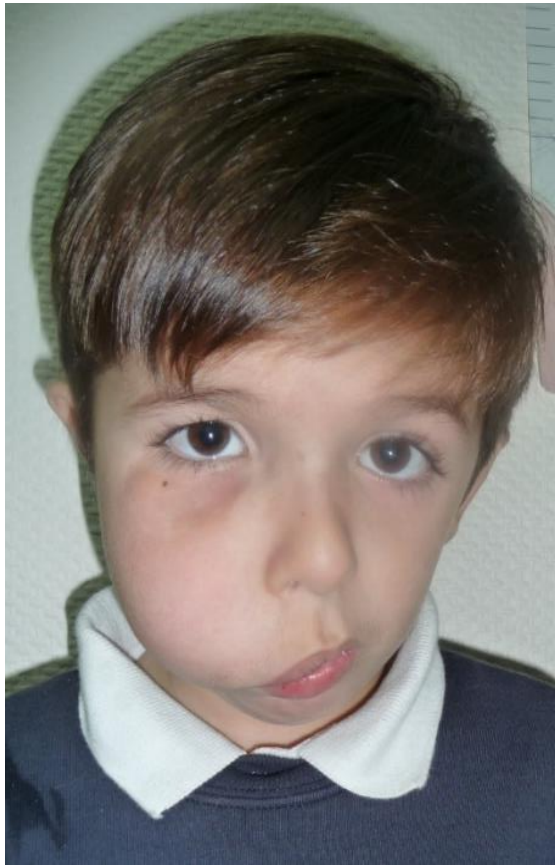
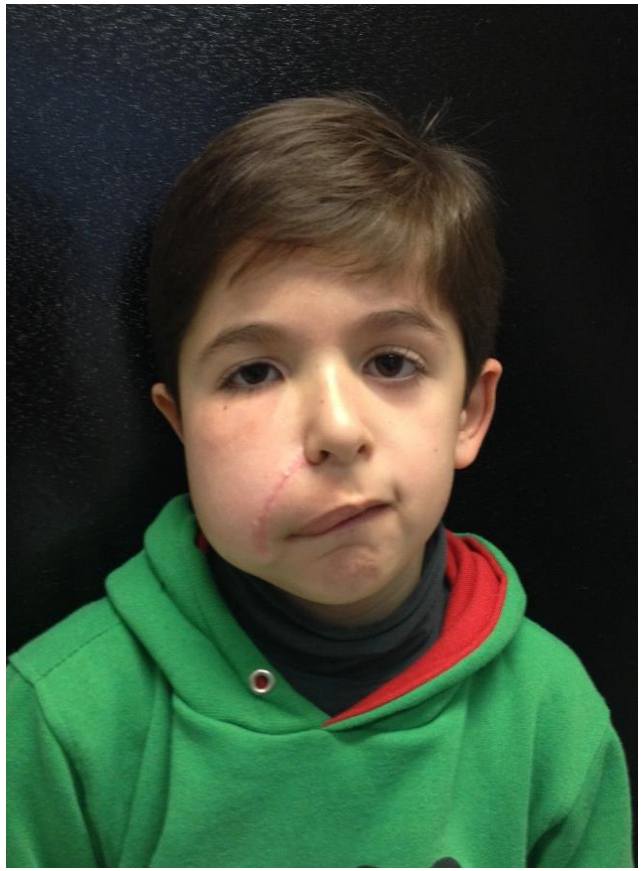
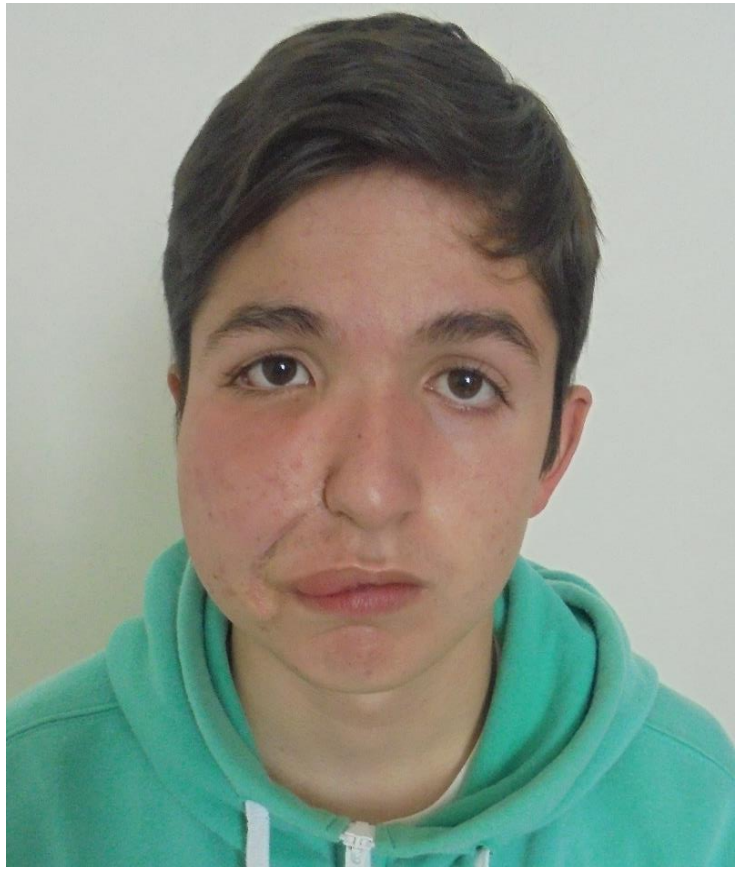
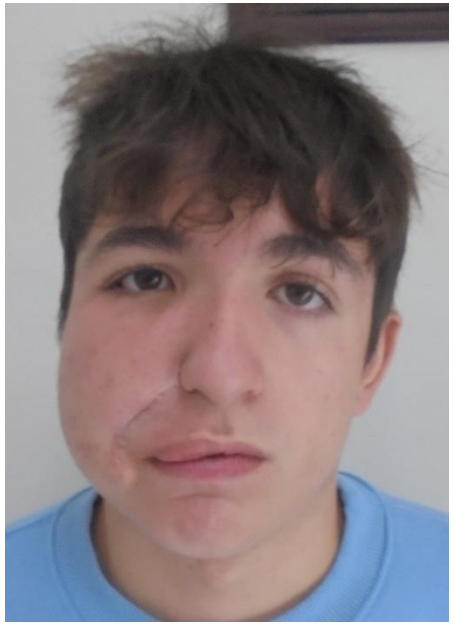


