

Integration of genotypic data into clinical trial design and reporting in hereditary hemorrhagic telangiectasia could help personalize treatment

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DATA SUPPLEMENT

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Supplementary Table 1- Published clinical trials with drug interventions in PubMed

Administration	Intervention	Title	First author, year
Local	Bevacizumab ¹	Randomized, controlled, double-blinded clinical trial of effect of bevacizumab injection in management of epistaxis in hereditary hemorrhagic telangiectasia patients undergoing surgical cauterization	Khanwalkar, 2022
	Bevacizumab ²	Intranasal submucosal bevacizumab for epistaxis in hereditary hemorrhagic telangiectasia: a double-blind, randomized, placebo-controlled trial	Riss, 2015
	Bevacizumab ³	Effect of Bevacizumab Nasal Spray on Epistaxis Duration in Hereditary Hemorrhagic Telangiectasia: A Randomized Clinical Trial	Dupuis-Girod, 2016
	Bevacizumab, estriol, tranexamic acid 10%, or placebo ⁴	Effect of Topical Intranasal Therapy on Epistaxis Frequency in Patients with Hereditary Hemorrhagic Telangiectasia: A Randomized Clinical Trial	Whitehead, 2016
	Bevacizumab ⁵	ELLIPSE Study: a Phase I study evaluating the tolerance of bevacizumab nasal spray in the treatment of epistaxis in hereditary hemorrhagic telangiectasia	Dupuis-Girod, 2014
	Flo seal ^{®6}	Prospective pilot study of Flo seal [®] for the treatment of anterior epistaxis in patients with hereditary hemorrhagic telangiectasia (HHT)	Lee, 2019
	Estrogen ⁷	Intranasal topical estrogen in the management of epistaxis in hereditary hemorrhagic telangiectasia	Minami, 2016
	Timolol ⁸	Efficacy of timolol in a novel intranasal thermosensitive gel for hereditary hemorrhagic telangiectasia-associated epistaxis: a randomized clinical trial	Peterson, 2020
	Timolol ⁹	Efficacy of timolol nasal spray as a treatment for epistaxis in hereditary hemorrhagic telangiectasia. A double-blind, randomized, placebo-controlled trial	Dupuis-Girod, 2019
	Estriol ¹⁰	Plasma surgery and topical estriol: Effects on the nasal mucosa and long-term results in patients with Osler's disease	Sadick, 2003
	Estrogens ¹¹	Topical estrogens combined with argon plasma coagulation in the management of epistaxis in hereditary hemorrhagic telangiectasia	Bergler, 2002
Systemic	Bevacizumab ¹²	Efficacy and safety of intravenous bevacizumab on severe bleeding associated with hemorrhagic hereditary telangiectasia: A national, randomized multi-centre trial	Dupuis-Girod, 2023
	Bevacizumab ¹³	Emerging role of bevacizumab in management of patients with symptomatic hepatic involvement in hereditary hemorrhagic telangiectasia	Chavan, 2017
	Bevacizumab ¹⁴	Bevacizumab in patients with hereditary hemorrhagic telangiectasia and severe hepatic vascular malformations and high cardiac output	Dupuis-Girod, 2012
	Carbazochrome-Sodium-Sulfonate ¹⁵	An Old Drug for a New Application: Carbazochrome-Sodium-Sulfonate in HHT	Passali, 2015
	Doxycycline ¹⁶	Randomized, double-blind, placebo-controlled, crossover trial of oral doxycycline for epistaxis in hereditary hemorrhagic telangiectasia	Thompson, 2022
	Doxycycline ¹⁷	North American Study for the Treatment of Recurrent Epistaxis with Doxycycline: The NOSTRIL trial	McWilliams, 2022
	Estradiol valerate ¹⁸	Estrogen treatment of hereditary hemorrhagic telangiectasia. A double-blind controlled clinical trial	Vase, 1981
	Ethinyl oestradiol and norethisterone ¹⁹	Georges Brohee Prize. Oestrogen-progesterone, a new therapy of bleeding gastrointestinal vascular malformations	Van Cutsem, 1990
	Itraconazole ²⁰	Oral itraconazole for epistaxis in hereditary hemorrhagic telangiectasia: a proof of concept study	Kroon, 2021
	N-acetylcysteine ²¹	The effect of N-acetylcysteine on epistaxis and quality of life in patients with HHT: a pilot study	de Gussem, 2009
	Octreotide ²²	Octreotide for gastrointestinal bleeding in hereditary hemorrhagic telangiectasia: A prospective case series	Kroon, 2019
	Pazopanib ²³	Pazopanib may reduce bleeding in hereditary hemorrhagic telangiectasia	Faughnan, 2019
	Tamoxifen ²⁴	Anti-estrogen therapy for hereditary hemorrhagic telangiectasia: a double-blind placebo controlled clinical trial	Yaniv, 2009
	Thalidomide ²⁵	Efficacy and safety of thalidomide for the treatment of severe recurrent epistaxis in hereditary haemorrhagic telangiectasia: results of a non-randomised, single-centre, phase 2 study	Invernizzi, 2015
	Tranexamic acid ²⁶	Tranexamic acid for epistaxis in hereditary hemorrhagic telangiectasia patients: a European cross-over controlled trial in a rare disease	Gaillard, 2014
Tranexamic acid ²⁷	Treatment of epistaxis in hereditary hemorrhagic telangiectasia with tranexamic acid - a double-blind placebo-controlled cross-over phase IIIB study	Geisthoff, 2014	

