

BMP9-Related Telangiectasia Syndrome

Indications for Ordering

Diagnostic test for individuals suspected to have a telangiectasia syndrome

Test Description

Bidirectional sequencing of entire coding region and intron/exon boundaries of *BMP9/GDF2* gene

Tests to Consider

Primary test

[Telangiectasia Syndrome \(*BMP9/GDF2*\) Sequencing 2010015](#)

- Diagnostic test for individuals suspected to have a telangiectasia syndrome
 - In the absence of pathogenic variants in the *ACVRL1*, *ENG*, or *SMAD4* gene

Related tests

[Hereditary Hemorrhagic Telangiectasia \(HHT\) Panel, Sequencing and Deletion/Duplication, 5 Genes 2009337](#)

- Most comprehensive test to diagnosis a telangiectasia/arteriovenous malformation (AVM) disorder

[Hereditary Hemorrhagic Telangiectasia \(*ACVRL1* and *ENG*\) Sequencing and Deletion/Duplication with Reflex to Juvenile Polyposis \(*SMAD4*\) Sequencing and Deletion/Duplication 2009008](#)

- Appropriate initial test for individuals with telangiectases clustered on face, hands, and mouth
 - In conjunction with recurrent nosebleeds
 - With or without internal arteriovenous malformations

[*RASA1*-Related Disorders \(*RASA1*\) Sequencing and Deletion/Duplication 2007852](#)

- Appropriate test for individuals with cutaneous capillary malformations, with or without telangiectasia and arteriovenous malformations

[Familial Mutation, Targeted Sequencing 2001961](#)

- Useful when a familial variant identifiable by sequencing is known

Disease Overview

Prevalence – ~1/5,000-10,000 for hereditary hemorrhagic telangiectasia (HHT)

- *BMP9*-related disorder – 1-2% of individuals with HHT

Symptoms

- Cutaneous telangiectasia located on face, mouth, hands, limbs and/or trunk
- Recurrent nosebleeds
- Solid organ arteriovenous malformations – unknown occurrence/incidence

Genetics

Gene – *BMP9/GDF2*

Inheritance – autosomal dominant

Function

- Encodes for protein called bone morphogenetic protein 9
- Involved in a common transforming growth factor-beta (TGFB)-signaling pathway with hereditary hemorrhagic telangiectasia genes *ACVRL1*, *ENG*, and *SMAD4*

Test Interpretation

Sensitivity/specificity

- Clinical sensitivity – ~1-2% of individuals suspected to have a telangiectasia syndrome in the absence of a pathogenic variant in *ACVRL1*, *ENG*, or *SMAD4* are expected to have a *BMP9* variant
- Analytical sensitivity/specificity – 99%

Results

- Positive – pathogenic variant detected
 - Cause of telangiectasia syndrome identified
- Negative – no pathogenic variant detected
 - No etiology for telangiectasia identified
- Inconclusive – novel variant of uncertain clinical significance may be identified

Limitations

- Not detected
 - Large deletions/duplications
 - Deep intronic variants
 - Regulatory region variants
- Diagnostic errors can occur due to rare sequence variations
- Variants in other genes associated with telangiectasia syndromes will not be tested