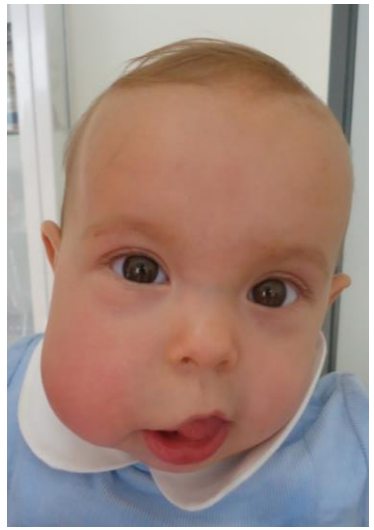
50 cms

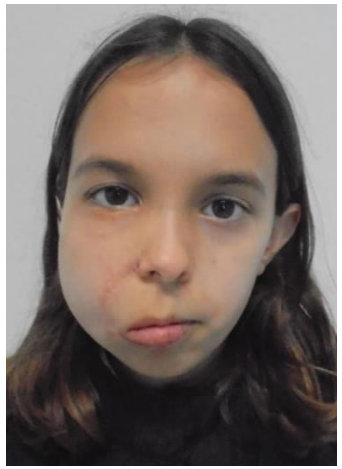
3 años después sigue habiendo respuesta

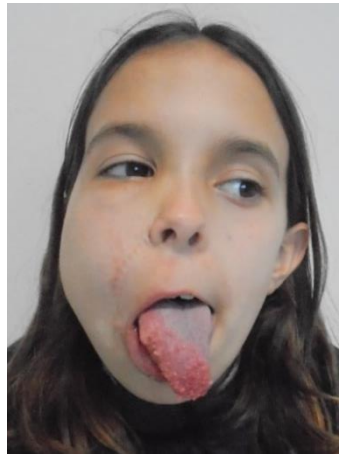


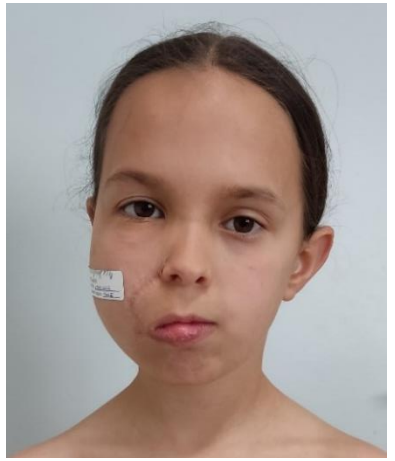
LIPOMATOSIS INFILTRATIVA FACIAL

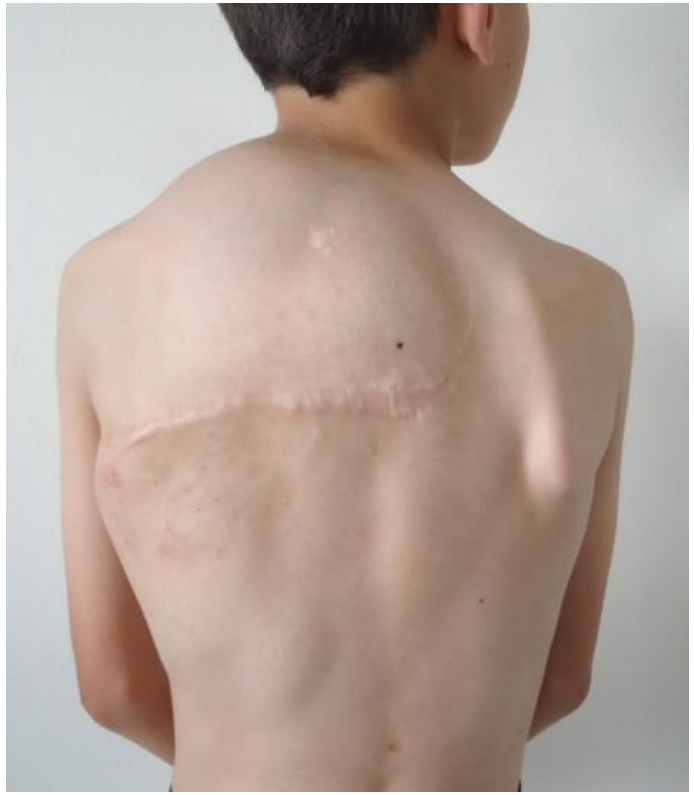





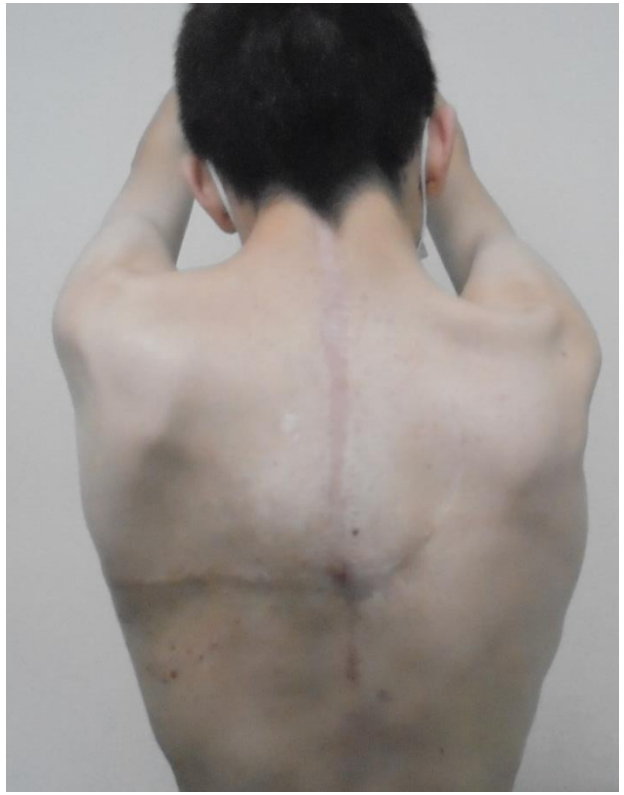


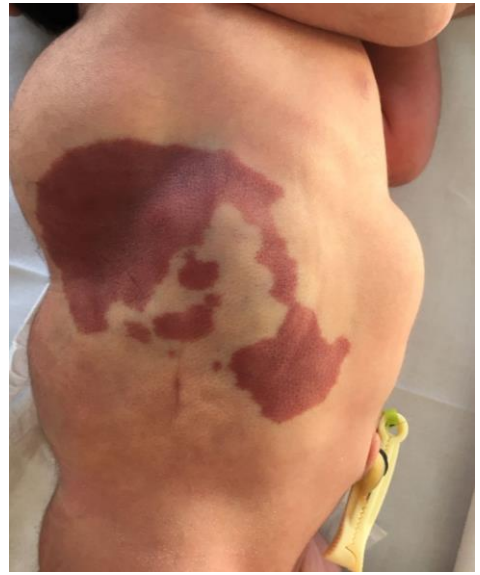


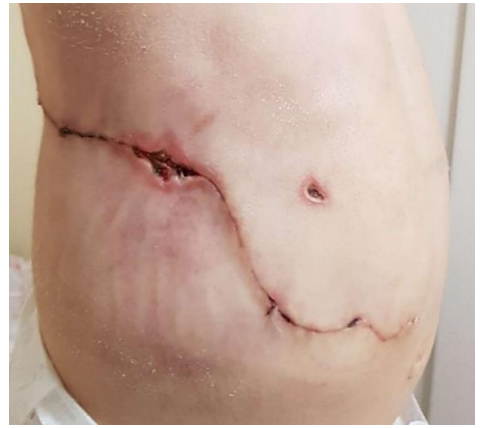


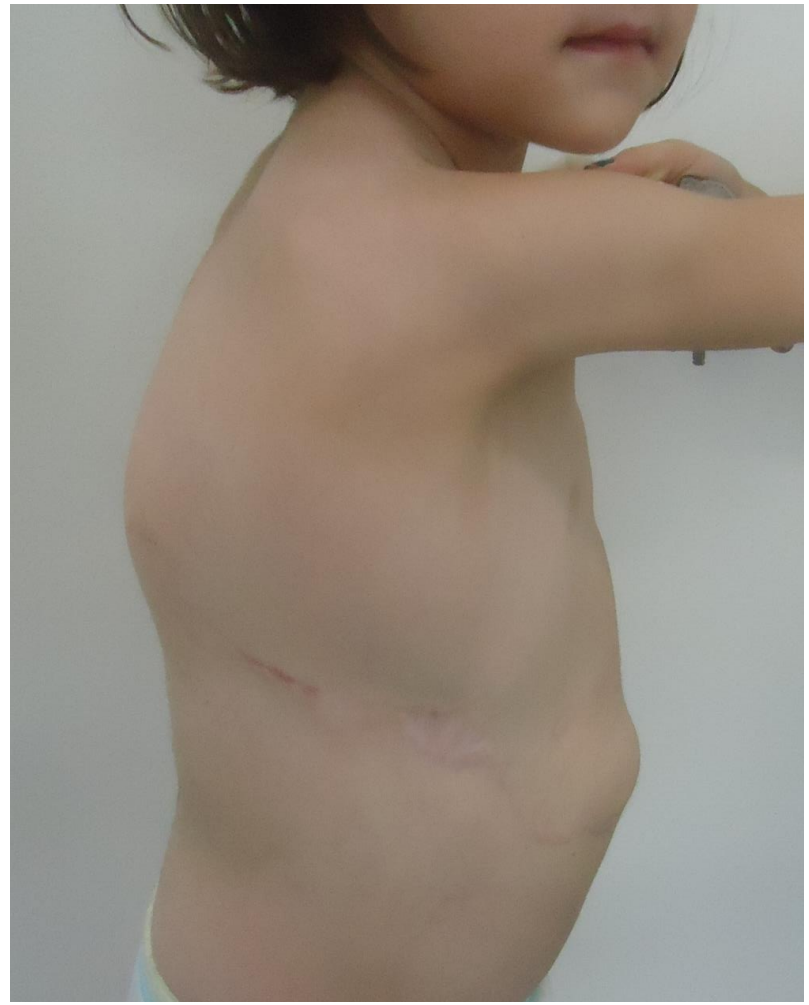


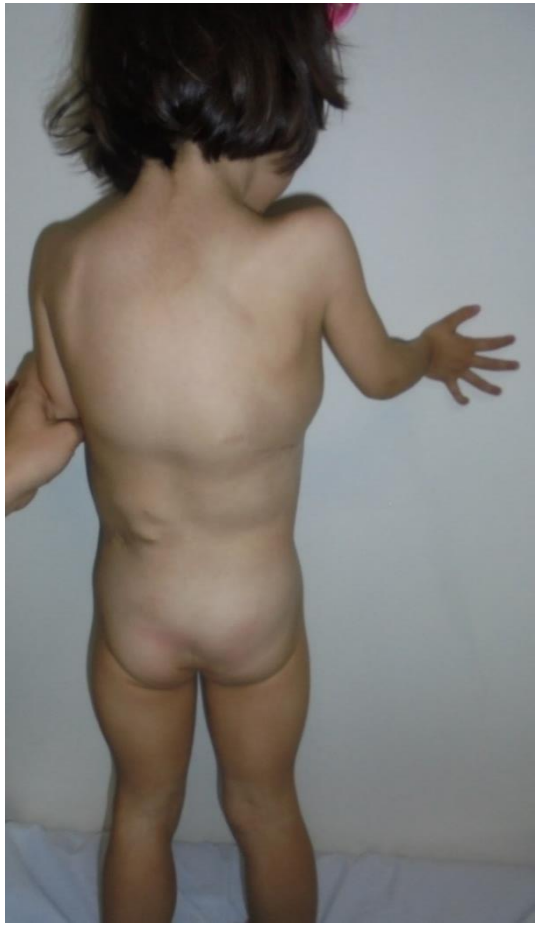


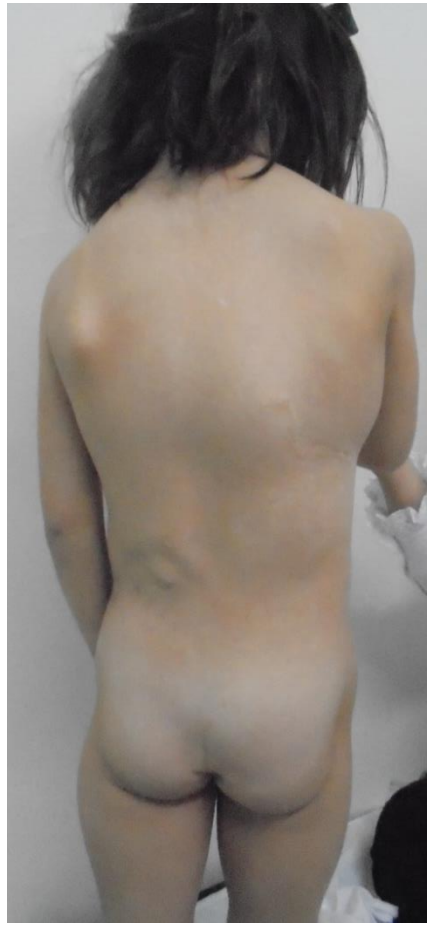






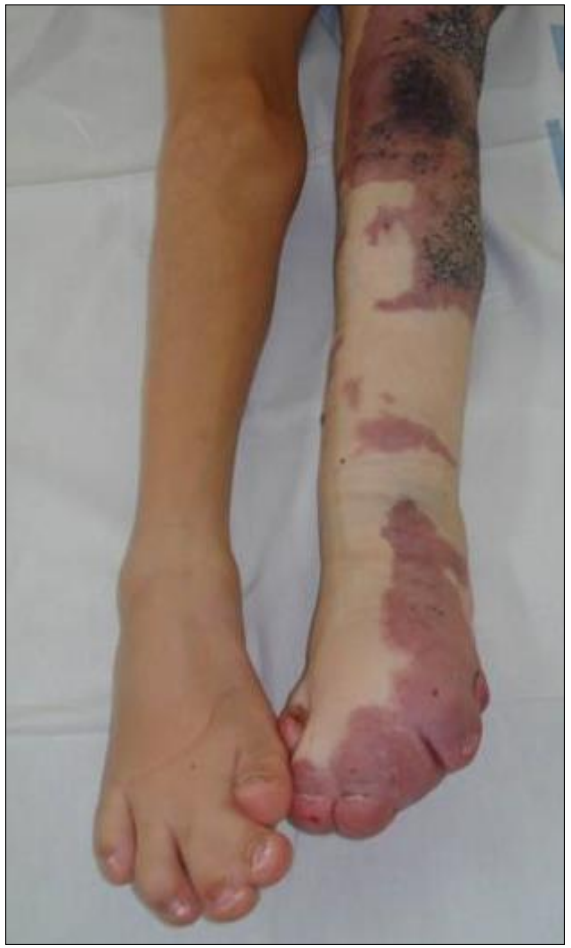


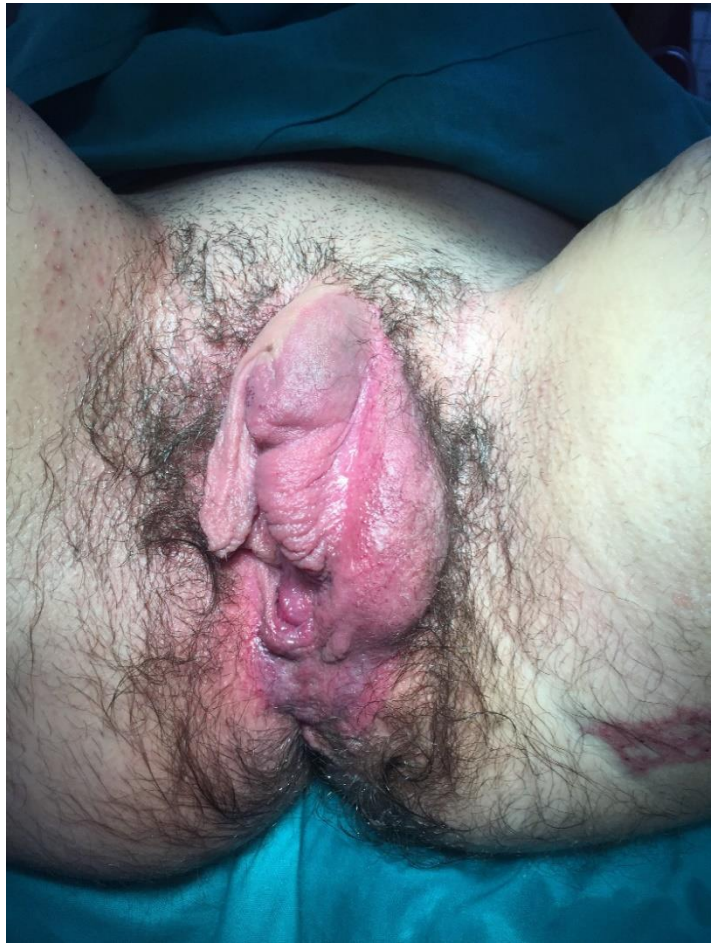


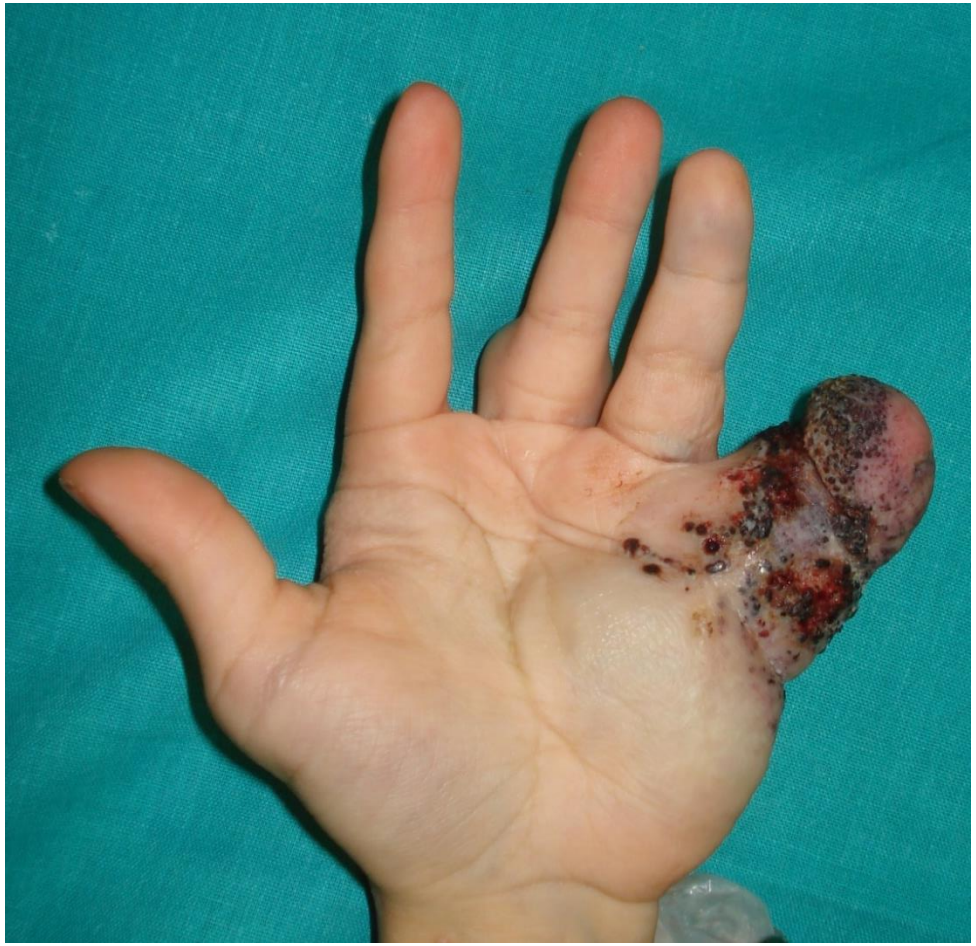


PIK3CA p.Glu542Lys

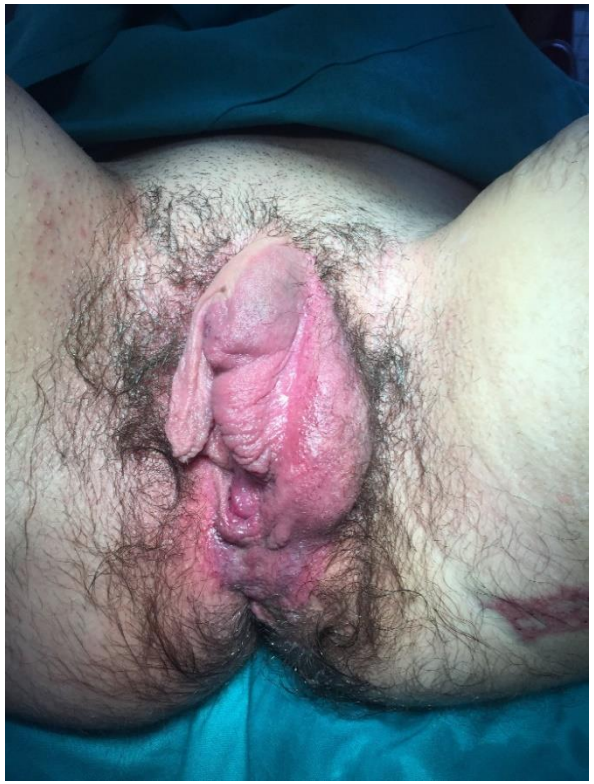
CLOVES SYNDROME

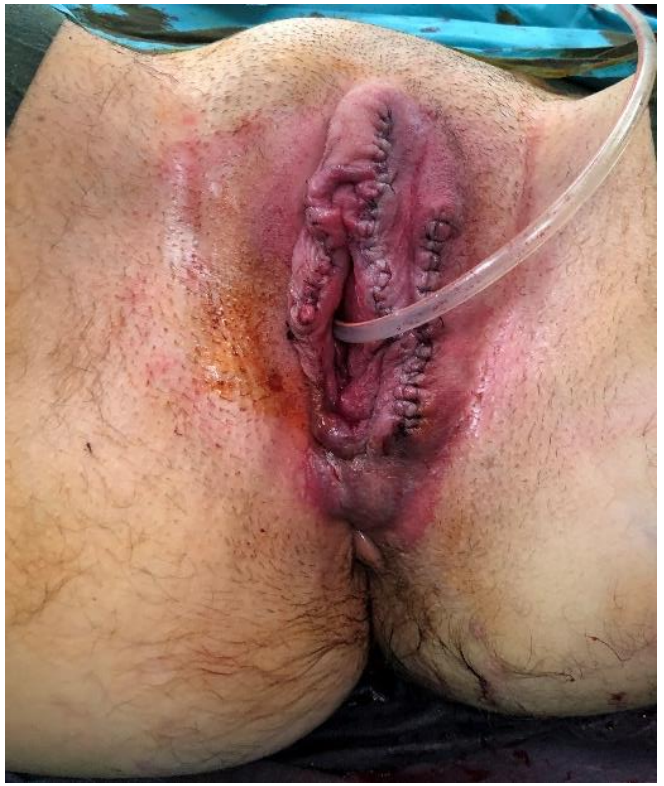






ALPELISIB 6 MESES





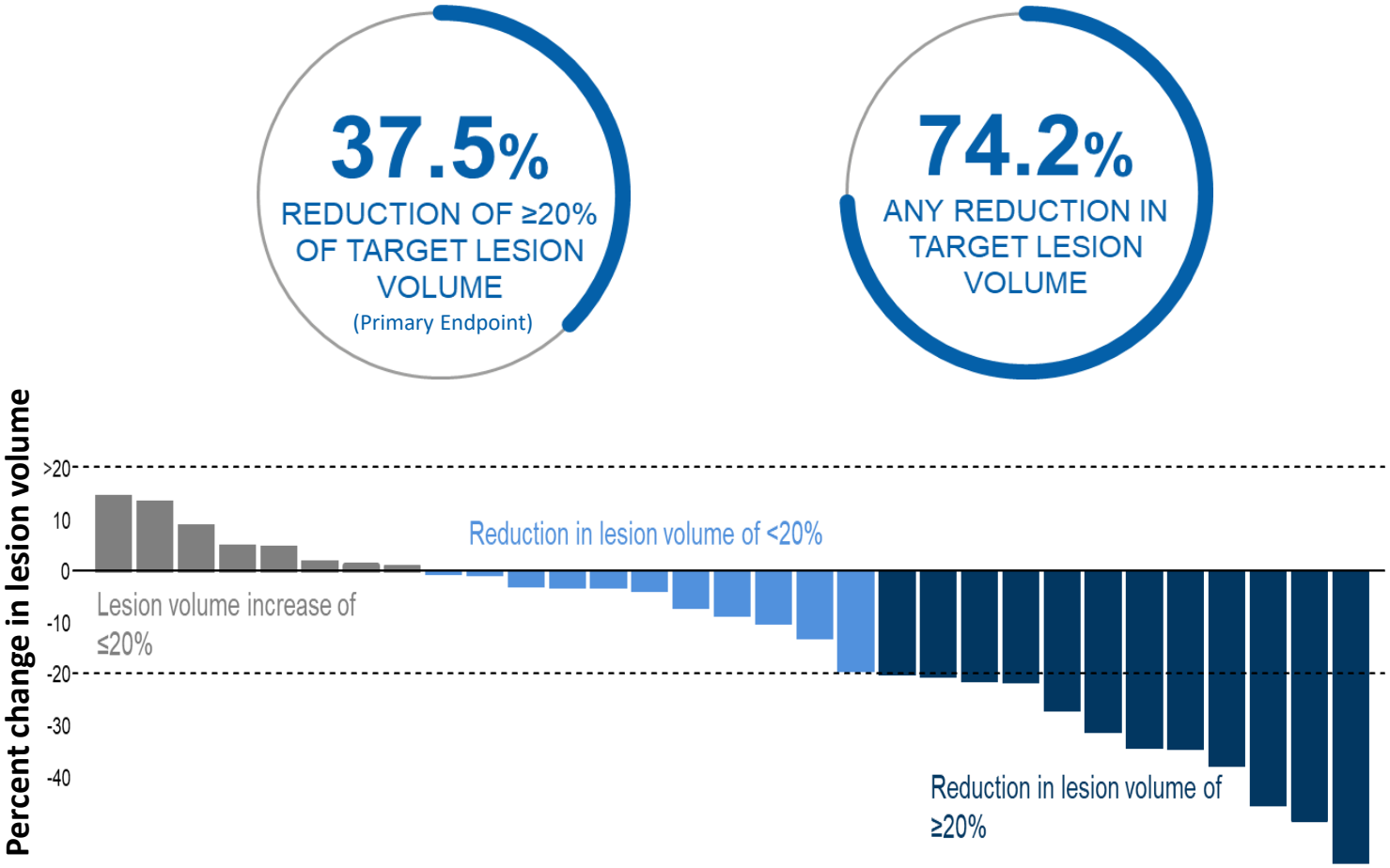
EPIK-P1: Retrospective Chart Review Study of Patients With *PIK3CA*-Related Overgrowth Spectrum (PROS) Who Received Alpelisib

Guillaume Canaud,[1] Juan Carlos López Gutiérrez,[2] Alan Irvine,[3] Nii Ankrah,[4] Athanasia Papadimitriou,[5] Antonia Ridolfi,[6] Denise M. Adams[7]

[1]Hôpital Necker, Université de Paris; [2]La Paz Children's Hospital; [3]Trinity College Dublin; [4]Novartis Pharmaceuticals Corporation; [5]Novartis AG Switzerland; [6]Novartis Pharma SAS;

[7]Children's Hospital of Philadelphia

EPIK-P1: Efficacy of Alpelisib at Week 24



- 37.5% (12/32; 95% CI, 21.1% - 56.3%) of the patients with complete cases responded (ie, ≥20% reduction in target lesion[s] volume as determined by ICRR)
- 74.2% (23/31) patients with imaging at index and week 24, experienced reduction in sum of target lesion volume
  - The mean ± SD reduction was 13.7±18.9%
- No patient experienced disease progression or death during the study period

CI, confidence interval; ICRR, Independent Central Radiological Review(er); SD, standard deviation.

EPIK-P1: Adverse Event Rate by Preferred Term in Full Study Population

- Pediatric patients received a median (range) dose of 50.0 mg (50.0-250.0) per day
- Adult patients received a median (range) dose of 250.0 mg (101.9-250.0) per day
- The most common AEs of any grade were diarrhoea (n=9, 15.8%), hyperglycaemia (n=7, 12.3%), and aphthous ulcers (n=6, 10.5%)
- The most common treatment-related AEs were hyperglycemia (7/57, 12.3%), aphthous ulcer (6/57, 10.5%), and stomatitis (3/57, 5.3%)
- The most common grade 3/4 AE was cellulitis (n=2, 3.5%); one adult case was considered treatment-related
- No AE lead to treatment discontinuation or death
- Overall, pediatric patients experienced lower rates of treatment-related AEs

Category[a]	Pediatric patients (<18 years) n=39	Adult patients (≥18 years) n=18	All patients N=57
Overall AEs, n (%)	31 (79.5)	16 (88.9)	**47 (82.5)**
Treatment-related	9 (23.1)	13 (72.2)	**22 (38.6)**
Serious AEs, n (%)	10 (25.6)	11 (61.1)	**21 (36.8)**
Treatment-related	0	3 (16.7)	**3 (5.3)**
AEs leading to dose reduction, n (%)	0	3 (16.7)	**3 (5.3)**
Treatment-related	0	1 (5.6)	**1 (1.8)**
AEs leading to dose interruption or adjustment, n (%)	2 (5.1)	5 (27.8)	**7 (12.3)**
Treatment-related	1 (2.6)	3 (16.7)	**4 (7.0)**
AEs leading to discontinuation, n (%)	0	0	**0**
Treatment-related	0	0	**0**

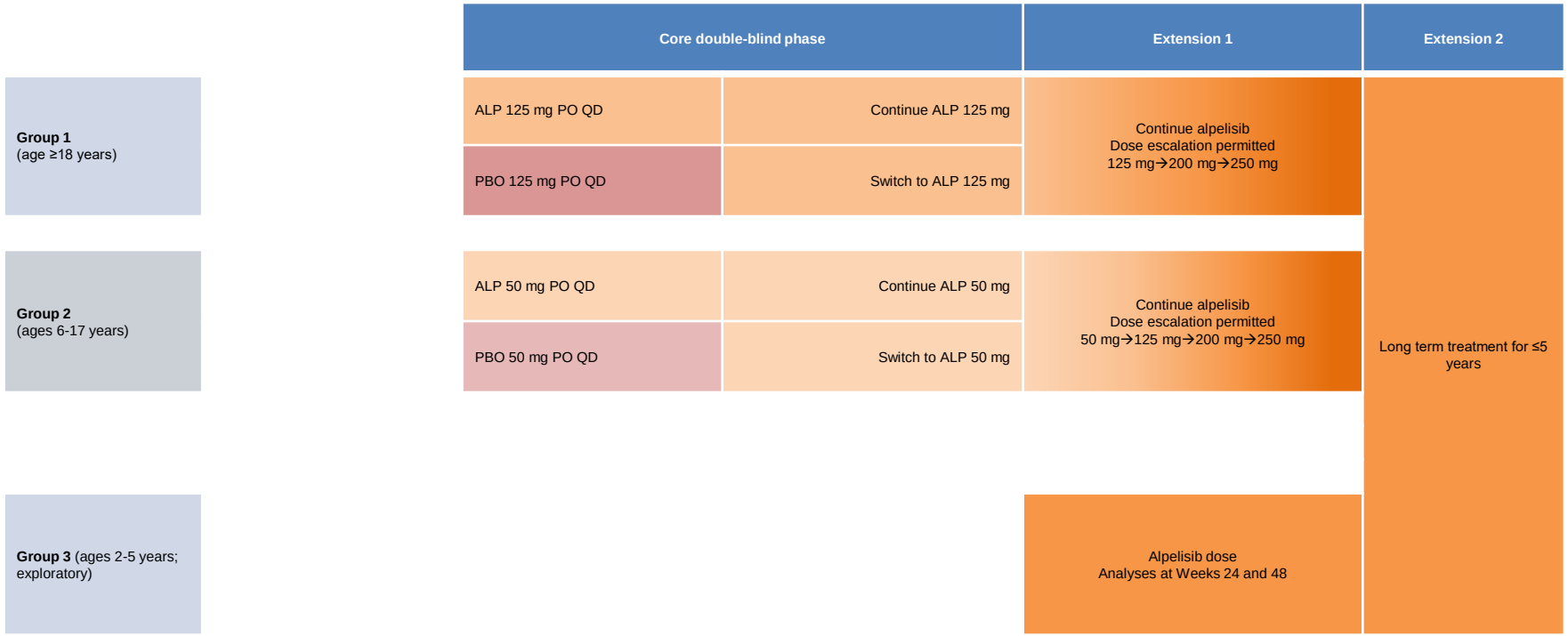
[a]Adverse events (AEs) of all grades; coded by preferred term (MedDRA version 24.0) and graded according to CTCAE (version 4.03).

AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; MedDRA, Medical Dictionary for Regulatory Activities.

EPIK P2

A Prospective Phase 2, Double-Blind, Randomized, Placebo-Controlled Study of **Alpelisib** in Pediatric and Adult Patients With *PIK3CA*-Related Overgrowth Spectrum (PROS)

150 patients



Study Assessing Long-term Safety and Efficacy of Alpelisib in Patients with *PIK3CA*-related Overgrowth Spectrum who Previously Participated in EPIK-P1 (EPIK-P3)

NCT04980833

EPIK-P3: A phase II study to evaluate the long-term safety and efficacy of Alpelisib in patients with *PIK3CA*-Related Overgrowth Spectrum (PROS) who previously participated in study CBYL719F12002 (EPIK-P1)

Key Inclusion Criteria:

- Males and females aged ≥2 years who previously participated in EPIK-P1 study and were treated with ≥1 dose of alpelisib after EPIK-P1 study data cut-off date of 09-Mar-2020
- Retrospective period: No patient with permanent discontinuation of Alpelisib on or prior to the cut-off date
- Prospective period: No patient with treatment discontinuation (after cut-off date) due to adverse events (AEs)
- Patients with no known impairment of GI function or uncontrolled diabetes mellitus (Type I or II) at time of informed consent

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	50 participants
Allocation:	N/A
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase II Study to Evaluate the Long-term Safety and Efficacy of Alpelisib in Patients With PIK3CA-Related Overgrowth Spectrum (PROS) Who Previously Participated in Study CBYL719F12002 (EPIK-P1)
Estimated Study Start Date :	November 25, 2021
Estimated Primary Completion Date :	April 28, 2027
Estimated Study Completion Date :	May 26, 2027

FDA approves alpelisib for PIK3CA-related overgrowth spectrum

Resources for Information | Approved Drugs

Oncology (Cancer) / Hematologic Malignancies Approval Notifications

Ongoing | Cancer Accelerated Approvals

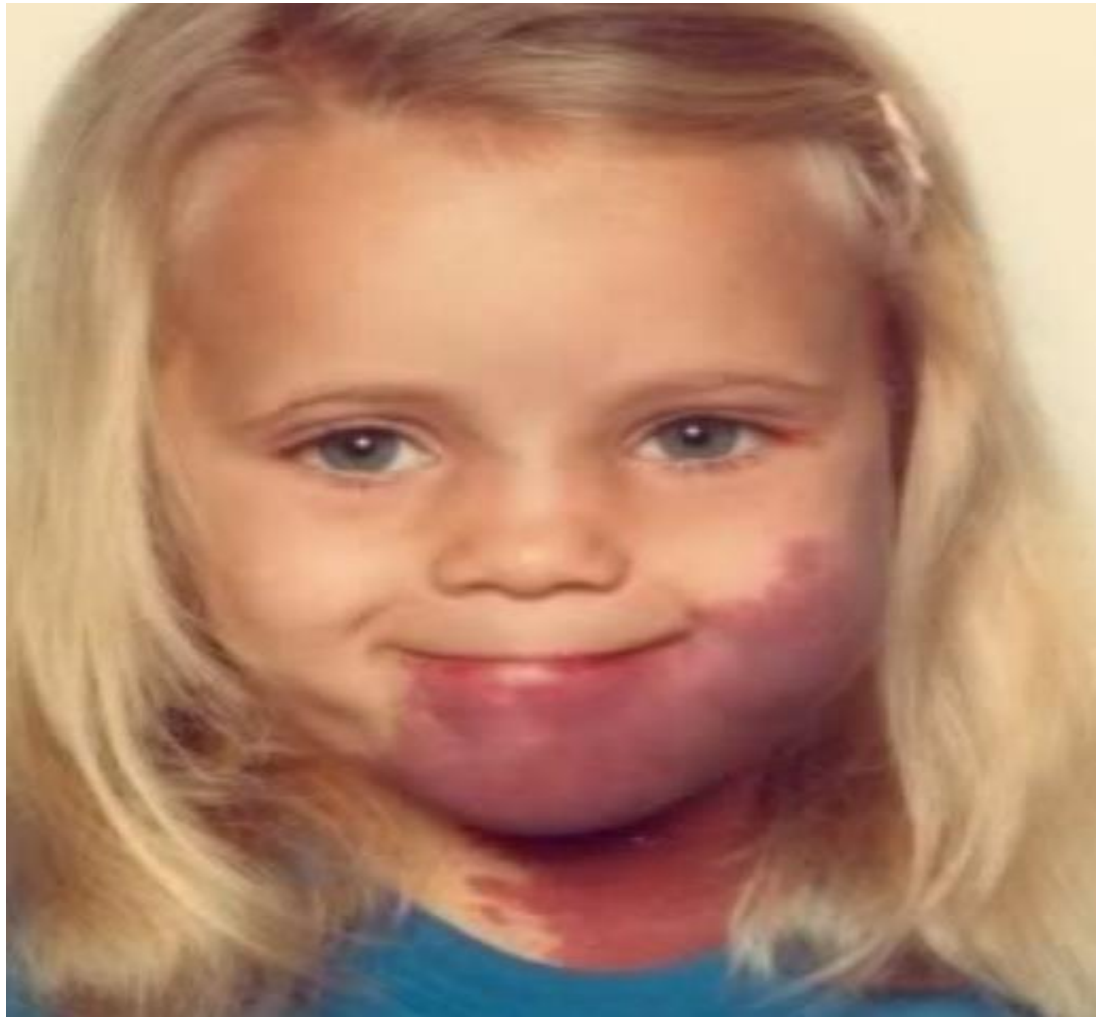
Verified Clinical Benefit | Cancer Accelerated Approvals

Withdrawn | Cancer Accelerated Approvals

On April 5, 2022, the Food and Drug Administration granted accelerated approval to alpelisib (Vijoice, Novartis Pharmaceuticals) for adult and pediatric patients two years of age and older with severe manifestations of PIK3CA-related overgrowth spectrum (PROS) who require systemic therapy.

Efficacy was evaluated using real-world data from EPIK-P1 (NCT04285723), a single-arm clinical study in patients two years of age and older with PROS who received alpelisib as part of an expanded access program for compassionate use. Eligible patients had clinical manifestations of PROS that were assessed by the treating physicians as severe or life-threatening and necessitating systemic treatment and had documented evidence of mutation in the PIK3CA gene. The efficacy of alpelisib was evaluated in a total of 37 patients with at least one target lesion identified on imaging performed within 24 weeks prior to receipt of the first dose.

