Benefit of phlebotomy and low-dose aspirin in the prevention of vascular events in patients with *EPOR* primary familial polycythemia on the island of New Caledonia

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Article	Clinical data	*EPOR* mutation
Kralovics R, Indrak K, Stopka T, Berman BW, Prchal JF, Prchal JT. Two new EPO receptor mutations: truncated EPO receptors are most frequently associated with primary familial and congenital polycythemias. *Blood*. 1997;90(5):2057-61.	Propositus: Headaches Asthenia 4 relatives: father and 3 paternal ones relatives	- *EPOR* exon 8 - 7bp deletion (**del5985-5991**) - **59 AA** truncated receptor
	Propositus: Arterial hypertension 1 relative: father	- *EPOR* exon 8 - Insertion (**5967insT**) - **65 AA** truncated receptor
Kralovics R, Prchal JT. Genetic heterogeneity of primary familial and congenital polycythemia. *Am J Hematol.* 2001;68(2):115-21.	No clinical data Propositus and 3 relatives	- *EPOR* exon 8 **c.1273G>T** - **G5959T (p.Glu425*)** - **84 AA** truncated receptor
Kralovics R, Sokol L, Prchal JT. Absence of polycythemia in a child with a unique erythropoietin receptor mutation in a family with autosomal dominant primary polycythemia. *J Clin Invest.* 1998;102(1):124-9.	Propositus: extensive coronaropathy Arterial hypertension 3 relatives	- *EPOR* exon 8 **c.1278C>G** - **C5964G (p.Tyr426*)** - **83 AA** truncated receptor
Al-Sheikh M, Mazurier E, Gardie B, Casadevall N, Galacteros F, Goossens M, et al. A study of 36 unrelated cases with pure erythrocytosis revealed three new mutations in the erythropoietin receptor gene. *Haematologica*. 2008;93(7):1072-5.	No clinical data Propositus and 3 relatives	- *EPOR* exon 8 **c.1271_1272del** - **p.Phe424*** - **85 AA** truncated receptor
	No clinical data Propositus and 1 relative (cousin)	- *EPOR* exon 8 **c.1142_1143del** - **p.Pro381Glnfs*2** - **127 AA** truncated receptor
	Asymptomatic Propositus and 2 relatives	- *EPOR* exon 8 **p.Leu429Trpfs*24** - **c.1285del** - **57 AA** truncated receptor
Bento C, Almeida H, Maia TM, Relvas L, Oliveira AC, Rossi C, et al. Molecular study of congenital erythrocytosis in 70 unrelated patients revealed a potential causal mutation in less than half of the cases (Where is/are the missing gene(s)?). *Eur J Haematol*. 2013;91(4):361-8.	Propositus and 2 relatives	- *EPOR* exon 8 **p.Pro438Metfs*6** - **c.1311_1312delTC** - **66 AA** truncated receptor
	No family data	- *EPOR* exon 8 **p.Ser412*** - **c.1235C>A** - **97 AA** truncated receptor
Toriumi N, Kaneda M, Hatakeyama N, Manabe H, Okajima K, Sakurai Y, et al. A case of primary familial congenital polycythemia with a novel EPOR mutation: possible spontaneous remission/alleviation by menstrual bleeding. *Int J Hematol*. 2018;108(3):339-43.	Propositus: ruddy complexion 1 relative (mother)	- *EPOR* exon 8 **p.Ser407*** - **c.1220C>A**
Oliveira JL, Coon LM, Frederick LA, Hein M, Swanson KC, Savedra ME, et al. Genotype-Phenotype Correlation of Hereditary Erythrocytosis Mutations, a single center experience. *Am J Hematol*. 2018; 93(8): 1029–1041.	Unknown	- *EPOR* exon 8 **p.Pro388HisfsX3** - **c.1161_1186**
	Headaches	- *EPOR* exon 8 **p.Gly390TrpfsX10** - **c.1166dup**
	Mild fatigue Chest pain	- *EPOR* exon 8 **p.Ser401*** - **c.1202C>G**
	Asymptomatic	- *EPOR* exon 8 **p.Leu436*** - **c.1307T>A**
Gross M, Ben-Califa N, McMullin MF, Percy MJ, Bento C, Cario H, et al. Polycythaemia-inducing mutations in the erythropoietin receptor (EPOR): mechanism and function as elucidated by epidermal growth factor receptor-EPOR chimeras. *Br J Haematol*. 2014;165(4):519-28.	Unknown	- *EPOR* exon 8 **p.Ser415Hisfs*18** - **c.1242_1276del** - **65 AA** truncated receptor
Chauveau A, Luque Paz D, Lecucq L, Le Gac G, Le Maréchal C, Gueguen P, et al. A new point mutation in EPOR inducing a short deletion in congenital erythrocytosis. *Br J Haematol.* 2016;172(3):475-7.	Asymptomatic	- *EPOR* exon 8 **p.Tyr454*** - **c.1362C>G** - **55 AA** truncated receptor
	No familial history of hematological disorders	- *EPOR* exon 8 **p.Arg437His** - **c.1310G>A**