Supplementary Table 2- Registered clinical trials with drug interventions on clinicaltrials.gov²⁸

Administration	Intervention	Trial ID	Study title	Study status
Local	Bevacizumab	NCT01397695	Topical Bevacizumab for the Management of Recurrent Epistaxis in Patients With Hereditary Hemorrhagic Telangiectasia (HHT)	Completed
	Bevacizumab	NCT02106520	Efficacy of a Bevacizumab Nasal Spray as a Treatment for Epistaxis in Hereditary Hemorrhagic Telangiectasia (HHT)	Terminated
	Bevacizumab	NCT01507480	The ELLIPSE Study: A Phase-1 Study Evaluating the Tolerance of Bevacizumab Nasal Spray to Treat Epistaxis in Hereditary Hemorrhagic Telangiectasia	Completed
	Bevacizumab	NCT01314274	Intranasal Submucosal Bevacizumab for Epistaxis in Hereditary Hemorrhagic Telangiectasia (HHT)	Completed
	Bevacizumab	NCT02389959	Intranasal Bevacizumab for HHT-Related Epistaxis	Completed
	Bevacizumab	NCT01402531	Submucosal Bevacizumab for the Management of Recurrent Epistaxis in Patients With Hereditary Hemorrhagic Telangiectasia (HHT)	Completed
	Bevacizumab	NCT02157987	Treatment of Hereditary Hemorrhagic Telangiectasia of the Nasal Mucosa by Intranasal Bevacizumab: Search for Effective Dose	Unknown status
	Bevacizumab, Tranexamic Acid, Estriol, Sterile saline	NCT01408030	North American Study of Epistaxis in Hereditary Hemorrhagic Telangiectasia (HHT)	Completed
	Floreal®	NCT02638012	Prospective Pilot Study of Floreal for the Treatment of Anterior Epistaxis in Patients With (HHT)	Completed
	Mupirocin	NCT02963129	Treatment of Nasal Staphylococcus Aureus Colonization in Patients With HHT	Unknown status
	Propranolol	NCT04113187	Propranolol for Epistaxis in Hereditary Hemorrhagic Telangiectasia Patients	Completed
	Tacrolimus	NCT03152019	Efficacy and Safety of a 0.1% Tacrolimus Nasal Ointment as a Treatment for Epistaxis in Hemorrhagic Hereditary Telangiectasia (HHT)	Completed
	Timolol	NCT04139018	Timolol Gel for Epistaxis in Hereditary Hemorrhagic Telangiectasia	Completed
	Timolol	NCT02484716	Efficacy of a Timolol Nasal Spray as a Treatment for Epistaxis in Hereditary Hemorrhagic Telangiectasia (HHT) - (TEMPO)	Completed
Timolol	NCT01752049	Topical Anti-angiogenic Therapy for Telangiectasia in HHT: Proof of Concept	Completed	
Systemic	Bevacizumab	NCT04404881	Bevacizumab In Hereditary Hemorrhagic Telangiectasia	Recruiting
	Bevacizumab	NCT03227263	BABH Study: Efficacy and Safety of Bevacizumab on Severe Bleedings Associated With Hemorrhagic Hereditary Telangiectasia (HHT).	Completed
	Bevacizumab	NCT00843440	Efficacy and Safety of Bevacizumab for the Treatment Hemorrhagic Hereditary Telangiectasia (HHT) Associated With Severe Hepatic Vascular Malformations. Phase II Study	Completed
	Doxycycline	NCT04167085	North American Study for the Treatment of Recurrent epistaxis With Doxycycline: The NOSTRIL Trial	Completed
	Doxycycline	NCT03397004	Doxycycline for Hereditary Hemorrhagic Telangiectasia	Active, not recruiting
	Ferrous sulphate	NCT01908543	Iron Deficiency and Hereditary Haemorrhagic Telangiectasia	Terminated
	Nintedanib	NCT04976036	Efficacy of Nintedanib for Treatment of Epistaxis in Hereditary Hemorrhagic Telangiectasia (HHT) Patients	Recruiting
	Nintedanib	NCT03954782	Efficacy of Nintedanib Per os as a Treatment for Epistaxis in HHT Disease.	Completed
	Octreotide	NCT00004327	Phase II Pilot Study of Octreotide, a Somatostatin Octapeptide Analog, for Gastrointestinal Hemorrhage in Hormone-Refractory Hereditary Hemorrhagic Telangiectasia and Senile Ectasia	Completed
	Octreotide LAR	NCT02874326	Octreotide in Patients With GI Bleeding Due to Rendu-Osler-Weber	Unknown status
	Pazopanib	NCT03850730	Pazopanib for the Treatment of Epistaxis in Hereditary Hemorrhagic Telangiectasia	Not yet recruiting
	Pazopanib	NCT03850964	Effects of Pazopanib on Hereditary Hemorrhagic Telangiectasia Related Epistaxis and Anemia (Paz)	Recruiting
	Pazopanib	NCT02204371	Evaluation of Pazopanib on Bleeding in Subjects With Hereditary Haemorrhagic Telangiectasia	Terminated
	Pegylated Interferon Alpha2b	NCT00588146	Phase 2 Study of PEG-Intron in Hereditary Hemorrhagic Telangiectasia	Terminated
	Pomalidomide	NCT02287558	Pomalidomide in Hereditary Hemorrhagic Telangiectasia and Transfusion-Dependent Vascular Ectasia: a Phase I Study	Completed
Pomalidomide	NCT03910244	Pomalidomide for the Treatment of Bleeding in HHT	Completed	