MALFORMACIONES CAPILARES

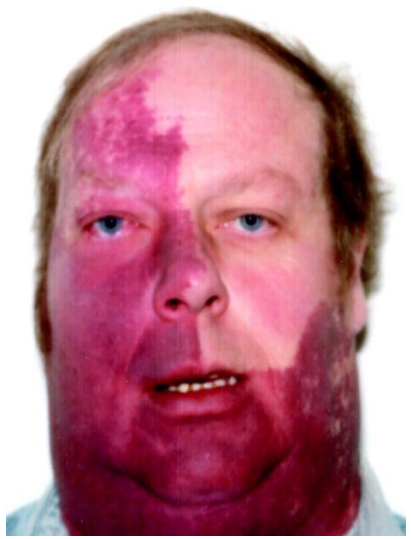


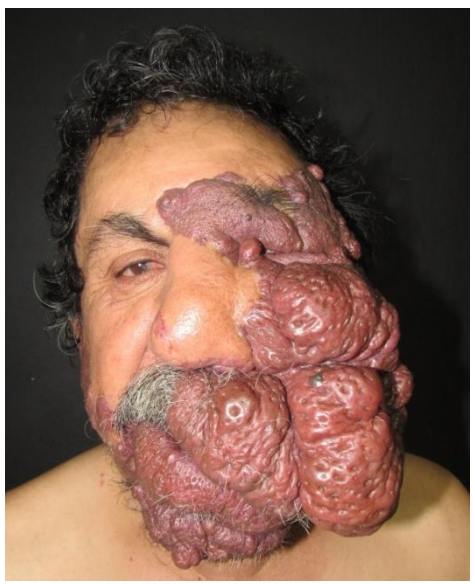
ORIGINAL ARTICLE

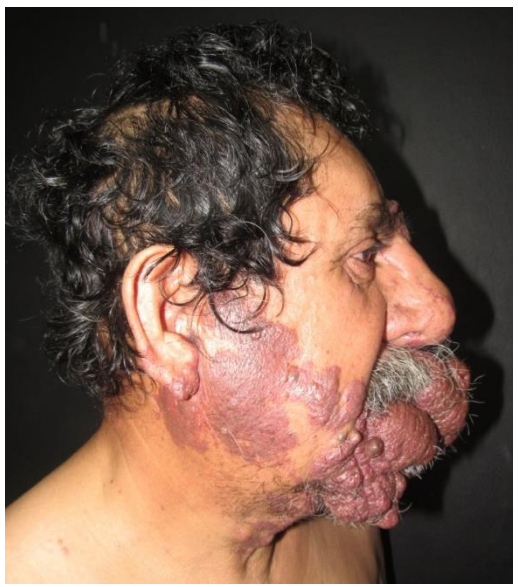
Sturge–Weber Syndrome and Port-Wine Stains Caused by Somatic Mutation in *GNAQ*

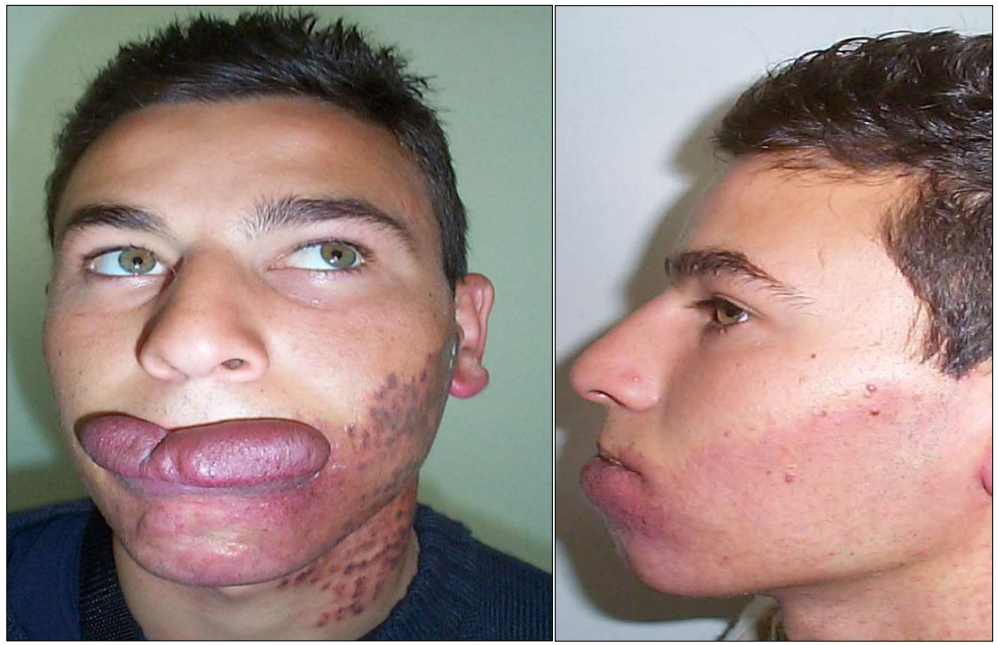
May 23, 2013
N Engl J Med 2013; 368:1971-1979

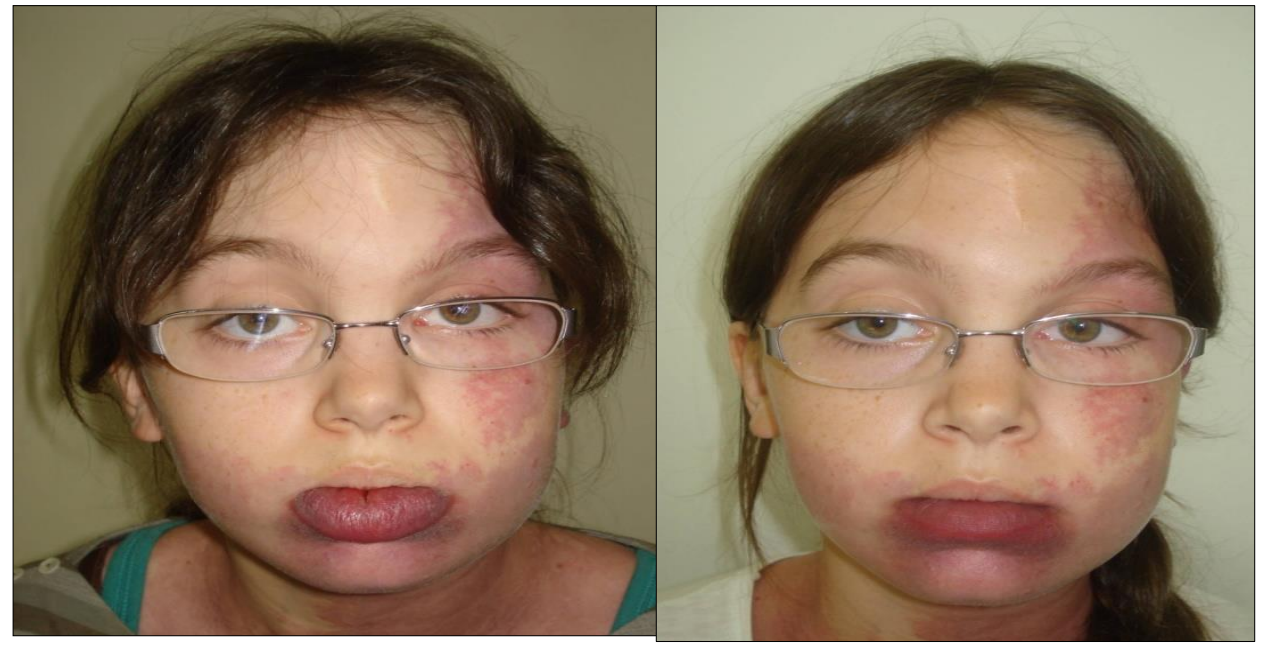
Matthew D. Shirley, Ph.D., Hao Tang, Ph.D., Carol J. Gallione, B.A., Joseph D. Baugher, Ph.D., Laurence P. Frelin, M.S., Bernard Cohen, M.D., Paula E. North, M.D., Ph.D., Douglas A. Marchuk, Ph.D., Anne M. Comi, M.D., and Jonathan Pevsner, Ph.D.

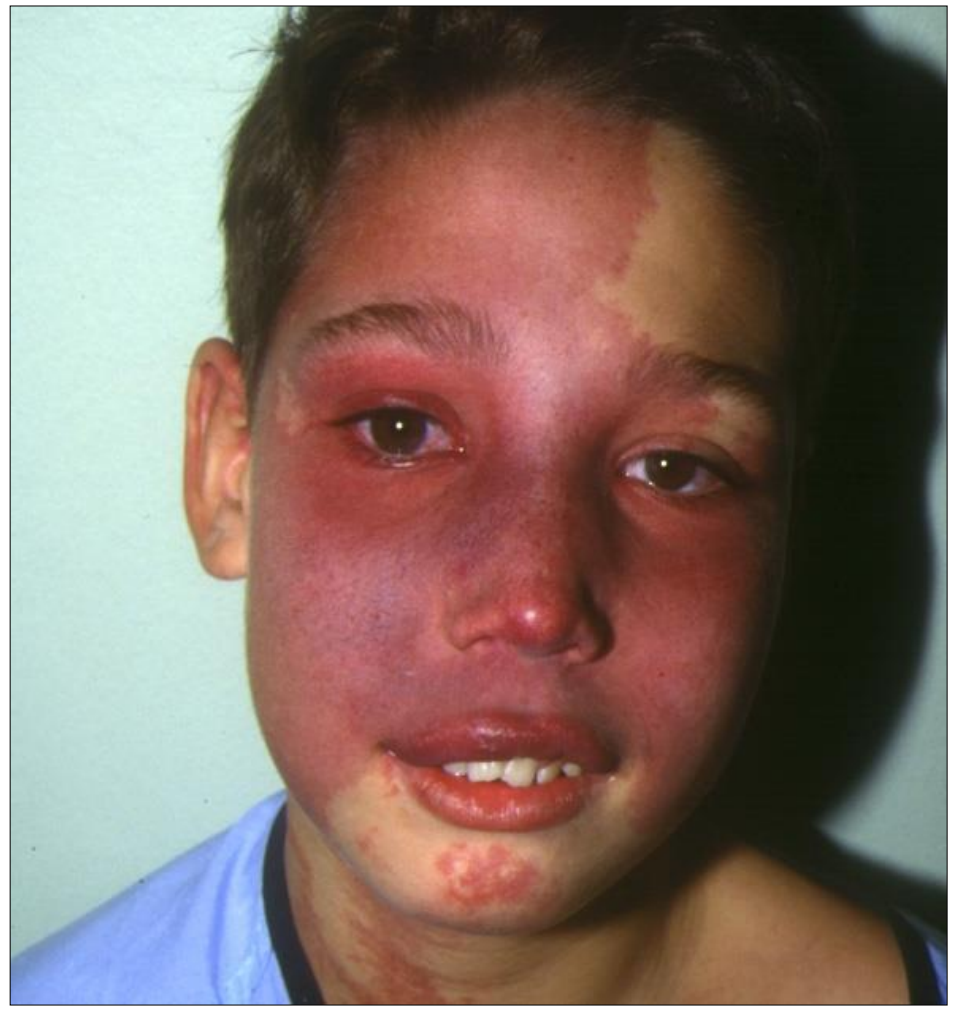


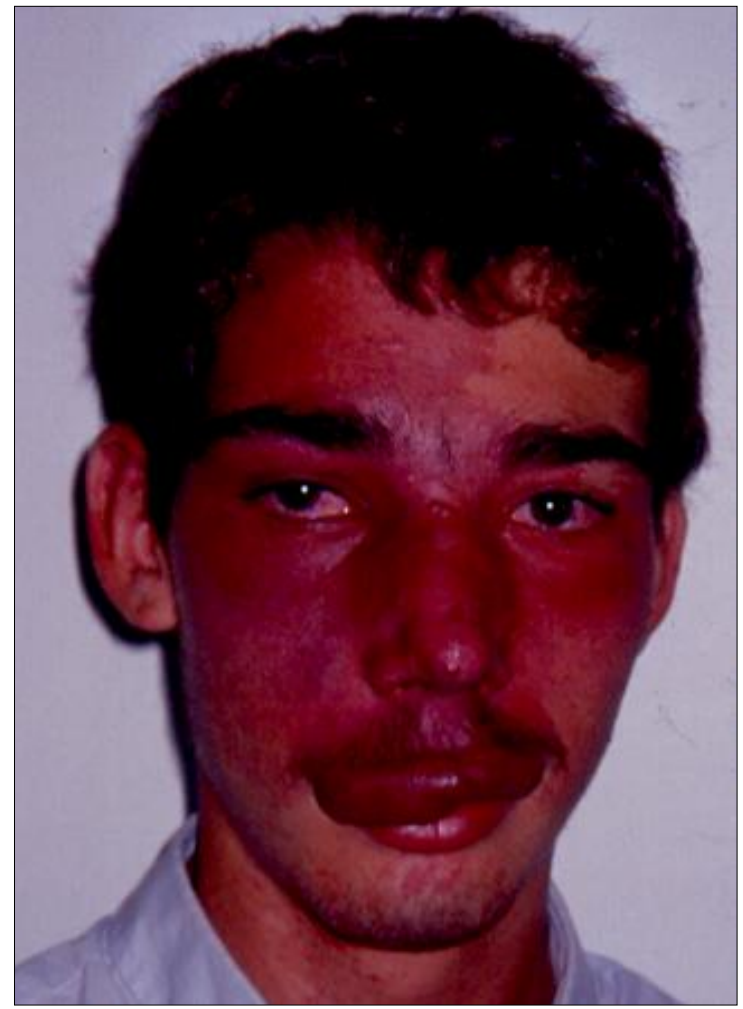












Pediatr Neurol. 2011 June ; 44(6): 443–449. doi:10.1016/j.pediatrneurol.2011.01.005.

CLINICAL OUTCOME IN BILATERAL STURGE-WEBER SYNDROME

Bálint Alkonyi, MD[*,†], **Harry T. Chugani, MD**[*,‡,†], **Samir Karia, MD**[*,‡,§], **Michael E. Behen, PhD**[*,‡], and **Csaba Juhász, MD, PhD**[*,‡,†]

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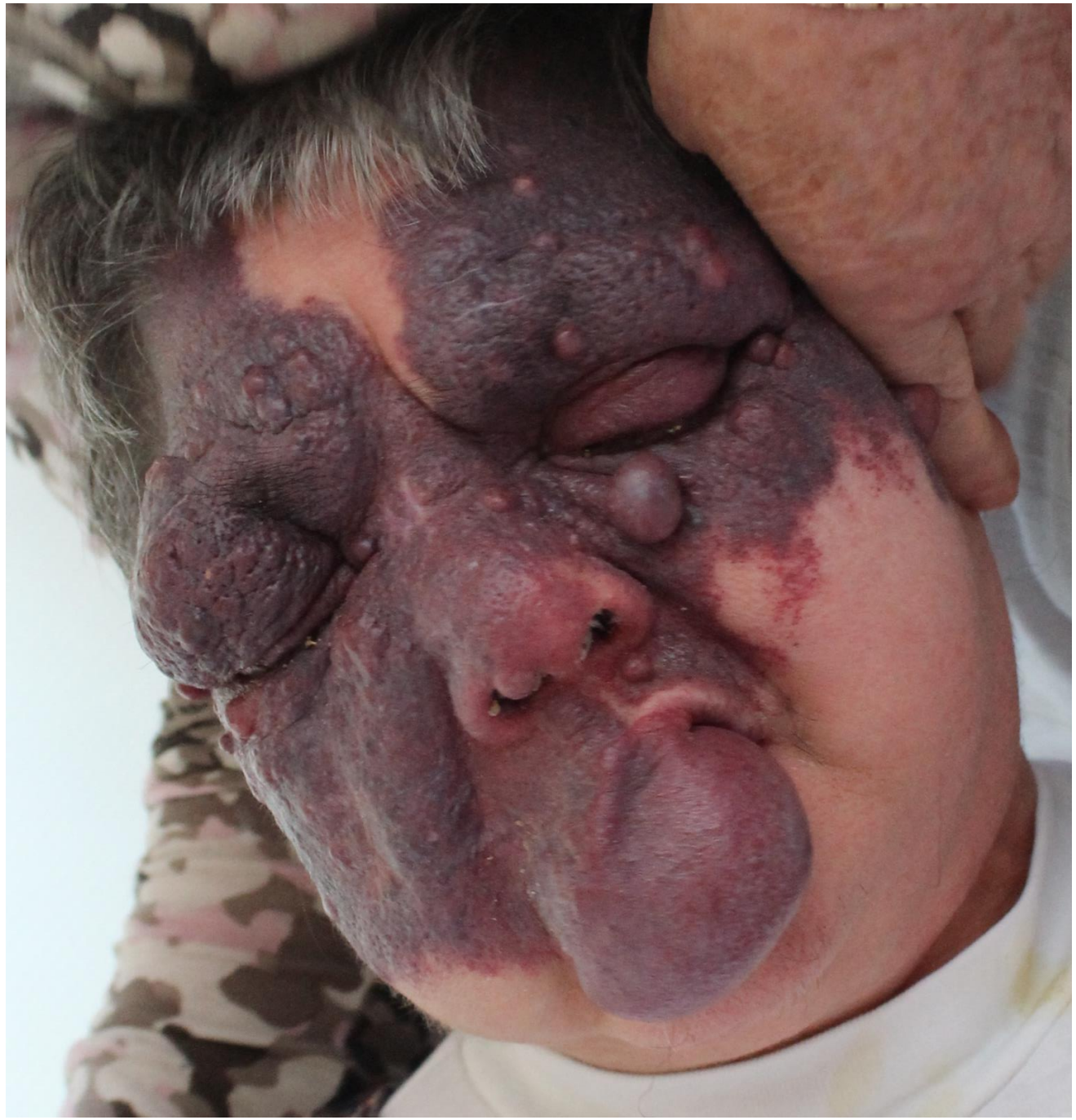
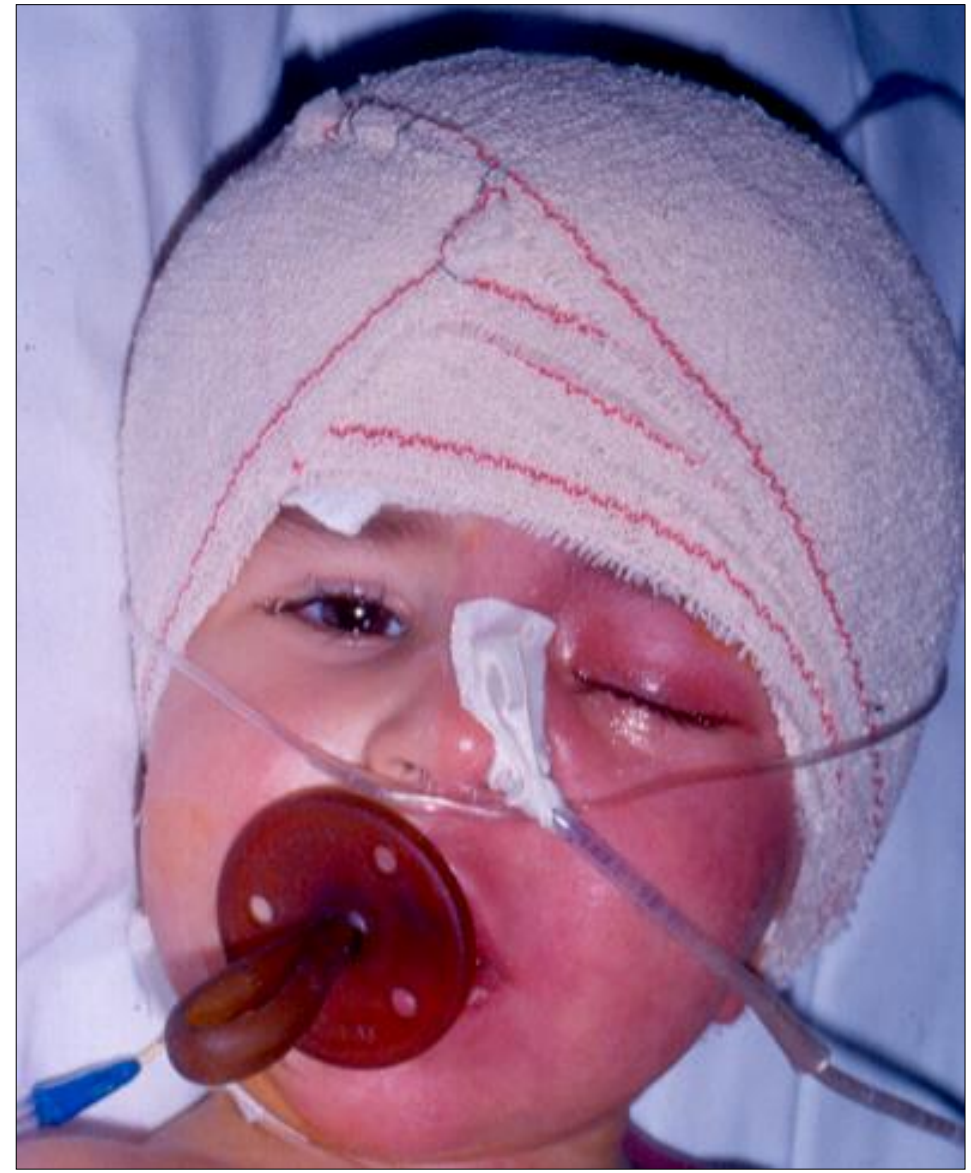
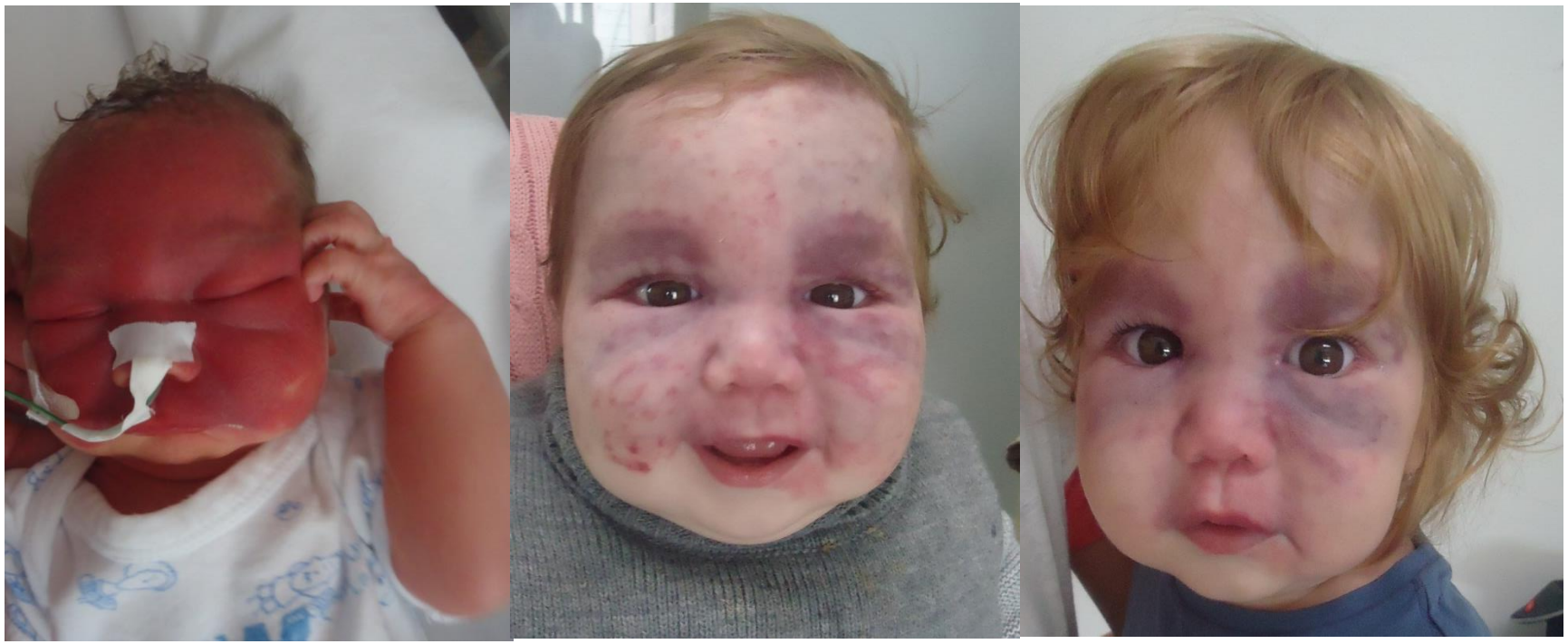
Clinical data of the patients

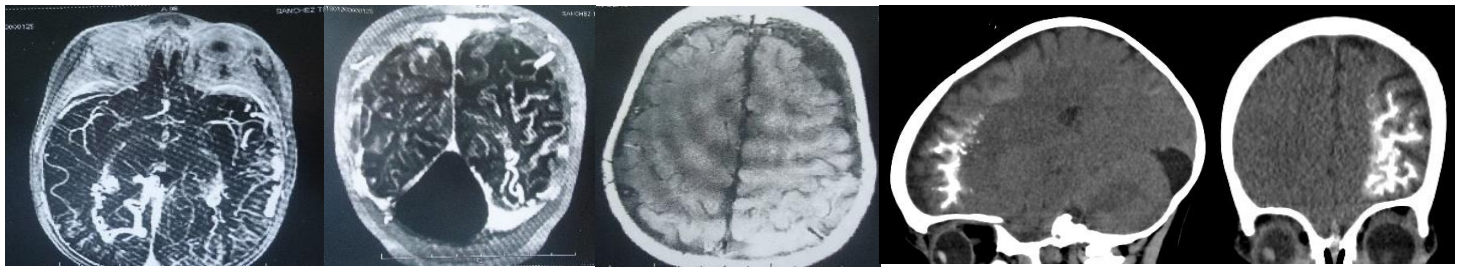
No/Sex	Age at PET scan	Age at last follow-up	Age at onset of first seizures	Type of seizures	Seizure control	Hemiparesis	Developmental impairment
1/M*	8 m	1.7 y	5.5 m	CPS/Gen	Poor	Left	Severe delay
2/M	1.0 y	16 y	6 m	CPS/Gen	Moderate	Left	Severe delay
3/F	1.7 y	2.8 y	3 m	CPS	Poor-Good (VNS)	Right	Severe delay
4/M	1.8 y	1.8 y	1.5 m	SPS, CPS	Poor (VNS)	Left	Severe delay
5/M	5.4 y	9.1 y	7.1 y	CPS	Moderate	None	Mild/moderate
6/F	6.4 y	6.5y	n.a.	CPS/Gen	Poor-Good	Left	Mild/moderate delay
7/M	7.5 y	7.5 y	6 m	CPS/SPS	Poor	Right	Mild/moderate delay
8/F	8.3 y	8.3 y	5 m	CPS/SPS/Gen	Poor-Good	None	Severe delay
9/M	9.8 y	9.8 y	2 w	CPS	Poor-Good	Left	Mild/moderate delay
10/M	10 y	22 y	22 m	CPS	Good	None	Mild/moderate delay
11/F*	11 y	27 y	4 y	Drop/CPS/GTCS	Poor-moderate	Right	Severe – Mild/moderate delay
12/F	15 y	15 y	n.a.	Drop, P	Poor	Right	Severe delay
13/M	26 y	32 y	18 m	CPS	Moderate	None	Mild/moderate delay
14/M	21 y	35 y	2.5 m	SPS	Good	None	Mild/moderate





Triana P, Lopez Gutierrez JC *"PREVENTIVE TREATMENT WITH ORAL SIROLIMUS AND ASPIRIN IN A NEWBORN WITH SEVERE STURGE-WEBER SYNDROME".*
Ped Derm 2019 Jul;36(4):524-527





Two years under sirolimus and aspirin treatment
No seizures, excellent response to PDL and
no neuro-developmental impairement

Trial of Sirolimus for Cognitive Impairment in Sturge-Weber Syndrome

ClinicalTrials.gov Identifier: NCT03047980

Recruitment Status : Recruiting
First Posted : February 9, 2017
Last Update Posted : January 8, 2019
See Contacts and Locations

Sponsor:
Anne Comi, MD

Collaborators:
Children's Hospital Medical Center, Cincinnati
Pfizer
National Institutes of Health (NIH)
Faneca 66 Foundation
National Institute of Neurological Disorders and Stroke (NINDS)

Information provided by (Responsible Party):
Anne Comi, MD, Hugo W. Moser Research Institute at Kennedy Krieger, Inc.