Furukawa T, Narita M, Sakaue M, Otsuka T, Kuroha T, Masuko M, et al. Primary familial polycythaemia associated with a novel point mutation in the erythropoietin receptor. *Br J Haematol*. 1997;99(1):222-7.	Propositus: ruddy complexion 3 relatives	- *EPOR e*xon 8 **p.Gln434*** - **c.1299C>G** - **75 AA** truncated receptor
Filser M, Aral B, Airaud F, Chauveau A, Bruce A, Polfrit Y, et al. Low incidence of EPOR mutations in idiopathic erythrocytosis. *Haematologica*. 2021;106(1):299-301.	Propositus and 2 relatives	- *EPOR e*xon 8 **p.Pro381Glnfs*2** - **c.1142_1143delCC**
	Propositus and 2 relatives	- *EPOR e*xon 8 **p.Ser407*** - **c.1220C>A**
	Asymptomatic	- *EPOR e*xon 8 **p.Ser432Alafs*21** - **c.1293del**
Arcasoy MO, Karayal AF, Segal HM, Sinning JG, Forget BG. A novel mutation in the erythropoietin receptor gene is associated with familial erythrocytosis. *Blood*. 2002;99(8):3066-9.	Propositus: headaches 23 relatives	- *EPOR* exon 8 **p.Glu399*** - **c.5881G>T** - **110 AA** truncated receptor
de la Chapelle A, Träskelin AL, Juvonen E. Truncated erythropoietin receptor causes dominantly inherited benign human erythrocytosis*. Proc Natl Acad Sci U S A.* 1993;90(10):4495-9.	Propositus and 28 relatives: asymptomatic	-EPOR exon 8 **p.Trp439*** - **c.6002G>A** - **70 AA** truncated receptor
Rives S, Pahl HL, Florensa L, Bellosillo B, Neususess A, Estella J, et al. Molecular genetic analyses in familial and sporadic congenital primary erythrocytosis. *Haematologica*. 2007;92(5):674-7.	No familial history	- *EPOR* exon 8 **p.Trp439*** - **c.1453G>A** - **70 AA** truncated receptor
	Propositus and 2 relatives	- *EPOR* exon 8 **c.1414C>G** - **p.Tyr426*** - **83 AA** truncated receptor
Arcasoy MO, Degar BA, Harris KW, Forget BG. Familial Erythrocytosis Associated With a Short Deletion in the Erythropoietin Receptor Gene. *Blood*. 1997;89(12):4628-35.	Propositus: chronic headaches 5 relatives	- *EPOR* exon 8 **c.1299_1305del** - **p.Gln434Cysfs*17** - **59 AA** truncated receptor
Sokol L, Luhovy M, Guan Y, Prchal JF, Semenza GL, Prchal JT. Primary familial polycythemia: a frameshift mutation in the erythropoietin receptor gene and increased sensitivity of erythroid progenitors to erythropoietin. *Blood*. 1995;86(1):15-22.	Propositus: facial erythrocytosis 3 relatives	- *EPOR* exon 8 **c.1288dupG** - **p.Asp430Glyfs*15** - **64 AA** truncated receptor
Lo Riso L, Vargas-Parra G, Navarro G, Arenillas L, Fernández-Ibarrondo L, Robredo B, et al. Identification of Two Novel EPOR Gene Variants in Primary Familial Polycythemia: Case Report and Literature Review. *Genes*. 2022;13(10):1686.	Propositus: severe headaches 1 relative	- *EPOR e*xon 8 **c.1275_1290dup** **p.Pro431Valfs*19**
	Propositus: severe headaches, asthenia, mental dullness	- *EPOR* - Exon 8 **c.1346del** **p.Pro449Hisfs*4**
Pasquier F, Marty C, Balligand T, Verdier F, Grosjean S, Gryshkova V, et al. New pathogenic mechanisms induced by germline erythropoietin receptor mutations in primary erythrocytosis. *Haematologica*. 2018;103(4):575-86.	Asymptomatic No familial history of erythrocytosis	- *EPOR* exon 8 **c.1300dup** **p.Gln434Profs*11** - **64 AA** truncated receptor

Supplemental table 1. Bibliographical review of *EPOR* mutations reported in the literature