	Ranibizumab	NCT01406639	Ranibizumab for the Management of Recurrent Nosebleeds in Patients With Hereditary Hemorrhagic Telangiectasia (HHT)	Withdrawn
	Sirolimus	NCT05269849	Sirolimus for Nosebleeds in HHT	Recruiting
	Tacrolimus	NCT04646356	Tacrolimus Trial for Hereditary Hemorrhagic Telangiectasia (HHT)	Active, not recruiting
	Tamoxifen	NCT00375622	Anti-Estrogen Therapy for Hereditary Hemorrhagic Telangiectasia A Double-Blind Placebo-Controlled Clinical Trial	Completed
	Thalidomide	NCT01485224	Efficacy of Thalidomide in the Treatment of Hereditary Hemorrhagic Telangiectasia	Completed
	Thalidomide	NCT00389935	Thalidomide Reduces Arteriovenous Malformation Related Gastrointestinal Bleeding	Completed
	Tranexamic acid	NCT00355108	ATERO: A Randomised Study With Tranexamic Acid in Epistaxis of Rendu Osler Syndrome	Completed
	Tranexamic acid	NCT01031992	Tranexamic Acid and Epistaxis in Hereditary Hemorrhagic Telangiectasia (HHT)	Completed
	VAD044	NCT05406362	Assess Safety and Efficacy of VAD044 in HHT Patients	Recruiting
	Vit D	NCT03981562	Vitamin D and Hereditary Haemorrhagic Telangiectasia	Unknown status

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