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PMCID: PMC8209677
NIHMSID: NIHMS1654819
PMID: 33316689

Sirolimus Treatment in Sturge-Weber Syndrome

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Arteriovenous malformations (AVM)	
Sporadic	MAP2K1
In HHT	(*HHT1* ENG, *HHT2* ACVRL1, *HHT3*, *JPHT* SMAD4)
In CM-AVM	RASA1 / EPHB4
Others	
Arteriovenous fistula (AVF) (congenital)	
Sporadic	MAP2K1
In HHT	(*HHT1* ENG, *HHT2* ACVRL1, *HHT3*, *JPHT* SMAD4)
In CM-AVM	RASA1 / EPHB4
Others	

ISSVA

Arteriovenous malformations (AVM)	
Sporadic	MAP2K1
In HHT	(*HHT1* ENG, *HHT2* ACVRL1, *HHT3*, *JPHT* SMAD4)
In CM-AVM	RASA1 / EPHB4
Others	***PTEN***
Arteriovenous fistula (AVF) (congenital)	
Sporadic	MAP2K1
In HHT	(*HHT1* ENG, *HHT2* ACVRL1, *HHT3*, *JPHT* SMAD4)
In CM-AVM	RASA1 / EPHB4
Others	

KRAS HRAS BRAF

Genotyping and clinical course in 100 patients with arteriovenous malformations

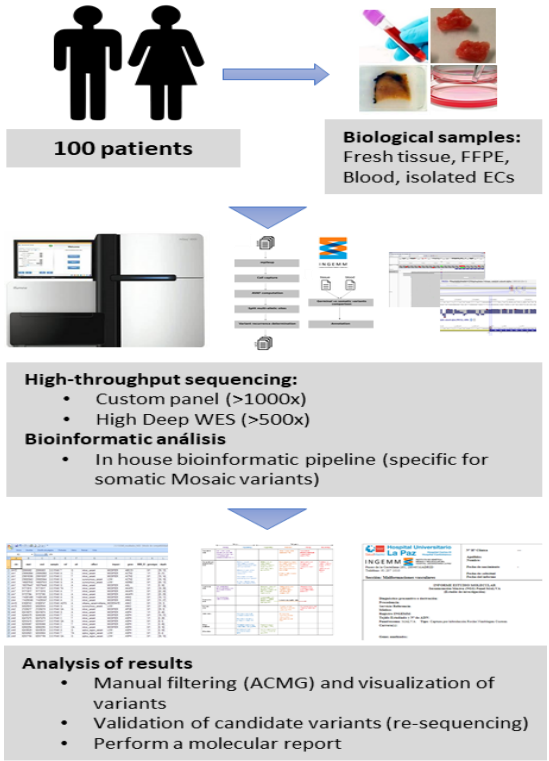
Rodriguez-Laguna L, Triana P, Martinez-Glez V, Lopez-Gutierrez JC
Hospital Universitario La Paz

Hospital Universitario La Paz
SaludMadrid
Hospital Carlos III
Hospital Cantoblanco

INGEMM
INSTITUTO DE GENÉTICA MÉDICA Y MOLECULAR DEL HOSPITAL UNIVERSITARIO LA PAZ

Genomic results

Pathogenic variants were detected in **67% of patients**. The remaining 37% of patients were negative for the screening of pathogenic variants.



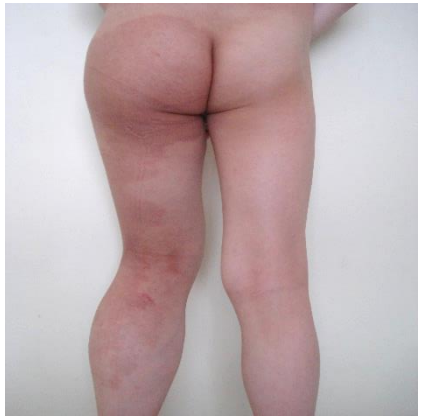
N=100 patients

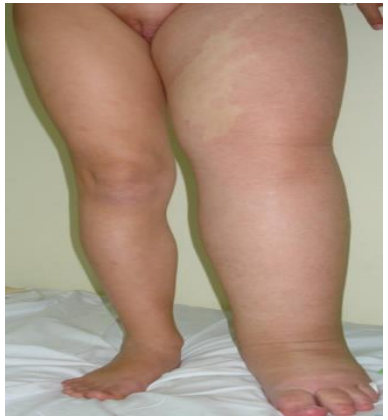
RASA1	n=9	***PIK3CA***	n=9*
EPHB4	n=2	***GNAQ***	n=3
PTEN	n=3	***GNA14***	n=1
MAP2K1	n=22	***FGFR3***	n=2
KRAS	n=17	***GJC2***	n=1
BRAF	n=4		
HRAS	n=1		

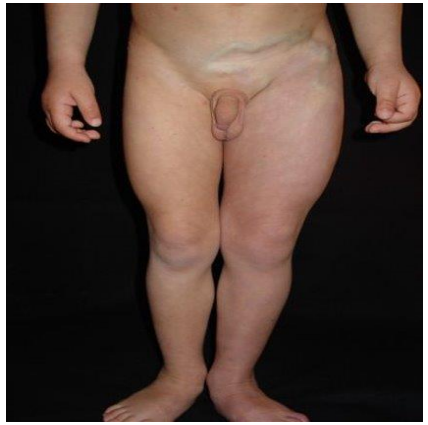
* 2 patients with no other pathogenic mutations detected and 7 cases with a concomitant pathogenic variants in other different gene.

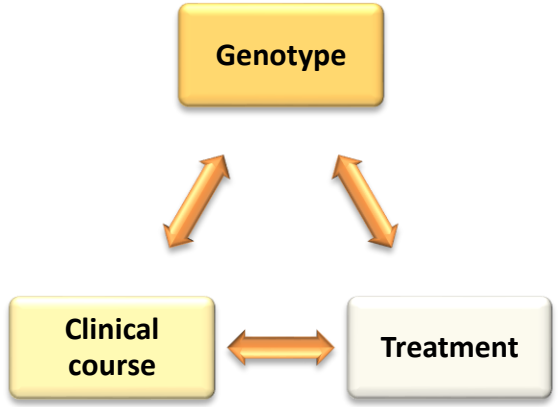
Parkes Weber Syndrome (PWS)

Parkes Weber Syndrome (PWS) phenotype features: capillary malformation, arteriovenous malformation, and overgrowth of the affected limb.







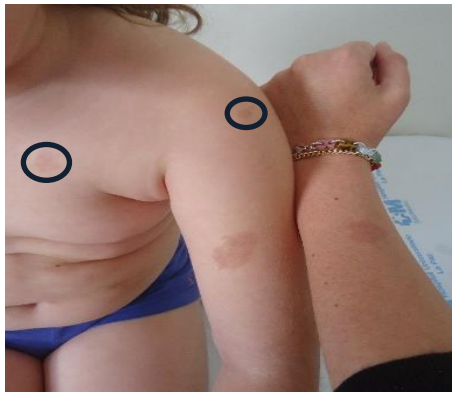


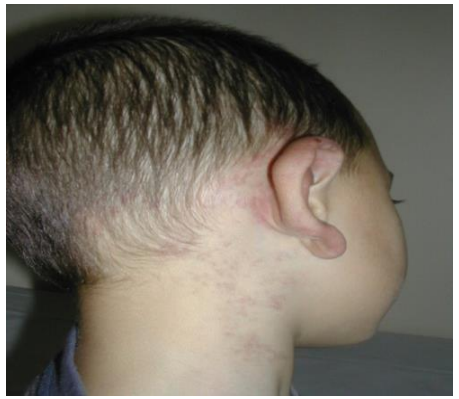
N=7 patients with PWS (pathogenic variants were detected in all)

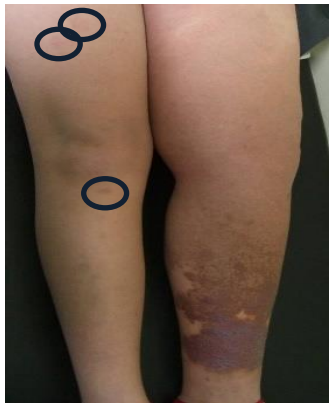
RASA1	n=3	Conservative treatment (3)
KRAS	n=2	Interventional treatment-Surgery (2) and amputation (1)
MAP2K1	n=1	Surgery (1)
GNAQ	n=1	Surgery (1)

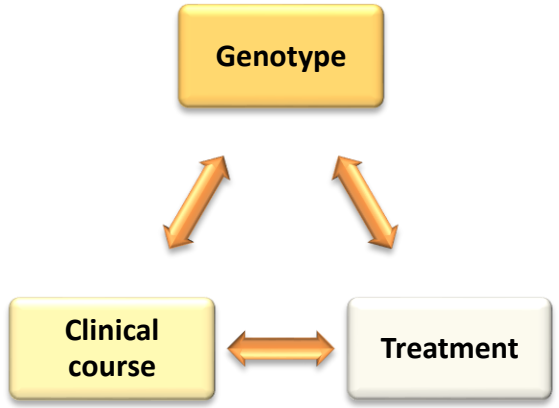
Capillary Malformation-Arteriovenous Malformation (CM-AVM)

Capillary Malformation-Arteriovenous Malformation (CM-AVM) phenotype features: one or multiple atypical capillary malformations together with a high flow vascular malformation.







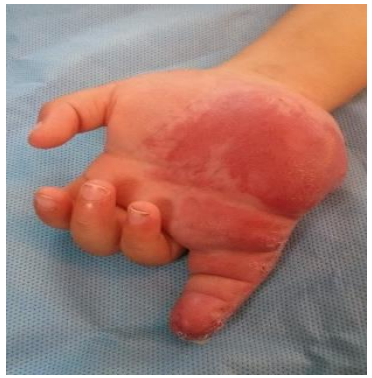


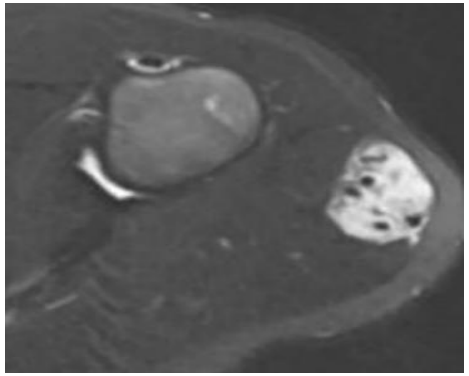
N=20 patients with CM-AVM (13 with pathogenic variants)

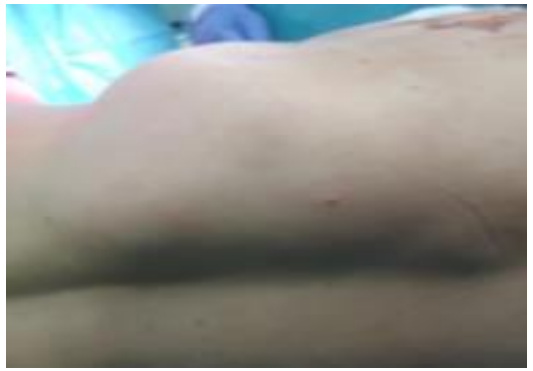
RASA1	n=6	Conservative treatment (6) and Sirolimus treatment (1)
EPHB4	n=2	Conservative treatment (2)
MAP2K1	n=3	Surgery (2) and resection (1)
BRAF	n=1	Interventional and Surgery (1)
FGFR3	n=1	Interventional and Surgery (1)

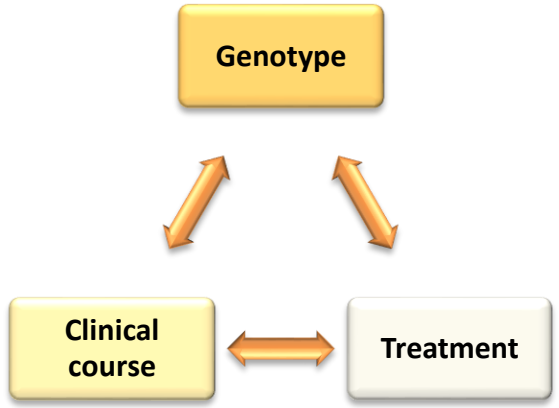
Intramuscular Fast-Flow Vascular Anomalies (or IHCT)

Intramuscular high-flow vascular anomaly, also known as **intramuscular hemangioma capillary type (IHCT)** is a fast-flow vascular lesion with a phenotype overlapping between tumor and AVM.







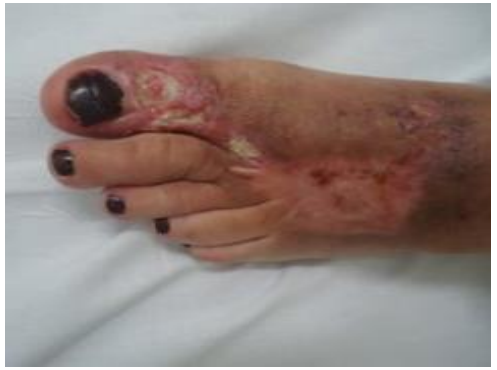


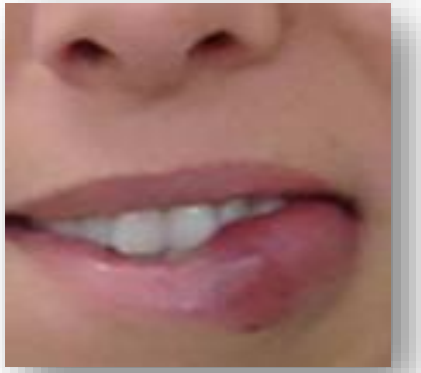
N=13 patients with IHCT (8 with pathogenic variants)

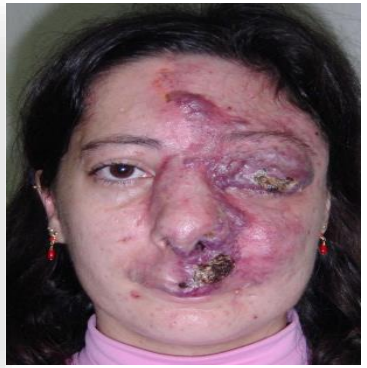
MAP2K1	n=1	Interventional treatment- Surgery (1)
KRAS	n=3	Surgery (2) Interventional treatment- Surgery (1)
PIK3CA	n=2	Surgery (2)
GNAQ	n=1	Surgery (1)
HRAS	n=1	Surgery (1)

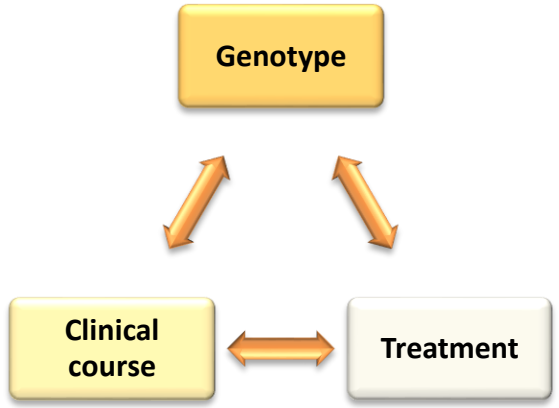
Sporadic AVMs

Isolated AVMs are localized lesions that could appear in any part of the body, mostly of them focus on the face and neck.









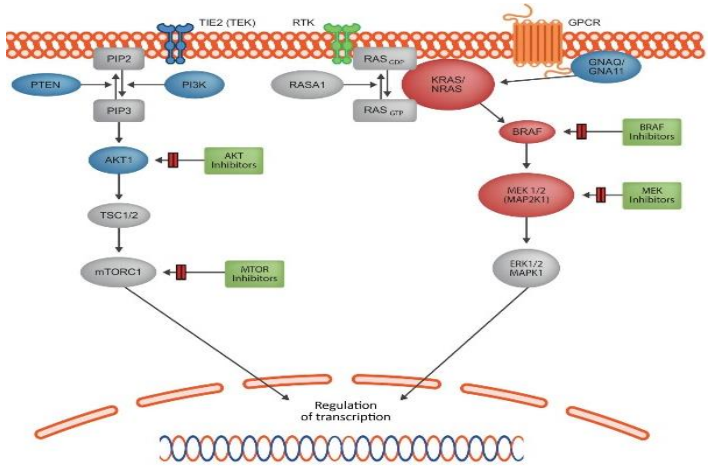
N=56 patients with isolated AVMs (35 with pathogenic variants)

MAP2K1	n=17	Interventional treatment- Surgery (6), Surgery (8), amputation (3)
KRAS	n=12	Interventional treatment- Surgery (7), Surgery (2), amputation (3)
BRAF	n=3	Interventional treatment- Surgery (3)
GNAQ	n=1	Surgery (1)
GNA14	n=1	Surgery (1)

GJC2 (n=1), no data

Genotype-Phenotype-Clinical Course correlation

Patients with **mild clinical course** harbor mutations in ***RASA1*** **and** ***EPHB4***, whereas those with pathogenic variants in ***KRAS, HRAS, BRAF,*** **and** ***MAP2K1*** show a more **severe progression** of AVM.



Al-Olabi L, et al. *J Clin Invest*. 2018

RASA1

EPHB4

→ Conservative treatment

MAP2K1

KRAS

BRAF

HRAS

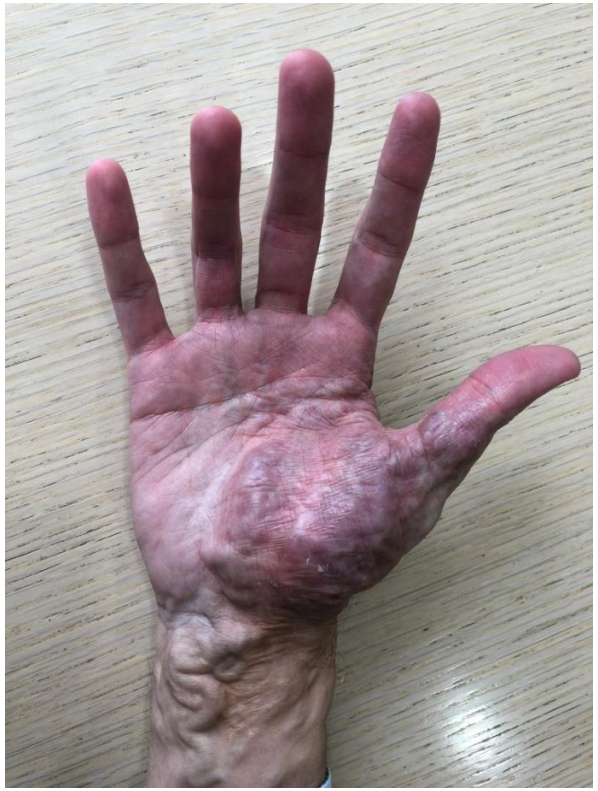
→ Interventional treatment

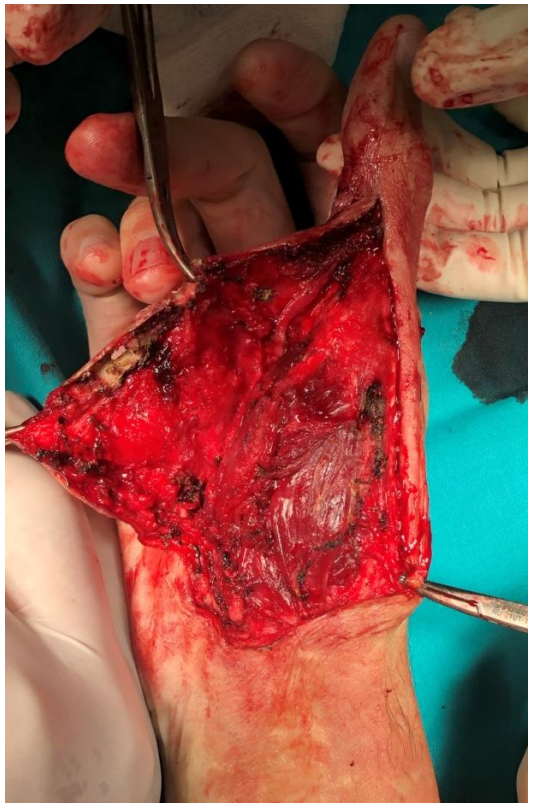
Interventional treatment and Surgery

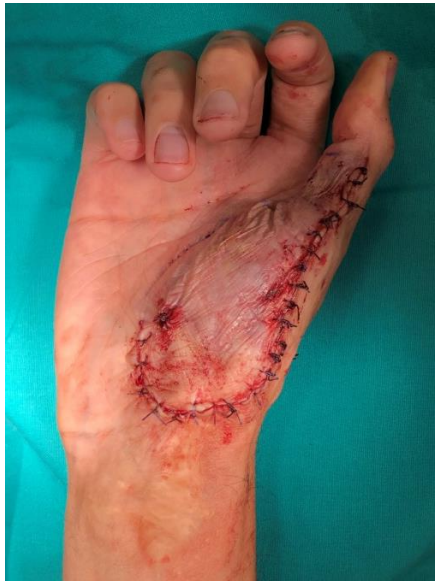
Surgery

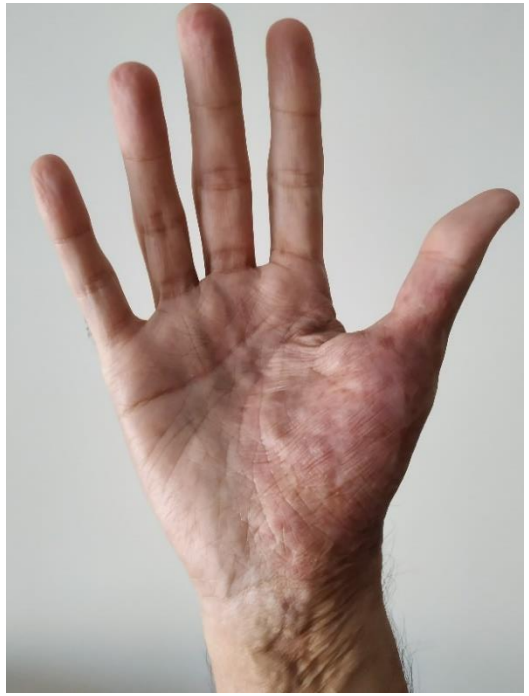
Full resection (amputation)

Genotype-clinical course correlation → It is necessary to increase the number of cases to establish a more robust correlation.

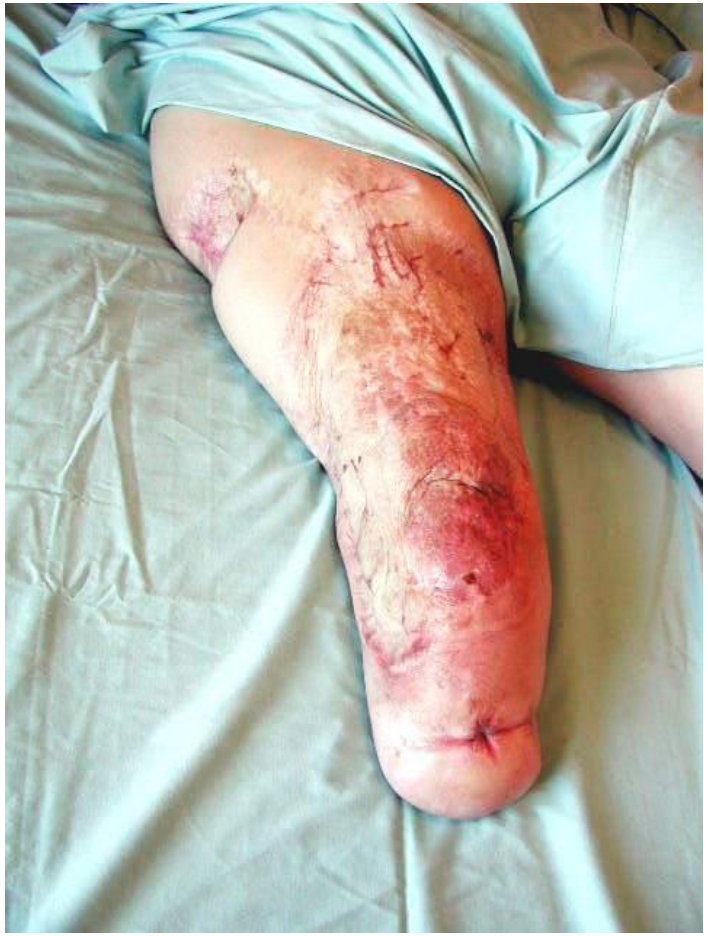


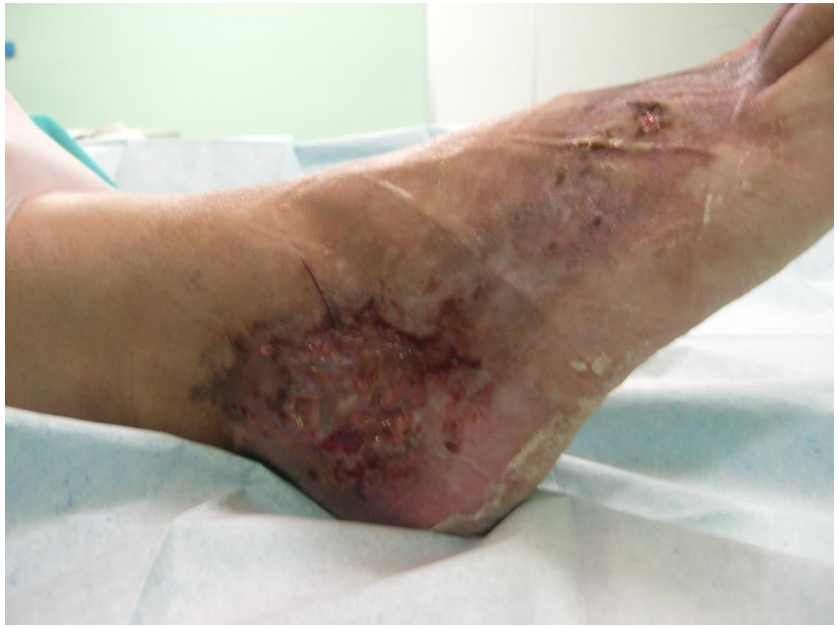


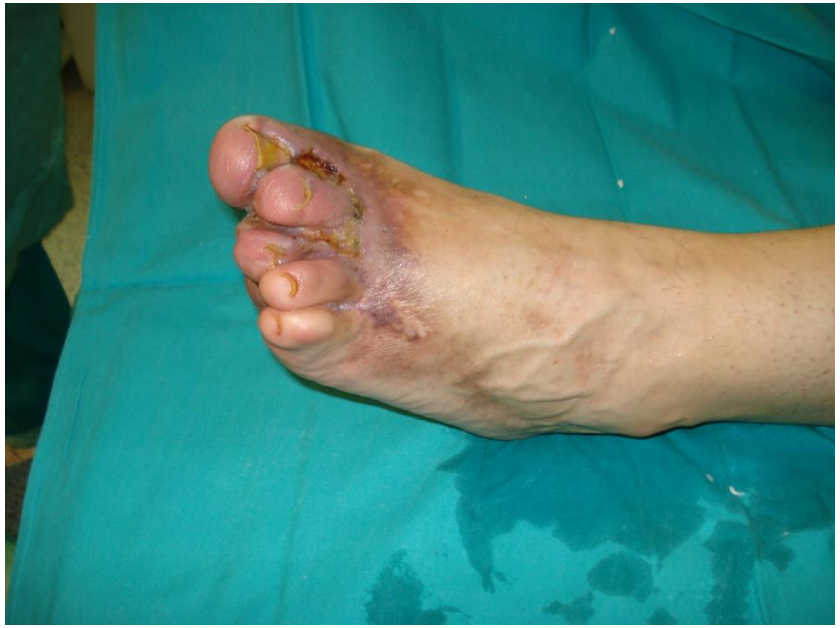


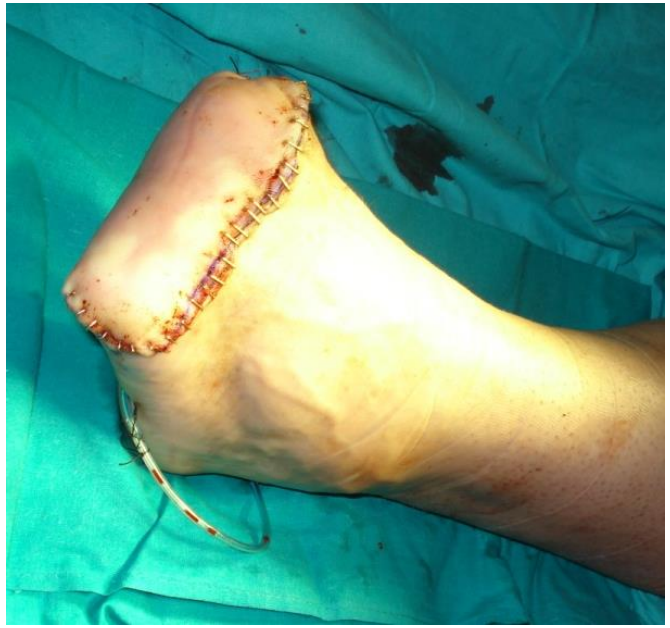


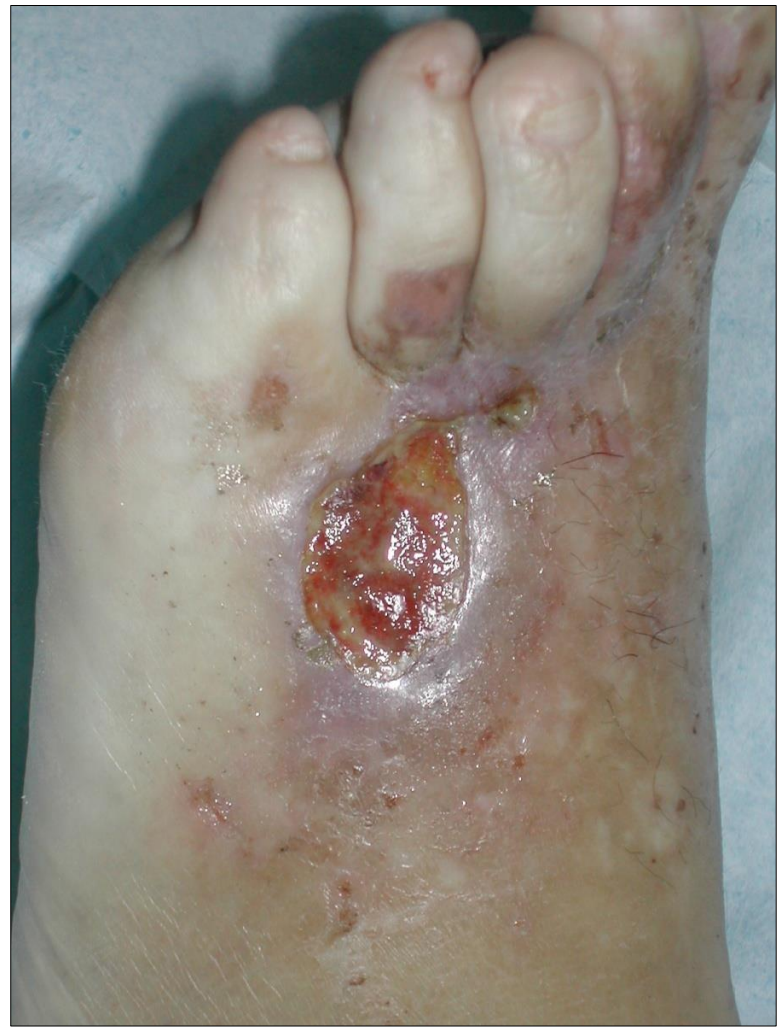
Sporadic AVM.....MAP2K1 mutation

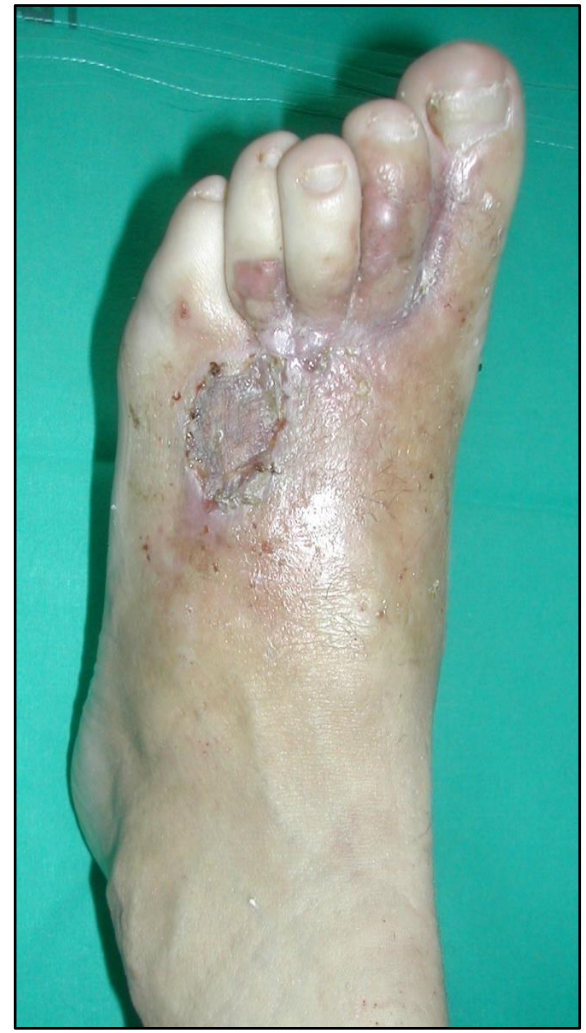


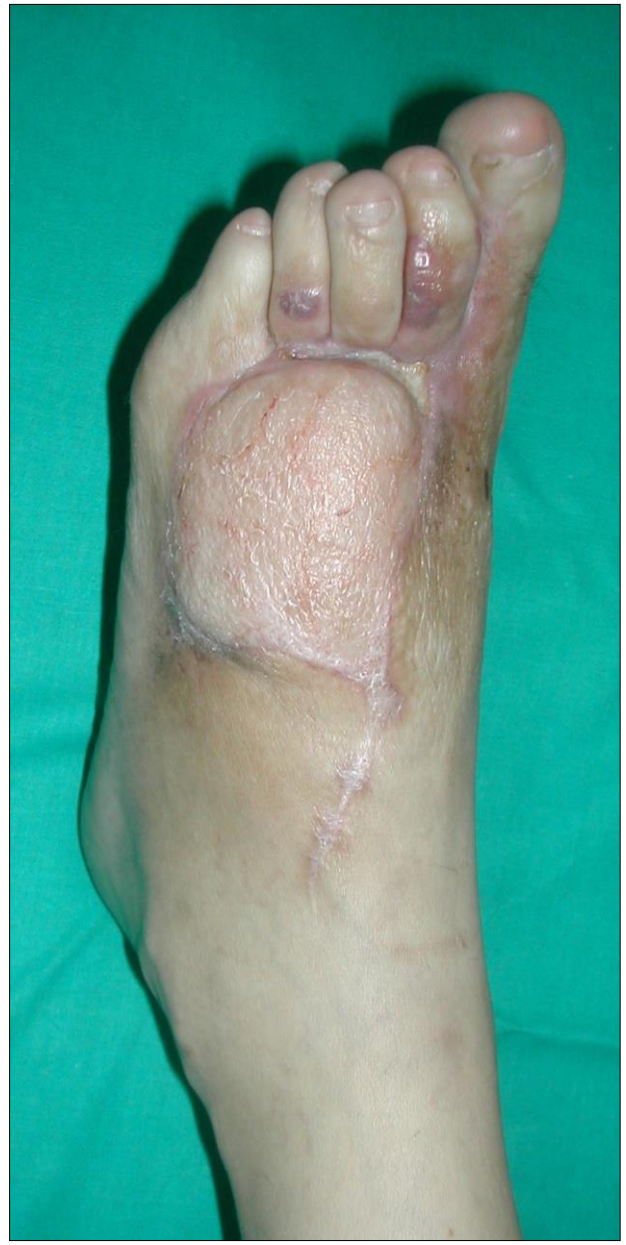


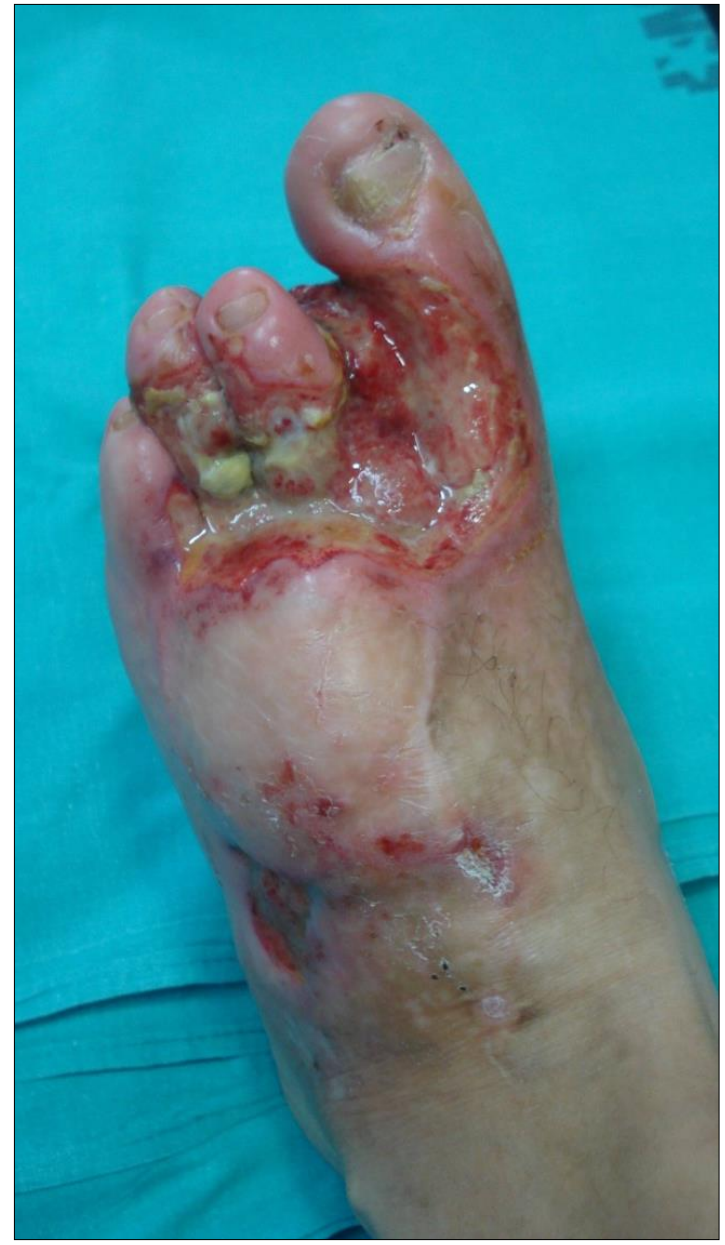


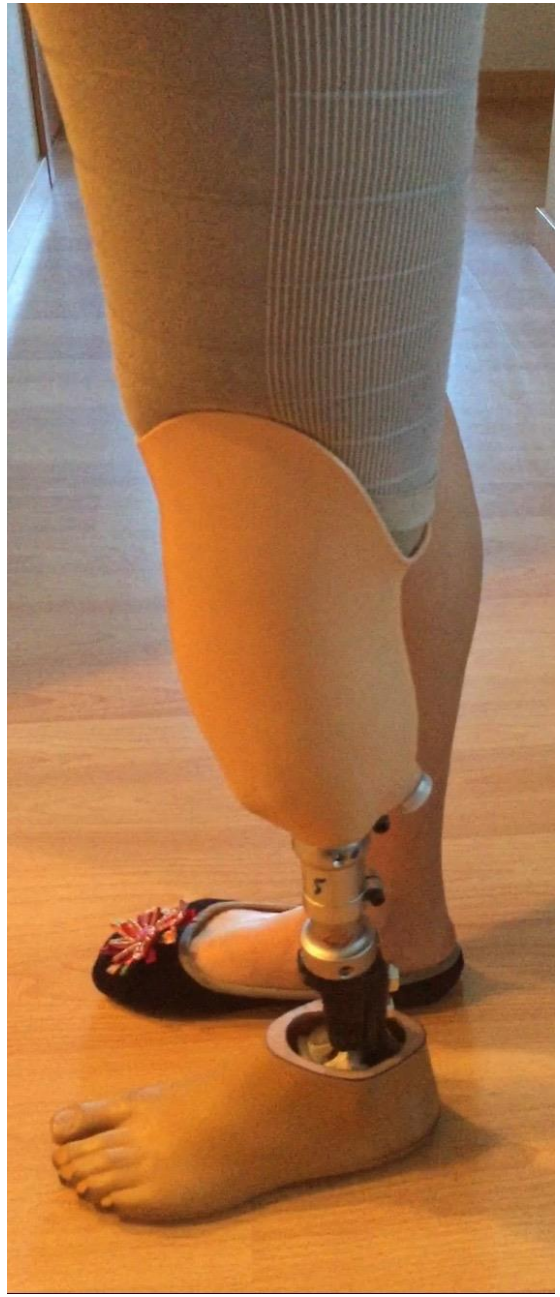


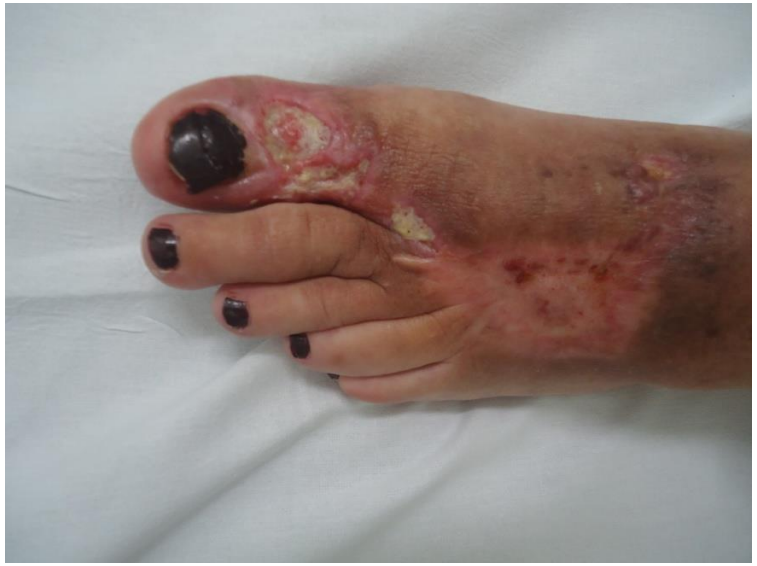


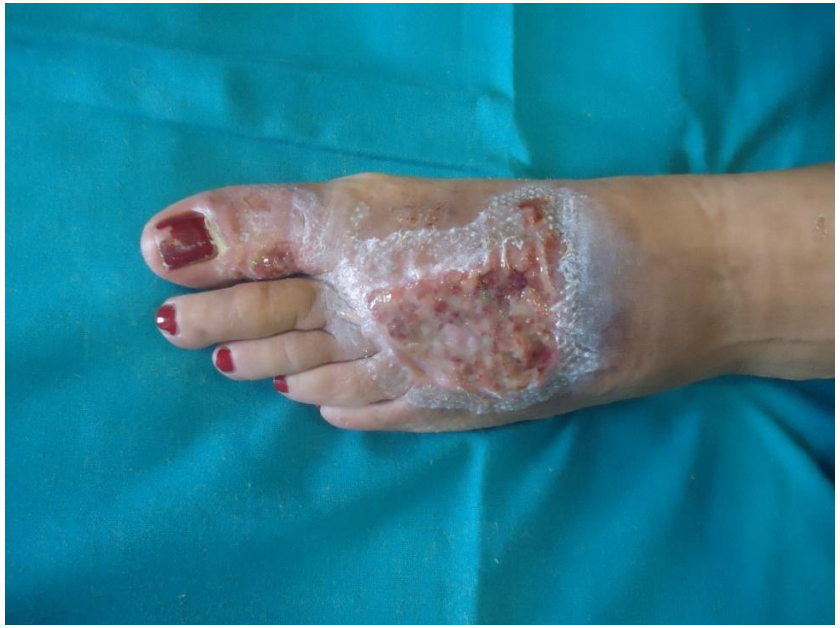


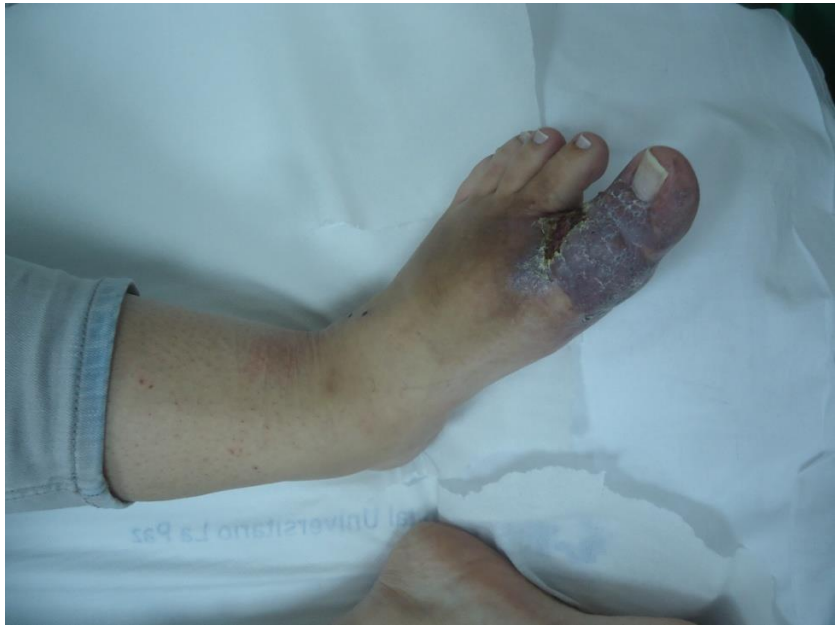


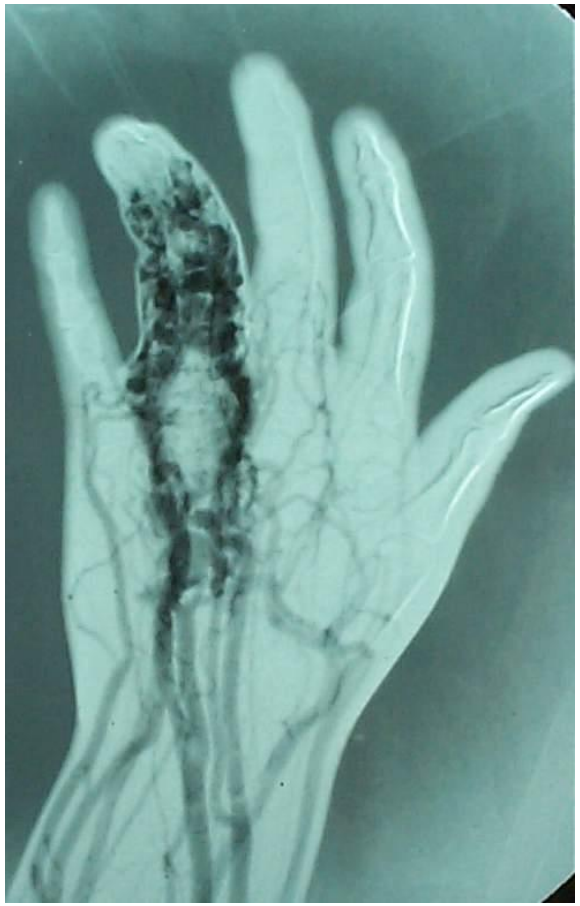


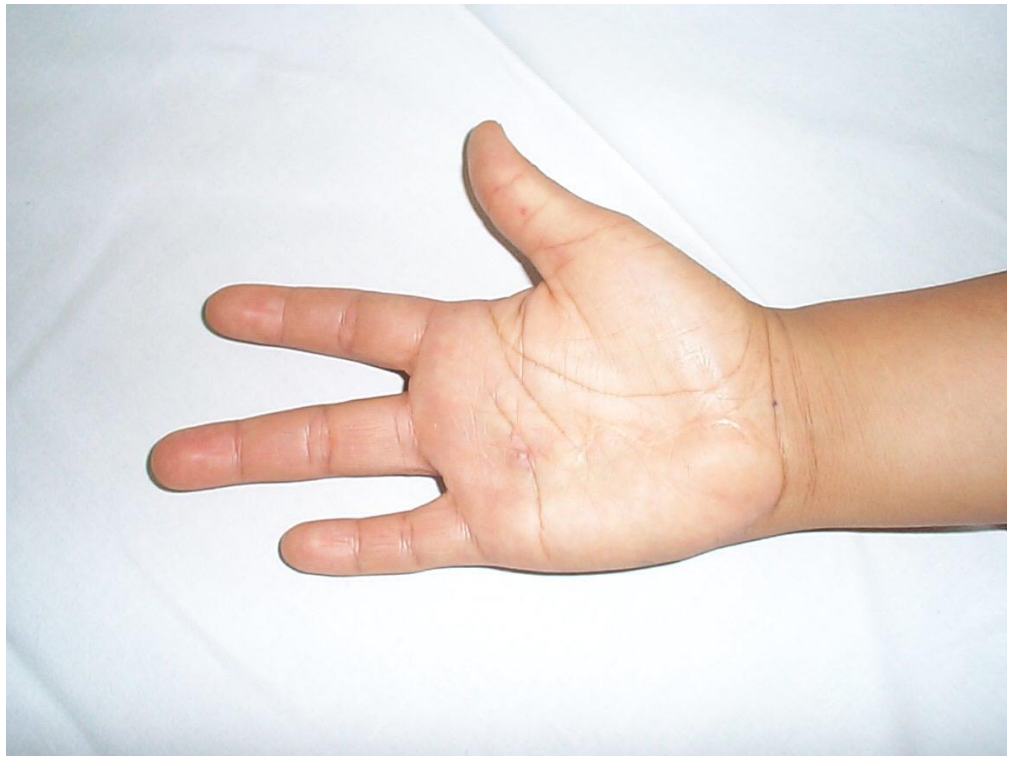


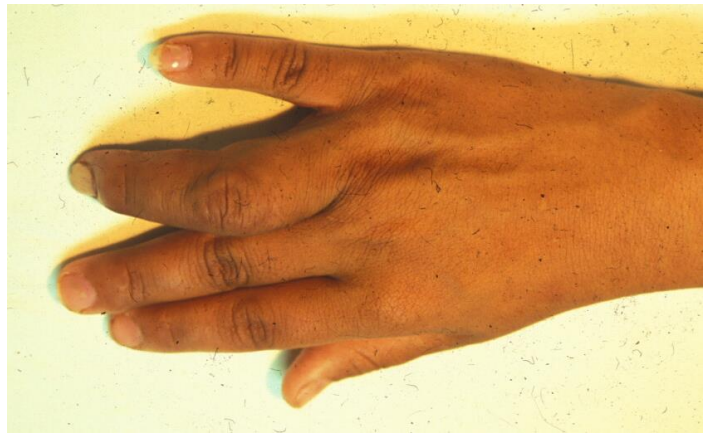


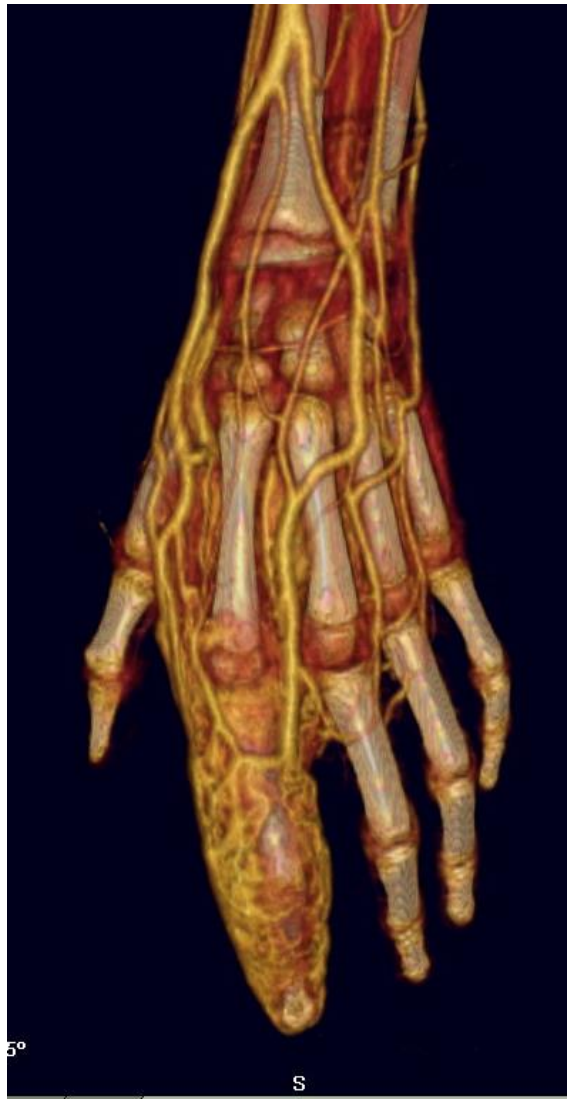








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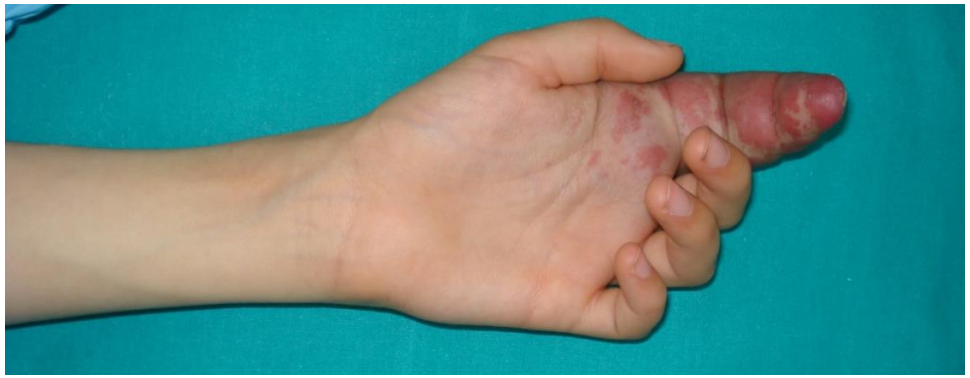

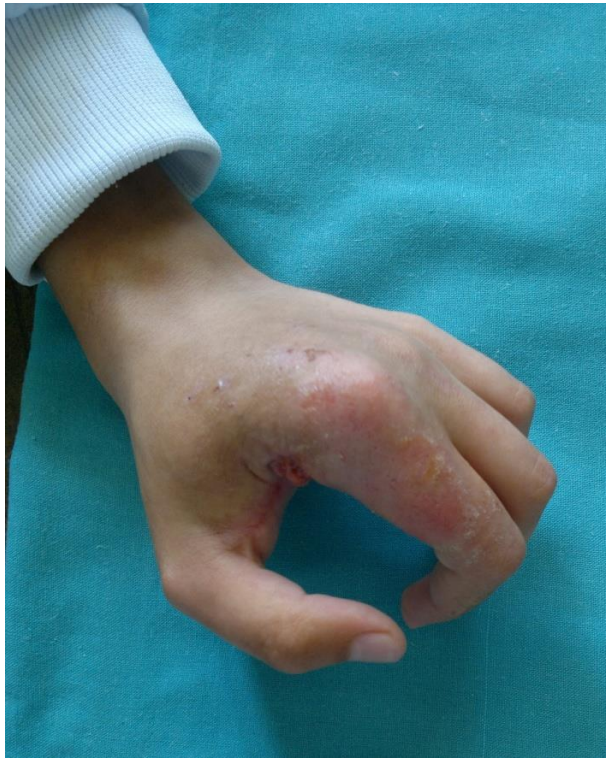

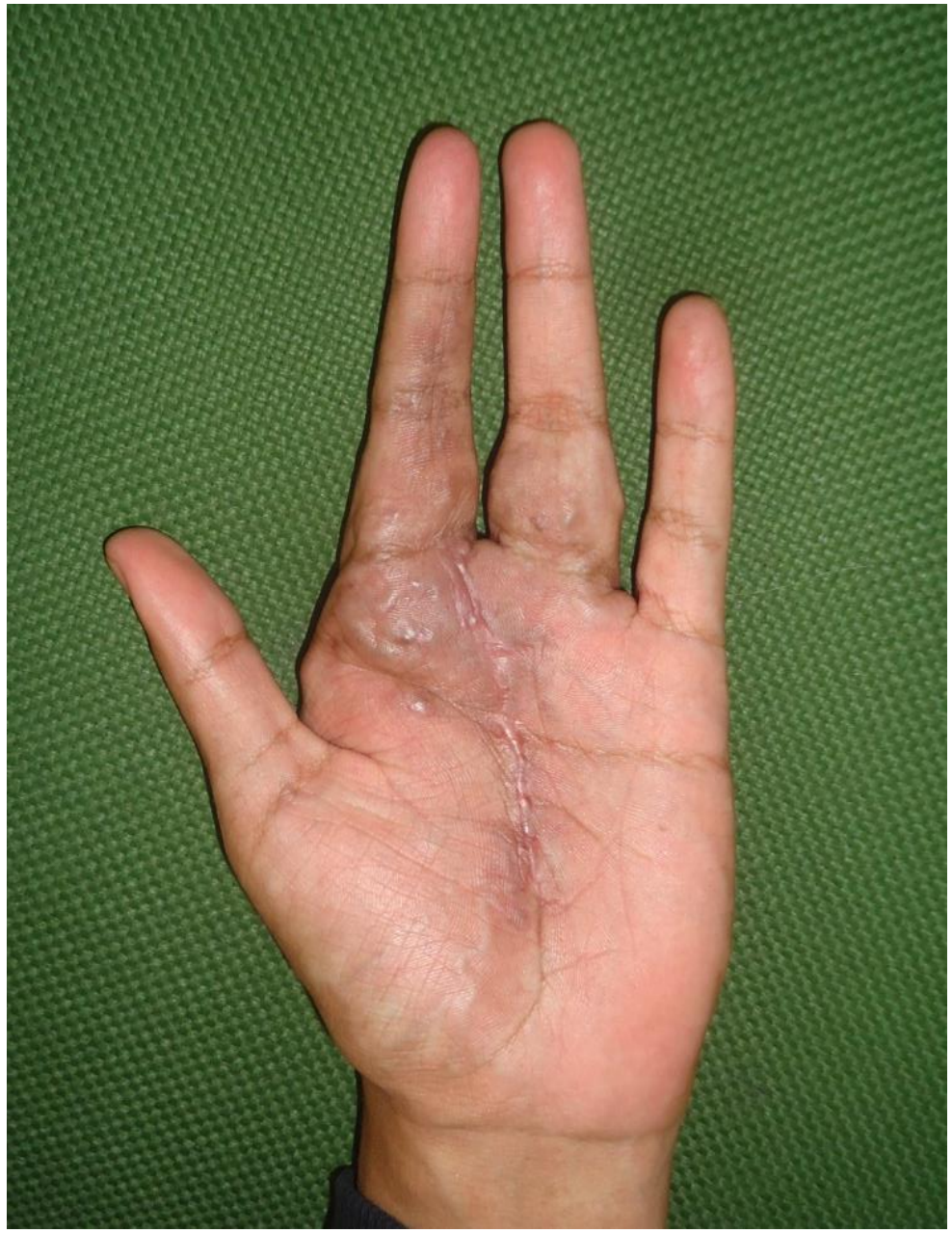

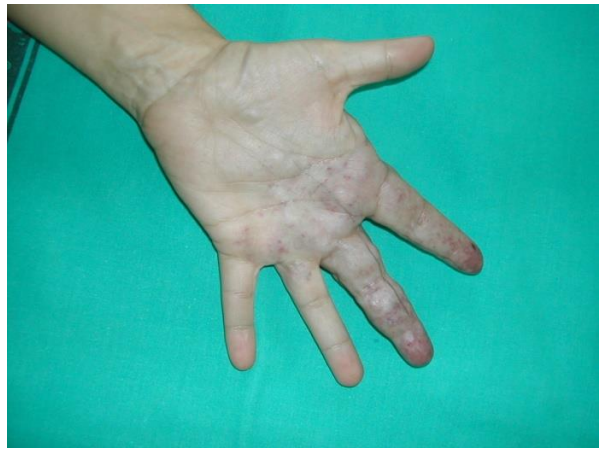
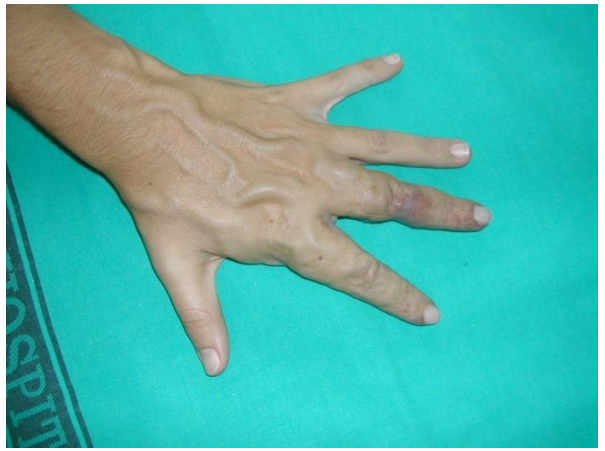
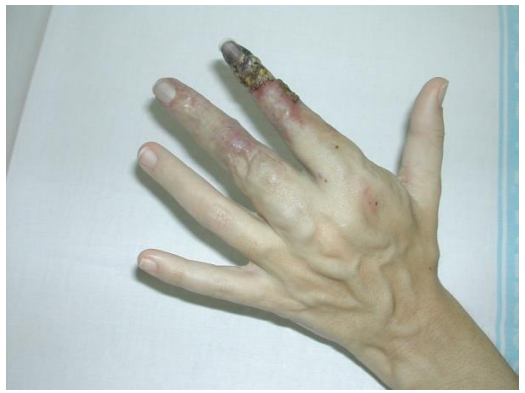
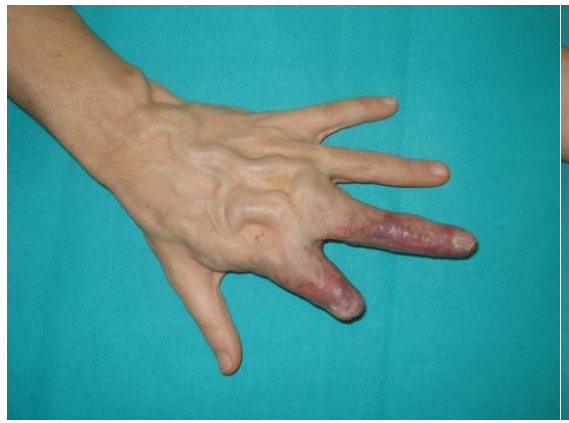
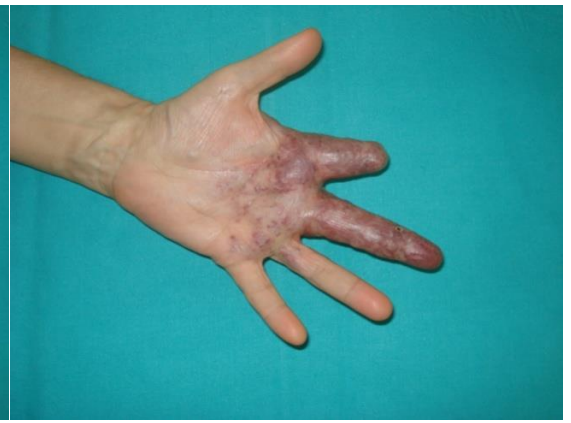

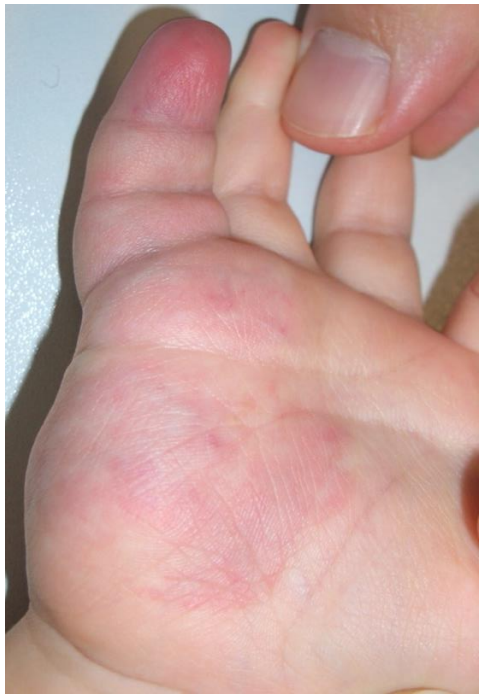
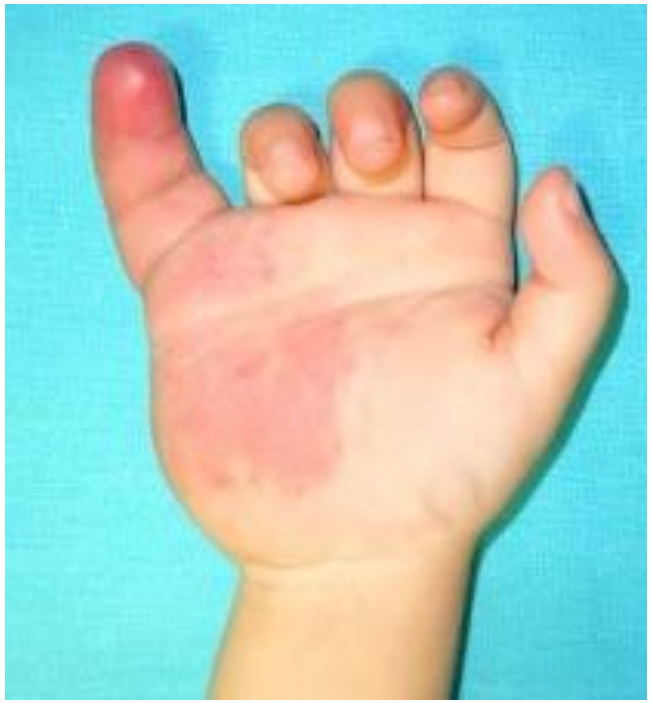
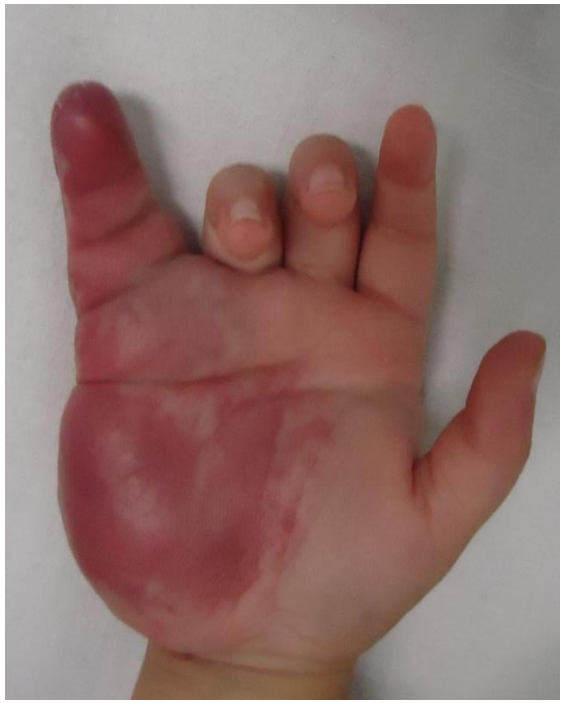


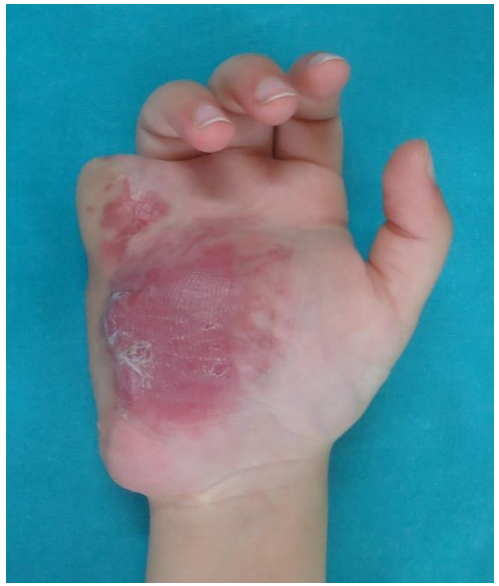
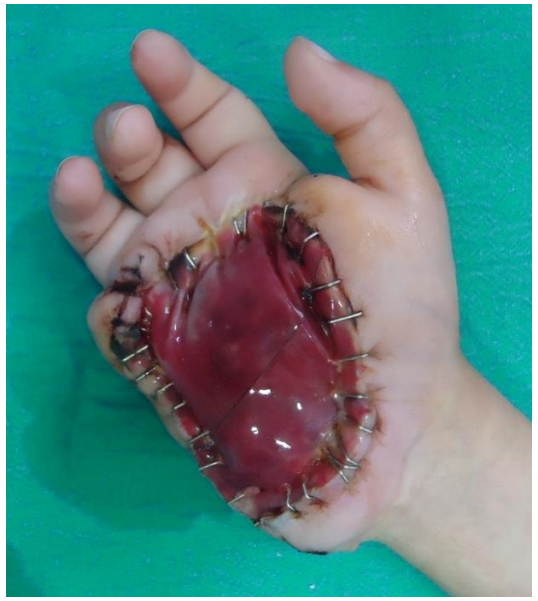
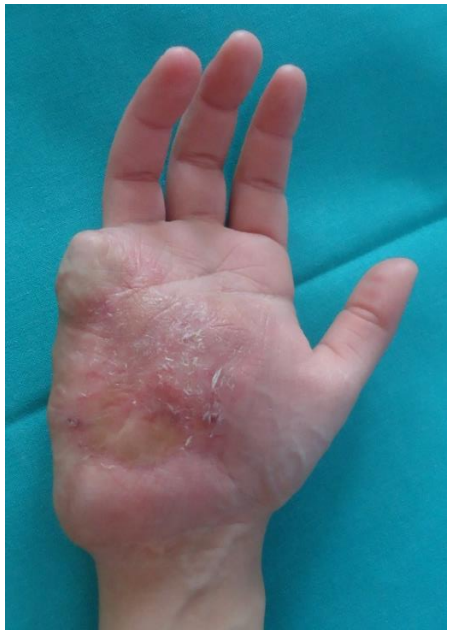

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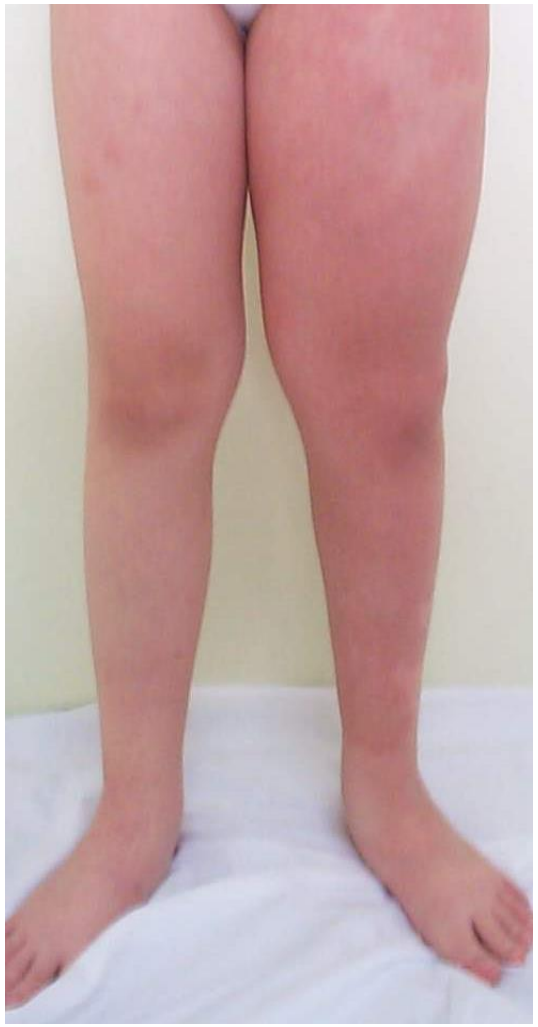
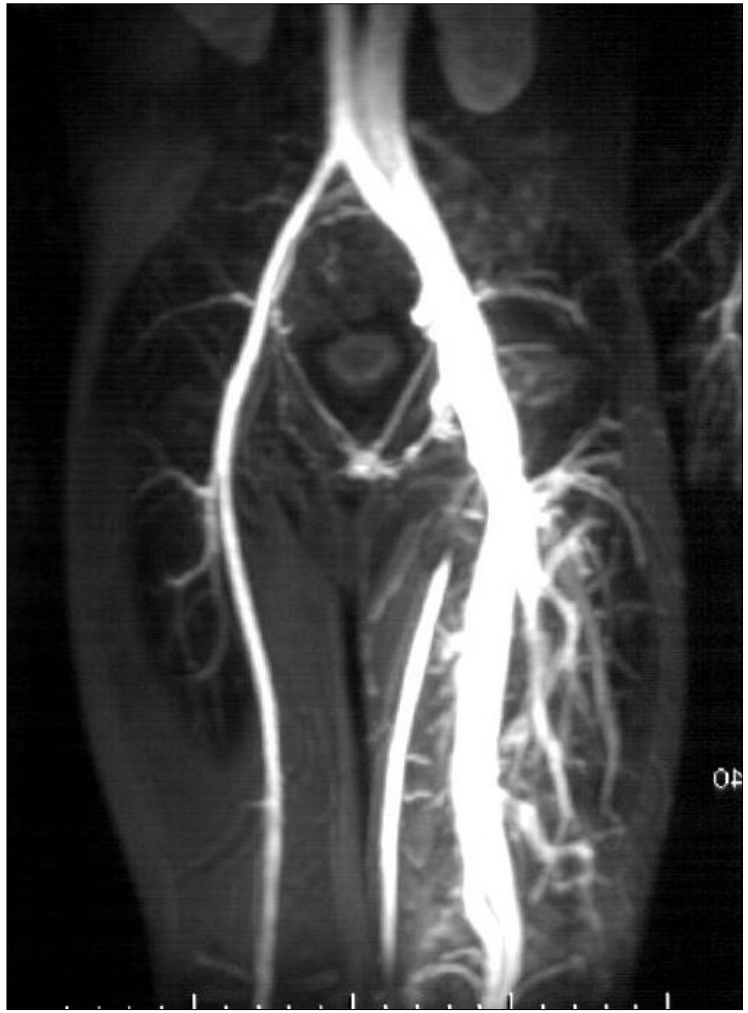
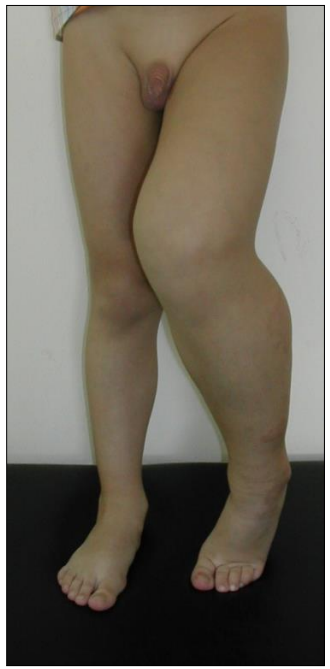
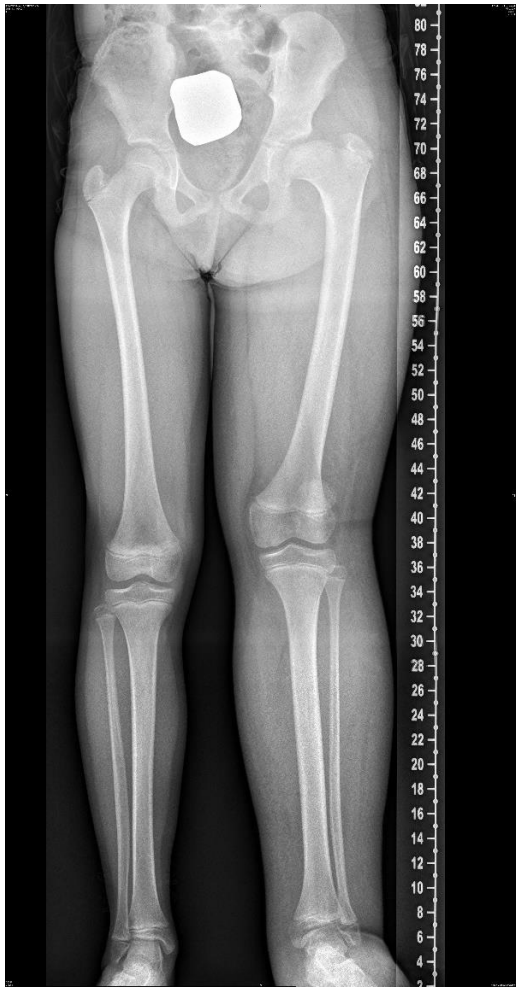
Ann Vasc Surg.2013 Aug;27(6):820-5

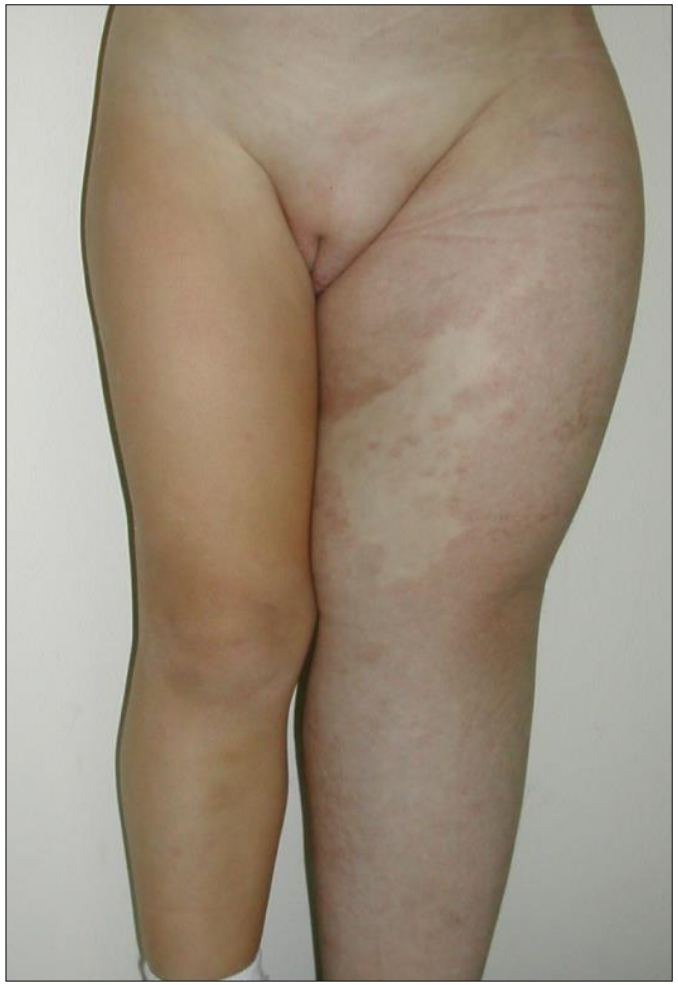
RASA 1 mutation

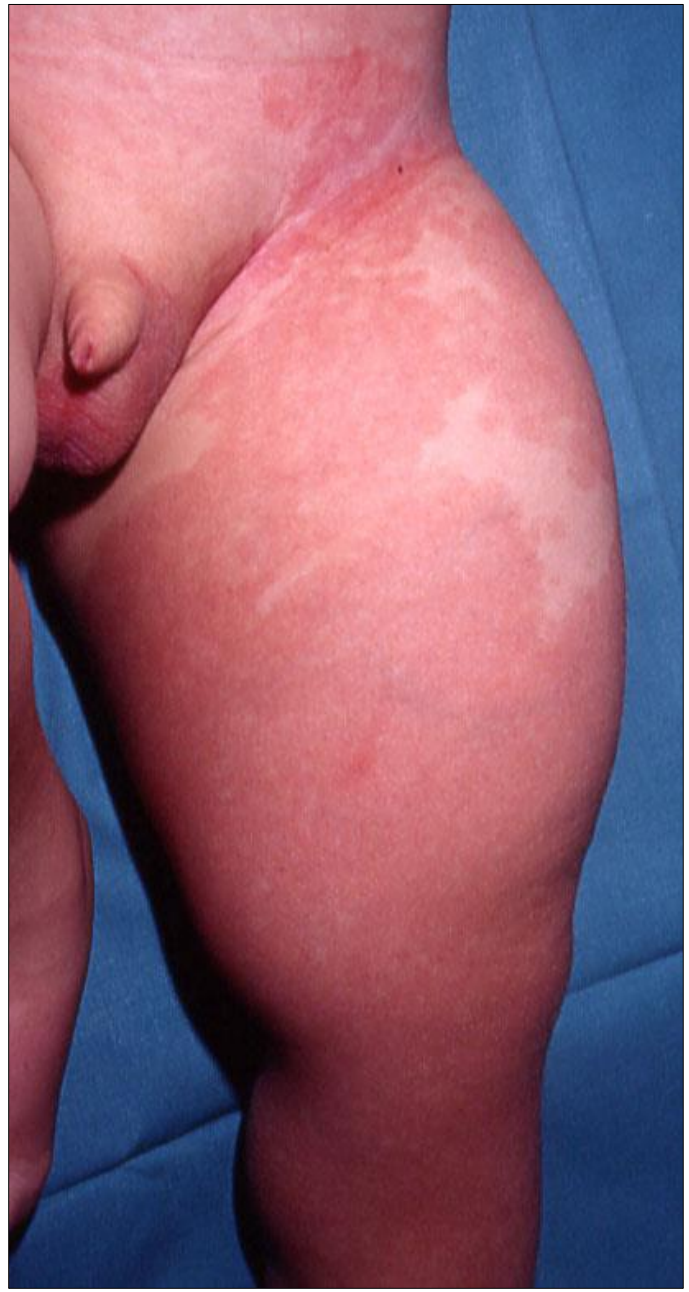


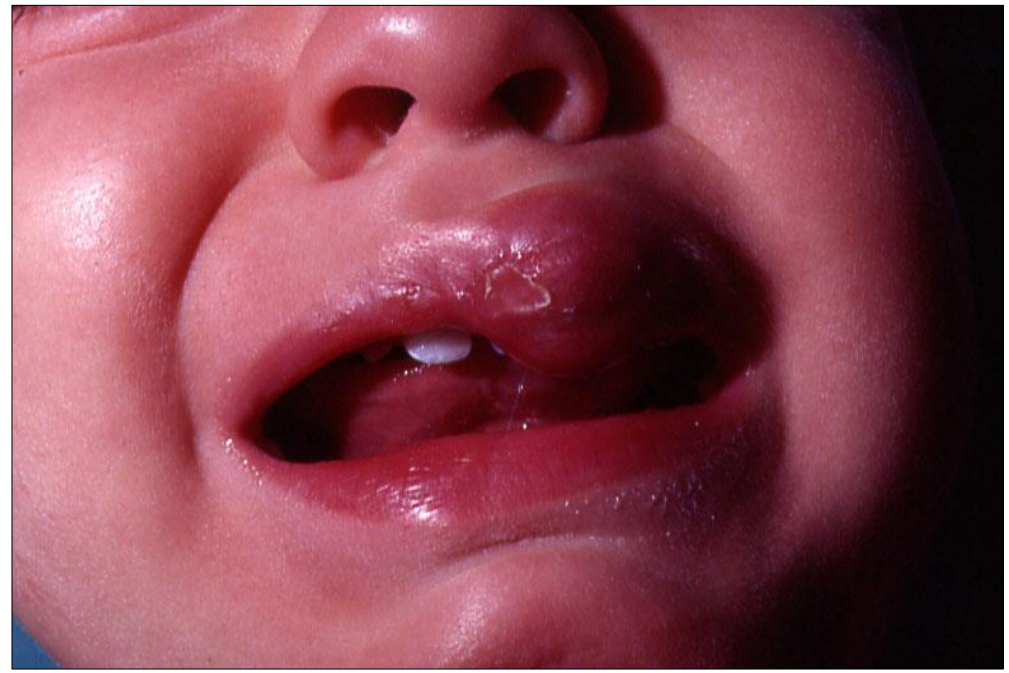


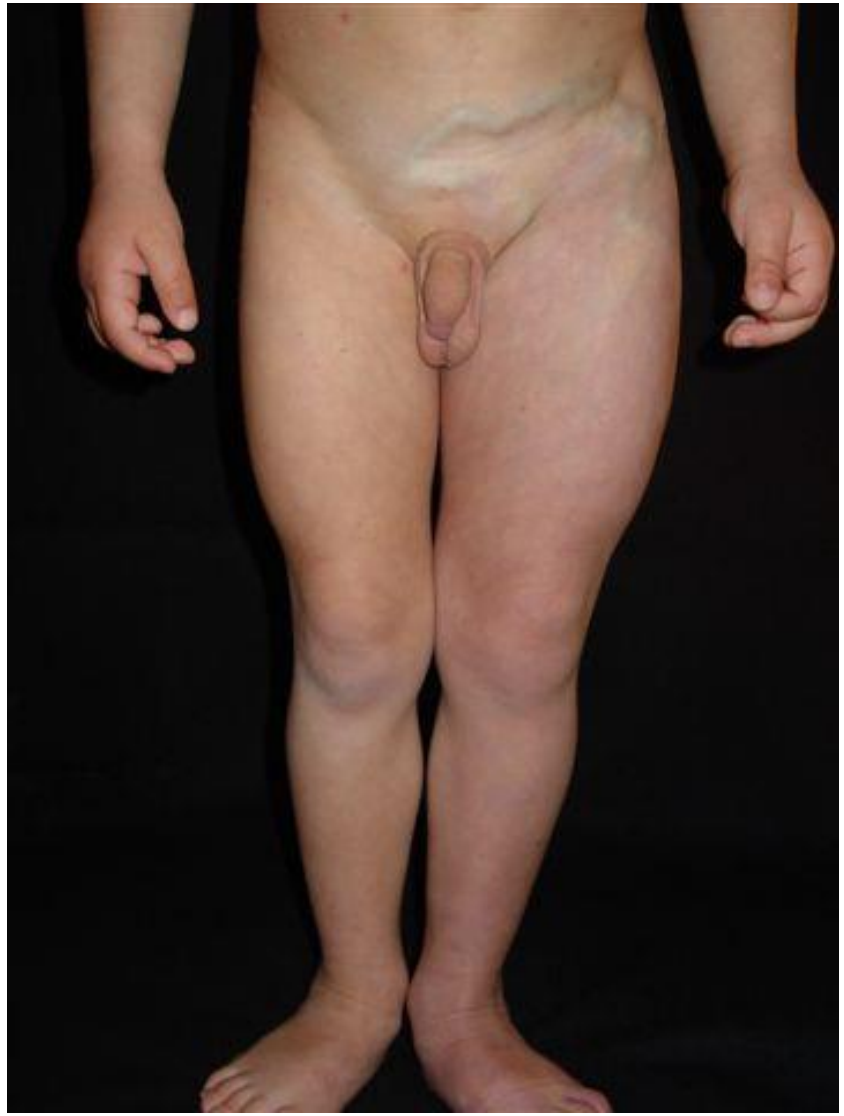


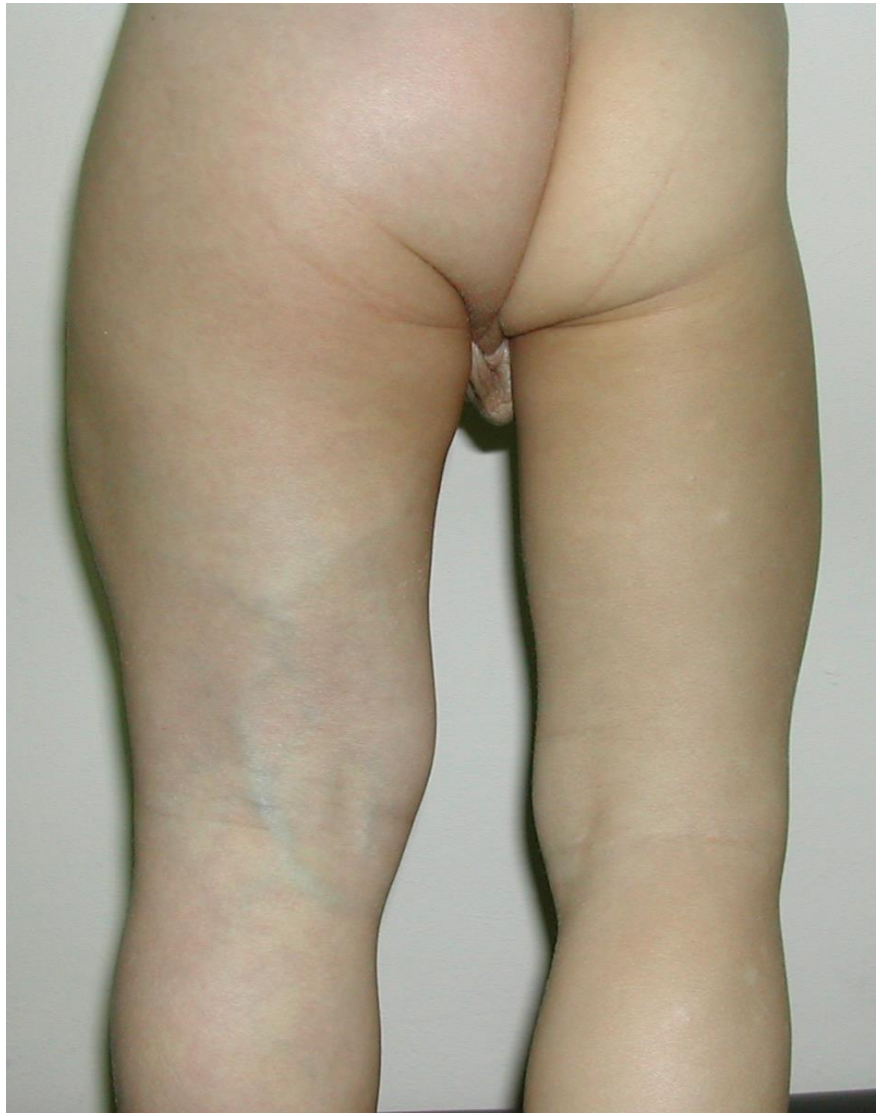


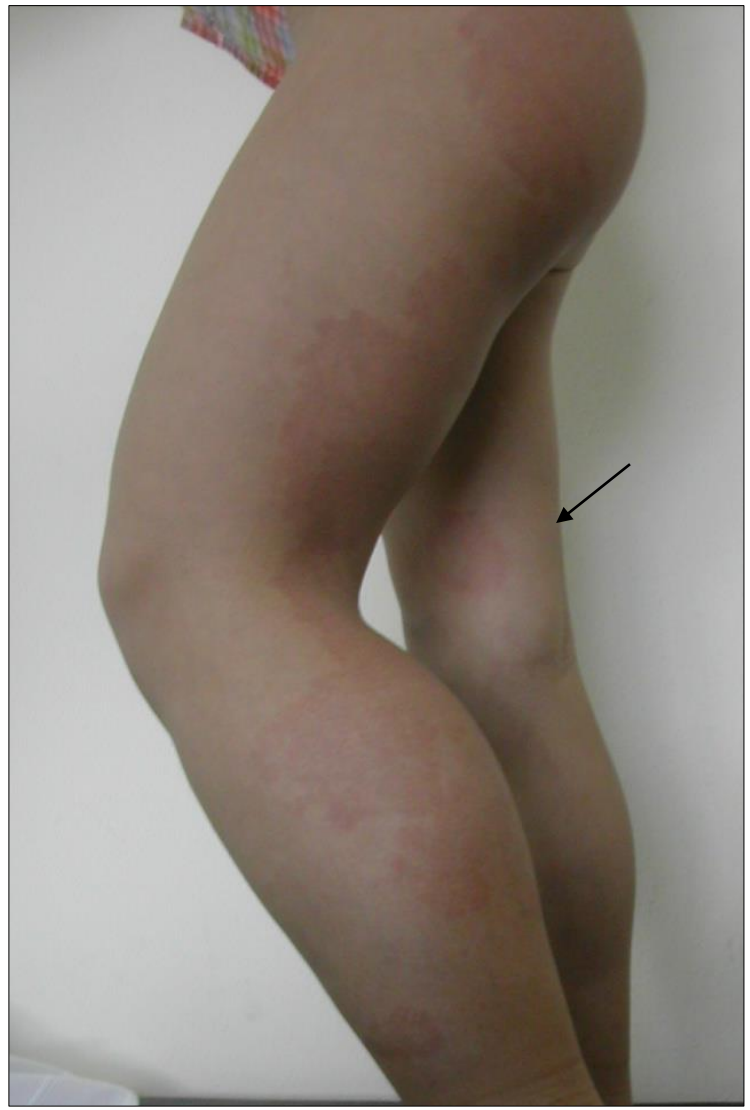


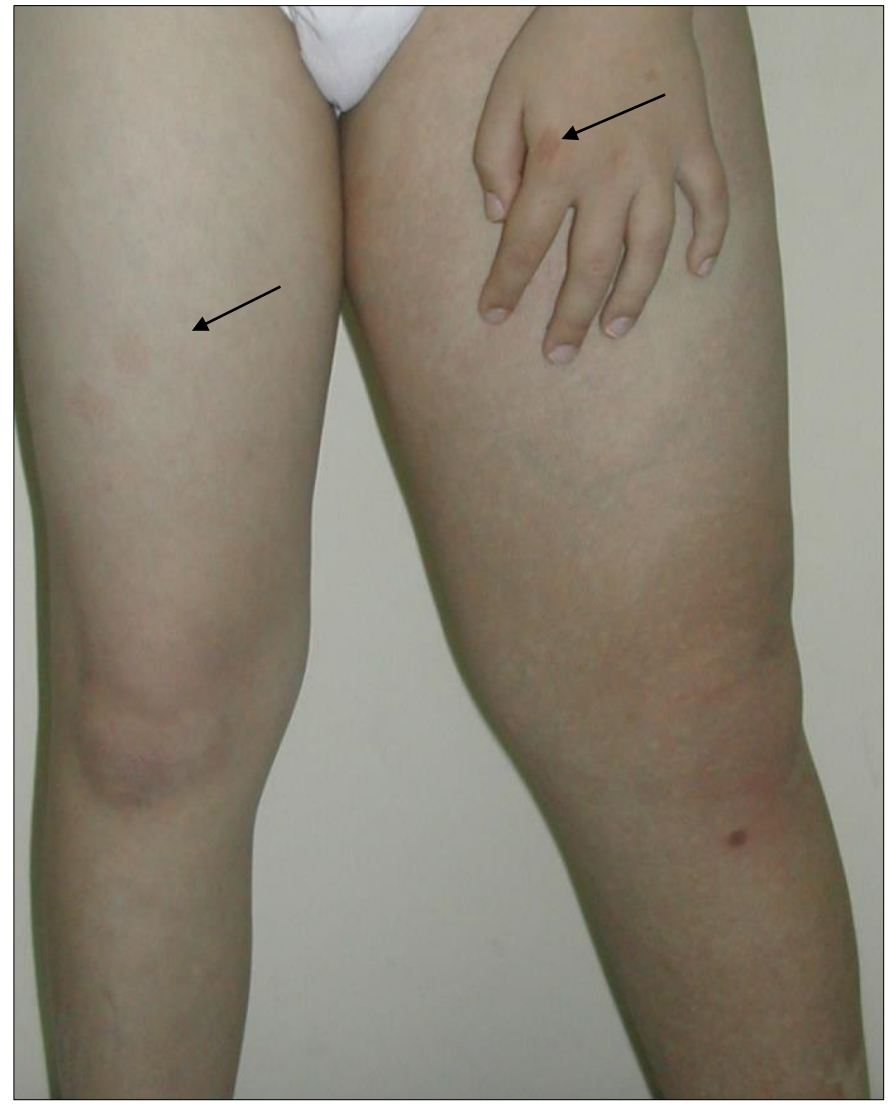


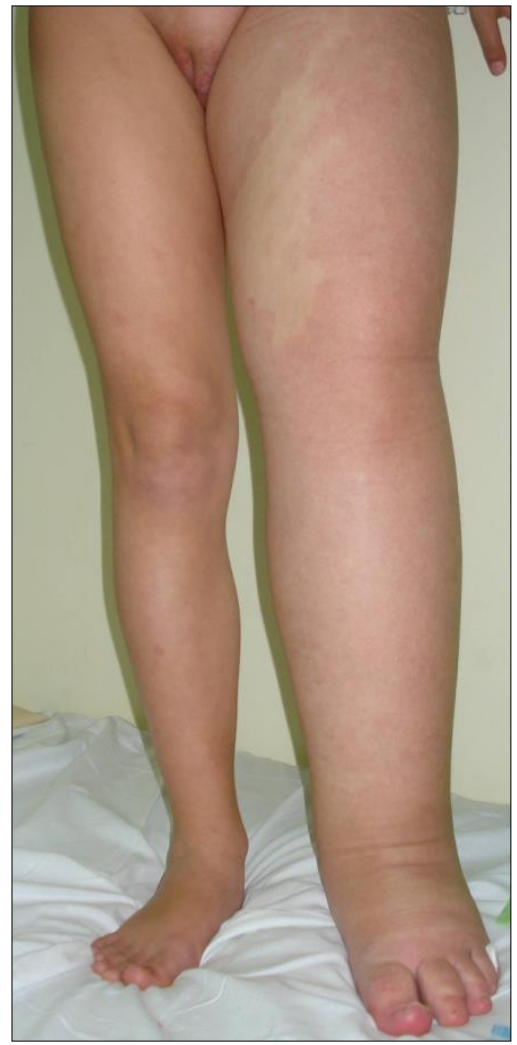


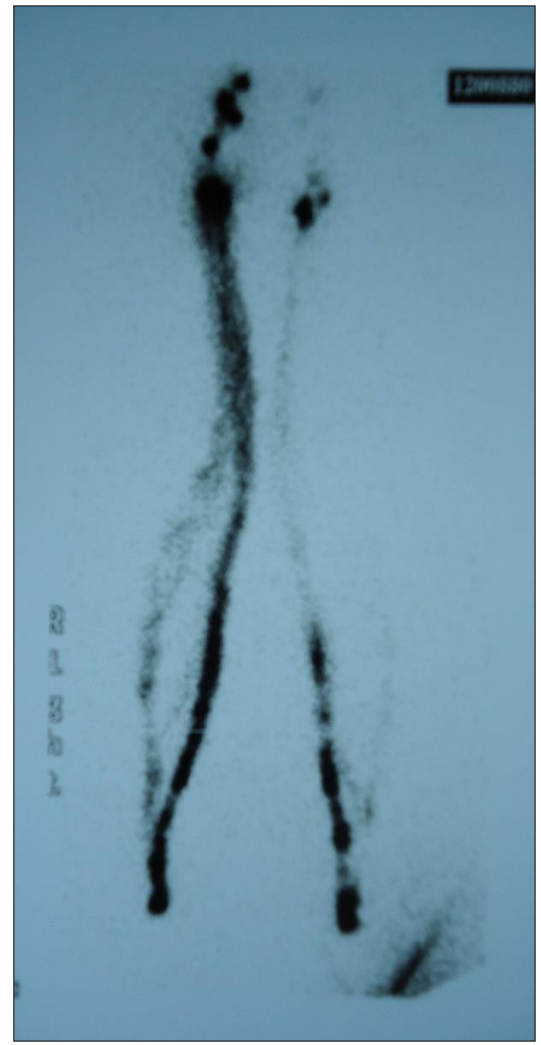


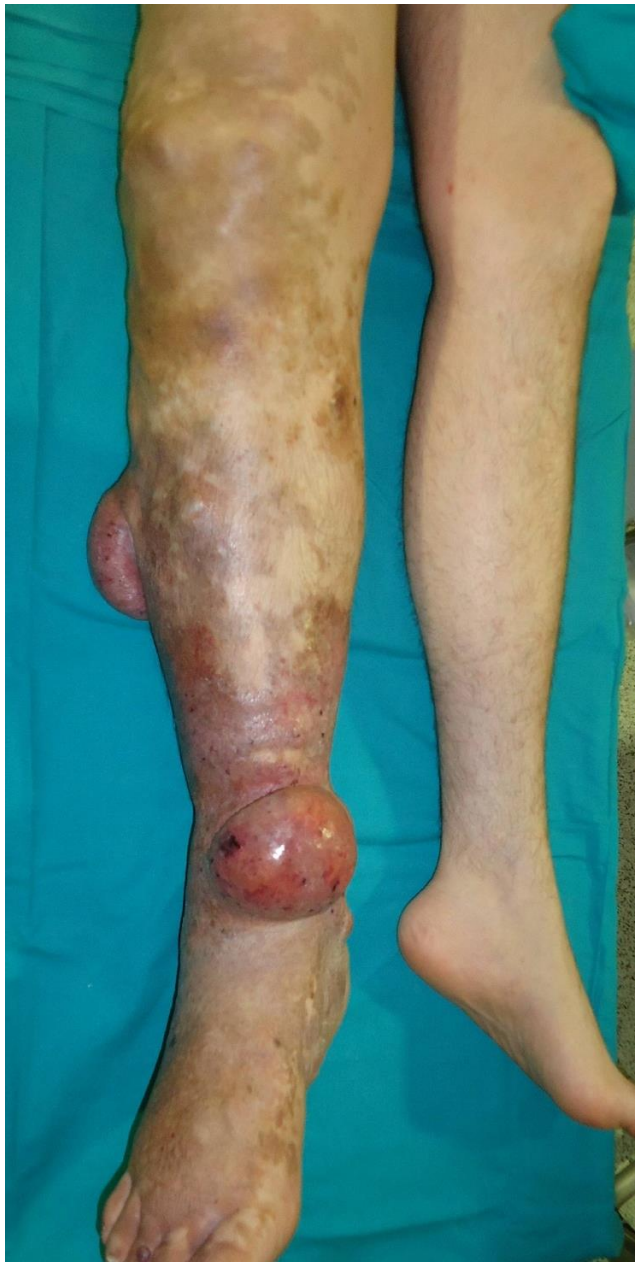


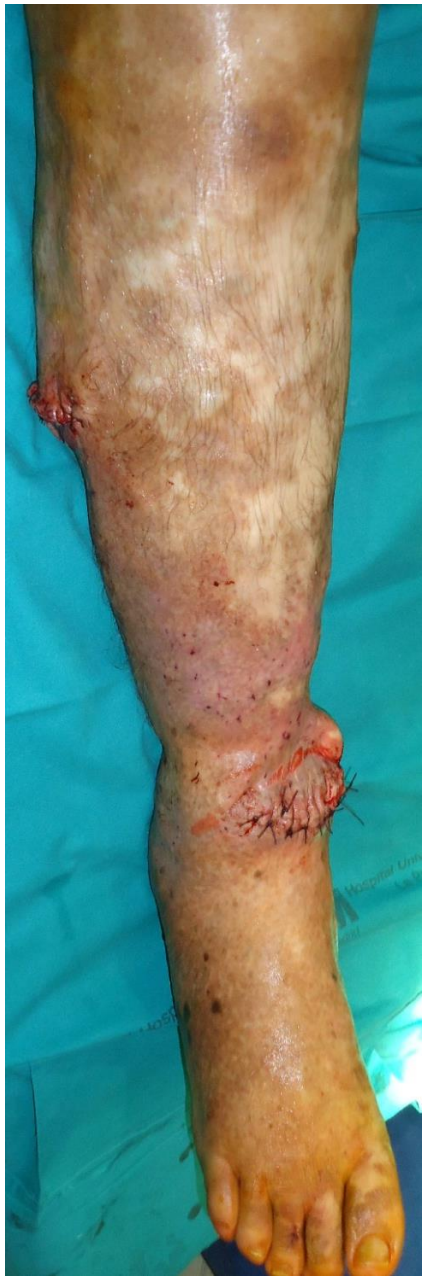


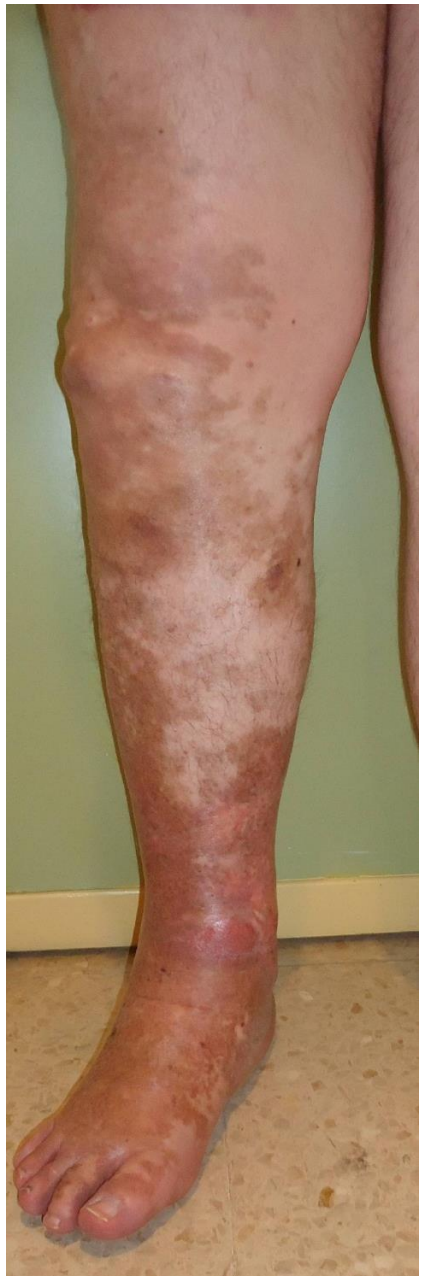


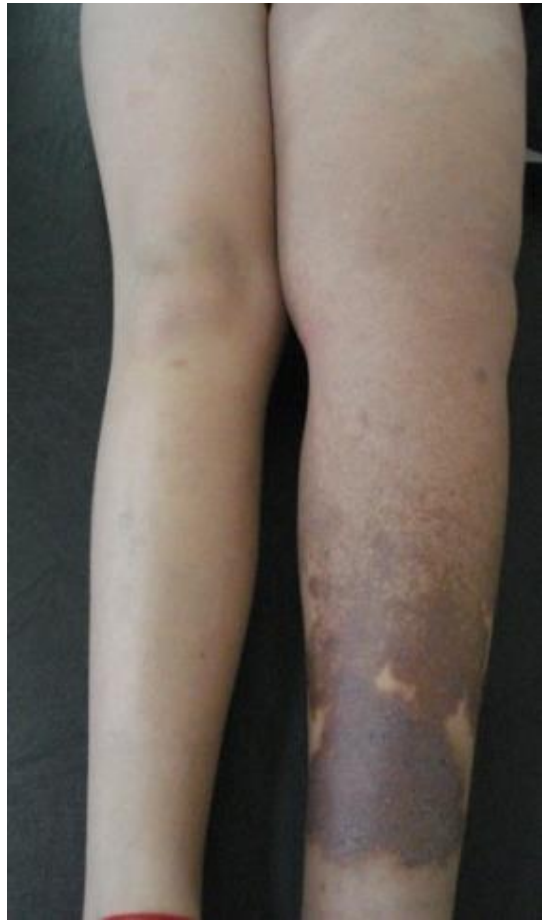


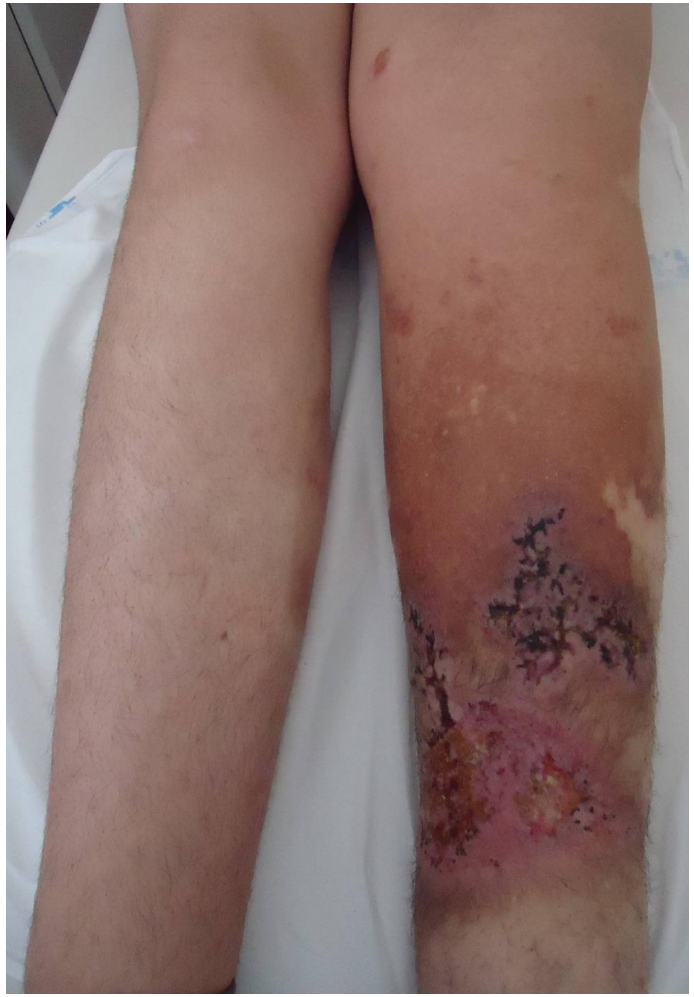


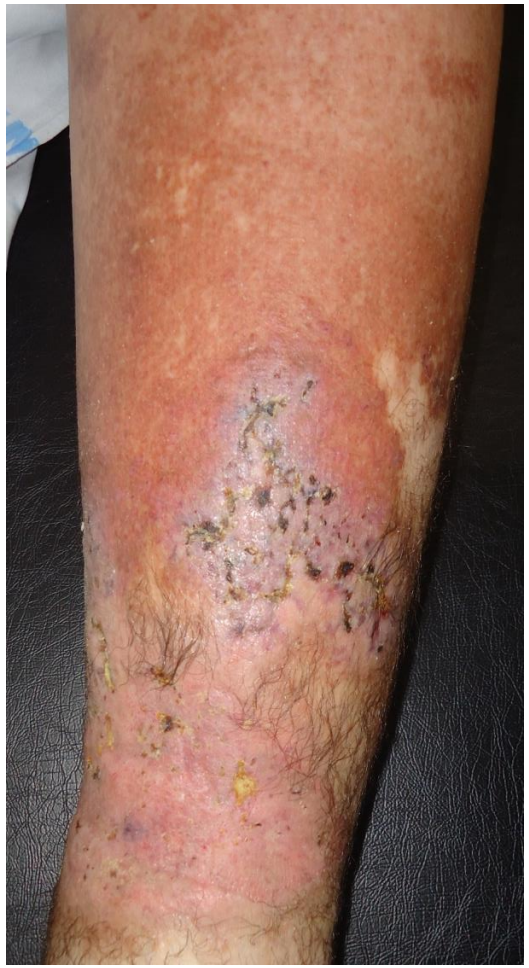


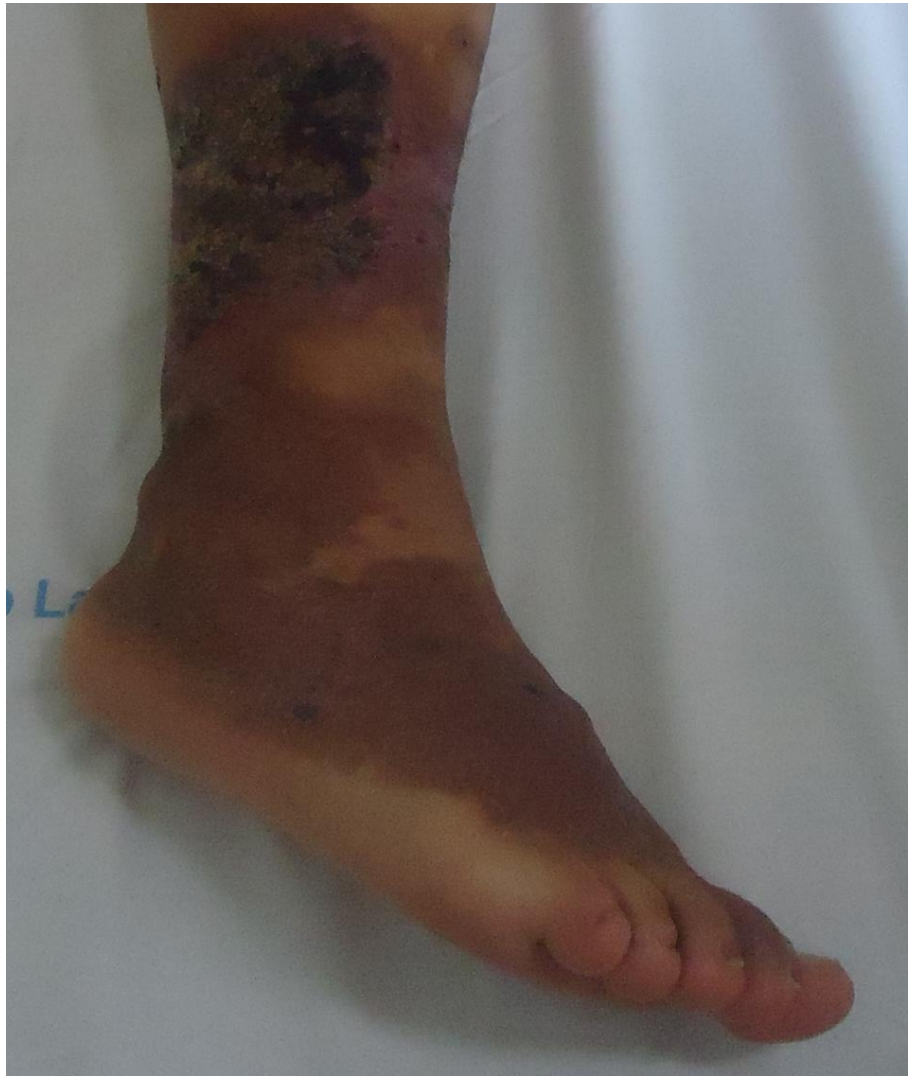


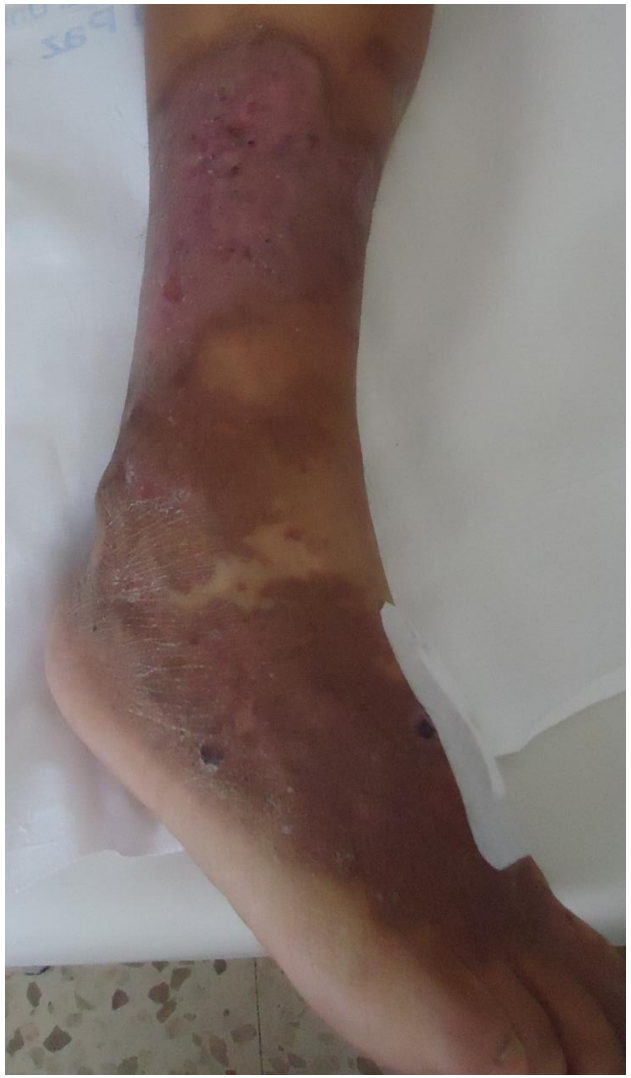












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Genetic profile of arteriovenous anomalies of the head and neck: Implications in progression and therapeutic approaches

Marta Maria Pampín Martínez • Lara Rodríguez Laguna • Elena Gómez García • Jose Luis Cebrián Carretero • Teresa González Otero • Juan Carlos López Gutiérrez

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	MAP2K1	KRAS	RASA1
Number of procedures	3,28	7,5	1,2
Mean hospital stay	9,7 days	22,5 days	3 days
Progression after treatment	50%	100%	16,6%

Table 4. Comparison between the three groups MAP2K1, KRAS and RASA1.

Hospital La Paz

Targeted Therapies in Vascular Anomalies

- PROPRANOLOL (320 patients.....99% RESPONSE)
- SIROLIMUS (178 patients.....90% RESPONSE)

- THALIDOMIDE.. 6 patients.....0% RESPONSE
- TRAMETINIB… 7 patients.....70% RESPONSE
- LAROTRECTINIB… 4 patients.....100% RESPONSE
- ALPELISIB.....67 patients.....80% RESPONSE

CONCLUSIONES

El tratamiento de las anomalías vasculares tiende a ser farmacológico en primera instancia, pero todavía es imprescindible el abordaje endovascular y quirúrgico.

Hoy más que nunca, clínicos , patólogos, radiólogos , genetistas y cirujanos debemos establecer puentes efectivos para ofrecer terapias a medida a cada paciente.

Se sigue explorando la liberación controlada e intralesional de fármacos

Avanzará el intervencionismo diagnóstico. Necesitamos tejido de malformaciones de difícil acceso o biopsia compleja para conocer la mutación y establecer un protocolo terapéutico farmacológico precoz